IN THE DISTRICT COURT OF THE FOURTH JUDICIAL DISTRICT OF

THE STATE OF IDAHO, IN AND FOR THE COUNTY OF ADA

IDAHO CONSERVATION LEAGUE, a non-profit corporation, and SAVE THE SOUTH FORK SALMON, a non-profit corporation, Petitioners, v. IDAHO DEPARTMENT OF ENVIRONMENTAL QUALITY, and IDAHO BOARD OF ENVIRONMENTAL QUALITY, Respondents.	Case No. CV01-25-13306 Agency Case No. 0101-22-01 OAH Case No. 23-245-01

AGENCY TRANSCRIPTS

Judicial Review from the Idaho Department of Environmental Quality
Idaho Board of Environmental Quality Presiding

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BEFORE THE BOARD OF THE ENVIRONMENTAL QUALITY
STATE OF IDAHO

IN THE MATTER OF AIR QUALITY PERMIT TO CONSTRUCT P-2019.0047	
NEZ PERCE TRIBE, IDAHO CONSERVATION LEAGUE, and SAVE THE SOUTH FORK SALMON, Petitioners,	BEQ Case No. 0101-22-01 OAH Case No. 23-245-01
vs.	
DEPARTMENT OF ENVIRONMENTAL QUALITY, Respondent.	
and	
PERPETUA RESOURCES IDAHO, INC., Intervenor.	

SUMMARY JUDGMENT HEARING
September 21, 2023
Boise, Idaho

Reported by:
Vanessa S. Gosney, CSR #752, RPR

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Also Present: Leslie Hayes

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HEARING OFFICER LAWRENCE: This is In The Matter of Air Quality Permit to Construct P-2019.0047. It is BEQ Case No. 0101-22-01 and the OA -- the Office of Administrative Hearings Case No. 23-245-01.

And before we get any farther, I just got to say, I do have serious imposter syndrome being in the room like this and up here. I was going to really freak out if I had to be up here, but thankfully Vanessa is able to set up shop over here.

So why don't we start off with some introductions and appearances. My name is Dylan Lawrence. I am the appointed hearings officer in this matter on behalf of the Office of Administrative Hearings. Also present is Leslie Hayes.

And I have a disclaimer that I am going to read about that in a second, but why don't we also take appearances with the parties starting with the petitioners.

MS. THROWER: Yeah. Julia Thrower for Save the South Fork Salmon.

MR. HURLBUTT: Bryan Hurlbutt for the Nez Perce Tribe and Idaho Conservation League.

HEARING OFFICER LAWRENCE: How about the DEQ?

MR. SHACKELFORD: I am John Shackelford with the attorney general's office representing the Department of Environmental Quality.

MS. FLOYD: Tiffany Floyd, I'm the air quality commission administrator for the DEQ.

MR. POOSER: Christopher Pooser with Stoel Rives representing the intervenor, Perpetua.

MS. MCINTYRE: Krista McIntyre, Stole Rives, also representing Perpetua.

MR. FOSTER: Wade Foster with Stole Rives also representing Perpetua.

HEARING OFFICER LAWRENCE: All right. Thank you everybody. So the disclaimer that I'm going to read here, bear with me, it is a little formal. This has to do with Leslie's presence here.

You will note that Lesley Hayes is in attendance at this hearing today. The Office of Administrative Hearings is statutorily charged with the duty to implement the system for monitoring the quality of contested case proceedings and such other proceedings as are conducted by the Office of

Administrative Hearings in accordance with Section 67-5280(2)(a) and (b) Idaho Code.

Ms. Hayes is here as part of that monitoring process and will not be participating in these proceedings, instead only observing the proceedings. Ms. Hayes will not be participating in the decision in this case or the outcome of these proceedings in any way as I am the hearing officer specifically appointed to make the independent and unbiased decision pursuant to Idaho Code Section 67-5282(1)(f).

If a process question arises during this hearing I have discretion to determine whether it is necessary to resolve in order for the hearing to proceed and to clarify for the parties what the process is for purposes of these proceedings only. If necessary, I may then confer with the Office of Administrative Hearings for purposes of determining how that process question should be resolved in future proceedings.

Before I begin, are there any questions?

No. Okay. Hopefully that is as much as you need to hear from me today at one time, at least.

So we're here on a hearing for pending

motions for summary judgment. The hearing is being recorded by Vanessa Gosney, our court reporter. So just if you could, make sure to project towards her direction, that would be helpful, because she does have a microphone over there as well.

Before we get started are there any stipulations among the parties that I need to be aware of that affects today's proceedings? You guys haven't settled the case, huh? Okay. I can check that one off the list.

So as you guys know, on Friday I issued a notice to try and put some side boards on the hearing today. I feel like there has been a lot of briefing, it has all been very good. To me it would seem like a waste of your time and resources to make you regurgitate everything to me that was in those. So my goal was to identify issues that I'm still sort of struggling with or can use some more sort of input on. And even since Friday I have reviewed stuff -- stuff, I shouldn't use that word on the record -- materials in more detail and feel even stronger that for my purposes today I'd like to focus on the exclusion of the access road from ambient air.

I know in that notice I also mentioned

potentially walking through the language of the -- the air rule was the 210-14 about T-RACT and the evaluation of economic and environmental factors. But I spent the better part of Tuesday morning going through all that and I feel much more up to speed on it now. So the list of questions that I issued on Friday dealing with the exclusion of the access road from ambient air is what I would like to focus on today.

But just for planning purposes before we get into that, do any of the parties feel like there's any other issues that we need to talk about here today? And I'll start with the petitioners.

MR. HURLBUTT: I was planning to hit on three of the sub-issues in the outline, just to clarify a few points quickly, if that's okay.

HEARING OFFICER LAWRENCE: Can you tell me which ones?

MR. HURLBUTT: Yep. So 2 -- 2B, the 93.3 percent of PM emissions. And then three parts, B and C, the T-RACTs and averaging of arsenic.

HEARING OFFICER LAWRENCE: Okay. How about DEQ? I mean, obviously, if they are going to present on that you will want an opportunity to

respond. But is there anything else that you want to cover today?

MR. SHACKELFORD: My thought had been to cover the standard of review, although I don't even think that was listed in your requested -- or suggested topic, so if there's nothing else that needs to be said on that, then no, no other talking points.

HEARING OFFICER LAWRENCE: Okay. Personally I feel like I am good on the standard of review. Early on in this case, and especially, as I mentioned, given my experience ten years ago or so in another case, I feel like I'm on top of it. But if you want -- if there's any last minute things you want to say or to put a finer point, that's great. But we'll leave that for the end if we have time remaining, how about that?

MR. SHACKELFORD: That would be fine.

HEARING OFFICER LAWRENCE: Okay. And Perpetua Resources?

MR. POOSER: There's nothing specific. We wanted to be here to be responsive to your questions as well as the issues that the petitioners raise.

HEARING OFFICER LAWRENCE: Okay. So why

don't we -- why don't we focus, to begin, on the exclusion from ambient air. My cognition peaks mid-morning after my second cup of coffee and then steadily declines as the day goes on. So we could really start with that one. I'd say let's really start with that and then take a break. And then I may even think about time limits on some of these other issues, but want to give you the opportunity to at least, if there are things that you think have flown under the radar or need to be highlighted, to do that.

So let's go ahead and proceed on the ambient air issue. I don't -- in terms of time limits, I'm inclined to just put everybody on the honor system. And if I feel that somebody is getting off track or repeating themselves, then I will jump in, but -- because to me, it is one I want to make sure we cover -- I kind of want to let that one have some room to breathe.

So I'd like to start with petitioners. Obviously it's your guys' petition that determines the scope of this and you ultimately have the burden.

After petitioners I would like to hear from DEQ because they are, of course, the

respondent and I think they have the most sort of substantive declarations in the record that deal with these issues.

And then once DEQ finishes, go to Perpetua Resources to see if there's anything you think anything DEQ has missed or you would like to emphasize.

And then briefly back to petitioners just to, you know, if there is anything you want to highlight or emphasize before we wrap up the discussion.

Does that sound like a reasonable procedure?

MR. SHACKELFORD: Yes.

HEARING OFFICER LAWRENCE: Okay. For the record, I'm taking -- any time I ask a question and there's silence, I am taking that as an affirmative answer.

Okay. Well, so -- and by the way, just to clarify. With those questions that I -- you issued about exclusion from ambient air, we don't have to go in that order, that was kind of a little bit of a brain dump and I definitely don't foresee us like walking through each one of those individually. When I'm talking about going to the

parties, it's like this is your time to tell me anything you want about exclusion from ambient air and then we move on.

So with that, the floor is yours, petitioners.

MS. THROWER: All right. Good morning, Mr. Hearing Officer. My name is Julie Thrower here for Save the South Fork Salmon and also Idaho Conservation League and Nez Perce Tribe.

HEARING OFFICER LAWRENCE: Can you speak up just a tad bit? There is some sort of background noise.

MS. THROWER: Sure. I am going to just follow the questions that we have in Attachment A, so obviously I'm sure you will jump in if there are other issues you want covered. I'll just start by reading the question and then I will go ahead and answer.

So the first question was, "Petitioners appear to assert two separate bases of error, one, Perpetua lacks the legal authority to complete access, claim number 11, and two, the permit provisions regarding access control are inadequate, number 12. Is that an accurate characterization?"

Generally, yes. I'll just start with a

little bit of background.

As you know, the Clean Air Act seeks to protect human health and the environment from emissions that pollute ambient air. The regulatory definition of ambient air, which is incorporated in DEQ's air rule, is that portion of the atmosphere external to buildings to which the general public has access. Accordingly, an applicant must establish an ambient air boundary and include modeling demonstrating that the proposed potential emissions from the facility will maintain ambient air quality standards at the point of compliance, or essentially outside that ambient air boundary.

It's been EPA's long-standing policy, as we discussed in our briefs, that the facility must have both legal authority and practical ability to preclude public access to areas that are not ambient air.

This permit, DEQ and Perpetua, have not claimed that the air along the Stibnite Road access route is ambient air. They never have. They have not tried to model the air above that access route as ambient air during this entire approval -- permit approval process. Yet, this permit does not preclude public access to that route. That's a

fundamental requirement under EPA's long-standing ambient air policy and the Clean Air Act, and this permit did not demonstrate that that is being done.

So one of the issues is, as you stated in your question, that Perpetua has not demonstrated it has a legal authority to preclude public access and therefore it cannot exclude the road from ambient air protections.

The second issue, you asked, "Is the permit provisions regarding access control inadequate?"

In a nutshell, yes, that -- that is our claim. Perpetua's plan to require the public to sign a waiver before traveling through this access road is insufficient to practically preclude access, particularly when they don't have legal authority to do so. The practical ability to preclude access -- the public's access is hampered by that lack of legal authority.

So in order to get around this problem, what DEQ decided is that they'll have the public sign a waiver. They've created a new class of people called "guests of the facility" that is not anywhere in EPA's air policy nor in DEQ guidance and, in fact, conflicts with that policy and

guidance.

So our claim is, is that based on that characterization and allowing people to go through this area, the road that is not ambient air, it is not monitored for public health protections in compliance with ambient air quality standards, that it was arbitrary and capricious for them to do so.

So question two. "Is there anything in the record regarding the general public's need to utilize the road through the SGP, or Stibnite Gold Project, for example, to access trails, campgrounds and other communities, et cetera?"

Yes. There are several statements in the record that document the public's interest on traveling through this road.

And if I may approach, I have a couple of maps that I think will help, because they're in color, help explain or understand some of the statements from the record that I'd like to pull out.

HEARING OFFICER LAWRENCE: So these documents are in the record already?

MS. THROWER: The first map, it is record number PET532. This is in Appendix E of the statement of basis, which is the draft access

management plan.

HEARING OFFICER LAWRENCE: I have a good color copy over here.

MS. THROWER: Okay. If I may approach, I will still give you this, because I do have another map for illustrative purposes only.

The second map is from the recreation specialist report for the Stibnite Gold Project supplemental draft environmental impact statement. And as I said, it just provides a little bit more detail compared to the first map from the statement of basis. And I just want to use it for illustrative purposes so that when I read these statements from the record, you'll be able to kind of place them on the map. And also, I'm directionally challenged. So if I say "east" I might mean west, so obviously you'll have some visual to realize the area in that respect.

So looking at the first map, I'm sure everyone is well-oriented with these maps, but the cross-hatched area on the top right-hand corner is the project operations boundary or the air -- ambient air boundary. West of that to the northwest is Yellow Pine, the community of Yellow Pine. And to the east of that cross-hatch there is

a black line going through the cross-hatched area and going out east into the Payette National Forest and Frank Church Wilderness -- Frank Church River of No Return Wilderness. That line represents a road that is open to the public, it's a forest service road, and that does access several important recreation areas.

What I would like to point out on this map is there's an intersection on the east side of the cross-hatch area, and that road, which is a red road, going south along the border of the operations boundary or the ambient air boundary, that road -- this is a map of the proposed project. That road, which is, if you follow it down, is later labeled Brent Law Road. Most of that road around the operations boundary does not exist; that is what is proposed to be built.

So currently people going to Yellow Pine -- and you can see on the left-hand side, the lake in the upper left-hand corner is where McCall is. Going down to the lake on the lower left-hand corner is where Cascade is. Those are the two major population centers in this area.

So access, a lot of people access Yellow Pine through the road going from north and

northeast from McCall, go through Yellow Pine, and then they go through the project area and out east on that road to other recreational areas.

So I will just point out a few statements in the record that establish that there are areas that are of important access to the community.

So on record number PET310, this is from the statement of basis. It says, "In response to comments from local community citizens" --

HEARING OFFICER LAWRENCE: Sorry to interrupt. Can you repeat that reference?

MS. THROWER: Yeah. It is PET310, from the statement of basis.

And it says, "In response to the comments from local community citizens, PRI," Perpetua, "will manage an access route to provide the general public with limited access through the SGP site between Stibnite Road and Sugar Creek and Thunder Mountain Road at Meadow Creek."

Continues down a sentence later, "The proposed Stibnite Road access route through the SGP site is meant to provide control through site access that is safe, provides travel time comparable to current conditions, and is consistent

with the United States Forest Service Travel Management Plan."

Also from the statement of basis, Appendix E, which is called the access management plan, on PET527, in the first -- excuse me, in the second paragraph it says, "The United States Forest Service system road that passes through Stibnite extends from the village of Yellow Pine eastward along the East Fork of the South Fork of the Salmon River approximately 14 miles. Stibnite Road then continues south through the historic mine site and connects with Thunder Mountain Road on the eastern portion of the proposed SGP. This route also allows for access to Meadow Creek Lookout Road."

And so if you look at that second map I handed out from the recreation specialist report, you can see in sort of the lower half of the map, there's the Stibnite Road on the left-hand side and kind of the third -- two-thirds of the way down there's Yellow Pine. And if you follow that out, that's Stibnite Road, which follows the East Fork of the South Fork of the Salmon River into the Stibnite mining district.

And it is a little hard to see, it's not -- it's not very prominent, but there is a gray

line that goes out east into that area where there's purple bubbles around it, and that is trailheads from Monumental Summit and Lookout Mountain and Thunder Mountain. So those are established trailheads in US Forest Service land.

And then again, on that same page, it says, "Following the representation" -- "Following the presentation of the proposed public access routes described above in Midas Gold's PRO, an alternative public access route has been proposed by Midas Gold and would pass through the SPG mine site."

So there is another statement, there's several others, but I'll just give you those cites. I don't want to take up time reading these.

Another one, also from the access management plan, at PET529. The first full paragraph talks about different points, Thunder Mountain Road and beyond, that are important recreational areas for the community to access.

Also, I haven't -- this is the community access. I haven't talked about access for the Nez Perce Tribe. They use the area for their hunting, fishing and gathering, and their access and their interest to a lot of the area and the recreation --

these areas around the Stibnite Gold Mine is vast and is --

HEARING OFFICER LAWRENCE: Right. And they went into a fair amount of detail on that in the declarations on the standing issue, right?

MS. THROWER: Right. Yes.

HEARING OFFICER LAWRENCE: I have read those pretty extensively.

MS. THROWER: And as you pointed out, on the standing declaration for Save the South Fork Salmon, in particular Zack Seres's declaration, talks about how he goes through that road to access that Monumental Summit area.

HEARING OFFICER LAWRENCE: Right.

MS. THROWER: So number three -- I think that will be the longest one. Number three, "Is there anything in the record regarding the nature of Perpetua's property interest in the Stibnite Gold Project and its legal ability to control access?"

Yes. Some of the statements are in that draft access management plan, Appendix E of the statement of basis. They provide some understanding of both Perpetua's property interest in the road and their legal ability to control or

preclude access.

HEARING OFFICER LAWRENCE: Was that back on 529?

MS. THROWER: 527, PET527. That talks about the US Forest system road that passes through -- passes through Stibnite and extends from the village of Yellow Pine. That's a statement I read for the other question. So that provides us with an indication that that is not a private road, that is a US Forest Service system road and therefore it is a public road. And it is managed in accordance with the forest service's travel management plan, which is also one of the statements I read before from the Appendix E.

So any legal ability for Perpetua to control access comes from the forest service once it approves the final record of decision. That decision, whether to open this road or to close this road, needs to be consistent with the forest service's access management plan for the Payette National Forest. That's the governing document that tells people what types of uses are allowed on different roads. And currently, that Stibnite Road is open to public use and public travel by motorized use.

The access management plan at PET528 through 529, Section 2.2, discusses or has a section that is labeled the "SGP NEPA." That discusses the whole process and provides insight into what authority Perpetua or DEQ have to keep this road open or closed. And basically it says this is what the forest service is trying to decide, not quite whether it is going to be open or closed, but the alternatives that are being proposed in the NEPA process are two different alternatives for a road that would remain open and go through the Stibnite Gold Project area.

So it is only the forest service that can give legal authority to Perpetua to be able to preclude public access. In other words, they could say the road can stay closed. It may potentially need to modify its travel management plan. They would do that in the NEPA process. But that road needs to -- it will remain open until the forest service makes that decision to close it. And as I said, right now, during that NEPA process, the two alternatives that are on the table leave that road open.

To the contrary, there's no documentation that I am aware of in the record that

validates Perpetua's claim that it does have legal authority to preclude access. And in fact, DEQ's response to comments also indicates that the agency did not review any documents to confirm that Perpetua has legal authority to close the road down or to preclude public access.

So on PET570, response to comments, it says, "PRI has asserted they have complete and sole authority to control access to or through the facility, granting or excluding access at their discretion to anyone wishing to visit the site or pass through the site." That statement indicates -- it is a response to a comment. So it's not even -- you know, this is a response of someone saying we don't -- this isn't right. EPS's response to comments didn't say, hey, we've documentation here, here or there. They have clearly just taken Perpetua's word for it, you know, trust but not verify, right?

HEARING OFFICER LAWRENCE: On that point, do you have -- are there legal authorities that talk about how far DEQ is supposed to go in verifying that sort of thing versus relying on -- relying on an application that you are certifying under penalty of perjury what you are saying is true? So

what -- what is out there that tells us how far DEQ has to go down that road --

MS. THROWER: Right. And that touches on question four --

HEARING OFFICER LAWRENCE: -- no pun intended.

MS. THROWER: -- question four. Well, you know, just one thing under the Idaho Administrative Procedures Act, you know, petitioners can bring a claim for that an agency made a decision without substantial evidence. So if there's nothing in the record and the agency, you know, just made a decision based on that, you know, there's just authority just in the process or in the claims in the Administrative Procedure Act that indicate that an agency when making a decision should base that decision on substantial evidence.

This is from the Ninth Circuit. But there is a recent case called the Rosemont decision that touches on that issue as well.

So in the Rosemont case, this is a copper company that had a valid mining claim for land work proposed to locate a mine, however, its mining plan of operations proposed to dump waste rock onto adjacent National Forest Service land.

The United States Forest Service argued that they approved the mining operation because dumping of waste rock was a use of reasonably incident to mining operations and it assumed that Rosemont had valid mining claims on the national forest where it proposed to dump the waste.

The district court found, and the Ninth Circuit affirmed, that the forest service could not proceed with just the assumption that those mining claims were valid. It didn't find that the forest service had any basis for concluding that. And thus its decision to allow the mine to dump its waste on national forest land was arbitrary and capricious. And that citation to that Ninth Circuit case is 33 F.4th 1202. And that's a 2022 decision.

HEARING OFFICER LAWRENCE: When did we get to the 4th of the federal reporters? That's news to me.

MS. THROWER: I don't know.

HEARING OFFICER LAWRENCE: Okay.

MS. THROWER: So question number 235, "To what extent are DEQ's enforcement authorities relevant to these issues?"

You know, I think they're relevant at

basically the permitting level. It must require an applicant to include modeling to demonstrate that a proposed potential emissions from the facility will maintain ambient air quality standards in areas of where the public is allowed to access. It can, as part of the permit, require that Perpetua monitor that route to ensure that the ambient air quality standard is maintained. However, once this permit is approved, as the permit now stands, there are no air quality standards that DEQ can enforce or do anything about over that road.

HEARING OFFICER LAWRENCE: But if -- if Perpetua wasn't doing the things that the permit says in terms of controlling access, is there ability to then redo anything of the permit and say, well, no, you're not doing -- you're not doing what you said you would do in terms of maintaining access so now we need to remodel and do everything over again?

MS. THROWER: I will leave that answer to Mr. Shackelford. I'm, you know, sure that they can go back and try and do some enforcement, I suppose. That's at the discretion of the -- of the agency. I'll let him answer that question and see if he has any -- any sense of whether DEQ can do that.

But with respect to whether this road stays open or closed, that stands with the forest service and not DEQ.

So, for example, DEQ or the State couldn't go back and say, no, you have to close this road because we realize that, you know, you're not following your access management plan, people are going through here, it's not -- it should have been ambient air, it's not ambient air. There's no controls over this. That would be a change in the plan of operations that is authorized by the forest service, again a change in travel management plan that manages use of that road. So they -- they could not do that.

Question number six, "Is there anything in the record discussing the difference between guests to the facility and members of the general public and how Perpetua will determine who is allowed to access and who is not?"

There's EPA's ambient air policy document that discusses the difference between persons that have legal and practical access to a source of property but are not considered members of the public. That is at PET776. It talks about things such as an employee of the owner or operator

who works at the site is not a member of the public, and business invitees such as contractors or delivery persons. IDEQ's guidance also discusses some situations of other persons can be considered the public and require ambient air protections. Here are some statements from DEQ's guidance, which are -- I think those are on PET743 and 744.

HEARING OFFICER LAWRENCE: And I don't mean to interrupt. I mean, I'm pretty familiar with the guidance document. With this question I was more trying to get at like nuts and bolts how that's actually going to happen in real life outside of the, you know, the EPA document.

MS. THROWER: Right. So, you know, the thing if you look at EPA's policy in the guidance documents, there's no mention of what this guest of the facility is. I mean, there's -- there's people invited as a normal part of business conducted at the facility, but guest of the facility is not mentioned in the statement of basis either. It wasn't until the response to comments that I see that DEQ added this term and defined it as though seeking access for a specific purpose.

So how this is going to work

practically, it's unclear because they basically subsumed everybody into this guest of the facility. So I don't see how they would preclude anyone from accessing that site. Everybody that's going there is going to be seeking access for a specific purpose, whether it's a legitimate purpose or not.

I suppose the practical aspect of it is they will have a gate and presumably, if someone doesn't sign their health protections away and signs their paper saying they are now a guest of the facility and not the general public, then, you know, if they sign it they're allowed to go through. And if not, then presumably they would say you can't go through.

But, you know, this -- this definition, as I said, it sort of -- it's everybody. I mean, there's no distinction. It's not consistent with the distinctions made in EPA's policy and DEQ's guidance. No one needs to be excluded in this case. And no one's afforded ambient air protections in this case. I mean, you know, this definition basically guts the entire ambient air protections that are there to protect public health.

Does that answer your question?

HEARING OFFICER LAWRENCE: Yes. Thank you.

MS. THROWER: And let's see, question seven. I believe this is the last question. "How did DEQ guidance documents in the record at PET743 through 744 and EPA e-mail attached to the Shilling declaration affect the determination of ambient air?"

You know, we believe DEQ's guidance is consistent with the EPA's ambient air protection policy. You know, it states that it shall be assumed that the air within facility boundaries is ambient air unless the facility can demonstrate that public access is precluded. It talks about right-of-way access, for instance, if the general public is allowed on the site as part of a right-of-way easement or common service road, then the right of way is determined to be ambient air. I think, you know, that is -- is pretty close to what we have here with the public road. I mean, there's a right of way for the public to go over forest service roads, yet this was not determined to be ambient air.

The e-mail from the EPA regional modeler, Jay Emmett Alpine, doesn't really change our assessment that -- that DEQ's decision to treat

everyone as guests of the facility is wrong. His e-mail states -- you know, it's based on a limited number of facts in the prior e-mail that was sent to him from someone from DEQ, so he clearly wasn't looking at the entire record. And it states it's just his understanding of the roadway, it's just his opinion and not an approval, and it directs the e-mail sender, Kevin Shilling, to get formal review by EPA's ambient air review team.

So the value of his opinion on this road is not very valuable, and it's undermined by EPA's official comment on the draft permit at PET672 where the EPA says, "the State needs to provide sufficient justification to demonstrate the measures and requirements to preclude public access and ensure members of the public to presume the road can be classified as guests of the mine sufficiently complies with the national ambient air policy.

"Given the uniqueness and ambiguity of the situation, a petition to the EPA national ambient air policy team for review and concurrence with the State's findings could be warranted."

And again, I think we can see from the August 10th, 2023, EPA letter that it confirmed

that comment in its official position that it still has legal access concerns whether the general public has a right or permission to enter a specific property.

So in short, we don't believe that e-mail has any -- any value in terms of -- or shouldn't really be given any weight in terms of it being an official EPA declaration that it is okay to leave this road open and not preclude access.

So that concludes the questions that you had listed in your notice.

HEARING OFFICER LAWRENCE: I have one question. To backtrack, I probably should have interjected this on number six. This is going to seem like kind of a mundane, like on-the-ground question, but it's something I have been wondering. To your knowledge, is there anything in the record that talks about once within the project area, so if someone is on the access road and they're a guest, are there any destinations within the SGP that somebody would be stopping at or allowed to stop at or is it literally they are going straight through from the north to the south and vice versa and that's it? If there's anything in the record on that, that's all I'm asking.

MS. THROWER: Right. Yeah. There are draft access management plan and there are statements in the record. Again, there's not a finalized access management plan like a lot of the other plans. The stuff is not finalized prior to issuing the permit. But there are statements about how the road is being built to be separate from mining activities. That people will not be able to stop or go off of that road. There might be a pilot car that they will have to follow.

So no, as far as I understand that, they would not allow people to go off of that road to go check out the blasting activities or even go to -- you know, there's not going do be any interpretive signs open.

HEARING OFFICER LAWRENCE: Okay. Thank you.

For the petitioners, we have, what, three petitioner entities, right? I just want to make sure I'm not overlooking --

MR. HURLBUTT: Yeah, I just want to make one last point before moving on.

THE COURT: Okay.

MR. HURLBUTT: And I think a number of the questions that you've asked about whether Perpetua can have or will have the authority to control the

road, whether DEQ could take enforcement action to make sure that indeed happens, I think those miss one of the larger points, which is that whatever authority Perpetua does have or is granted, they've been stating throughout this process that they will be letting people access the site as long as they go through the check point and sign the waiver. So whatever authority they have, the plan, and what DEQ has approved in the permit process is this situation where people will be allowed to use the access road through the site.

HEARING OFFICER LAWRENCE: Okay.

MR. HURLBUTT: Thank you.

HEARING OFFICER LAWRENCE: Okay. DEQ, Mr. Shackelford.

I avoided calling you "Shackleton." I've always been into Ernest Shackelton so I always feel like I'm about to say that name instead of you.

MR. SHACKELFORD: I would just start, before getting to the questions, I will probably skip down to number four anyway, start by saying that this is an unusual situation regarding access management plans. I think the declaration of Kevin Shilling, which is probably our most extensive explanation of

the decision-making behind this problem, illustrates that this is not a normal thing for us to do, to do an access management plan for facilities. Since -- and my assignment also indicates we do approximately 100 or so air permits per year in the air quality program. So since this issue, this permit was issued, we have probably done 100 more.

Given that, and I think that you alluded to this earlier, as to number four, DEQ is reasonable in relying on the certification of documents that IDAPA 58.01.01.23, what I think you were alluding to earlier, which essentially requires sworn statements in the application so that we can reasonably rely on those. We can't go and fact check all 100 applicants every year for every little detail that they provide for us. This is also why we have the guidance documents that has also been referred to here. Because for all the different parts of the state and all the different activities, whether it be some sort of metal mining or sand mining or asphalt production, whatever it is, whatever the emissions are, we have to have some sort of flexibility in determining what will actually work on the ground.

So that's in my view the relevance both of the evidence that we relied upon and the guidance documents that are referred to as well.

HEARING OFFICER LAWRENCE: Before you move on, can I just ask a couple of follow-up questions? So is there -- and I have gone through the record, I mean, I've read the briefs and then when people would cite to things I would see if I could lay eyes on that myself. But is there some place in the record where -- that you're aware of that Perpetua has actually made that representation about the ability to control access?

Because what I recall is, when I would go back to documents in the record based on the citations and the briefs, I'd see what looked to me like sort of descriptions of a prior representation that had been made, but I don't know that I've actually seen where that representation is. So I was wondering if that is somewhere in the record, if that question makes sense.

MR. SHACKELFORD: No, that does make sense and I can't recall one either. I suspect it is in the actual permit application. All I know is I'm referencing Kevin Shilling's declaration, which in turn refers back to what representations that were

made to him in the modeling team.

HEARING OFFICER LAWRENCE: Right.

MR. SHACKELFORD: But further than that, I'm not sure.

HEARING OFFICER LAWRENCE: Okay. Thank you.

MR. SHACKELFORD: And I think, to put a finer point on one of your earlier questions, I'm not -- I'm not aware of any existing authorities, I think you asked about legal authorities addressing the extent to which DEQ is responsible for verifying any of that information.

HEARING OFFICER LAWRENCE: Right.

MR. SHACKELFORD: I'm not aware of any law that was violated here that says, well, DEQ needs to go and fact check all the different parts of the application that have been certified.

HEARING OFFICER LAWRENCE: So when I asked Mrs. Thrower that question, her answer was, well, it's an issue of evidence in the record.

Do you have any particular thoughts on that point?

MR. SHACKELFORD: No. I think that's fairly put. It's what's relied upon by -- by the permit writers in the modeling team.

HEARING OFFICER LAWRENCE: So DEQ would say,

well, the reliance on the representation, that's the sufficient record evidence or under the standards that govern --

MR. SHACKELFORD: Yeah. This isn't just for the air quality program. I mean, if you -- there's all kinds of permits that require maybe legal descriptions of land that we don't get into. So most -- most facilities are going to be a normal parcel. We don't ask who owns it? What are your leasehold rights? Does your lease specifically indicate that you can exclude people? Does it require you to allow anybody on that may not be directly associated with the facility?

If you were applying for reapplication of recycled water, for example, you need a place to put that recycled water. Maybe you have a lease with a farmer who then decides, well, I don't like the way that you're spraying my fields, you no longer have that. What does that mean for our permit that was reliant on some place where we can put it? Well, it means you can't really use it anymore. So that's how it would happen in the practical world.

So to what extent of DEQ's enforcement authority is relevant to the issues, they -- they

are very relevant. In my time with the air program, I've seen that their enforcement typically is commensurate with the level of the -- of the violation. So if it's a very minor violation it may be simply a letter or a small fine. And for larger violations, consent orders, consent decrees, CASAs, and larger fines.

I don't know how deep into hypotheticals we should really get, but I think if this were just somebody crossing over the boundary far away from the mine and that were to be found out by DEQ, that would probably be seen as a minor violation. But if they were just -- if Perpetua were to decide to just let everybody in, we are not really doing the whole escort vehicle, we are not putting up any trespassing signs, anybody who wants to come in and go through that's fine, that would be a major violation of the permit.

To the extent that the forest service, if that is true, somehow reneges or doesn't give Perpetua the right over some portions of this land, although my understanding is that a lot of these are fee simple parcels with patented mining claims, then that would require a permit modification. But at this point we don't have that evidence, which is

why DEQ's decision was reasonable with the record before it.

That said, as Kevin Shilling mentioned, there is an option. I think on Page 5 and 6 it discusses the other option, which would be to include the road and ambient air, and that compliance could have been demonstrated. It would have required considerable analytical scenarios and extensive number of permit conditions to make such scenarios enforceable, which is why option two is preferred by the team.

As for number six, I think the answer is likely no, whether there's anything in the record discussing the difference between guests of the facility. From DEQ's point of view, that's not its responsibility to dictate who gets to enter, enter different facilities. Lots of places do provide tours. So it's not really up to us to decide how that -- how that works.

What is up to us is to ensure that it's not the general public that has access, that they are reasonably precluded, that they are discouraged from entering the property.

For number seven, I would say I touched briefly on the guidance document. And it's

important because it provides a lot of flexibility for all different kinds of stationary sources throughout the state and it requires reasonable preclusion. I think on the second page, on PET744, there's essentially a series of questions, and you answer yes or no. And based on the answers to those questions, you can decide whether the general public is reasonably precluded from gaining access to the facility. And based on the permit application, we could see that the general public was reasonably precluded based on the number of parameters that they provided as well as permit conditions that would be required. And then, of course, the more specific access management plan, which would be their -- incorporated thereafter.

As to e-mail attached to Kevin Shilling's declaration. It is an opinion by one of EPA's PhD-prepared staff members. I don't think it is fair to say it's not relevant. I think it's fair to say that this is a nuanced and difficult issue, that DEQ -- DEQ took considerable time and paid considerable attention to figuring out a scenario that could work for the permit applicant while protecting the public's health. And I think that opinion helps go to show DEQ's effort in

trying to bring in more support for its decision and trying to bounce this idea off of others to make sure that they got it right.

HEARING OFFICER LAWRENCE: All right. Actually, I have a question that relates to that and I think something you said at the beginning, which is this is kind of -- this is not a typical situation for DEQ. What makes this unusual?

And the reason I ask is obviously we all know Idaho has -- we have so much federal land within our borders. So what -- why is it that this is sort of such a unique type of situation? And that may not be relevant to anything at all, but I'm curious.

MR. SHACKELFORD: Well, I think for the most part, stationary sources aren't places people want to go, right? So if you see a big stack emitting things, it's probably not a fun place to recreate in the first place.

But you're right, there are other mines in very rural places in Idaho where there might be nearby lakes or forests to visit that could be somewhat similar, but maybe the topography are such that there aren't any kinds of roads for people to get in and out and there they're even more rural

and rugged.

So I can't really speak beyond that because I haven't had in-depth conversations with the permitting team on all the different permits that they've seen.

HEARING OFFICER LAWRENCE: Right.

MR. SHACKELFORD: All I know is that from their perspective, and I think there was a discovery request on this, any other type of scenario they could come up with when there was some sort of public right of way. The closest they could come up with, a place down in Owyhee County, when there was an actual road, like a public road, and that could not be permitted because the permit applicant had no authority and it was beyond question, didn't represent that they had the authority to close it down. That's what DEQ considered a right of way. Literally you have the right to go through, you cannot possibly preclude it, and so you can't represent such.

HEARING OFFICER LAWRENCE: All right. Like you mentioned, other mines, like Thompson Creek Mine or the Cobalt project up near Salmon, it seems like this might replicate itself. It's funny to me that it is so unusual. But anyway, so that was my

last question.

MR. SHACKELFORD: Great. I don't have anything further.

HEARING OFFICER LAWRENCE: Okay. Thank you.

Mr. Pooser.

MR. POOSER: Thank you, Mr. Hearing officer, Counsel.

I think I will probably just go through these questions as the parties have already done. And with respect to the first question, I do want to address kind of this idea of legal authority to preclude access. And I want to make sure we're actually looking at that with the right perspective, and that's what the actual allegations are by the petitioners. And it's quite limited when you actually look at their -- at their briefing.

Their opening brief doesn't actually address legal control at all. In their reply, it is at Pages 14 and 16, they talk about legal control, but it's only within a very specific allegation and assumption, and that is, that the forest service is requiring that Perpetua include this road and that then allows public access across the road. And that is an assumption that is flawed

and it's also not -- is unsupported by the record.

So I want to just make sure when we're talking about legal authority that we're looking at it as the issue has been presented and the issue has been kind of briefed and discussed already. It is very limited to just simply the assumption that the forest service here is -- is mandating that this access road exist, is mandating that the public be pro- -- the general public be provided access across the site, and that is just simply not the case.

HEARING OFFICER LAWRENCE: So you're saying that there's nothing in the record where the forest service is saying that access has to be allowed through the project site?

MR. POOSER: Yeah. And this kind of -- this kind of goes back to some of the other questions about, you know, the questions too about the public's need to access it, also kind of what Perpetua's interests are.

So, I mean, there's simultaneous permit -- permit actions going on here, and so one is with the forest service. And so Perpetua has submitted a plan of operation, and that plan of operation is seeking to establish an operational

boundary for the project. That operational boundary is also being used as the ambient air boundary. So there's a fundamental assumption in the operation -- in the plan of operation that there will be an ambient air boundary around the site, that Perpetua has legal -- full legal control over and can exclude the public for operational reasons, for safety reasons, and also for air quality permitting. So that process is ongoing.

At the same time, we're here in front of DEQ saying, hey, can you confirm what our air -- air ambient boundary is? And that is what we're kind of talking -- that's ultimately what we're talking about here, which is the operational boundary of the facility.

And so when we're -- when we're looking at these two permit processes actually kind of go hand in hand and they're going -- they're coming together kind of simultaneously. And so when you look at the assumptions that are kind of being made and the representations of legal -- of legal authority, those are being made because that is what is -- that is what the plan of operation actually calls for. So that's when we kind of talk about this legal control.

Now the other aspect of the plan of operation is that there is going to be this access road. And I think it's kind of important to kind of look at the timeline and you've kind of asked where in the record is some of this information available in and in particular, it is in the application materials and it is in -- some of those are supplied as part of the statement of basis, some of those were supplied in the application that we submitted as part of our summary judgment briefing.

And so if you look at the draft access management plan, I mean, it does kind of sort of, you know, give this background as far as, hey, we're going in front of the forest service, we have this plan of operation and this plan of operation includes our operational boundary, which is our air -- ambient air boundary and it also includes this -- this access road that we would also control. And so that is all -- so that is all in the record.

And I think in looking at kind of the timeline of this, it is kind of important just to understand how this kind of came about and that's in the access management plan.

And so in September 2016, that's when the plan of operation was submitted to the forest service. And again, as proposed, it is creating this operational boundary. And at that time the public access through the mine site was completely prohibited under the plan of operation. And in public comments, particularly the Yellow Pine residents, expressed concerns about that and Perpetua was asked to consider, are there other options? So it came up with this option. And so now that is -- that is -- the plan of operation was refined and so now that option is in there as far as having this access and this controlled access that Perpetua would have full control of this road, they would protect its ambient air boundary, and that is kind of, again, part of this plan of operations.

And so you can -- you can see this, you know, in the application materials. Perpetua applied August 2019. It submitted a final application in June of 2020. In December of 2020 it submitted another refined plan of operation. And then it updated its modeling at that time with DEQ.

HEARING OFFICER LAWRENCE: Are those in the

record?

MR. POOSER: Yes, they are.

So when I'm talking about the timeline that is largely set forth in the access management plan, which we've already talked about, which is petition 527 through 533. That has a lot of the background. You know, the application itself kind of indicates that there's a record of decision that is still required from -- from the forest service, that's at PRI382. And then you have the application itself with respect to kind of the air quality modeling report, and then there's also kind of an addendum to that report. And those reports are at PRI411 through 419. And also at PRI818 through 825. And those talk about -- what the situation here is as far as how Perpetua is having to go through this forest service process and present a plan of operation.

So you asked specifically like where did Perpetua make the representations that it has control? There's a couple, and one is just the permit and the air quality analysis. Again, it is assuming that we have this operational boundary and the operational boundary is the -- is the ambient air boundary. And so that is a fundamental

assumption that is in the permit application. It is a fundamental assumption that goes into the air quality analysis, the NAAQS analysis, et cetera, et cetera.

And the statements are made again, kind of pointing to the access management plan, that we will have full control over this road, and that we have the legal authority to exclude the general public. And so those representations were made and, again, kind of where that -- where that is in the access management plan.

Kind of see, perhaps move to question five. And you're kind of asking sort of about DEQ's enforcement authorities relative to this.

And I think enforcement authority is kind of relevant, but also the sequencing of events here is also kind of relevant because there is, as I mentioned earlier, there is sort of this challenge in sequencing because Perpetua has to get forest service approval for its operational boundary. At the same time, Perpetua needs DEQ to recognize what the actual ambient air boundary is, you know, based on that operational boundary. So, you know, we can't commence construction -- if we don't have a project, we've got no air permit. So,

you know, this is fundamentally sort of based on that -- that, you know, we can't commence construction unless we have a project.

So I want to kind of turn just real quick back -- well, actually, maybe I will just kind of move forward and get to that later.

So question six, as far as kind of you're asking whether or not there's anything in the record that kind of discusses this sort of difference between guests of the facility and members of the general public, and Mr. Shackelford said there's really not, but I think there is and that's in the permit -- that's in the permit. And that's in permit condition 2.7, which makes that distinction between the general public and people -- and the folks that are actually allowed to cross the site. And so that kind of distinction between the general public and, you know, guests to the site, that is how that is defined. That is how the DEQ chose to address the situation. And that's where you find that fundamental distinction.

HEARING OFFICER LAWRENCE: As I recall, is there anything that says what the difference between a guest and a member of the general public actually is?

MR. POOSER: Yes. Yes. I mean, so a member of general public would be somebody that can just come through the site unrestricted, right? They could just pass through it like a county road. They could just kind of pass through the site without any obligation whatsoever. It is just the general public has access to go through there. And that's not what we have here.

This is a controlled -- this is a controlled road. It is monitored, it is -- there is surveillance provided, there are barriers put up. When people come to this site, they know they are not the general public. They know that they are going to be a guest. They know they don't have a right to be there other than as allowed to go through -- to pass through on the road. And so those conditions are very clear and that is what kind of makes that distinction between the general public and the guest.

On number seven, as far as the DEQ guidance document, I thought Kevin Shilling addressed that very well in his -- in his declaration about how he kind of sort of -- how the DEQ guidance and EPA guidance are the same and how they kind of sort of went through this analysis.

As far as the EPA e-mail goes, I think it is, you know, important because it does show that DEQ actually consulted with -- with EPA on this issue. It is not like DEQ just kind of made a mandate and just said, this is how we're going to do it. It actually consulted with the EPA to try to get its thoughts and those are the thoughts that they got back.

And that kind of gets me back to sort of the original point as far as kind of the legal -- the idea of legal authority and the specific challenge here, again, which is that the forest service requires public access. And the only proof that they provide, that the petitioners provided in the record, are two memos. One is a Stantec memo, which I understand is kind of like a -- I suppose a consultant of the forest service that's kind of consulting on air quality issues. And then there is also a much lengthier document that is an actual air quality analysis.

And both of those documents do what DEQ does, they're assuming that there is a plan of operation that includes an operational boundary and an ambient air boundary. And so their analysis is based on there being an ambient air boundary.

Their analysis is also based on the fact that Perpetua is going to have legal control of this access road.

So all of those are assumed in these two documents. And those documents in no way show that the forest service is requiring public access. Frankly, it is the opposite because those documents, again, are kind of reporting what is in the plan of operation and what is -- what is going to happen with this project when it gets off the ground.

The other aspect of those two -- of those two documents, which I think are quite interesting, is that they also refer to EPA's response to this question on whether or not the road should be excluded from the ambient air.

And so if you look at Petition 964, and this is the -- this is kind of that larger air quality analysis -- yes, this is the large air quality analysis. On Petition 964 it specifically talks about that there was a November 18th, 2020, response to comments letter authored by EPA that is accepting DEQ's findings on the -- on the road. And on Page 25 of the letter it states that EPA are recognizing that this control access road would not

be ambient air. It also -- and so that's that air quality analysis.

When you turn to the Stantec memo, which is at Petition 838 and 839, if you look specifically at Page 839, you will see there it says, "EPA approach" -- "EPA approach to the access road." And it talks specifically about that same November 18th, 2020, response to comments that EPA did where it acknowledges and accepts DEQ's findings.

And then in addition, they talk about an April 15th, 2021, conference call with Stantec and the forest service. And what this says is "EPA representatives affirm that control public access road is consistent with the December 2nd, 2019 revised policy on exclusions from ambient air memorandum."

So it's not just that -- that e-mail that was attached to Mr. Shilling's declaration. There's other -- there's other evidence in the record as far as EPA's approval -- approval of the ambient air boundary and specifically with respect to that access road.

So I'm happy to address any additional questions you may have.

HEARING OFFICER LAWRENCE: No, I don't have anything else.

Thank you.

Petitioners, do you want to follow up?

MS. THROWER: Just a couple quick points. As DEQ mentioned, you know, that they should be able to rely on sworn statements of an applicant, you know, I would just like to point out that these were comments that were brought up to the agency indicating that there was potential issue about, you know, whether -- whether they could preclude access, whether they have the control to preclude access. So, you know, to that extent, the agency should have had a little bit of more heightened awareness and should have -- it would have been reasonable for them to look into that and respond to comments with that information saying, yes, they've looked at it.

You know, I -- like I said, I mean, you know, in the Rosemont case, that was the same issue. The mining company said, hey, we have valid mining claims, but there was never any indication that the forest service looked to see if those really were valid mining claims. Having a valid mining claim there are certain -- certain things

that you have to meet, for instance, that you have valuable minerals underground. They never checked that. And the Ninth Circuit said you can't make those assumptions. You need to have some basis for -- you know, if you are going to make a decision based on those assumptions, you need to have looked at those and have made a reasonable assessment if those claims are true.

You know, this issue with guests versus the general public, you know, the guests of the facility is, as I said, this is a category of people that was made up for this permit. It's based -- it's not based -- like EPA policy and IDEQ guidance. If you look at the people that are either not the general public or the general public, they are -- those situations or those classes of people are based on what people are doing at that site or trying -- or why they are trying to access that site. They are not based on someone signing a paper. And so by doing this, they really, like I've said, there is no general public anymore. And it's completely gutted any protections that the general public has by, you know, this new class of people.

So, you know, just for instance, DEQ

decided that the general public is considered anyone not directly associated with the facility. You know, people trying to access the road to get to the public land are not directly associated with the facility. Most people are probably not going to want to, you know, hang out there. Someone not subject to worker exposure regulation or someone not onsite. It is probably going to be someone who is trying to drive their car through there. People invited as part of a normal business conducted on the facility site like a commercial establishment or service provider, those are people of the general public. They need ambient air protections.

You know, I don't think it is consistent with this guidance to say, oh, okay, well, if you walk on to -- maybe the facility has a taco shop, right? If you walk on there to get a taco and they have you sign a piece of paper that you're not the general public, is that okay? I mean, that just seems to completely, like I said, gut the whole -- whole purpose of this ambient air policy and precluding the public from areas that are not ambient air.

You know, there's other, as I mentioned, general public allowed as part of a right-of-way

easement or common service road. Even if the facility is under common ownership but there's a different facility and the employees have to pass through the one source to get to where -- to where they work, they are still considered the general public. You know, can they sign a waiver every time they have to go to work to say, okay, well, if we pass through this facility we get to breathe all the pollution that the facility is emitting and we don't get ambient air protections?

You know, I don't think there's a case, I haven't seen anything that says that's okay. But like I said, I mean, this whole new guest of the facility thing, there isn't any general public anymore. Anybody can just sign they are a guest of the facility and it's done.

I get the -- I get the whole, you know, the permits, there's a lot of permits that Perpetua has to get. There's a lot of assumptions they need to make, you know, about the project because the forest service has not permitted the project. We don't know exactly what the plan of operations or what the final approval is going to look like.

What we do know is that the two options are to keep that road open just the alignment is a

little bit different. But both of those options would be going through the mine site, and both of those options would allow the public to access these recreational sites that are really important to the community.

So, you know, you talk about a larger air -- ambient air boundary and giving Perpetua complete control over that, you know, that's -- you know, that's what the forest service's approval gives them in terms of blocking people out from using the rivers there, blocking trails, that kind of thing. If they -- if the forest service gives them that authority to do that, that's fine. But to the extent that they don't have the authority to preclude people from accessing this road to go through to other public lands, I just -- you know, I don't see how Perpetua can claim they have legal authority to preclude access that's required under EPA's policy.

And about other comment letters, about other statements from EPA about, you know, that the ambient -- the excluding the road from ambient air protections is okay and other things, you know, I'm sure you'll be going through all the citations and all the documents to see, but we do know that the

last -- on the last draft permit EPA's comment letter was not -- was -- basically said that this doesn't seem right. You need to, you know, check this out more, that there's -- the public is going to be going through there.

Same thing with the August 10th, 2023, letter. EPA clearly made a point there that the assumptions that Perpetua's making in terms of being able to preclude access to the public are not substantiated and they had issues there.

We don't have a final determination as the EPA letters, both of them said, you know, get an EPA determination, get an EPA determination. DEQ hasn't done that.

So, you know, as far as EPA's official policy on this road, I suppose that we don't have that official policy from the ambient air team. It's not something EPA is going to impose on the State. The State has delegated authority to issue these permits. So I understand that EPA's not going to mandate that, but that is available and that hasn't been done. And so, you know, the latest official policy, I suppose, or the official opinion that we have from EPA is the latest they have submitted on the last draft permit on the 2022

and 2023 letter that we have been talking about.

And, you know, I think that concludes my comments. You know, currently that road is being used, you can drive up there, you can go through there and have fun. It is a rough road, but, you know, it's a public road. As -- as far as the forest service is reviewing the plan of operations and reviewing the environmental impact statement, that road will stay open to the public. And if it's not excluded from -- or if it is not included in the ambient air and people are going to be driving through there. A lot of those cars are these Razors and everything --

HEARING OFFICER LAWRENCE: I'm having trouble hearing you now.

MS. THROWER: A lot of those cars are these Razors and stuff that are open air. People are going to be, you know, enclosed in their cars with air-conditioner and they are going to be breathing all of that dust, all of that particulate matter, all of that arsenic, which, you know, as we've argued, is also been underestimated to begin with. And I don't think people are going to make that distinction of, oh, I signed a paper so I'm no longer the general public so I'm protected, you

know, I'm protected now from this pollution. Nobody is going to understand that. And the truth is that they're not.

HEARING OFFICER LAWRENCE: All right. Thank you.

MS. THROWER: Thank you.

HEARING OFFICER LAWRENCE: Okay. Well, that was helpful for me, and that concludes the exclusion from ambient air argument.

Do you guys still want to present argument on those few issues you mentioned in the beginning, Petitioners?

MR. HURLBUTT: If that's okay with you, Mr. Hearing officer, and I don't -- I don't want to take up too much time, but yes.

HEARING OFFICER LAWRENCE: Do you have an idea how much time? I'm kind of inclined to take a break just to give my brain a chance to recover a little bit, unless you're going to tell me it's going to be super short.

MR. HURLBUTT: I mean, I think ten to 15 minutes.

HEARING OFFICER LAWRENCE: Let's go ahead and take a ten-minute break because obviously these folks need time to respond too. So that would be

helpful for me. So I have we are at 10:49, so why don't we make it that we reconvene at 11 a.m. even.

(Break taken from 10:49 a.m. to 11:00 a.m.)

HEARING OFFICER LAWRENCE: We're back on the record in the matter of air quality permit to construct P-2019.0047.

So we have concluded the argument about the exclusion of the access road from ambient air and now the petitioners would like to present argument on a few other issues. Given it's only three of them, I would be inclined to just go party by party on this one and not issue by issue so that everyone is getting up three different times and all that.

Is that okay with you?

MR. HURLBUTT: Yes.

HEARING OFFICER LAWRENCE: Okay. And disclaimer. I did my best during the ten-minute break to refresh my recollection of a couple of these issues. My attention more recently has been focused on the ambient air and the second issue you raised, the T-RACT analysis, so that one I'm pretty up to speed on. It's been a while since I have looked at the other two, so you may want to talk to me like you are explaining the issue to a fifth

grader, is all I am trying to say, if you want it to land.

So Petitioners, you are free to go.

Oh, is someone trying to come in?

MR. HURLBUTT: Yeah.

So I wanted to hit on just three of these sub-issues which I think are really important and require a little bit of clarification after -- after all the briefing.

So first on issue 2B, the assumption of 93.3 percent dust control. I'd like to point out that this is a big deal, the 93.3 percent. They're operating on a razor thin margin to comply with the national ambient air quality standards for particulate matter. This is in the statement of basis attachments at PET325 through 326 where DEQ modeled a slightly different scenario. Instead of what's been approved, which is 180,000 tons per day of mining operations and 93.3 percent dust control, what if instead they cut the operations by a third and only did 120,000 tons per day of mining operations, but also were only able to achieve 90 percent dust control. So just a little bump down in the dust control efficiency and a one-third drop in the amount of mining that would occur.

And in that modeling, DEQ found that that would violate the PM10 daily standards for the NAAQS. Again, that's in the record. I think that's at five receptors around the site, those would be exceeded. So even with a huge reduction in mining but just a small reduction in control efficiency we had violations of the air quality standards. And that's why DEQ says this throughout the statement of basis, 93.3 percent is critical for NAAQS compliance. It is an aggressive level of control. It is challenging to consistently and continuously achieve 93.3 percent control. And the permit therefore requires aggressive implementation measures to achieve that.

HEARING OFFICER LAWRENCE: So sorry to interrupt. So am I correct in the ultimate alleged error is that because this is such an important issue and maybe -- if that's accurate, that it's a razor-thin margin, but the ultimate alleged error is that it was error not to include an enforceable limitation on that.

Am I accurately describing what the alleged error is?

MR. HURLBUTT: The error is that there is -- there is no 93.3 percent enforceable limitation or

there is no other limitations that reasonably assure that that 93.3 percent would be left. So, yeah, it's true there's no, you know, limitation that you shall achieve 93.3 percent. All there is is this future fugitive dust control plan, not yet been submitted, that DEQ and Perpetua claim will help achieve that 93.3 percent.

But really DEQ is hiding the ball here. We don't know how Perpetua plans to use magnesium chloride and water to actually achieve 93.3 percent control at this particular site. They've not yet identified the frequencies and rates of spraying that are going to be used and when and where that's all going to happen. They're hiding the ball, shielding it from public scrutiny. EPA in its comments have not been able to comment on the actual plan that Perpetua is going to employ. Neither is Save the South Fork, neither is the Nez Perce Tribe air division, neither has ICL or any other member of the public. DEQ is shielding that view.

The super important issue is to whether the plan Perpetua comes up with can actually achieve 93.3 percent, and we have no idea yet what that plan is going to be. And the requirements in

the facility -- the fugitive dust control plan, though they do require Perpetua to set specific tasks that it's going to perform and monitoring to make sure it performs those tasks, none of that is actually in any way tied to specifically achieving 93.3 percent.

And these points are backed up by EPA's original comments where they thought that an 80 percent air control was a more appropriate thing to assume, and also by EPA's recent letter from August 10th. And I would just like to point out that in that enclosure to the EPA letter at Page 14, after EPA raises concerns about the lack of information to support that 93.3 percent could be achieved specifically at this project site, EPA then warns, "ultimately IDEQ appears to have back-calculated the control efficiency necessary to demonstrate NAAQS compliance rather than determine a control efficiency that's achievable in practice."

And if you don't have any further questions on the 93.3 percent I'll move on.

HEARING OFFICER LAWRENCE: I -- can you -- well, this may be more of a question for Mr. Shackelford. But do you recall -- and I'm

asking just because, again, I haven't looked at this particular issue recently. Do you remember what the Simon and Shilling declarations say on this issue in terms of how they explained the 93.3?

MR. HURLBUTT: I don't. Sorry.

HEARING OFFICER LAWRENCE: Okay. No questions.

So we'll move on to -- the next one was the T-RACT issue, right?

MR. HURLBUTT: Yeah, 3B, T-RACT. Perpetua doesn't have a right to be granted a T-RACT adjustment, which lets the acceptable levels of carcinogenic arsenic be ten times higher than what's normally acceptable. They have to follow the rules and go through a T-RACT process. And I realize you now said you have gone through those rules, but with the air rules at 210.14 say that on a case-by-case basis DEQ has to decide whether to grant T-RACT. It then says the applicant shall submit and what DEQ shall consider when making its determination and that includes both environmental information about the environmental impacts of the control technology that is going to be used, here this spraying the roads with magnesium chloride and water, and the economic feasibility of doing that.

The case-by-case thing is important, and this is a unique case that a lot of Perpetua's reply brief focused on the fact that magnesium chloride has been used in other situations so why do they need to, you know, consider it here. But again, the rules say case by case.

Nothing in the T-RACT analysis that's in the record talks about the environmental impacts of using magnesium chloride. This is a unique project site. It's up in the mountains in narrow valleys. Most of the roads are near live water. And to achieve this super high 93.3 percent control efficiency, presumably they're going to be spraying a lot of magnesium chloride. So the idea that because maybe this has been used out in the phosphate patch or at a gravel mine on the Snake River plain, that somehow shows DEQ knows what the environmental impacts of using this high amount of magnesium chloride at this particular site, that's just not -- not accurate and needs to be considered here.

And the same goes with economic feasibility. Again, maybe other projects have used these types of controls before, but what's the feasibility of doing it here where they're trying

to achieve such a high and aggressive level of control?

Any questions on T-RACT?

HEARING OFFICER LAWRENCE: No.

MR. HURLBUTT: And so moving to -- this is issue 3C.

HEARING OFFICER LAWRENCE: Averaging?

MR. HURLBUTT: Averaging of projected arsenic emissions. Again, DEQ needs to follow the air rules as they're written, which require meeting ambient arsenic concentrations. Those concentrations are laid out in the rules and they provide for two specific instances in which those standards can be adjusted. That's the T-RACT which we've already talked about. So with the T-RACT demonstration, ten times as much arsenic can be found in the ambient air during the project than would otherwise be able to.

The other exemption in the rule that allows for adjusting the arsenic, AAC, is for a short-term project. This is in the air rules at 210.15. And then the definition for a short-term project is in the air rules at Section 007.08 in the definitions. Those are five-year sources or less.

Even if the Stibnite Project is granted the T-RACT adjustment, so allowing ten times as much arsenic to be found in the air, the project would not comply with the arsenic ambient air levels, and that's why DEQ came up with this 16/70ths adjustment. Multiplying the annual arsenic that can be actually found in the air when the project's underway as well, multiplying it by the 16 years of the life of the mine and dividing by a 70-year lifetime, effectively cutting 77 percent of what's actually modeled to be in the air for arsenic each year down to just about 23 percent by spreading it out over this longer period.

That's not in the rules. That's not one of the exceptions of the rules. If DEQ's allowed to just come up with other things like that, I mean, why is there an actual arsenic number rule? Why are these two specific ways to adjust that, the T-RACT and the short-term source? This is just a third exception that DEQ made up. It's not found in the rules. And without it this project would not comply with the ambient arsenic standards.

Any questions on that?

HEARING OFFICER LAWRENCE: No.

MR. HURLBUTT: Thank you.

HEARING OFFICER LAWRENCE: Thank you.

All right. Mr. Shackelford.

MR. SHACKELFORD: Well, I'd like to start, given that it's been mentioned several times throughout this hearing, with the EPA's recent letter, which has now found its way into this administrative record, there's something important in the attachment, there's an incomplete citation to a reference document. And that document was issued by the environmental appeals board, and I think that document can help put some of these arguments into context. That document is called the Order Denying Relief, and that is dated February 18th, 2005. And it was issued in the case In re: Peabody Western Coal. So you'll see footnotes throughout that attachment to the letter, which is now in our administrative record.

In that case, the board denied the coal company's petition to review the EPA's decision declining to impose a potential to emit on the coal company's operations. And that was because the board found, and I will quote it, "in light of the considerable deference that the board typically affords the permit issuer in questions on technical judgment, the board concludes that the regent

adequately explained the basis for its decision and that the regent's rationale was reasonable based on the information in the administrative record."

And then in reaching that conclusion, the board highlighted the particularly heavy burden that petitioner -- that is assigned to the petitioner that seeks review of a permit that is based on issues that are fundamentally technical in nature.

So technical judgment, deference, heavy burden, reasonable basis, these are the themes prevailing in this order that was provided by EPA to DEQ.

HEARING OFFICER LAWRENCE: So just to clarify. So we are talking about sort of general standards that apply. This -- this Peabody, this isn't relevant to one of these three specific issues.

MR. SHACKELFORD: Yes, it is.

HEARING OFFICER LAWRENCE: Oh, it is. Sorry to interrupt.

MR. SHACKELFORD: No, that's all right. No, I can see. It's a long lead up, I guess.

The point is that when a matter is open to interpretation or subject to many variables

you're inevitably going to see a rise in multiplicity opinions. And the petitioner's arguments are opinions, and these opinions are not favored by our law which grants great deference to the agencies tasked with making the complex technical judgments that are at issue today.

So coming to things like the 93.3 control efficiency, okay. To make these arguments that it's razor thin means you have to ignore the entire declaration of Kevin Shilling and Mike Simon as well, bureau chief Mike Simon, who together have a combined relative experience of 60 years doing this.

Built into all of their engineering, all their modeling are conservative values. That's what gives them the confidence to say within a reasonable degree of engineering certainty we can have a high assurance the NAAQS won't be violated over any of the time periods. It's ignoring all the conservative principles that are going into this. It is not razor thin. Modeling was based on worst case scenarios. That's found throughout the declaration of Kevin Shilling about Pages 16 through 18.

Regarding hiding the ball, I'm not sure

what ball is being hidden. It sounds like the idea is that the actual operations, the specific timetables for sprays, the combination mixtures of water to magnesium chloride or some other chemical dust suppressant, that is the ball being hidden.

DEQ issues permits all the time requiring fugitive dust control plans. Unlike the access management plan, this is a much more typical thing that DEQ does all the time. And DEQ enforces when there's permit violations.

Now, typically that will require neighbors complaining. And it is my understanding that this site, although I haven't visited it, doesn't have much in the way of neighbors to complain about dust. But the fact is that DEQ has experienced controlling those fugitive dusts based on plans that it approves.

And there's nothing in the record to suggest that DEQ is somehow now going to approve a plan that doesn't meet its level of expectation for control. And in fact, overriding all of this is there's a ten percent opacity, instantaneous opacity test, that needs to be conducted such that anything is beyond ten percent, operations shut down.

The permit requires daily inspections of all fugitive dust sources. So there's all kinds of protections built in here that precludes all of the various hideous scenarios that are being alleged.

Regarding T-RACT, that's a misstatement of the law -- of the rule. Never does it say DEQ shall do anything. That is wishful thinking. The rule literally says, "will on a case-by-case basis consider factors to determine whether technological feasibility of any particular proposed control technology."

If you see the declaration of Mike Simon, it talks about how paving was one of the controls that was proposed and that was eliminated because it was not found technologically feasible based on the very first prong. So that was based on the process and operations. There was no need to go further.

The next one, that's what's remaining. DEQ has essentially no choices at this point, other than to say we have chemical dust suppressants combined with water. PRI, or Perpetua, provides us with studies indicating a control efficiency of 90 to 99 percent. We go ahead and take the most conservative one at 90 percent and applied that to

our modeling. Then when we do non-bulk RN process meteorological data there are no 24-hour NAAQS exceedences. Only when you use the bulk RN is there then NAAQS exceedences and only then at only five receptors, at only five of the receptors. And then later the company decides to eliminate those facilities with where the exceedences were found. That is all on Page 17 of Kevin Shilling's declaration.

If DEQ were to find that Perpetua's permit application were incomplete, why would DEQ then go on to, well, it says we have to or we will consider all these factors. We found it incomplete for some other reason, maybe they didn't certify it, but let's go ahead and look at all these other factors. It would be an exercise in futility.

And in this case it's the same. We have one control technology that is proven in the field that there's really no reason to look into at this point since there's no other control technologies available at this site.

So for these reasons, there's no basis to question DEQ's technical judgments in this case on those issues. Thank you.

HEARING OFFICER LAWRENCE: Thank you. Did

you want to say anything about the averaging?

MR. SHACKELFORD: So regarding the averaging, again, I think that's -- that's fairly well explained also by the declarations about how they applied the five-year rule by analog and extending it to a 16-year projected mine site. This is -- it is different because most stationary sources don't have projected life frames. We're going to set up a potato processing plant and it is going to be there until we run out of potatoes or whatever the case may be.

So this is unique, and DEQ didn't have any rules indicating that this would be inappropriate and would fit with health concerns given that the standard is a lifetime exposure rate.

So again, I think that's -- I don't need to get too into the weeds in that one because it is explained by both Mr. Shilling and Mr. Simon.

HEARING OFFICER LAWRENCE: Okay.

Okay. Thank you.

Mr. Pooser.

MR. POOSER: Just one question. Will we have a chance to kind of provide final thoughts or are we done after this?

HEARING OFFICER LAWRENCE: We can do -- we can do some final thoughts. I may do a time limit on those.

MR. POOSER: Okay. Completely fine with me. I was just kind of wondering.

So let me first start with the 93.3 percent and -- and the reference to, you know, the model analysis that DEQ did. DEQ did multiple model analyses. I think Kevin Shilling's declaration at Pages 14 to 18 does a really good job of sort of kind of explaining all the different angles that DEQ was -- was looking at, trying to make sure that it reached the best decision in this permit in determining whether or not the NAAQS were protected. And so it did multiple, multiple analyses looking at -- at this from a lot of different perspectives.

And when we get to the 93.3 percent and you ask the question, you know, where was -- what did -- what did DEQ base that on, and that's explained in our -- in our briefing. And specifically we talked about how, you know, DEQ is very deliberate in looking at this 93.3 percent. And in particular, it considered there was a review that Perpetua had done of AP42, Section 13.2.2,

which addresses unpaved roads. And it actually looked at the underlying test studies to see what was the actual control efficiency on with the use of chemical dust suppressant and water, what was it -- what was it just for chemical dust suppressant, what was it for water and what was it combined, and it provided that information.

And that showed very specifically that the chemical dust suppressants was 90 to 99 percent. And so that is also in the record.

They also relied upon -- there was kind of an analysis of the RACT/BACT/LAER Clearinghouse, and that looked at these different projects that were using chemical dust suppressant with and without water. And that, again, came to 90 to 98 percent control for chemical dust suppressant. AP42 also indicates that the control for water can be between 75 and 100 percent depending on the moisture content. So that is what DEQ relied upon that is in the record.

The question is here is whether or not DEQ's decision to choose 93.3 percent was arbitrary and capricious. And there's a rational basis for this. It looked at these different studies, it made its determination.

As far as a lack of enforcement, I think we've kind of -- we've hit this very hard in our briefing. The control efficiencies for chemical dust suppressant and water has many, many different variables, and so, you know, DEQ sort of built this permit based on numerous conditions and limits, you know, particularly with respect to the fugitive dust control plan.

But not just that. There was monitoring, there's daily inspections, all these different control measures. And then that kind of leads to some of the comments that were -- that were made about the plans.

And to kind of follow up on Mr. Shackelford's points. The con- -- the contents of the plans were very detailed in the permits themselves and that went out to public comment. Petitioners had an opportunity to get public comment on what those minimum requirements were. And these work plans, as is explained in Mike Simon's declaration, are common in DEQ permits and there's a good reason for them. They're typically -- and they're all, they're all prepared kind of post permit. And there's kind of a balance between --

HEARING OFFICER LAWRENCE: Can I jump in for a second? Which of the three issues -- I'm aware of the whole concept of the future plans, but if you could ground me in terms of which of the three particular issues we're --

MR. POOSER: This is responding to Mr. Hurlbutt's comments with respect to that there was -- they didn't have a chance -- there was kind of no review as far as what the plans are going to be and that, you know, DEQ's kind of hiding the ball on what these plans are going to be. And I think this is specifically responsive to that.

HEARING OFFICER LAWRENCE: Okay.

MR. POOSER: And so -- I mean, because these work plans are common and it makes complete sense from DEQ's perspective. Mr. Simon kind of addresses that in -- in his -- in his declaration. And I think that is owed -- that is owed discretion, particularly the comments about public comment. These did go to public comment. The minimum requirements are in there.

So turning to the T-RACT analysis. So very -- very briefly. I think Mr. Simon addresses that in his declaration as well. And, you know, there were three -- for the haul roads there were

three options, there was paving, there was chemical suppressants and water. And looking at the technical feasibility, they said paving is not -- not feasible. And because trucks are heavy and you're also having to reroute the roads as -- as the mining operation evolves.

And so what we're left with is chemical suppressants and water. And it's obviously widely recognized and actually required in -- in DEQ's rules. So we don't believe there is really any issue with that.

With respect to the arsenic averaging, I think enough has been said about that. I think Mr. Shilling's declaration, Mr. Shackelford kind of pointed out at Pages 10 through 11 kind of talks about that very clearly.

And then let me very quickly just sort of -- I want to provide you a cite with respect to the 93 percent findings just so I don't lose that. And that is specifically with respect to the study of AP4213.2.2. That is at PRI2.9. And then with respect to sort of the T-RACT analysis and consideration of the clearinghouse, that is at Petition 544 through 548, PET544 to 548.

HEARING OFFICER LAWRENCE: Okay.

All right. Thank you.

So Petitioners, how about five minutes to both rebut anything that they said and if you want to have sort of final comments to high level wrap things up.

MR. HURLBUTT: I'm just going to focus on rebuttal and no final comments from us.

HEARING OFFICER LAWRENCE: Okay.

MR. HURLBUTT: So on the 93.3 percent issue, Mr. Shackelford pointed out that the issue and, you know, practice of deferring to an agency's technical judgment, and I would ask you here what are they asking you to defer to? What technical judgment? There is no specific plan yet as to how Perpetua is going to spray magnesium chloride and water on the roads. They are asking you to defer to their judgment that some future plan that has not yet been developed that we don't know the actual parameters to will somehow be at 93.3 percent. Everyone knows this case this is from, I think it's a famous federal court case saying that courts don't have to defer to a void when it comes to deferring to agency expertise. They're just asking you to defer to their hope that they can cross their fingers that this will

hopefully work.

On the -- also on the 93.3 percent, one of the conditions for the plan is to have a ten percent opacity test which was mentioned. And I would just like to point out that this is a visual opacity test. If it looks too dusty you need to shut down operations. That all may be well and good in general, but there is nothing in the record that specifically ties that to somehow meeting 93.3 percent dust control efficiency as is necessary here. EPA hammers on that in their enclosure to their August 10th letter. This is on Pages 16 and 17 of that. "Finally, IDEQ's response to EPA's comment on the basis for the ten percent opacity limit in condition 2.5 does not provide additional basis for correlation between opacity and the 93.3 percent control."

Moving on to T-RACT. I was a little surprised to hear it stated that the T-RACT does not say "shall." And just in the first few sections of air rule Section 210.14 on T-RACT, "shall" is used many times. First, opening part it says, "T-RACT shall be determined on a case-by-case basis by the department as follows." In the "as follows," part B, "the department shall review the

information submitted by the applicant and determine whether the applicant has T-RACT." Part C, "the technological feasibility of the control technology or other requirements of a particular source shall be considered in several factors then listed below which includes environmental impact factors. Part D, economic feasibility also shall be considered. "Shall" is used a lot. These factors were not considered in the T-RACT analysis ignoring all those "shalls."

And then on the arsenic averaging, the 16 out of 70 issue, DEQ's counsel admitted this is not in the rules. And that's our key point here. This is not in the rules. This is a made-up adjustment. They might be able to explain why they think it's a good idea, but it's not in the rules. Permits need to be issued based on what is in the air rules. DEQ can go through a rule making and change the rules and adjust what counts as a short-term source or come up with any other thing it wants to through the rule-making process. This is not in the rules, it's a made-up exception to the ambient air concentrations for arsenic. Thank you.

HEARING OFFICER LAWRENCE: Okay. Thank you.

DEQ, they declined their opportunity to have a wrap-up comment.

Do you -- is there anything you want to say briefly in order to wrap things up?

MR. SHACKELFORD: No. Thank you.

HEARING OFFICER LAWRENCE: Okay. Petitioners, how about you guys -- I'm sorry, Perpetua.

MR. POOSER: Just a few things, some things that I can't get a chance to sort of respond to.

Just to kind of clean things up. With respect to kind of the Rosemont decision that's addressed, we understand that's -- that has not been, you know, that has not been briefed. However, it is resolving. The issue, I understand, is whether the mining claims are valid. We're on an air quality permit. I don't know how that -- how that case has any bearing here.

With respect to kind of the control of the access road, you know, there's an example of control that's just right down the hall and the general public can't access this room. I had to get permission to be here. I know I'm a guest. And that is the exact same conditions that are in the permit with respect to the access road.

With respect to the 93.3 percent, again, you can't look at just one condition and say, oh, ten percent opacity, how does that relate? You have to look at the entire suite of control and limits that are in the permit. And that's what we tried to emphasize in our briefing, and that is what DEQ emphasized in its response to comments and statement of basis. There's a whole suite of -- of limitations and controls that are seeking to enforce this 93.3 percent. That's what's important and I think kind of gets lost in some of the petitioners' arguments.

HEARING OFFICER LAWRENCE: Can you be a little bit more specific on that? What -- what specific instances are you talking about?

MR. POOSER: Well, when we were talking about control he mentioned, like, opacity, ten percent, how does that control 93.3 percent? I think you have to consider that that's part of an entire suite of permit conditions and limits that are in the permit as far as daily inspections, the record keeping and reporting, the monitoring that's involved, all of it. You know, the conditions in that Section 2 of the permit, there's a whole suite of things. There's a fugitive dust control plan as

far as minimum requirements, what has to be in there. So I think you have to look at all of those things as a whole, not just one single permit condition.

HEARING OFFICER LAWRENCE: Okay.

MR. POOSER: And then finally, I just -- to reiterate DEQ's comments about -- these are technical determinations. DEQ was using its technical judgment here. And I think when you -- when you look at the petition you look at the arguments that are in the brief, you will see that DEQ adequately explained the basis for its decisions and that its rationale was reasonable. There is support for it in the record. And it was using its technical judgment and that requires some deference from the board. Thank you.

HEARING OFFICER LAWRENCE: Okay.

All right. Thank you all. As far as I'm concerned, this is all fully submitted and I'm on the clock now to issue a decision. Just so you guys know, the Office of Administrative Hearings goes by the judicial guideline of once a motion is fully submitted the goal is to get a decision issued by the end of the following month. So that's my goal.

Thank you all. I appreciate it. This was very helpful for me. Thank you for all the time and preparation. As I've said before, all of the briefing has been topnotch and I appreciate all the work that has gone into that. I don't have an easy job, but you guys have at least helped take the edge off of it a little bit with all that. So thank you.

We can adjourn.

(Proceedings concluded at 11:35 a.m.)

REPORTER'S CERTIFICATE

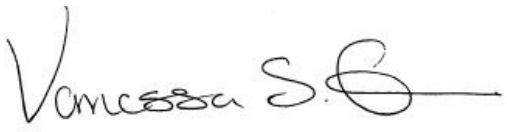
STATE OF IDAHO)
) ss.
COUNTY OF ADA)

I, VANESSA S. GOSNEY, Certified Shorthand Reporter and Notary Public in and for the State of Idaho, do hereby certify:

That I am the reporter who took the proceedings had in the above-entitled action in machine shorthand and thereafter the same was reduced into typewriting under my direct supervision; and

That the foregoing reporter's transcript contains a full, true, and accurate record of the proceedings had in the above and foregoing cause, which was heard in Boise, Idaho.

WITNESS my hand and seal this 9th day of October, 2023.



VANESSA S. GOSNEY
RPR and Notary
Public in and for the
State of Idaho.

My Commission Expires: 10-29-25

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BEFORE THE BOARD OF ENVIRONMENTAL QUALITY
STATE OF IDAHO

IN THE MATTER OF AIR QUALITY PERMIT TO CONSTRUCT P-2019.0047	Agency Case No. 0101-22-01
NEZ PERCE TRIBE, IDAHO CONSERVATION LEAGUE, and SAVE THE SOUTH FORK SALMON, Petitioners, vs. IDAHO DEPARTMENT OF ENVIRONMENTAL QUALITY, Respondent, and PERPETUA RESOURCES IDAHO, INC., Intervenor-Respondent.	OAH Case No. 23-245-01

CONTESTED CASE HEARING
MARCH 14, 2023
IDAHO DEPARTMENT OF ENVIRONMENTAL QUALITY
1410 NORTH HILTON STREET
BOISE, IDAHO

REPORTED BY: DORIS M. BAILEY, CSR, RPR, CRR
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JOHN SIGLER
CLAYTON STEELE
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ELAINE GANINO, Clerk to the Board

--oOo--

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MARCH 14, 2024 9:00 AM

P R O C E E D I N G S

BOARD CHAIR BOWEN: I call to order the meeting of the Idaho Board of Environmental Quality. In addition to being a public meeting, we are also on the record in the matter of the air quality permit to construct issued to Perpetua Resources Idaho, Inc., agency case number 0101-22-01, OAH case number 23-245-01. This meeting is being held in the state office of the Department of Environmental Quality.

For those present in the meeting room, please sign in on the sheet provided by the entrance. There won't be an opportunity for public comment today.

Elaine, could you please take the roll?

BOARD CLERK GANINO: Yes, Mr. Chairman.

Mark Bowen.

BOARD CHAIR BOWEN: Here.

BOARD CLERK GANINO: Dr. Randy MacMillan.

VICE CHAIR MACMILLAN: Here.

BOARD CLERK GANINO: Carol Mascarenas. Carol?

BOARD MEMBER MASCARENAS: Here. I'm here.

BOARD CLERK GANINO: Beth Elroy.

BOARD MEMBER ELROY: Present.

BOARD CLERK GANINO: John Sigler.

BOARD MEMBER SIGLER: Present.

BOARD CLERK GANINO: Clayton Steele.

BOARD MEMBER STEELE: Here.

BOARD CLERK GANINO: Pat Purdy.

BOARD MEMBER PURDY: Here.

BOARD CHAIR BOWEN: Before we get started, I'd like to take a moment to introduce the parties and talk about some of the logistics for today.

You will notice that unlike normal DEQ Board meetings we have a court reporter here today. The reporter will be on the record throughout the proceeding today, so please speak slowly and clearly, try not to talk over one another, and use yes or no instead of uh-huh or nodding your head, please. That will make the court reporter's job easier today.

I'd also like to take a moment to introduce the parties and get everyone's names and spellings down for the record so the reporter has those going forward.

Let's begin with the parties.

The petitioners in this matter are the Nez Perce Tribe, the Idaho Conservation League, and Save the South Fork of the Salmon. Would you all take a moment and please identify yourselves, the attorney representing each party.

Let's begin with the South Fork of the Salmon attorney.

MS. THROWER: Julia Thrower, T-h-r-o-w-e-r.

BOARD CHAIR BOWEN: Thank you.

Nez Perce Tribe and ICL. I assume they have the same attorney?

MR. HURLBUTT: Bryan Hurlbutt, H-u-r-l-b-u-t-t.

BOARD CHAIR BOWEN: Thank you.

The respondents in this matter are the Department of Environmental Quality and Perpetua Resources. Would you please identify yourselves for the record?

DEQ attorney.

MS. YOUNG: Hannah Young, Y-o-u-n-g.

BOARD CHAIR BOWEN: Thank you. Perpetua attorney?

MR. POOSER: Good morning. Christopher Pooser, P-o-o-s-e-r.

BOARD CHAIR BOWEN: Thank you.

Also in the courtroom today we have Deputy Attorney General Ann Yribar. She's representing the Board.

And we have DEQ board staff Paula Wilson and Elaine Ganino here to help with logistics.

Is there anyone else that I missed who wants their attendance put on the record?

(No response.)

BOARD CHAIR BOWEN: Thank you. So we have a joint motion to supplement the record with a March 12th, 2024 letter from EPA to DEQ. This is not on the agenda so we need a motion to add it to the agenda.

VICE CHAIR MACMILLAN: Mr. Chairman.

BOARD CHAIR BOWEN: Yes, Randy.

VICE CHAIR MACMILLAN: I make a motion to amend the agenda to include and to supplement the record with the letter received yesterday.

BOARD CHAIR BOWEN: Thank you.

VICE CHAIR MACMILLAN: Or the 12th, whichever day that was.

BOARD CHAIR BOWEN: Okay. Do I have a second?

BOARD MEMBER MCELROY: I have a second.

BOARD CHAIR BOWEN: Thank you.

Elaine, would you call roll?

BOARD CLERK GANINO: Yes, Mr. Chairman.

Mark Bowen.

BOARD CHAIR BOWEN: Just a minute.

Randy, could you state the reason clearly why it was not added to the agenda initially?

VICE CHAIR MACMILLAN: Yes, Mr. Chairman. The supplement to -- the joint motion to supplement the record was received by the Board anyway yesterday, so it

had not been added to the -- or included in the agenda for today.

BOARD CHAIR BOWEN: Right. Thank you, Randy.

Elaine, would you call the roll on the motion, please?

BOARD CLERK GANINO: Yes, Mr. Chairman.

Mark Bowen.

BOARD CHAIR BOWEN: Aye.

BOARD CLERK GANINO: Dr. Randy MacMillan.

VICE CHAIR MACMILLAN: Aye.

BOARD CLERK GANINO: Carol Mascarenas.

BOARD MEMBER MASCARENAS: Aye.

BOARD CLERK GANINO: Beth Elroy.

BOARD MEMBER ELROY: Aye.

BOARD CLERK GANINO: John Sigler.

BOARD MEMBER SIGLER: Aye.

BOARD CLERK GANINO: Clayton Steele.

BOARD MEMBER STEELE: Aye.

BOARD CLERK GANINO: Pat Purdy.

BOARD MEMBER PURDY: Aye.

BOARD CHAIR BOWEN: Thank you. Motion carried.

Is it the desire of the Board to enter into executive session to discuss this matter? I'll entertain a motion.

VICE CHAIR MACMILLAN: Mr. Chairman, I move the

Board enter into executive session pursuant to Idaho Code 74-206(1)(f) to communicate with legal counsel for the public agency to discuss the legal ramifications of and legal options for pending litigation for controversies not yet being litigated but imminently likely to be litigated.

I request that a roll call vote be taken and that vote be recorded in the minutes of this meeting.

BOARD MEMBER PURDY: I second that motion.

BOARD CHAIR BOWEN: Thank you. Any discussion?

(No response.)

Elaine, will you take roll, please?

BOARD CLERK GANINO: Yes, Mr. Chairman.

Mark Bowen.

BOARD CHAIR BOWEN: Aye.

BOARD CLERK GANINO: Dr. Randy MacMillan.

VICE CHAIR MACMILLAN: Aye.

BOARD CLERK GANINO: Carol Mascarenas.

BOARD MEMBER MASCARENAS: Aye.

BOARD CLERK GANINO: Beth Elroy.

BOARD MEMBER ELROY: Aye.

BOARD CLERK GANINO: John Sigler.

BOARD MEMBER SIGLER: Aye.

BOARD CLERK GANINO: Clayton Steele.

BOARD MEMBER STEELE: Aye.

BOARD CLERK GANINO: Pat Purdy.
BOARD MEMBER PURDY: Aye.
BOARD CHAIR BOWEN: Thank you. Motion carried.
We'll now enter executive session. So we have to clear the room. Sorry.
(Thereupon the Board convened into executive session off the record.)
BOARD CHAIR BOWEN: I'll entertain a motion.
VICE CHAIR MACMILLAN: Mr. Chairman, I move that the Board resolve off of executive session, and that the minutes of the meeting reflect that no action was taken during executive session.
BOARD CHAIR BOWEN: Thank you.
Do I hear a second?
BOARD MEMBER SIGLER: Second.
BOARD CHAIR BOWEN: Thank you.
Elaine, can you take a roll call?
BOARD CLERK GANINO: Yes, Mr. Chairman.
Mark Bowen.
BOARD CHAIR BOWEN: Aye.
BOARD CLERK GANINO: Dr. Randy MacMillan.
VICE CHAIR MACMILLAN: Aye.
BOARD CLERK GANINO: Carol Mascarenas.
BOARD MEMBER MASCARENAS: Aye.
BOARD CLERK GANINO: Beth Elroy.

BOARD MEMBER ELROY: Aye.
BOARD CLERK GANINO: John Sigler.
BOARD MEMBER SIGLER: Aye.
BOARD CLERK GANINO: Clayton Steele.
BOARD MEMBER STEELE: Aye.
BOARD CLERK GANINO: Pat Purdy.
BOARD MEMBER PURDY: Aye.
BOARD CHAIR BOWEN: Motion carries.
We're back in general session. The Board is going to take a five-minute break, a bathroom break, and we will readjourn. Thank you.
(Thereupon there was a brief recess.)
BOARD CHAIR BOWEN: All right. Call back into order the general session.
We're under the amended agenda item Joint Motion to Supplement the Record with a March 12th, 2024 letter from EPA to DEQ.
As a Board we're a little bit concerned that we haven't had a chance to review this letter. I'd be interested in other Board members, what your thoughts are receiving the letter, where we are on that? Any discussion?
Dr. MacMillan.
VICE CHAIR MACMILLAN: Mr. Chairman, I have considerable reservation discussing very much of the

substance of the -- of that letter, simply because I've hardly had an opportunity to look at the letter, and surely others would be in the same boat.

So in the interest of fairness, I think that's something that we should allow the parties to fully digest that letter and provide response to that letter.

BOARD CHAIR BOWEN: Okay.

BOARD MEMBER STEELE: I agree.

BOARD CHAIR BOWEN: Any other thoughts?

BOARD MEMBER MCELROY: Mr. Chairman.

BOARD CHAIR BOWEN: Yes.

BOARD MEMBER MCELROY: I would like to share the disappointment that this letter was received at the last minute. And I'm not sure how we message that back to EPA, but I'm assuming that they were well aware of the dates and what's been happening with this issue. And to have a last minute letter submitted to the department, they need the feedback that it makes this whole process more challenging to receive that type of information very last minute.

BOARD CHAIR BOWEN: Okay. Any other thoughts?

I think at this point the Board would like to hear from the parties. We'd like to give the parties a five minute opportunity just to give us your position on this current agenda item.

Let's start with DEQ. Five minutes, please.

MS. YOUNG: May I approach and sit at the table?

BOARD CHAIR BOWEN: Please, yeah.

MS. YOUNG: Thank you for this opportunity. I'd love to have the five minutes to speak to you about this. And again, my name is Hannah Young. I represent the Department of Environmental Quality in this matter.

And I did want to note that I understand that you have two motions truly before the Board to supplement the record, and if I may, I'd like to talk about both of them because they're obviously interrelated as they relate to the same subject matter ultimately.

BOARD CHAIR BOWEN: Excuse me.

MS. YOUNG: Yeah.

BOARD CHAIR BOWEN: Could you stick to the one agenda item at this point?

MS. YOUNG: Oh, absolutely.

BOARD CHAIR BOWEN: You'll have an opportunity to talk about the other one later.

MS. YOUNG: Oh, okay. Sure. I wasn't clear on that, so thank you for that clarification, chairman.

As Ms. Elroy just pointed out, we only received this letter two days ago late in the afternoon, and so the parties, Perpetua and DEQ, made the motion to supplement the record with this March 12th letter

yesterday.

And the reason that we are moving to put this in front of the Board today is because in the underlying contested case proceeding, the petitioners in this case moved to enter EPA's original letter, which was issued in 2023 of August. And at that time DEQ and Perpetua objected to the inclusion of that letter, primarily because EPA is not a party to this case -- although they could be if they wanted to be, they are not.

And because the letter was being introduced at a very late juncture during the contested case proceeding, over a year after the contested case proceeding had been initiated, and so the parties objected to the inclusion.

However, the hearing officer did allow that original EPA letter to be introduced into the record. And because of that -- well, and I should back up.

He allowed it to be introduced in the record, but only for limited purposes. It wasn't a carte blanche, you know, it wasn't allowed in for you to read anything you wanted into it, he had three limitations: One was that the letter could not add new allegations of error; it could not add factual information that was not already part of the record, or the proxy for expert testimony to the Board.

And so under those limitations, the hearing

officer allowed that original EPA letter to be introduced. Since the hearing officer made his decision, two more letters have been issued between the parties, between DEQ and EPA.

DEQ responded, that is the first motion which we will take up later.

And then EPA finally responded to us two days ago, about four months after DEQ issued its letter.

And so now here we are in a bit of an uncomfortable position putting something, you know, before the Board at a very late hour.

But the only reason that we're doing that is because we'd like the Board to have the complete story. If you were just left with what the record entails today, which is just that initial EPA letter, you would have a false impression of the story. It may lead you to believe that the conversation ended there, but that's absolutely not the case.

In reality, DEQ responded to that letter, continued to defend the permit, provided a lot of helpful information that EPA as the agency not writing the permit didn't know, and ultimately this final letter -- which we received two days ago, which now in our minds we consider the matter closed based on this letter -- is another very critical part of that story which is that DEQ essentially

was able to come to a common understanding with EPA and find that the letter does meet the Clean Air Act and that it's -- the matter is closed.

And so, again, we did not start this process of putting these letters into the record, but now that it's here, out of fairness and to not prejudice any of the parties, we would strongly argue that all of the letters be allowed in.

And the final point I'd like to make is that just because you allow the letter into the record today doesn't mean that you don't have time to study it, consider it, think about the merits of what's being raised, you know, under those limitations set by the hearing officer, of course, and analyze it in your own time, and decide what weight to give it.

By allowing it to be introduced into the record today though, it's at least something that you can do, you can consider it and make your judgment when you're ready and when you have time to review it fully.

And to that end I did bring courtesy copies of our motion and declaration that was filed yesterday. I don't know if that would be helpful to pass around, because I do realize and apologize for its very late filing.

If you want a copy you can certainly take one

and pass it around, but there's both the declaration of Ms. Floyd with the letter attached as well as our motion. So provide that.

So with that, I would absolutely stand for any questions, but that's all I have to say.

BOARD CHAIR BOWEN: Could I ask you a question?

MS. YOUNG: Yeah.

BOARD CHAIR BOWEN: I think one of the concerns the Board has is what about the opportunity to fair response to this letter? Do you have an opinion on whether the parties should be given a chance to have fair time to respond to this letter before it's considered entered into the record?

MS. YOUNG: Mr. Chairman, if I may ask a clarifying question? Who do you mean by parties? Do you mean the petitioners?

BOARD CHAIR BOWEN: To them and the respondents to this motion.

MS. YOUNG: I don't think that that's necessary.

If the Board did want to allow the petitioners to write an objection or write some sort of response to our motion, that would certainly, you know, be fine.

They were allowed that opportunity to file an objection to our first motion to supplement the record and have their voices heard.

But again, the substance of the EPA letter is really not incredibly relevant to the issues today, because EPA is not a party to this case, and because we see this dialogue with EPA as sort of a separate matter. They're talking about issues that don't completely overlap with what is in front of the Board today. As we'll talk about later, of course, the petitioners have sort of narrowed down their issues as this process has gone on, and so we don't have that same overlap.

I don't think we're really here to discuss or debate the merits of what EPA said, it's more just for the Board to understand from a high-level perspective that when we received that letter from EPA in August of 2023, it didn't end there; the story didn't end there, and we continue to defend the permit just like we are today.

BOARD CHAIR BOWEN: Okay. Thank you.

Any other questions from the Board?

BOARD MEMBER STEELE: So in the letter from EPA, there's no new facts in that letter for us to consider?

MS. YOUNG: No, I would say there are no new facts. From the most recent EPA letter?

BOARD MEMBER STEELE: Yes.

MS. YOUNG: Sorry, Mr. Steele.

No, there's really no new facts. There are --

and I hesitate because I don't want to get into the first two separate. But, you know, it's really --

There's been a dialogue between DEQ and EPA since that letter, and there are things that have transpired, there's information that's been shared. Again, that is all information that, you know, has been vetted during the public comment process, during the dialogue with EPA. As far as the response to comments documents and things like that, the EPA has raised some of these same issues, has raised the same issues during the permit development as they did in their letter, so there's really no new facts.

Again, we are just hoping to put it in front of the Board. Because petitioners moved to enter the August 2023 letter, we don't want the Board to have a false impression that DEQ didn't respond and take, you know, serious, take it very seriously the statements and, quite frankly, accusations made in that letter from EPA.

BOARD MEMBER STEELE: Thank you.

BOARD CHAIR BOWEN: All right. Thank you.

MS. YOUNG: Thank you.

BOARD CHAIR BOWEN: Does Perpetua's attorney want to make a statement?

MR. POOSER: Yeah. Thank you. Christopher Pooser for Perpetua.

Only to say that we join in the motion and we concur with Ms. Young's remarks. We don't really have anything to add to what she said. I'd be happy to stand for any questions.

BOARD CHAIR BOWEN: Thank you.

Let's give the respondents an opportunity. Let's begin with -- go ahead. Decide. Tell us who you are.

MR. HURLBUTT: Bryan Hurlbutt representing the Nez Perce Tribe and the Idaho Conservation League.

We do not oppose adding the new EPA letter to the record.

And relatedly, in interest of completing the record, we are willing to withdraw our opposition to the motion to add DEQ's previous letter to the record. It seemed fairly incomplete before without EPA's response, but now with that, we do not oppose having both of these documents before the Board to consider.

And as far as whether there should be an opportunity to respond to that letter, we're prepared to talk about the letter today to the extent that the Board wants to, and how it relates to the merits of our claims, and we are happy to provide supplemental briefing or something like that if the Board thinks that would be helpful for considering the EPA letter. Yeah.

BOARD CHAIR BOWEN: Okay. Questions?

BOARD MEMBER STEELE: So with that statement, I mean, would you formally want to provide written comments? Or you said you'd be happy to provide written comments?

MR. HURLBUTT: We are happy to if the Board thinks that that would be helpful to reach a decision. And if not, we're happy to just say some things about it today during our argument.

BOARD MEMBER PURDY: So I guess an additional follow-up then. If you had the opportunity to provide oral argument today, then do you feel like you need to still have the time frame in statute to respond in writing? Or do you feel like just today's would be -- you don't have an opposition, so it seems like you're saying that today would be enough; is that what I'm hearing?

MR. HURLBUTT: Correct. As far as responding to the actual motion that was filed yesterday.

BOARD MEMBER PURDY: Okay.

MR. HURLBUTT: Yeah.

BOARD CHAIR BOWEN: Okay. Thank you.

Any other parties want to speak to that?

MS. THROWER: No. Thank you.

(Reporter clarification.)

MS. THROWER: Julia Thrower for Save the South Fork Salmon.

BOARD CHAIR BOWEN: Any other discussion?

Yeah, I, for one, after that new information would like to entertain -- if the Board would like to entertain moving to executive session?

Randy, do you want to make a motion?

VICE CHAIR MACMILLAN: Yes, sir. I move that the Board enter into an executive session pursuant to Idaho Code 74-206(1)(f) to communicate with legal counsel and the public agency to discuss the ramifications of and legal options or controversies not yet being litigated but imminently likely to be litigated.

I request that a roll call vote be taken and that vote be recorded in the minutes of this meeting.

BOARD CHAIR BOWEN: Do I hear a second?

BOARD MEMBER MCELROY: Second.

BOARD CHAIR BOWEN: Thank you.

Elaine, let's take a roll call, please.

BOARD CLERK GANINO: All right, Mr. Chairman.

Mark Bowen.

BOARD CHAIR BOWEN: Aye.

BOARD CLERK GANINO: Dr. Randy MacMillan.

VICE CHAIR MACMILLAN: Aye.

BOARD CLERK GANINO: Carol Mascarenas.

BOARD MEMBER MASCARENAS: Aye.
BOARD CLERK GANINO: Beth Elroy.
BOARD MEMBER ELROY: Aye.
BOARD CLERK GANINO: John Sigler.
BOARD MEMBER SIGLER: Aye.
BOARD CLERK GANINO: Clayton Steele.
BOARD MEMBER STEELE: Aye.
BOARD CLERK GANINO: Pat Purdy.
BOARD MEMBER PURDY: Aye.
VICE CHAIR MACMILLAN: So motion passes?
BOARD CHAIR BOWEN: Motion passes.
Moving to executive session. Thank you.
(Thereupon the Board convened into executive session off the record.)
BOARD CHAIR BOWEN: Okay. I'll entertain a motion.
VICE CHAIR MACMILLAN: Mr. Chairman, I move that the Board resolve out of the executive session, and that the meeting of the minutes reflect that no action was taken during the executive session.
BOARD MEMBER PURDY: Second.
(Unreportable simultaneous cross-talk.)
BOARD CHAIR BOWEN: Carol, can you hear us?
BOARD SECRETARY MASCARENAS: Yes, I can.
BOARD CHAIR BOWEN: Okay.

BOARD MEMBER MASCARENAS: Thank you.
BOARD CHAIR BOWEN: All right. We have a motion and a second.
Elaine, will you take the roll?
BOARD CLERK GANINO: Yes, Mr. Chairman.
Mark Bowen.
BOARD CHAIR BOWEN: Aye.
BOARD CLERK GANINO: Dr. Randy MacMillan.
VICE CHAIR MACMILLAN: Aye.
BOARD CLERK GANINO: Carol Mascarenas.
BOARD MEMBER MASCARENAS: Aye.
BOARD CLERK GANINO: Beth Elroy.
BOARD MEMBER ELROY: Aye.
BOARD CLERK GANINO: John Sigler.
BOARD MEMBER SIGLER: Aye.
BOARD CLERK GANINO: Clayton Steele.
BOARD MEMBER STEELE: Aye.
BOARD CLERK GANINO: Pat Purdy.
BOARD MEMBER PURDY: Aye.
BOARD CHAIR BOWEN: Okay. We're back in general session here. I'd like to thank the audience for indulging the Board. I think with this new information we've received -- any discussion from the Board?
VICE CHAIR MACMILLAN: Mr. Chairman.
BOARD CHAIR BOWEN: Yes.

VICE CHAIR MACMILLAN: It would seem that all the parties have agreed that the correspondence between DEQ and EPA is appropriate to include in the record, and that resolves our concern about making sure that this whole process is fair and open.

BOARD CHAIR BOWEN: Okay. Any other comments?

(No response.)

BOARD CHAIR BOWEN: I think the Board would like to hear from the parties that they agree to stipulate bringing these two letters into the record under the stipulation that -- under the same conditions as found by the previous hearing officer:

That the EPA letter cannot be used, one, to add new allegations of error.

Two, to add factual information that was not already part of the record.

Or three, as a proxy for expert testimony to the petitioners.

Do the parties stipulate? DEQ?

MS. YOUNG: Yes, Mr. Chairman, we would stipulate to that. Thank you.

BOARD CHAIR BOWEN: Perpetua?

MR. POOSER: Yes, Mr. Chairman, we stipulate.

BOARD CHAIR BOWEN: ICL?

MR. HURLBUTT: Yes, we stipulate.

BOARD CHAIR BOWEN: And does that include the other parties?

MS. THROWER: Yes, it does. Thank you.

BOARD CHAIR BOWEN: Okay. Nez Perce.

MR. HURLBUTT: Yes, for the Nez Perce as well.

BOARD CHAIR BOWEN: Thank you. Okay. With that I'll hear -- I'll entertain a motion.

VICE CHAIR MACMILLAN: Mr. Chairman, I move that the Board accept into the record, under the same conditions as identified by the hearing officer with regard to the August 10th, 2023 letter, the November 22nd, 2023, and the March 12th, 2024 correspondence between DEQ and EPA.

BOARD CHAIR BOWEN: Do I have a second?

BOARD MEMBER STEELE: Second.

BOARD CHAIR BOWEN: Any discussion?

(No response.)

BOARD CHAIR BOWEN: We'll entertain a vote. Elaine, will you call roll?

BOARD CLERK GANINO: Yes, Mr. Chairman.

Mark Bowen.

BOARD CHAIR BOWEN: Aye.

BOARD CLERK GANINO: Dr. Randy MacMillan.

VICE CHAIR MACMILLAN: Aye.

BOARD CLERK GANINO: Carol Mascarenas.

BOARD MEMBER MASCARENAS: Aye.
BOARD CLERK GANINO: Beth Elroy.
BOARD MEMBER ELROY: Aye.
BOARD CLERK GANINO: John Sigler.
BOARD MEMBER SIGLER: Aye.
BOARD CLERK GANINO: Clayton Steele.
BOARD MEMBER STEELE: Aye.
BOARD CLERK GANINO: Pat Purdy.
BOARD MEMBER PURDY: Aye.
BOARD CHAIR BOWEN: Motion carried. Thank you.
So that was essentially amended agenda item number 1.
Item number two was the second letter which we've just handled.
Any further comment on those two agenda items?
(No response.)
BOARD CHAIR BOWEN: If not, we'll move to the last agenda item. This next item on the agenda is oral argument on the amended petition for review of the preliminary orders that was filed by the petitioners, the Nez Perce Tribe, ICL, and Save the South Fork of the Salmon on December 15th, 2023, in the matter for Air Quality Permit to Construct P-2019.0047, case docket number 0101-22-01, OAH case number 23-245-01.
The amended petition asked this Board to review

the amended preliminary order issued by the hearing officer on December 5, 2023. The matter has been fully briefed.

We'd like to provide 30 minutes to each party to argue the amended petition. In addition, there will be 10 minutes allotted to the petitioners for rebuttal.

Let's begin with the petitioners first, the Nez Perce Tribe, then ICL, then Save the South Fork Salmon.

MR. HURLBUTT: And if it's okay with you, we planned to sort of do this together instead of dividing, you know, by parties.

Ms. Thrower is going to handle two of the four issues that we raised, and I was going to handle the other two, if that's okay.

BOARD CHAIR BOWEN: Okay. Are you okay with 30 minutes between you?

MS. THROWER: Yes.

BOARD CHAIR BOWEN: Okay. Thank you. Begin.

MS. THROWER: Thank you, Mr. Chairman.

And just as a technical question, are we able to put up some of the record documents?

MS. WILSON: Uh-huh.

MS. THROWER: Okay. Can I have you please go to REC 0145?

MS. WILSON: Do you know which number it is? Or

REC which again?

MS. THROWER: 415. So yeah, you have to scroll up quite a bit.

VICE CHAIR MACMILLAN: Carol, can you hear us?

BOARD SECRETARY MASCARENAS: If the respondents can talk a little louder, that would be great.

VICE CHAIR MACMILLAN: There is a chair up here if you'd like.

BOARD CHAIR BOWEN: Move the microphones back there.

MS. WILSON: Can you repeat the REC number?

MS. THROWER: It's document 36 REC 145.

MS. WILSON: Okay.

BOARD MEMBER STEELE: Which two were you going to talk about? Is it ambient air or --

MS. THROWER: I'm going to talk about ambient air, the access road issue, and also the fourth issue in our brief, the arsenic issue.

BOARD MEMBER STEELE: Okay. Thank you.

MS. WILSON: Do you know what page number other than the --

MS. THROWER: It's REC 415 on the bottom.

MS. WILSON: I'll just do math, I'll figure it out

MS. THROWER: Sorry, I don't have the PDF page

number.

MS. WILSON: That's okay.

MS. THROWER: Well, I can go ahead and start, Mr. Chairman, while that comes up.

BOARD CHAIR BOWEN: Thank you.

MS. THROWER: So, you know, we've heard, and I'm sure we'll hear more today, but we've read in petitioners' and Perpetua's brief about this pioneering approach for this proposed mining project to access some minerals. But what we're talking about here is an age-old problem of dust from roads that are created by vehicles traveling on unpaved roads.

There's no pioneering approach here to controlling dust. We at times will call that fugitive dust. There's no technological advances for controlling fugitive dust like there are for controlling pollution like out of a smoke stack, something that's more of a point source.

The pollution that we're concerned about here is creating a public health risk for those traveling and recreating through and around the proposed mine site. Some of that will be created, that dust will be created by blasting and crushing ore, but most of it is going to be caused by heavy trucks hauling ore up from blasting sites to ore processing facility and traveling on 55

miles of unpaved roads that are within the proposed mine site. And that's been the problem, most of the problems that petitioners have focused on.

All through the versions of the various draft permits, Perpetua and DEQ have had trouble on figuring out how to deal with this dust. It's not just a problem with compliance with the National Air Quality Ambient Air Quality Standards or NAAQS which in this case does involve, in particular, particulate matter, but it is also an issue with the state's Toxic Air Pollutant rules or TAPs, and in this case we're talking about arsenic which is a carcinogenic pollutant.

The approved permit and records supporting its decision demonstrates that DEQ still cannot comply with the NAAQS for particulate matter and for the TAPs for arsenic emissions.

Rather, the record demonstrates that DEQ took unprecedented, unsupported, and groundless measures to make it appear that the permit will comply with the law and the regulation.

As I said at the beginning, and Mr. Hurlbutt said, I'll talk about the Stibnite Road access route, and how we feel that that, including their excluding that route from ambient air protections violates the Clean Air Act and creates a public health risk for those using that

road.

I'll also talk about the arsenic emissions.

And as Mr. Hurlbutt says, he'll talk about the other two issues, the fugitive dust control efficiency, and also the plans that were not developed -- that are supposed to contain the enforceable permit conditions that were not developed in time for public review.

So indeed, if this permit is approved and this mine continues or is allowed to operate under the guise of the state's approval, this suggests that it complies with the Clean Air Act and Idaho state rules. And this creates a grave risk to public health for those who travel, recreate, and use the area to support their livelihood.

That's why we ask the Board to carefully consider the evidence before it and vacate this permit and remand it back to DEQ for reconsideration.

So I had an exhibit pulled up because there's a lot going on in this area. And I know it can be a little confusing if you're not -- if you haven't studied this map and aren't really familiar with the area.

So what this map shows is the ambient air boundary, sometimes it's called the operations boundary as well. And that's that blue line that encircles the entire mine site and several other thousand acres. That

ambient air boundary is, you can think of it sort of as a bubble.

Inside that ambient air boundary, the air quality does not meet -- does not need to meet the NAAQS, and it does not need to meet the state's toxic air pollutant standards.

Outside that ambient air boundary, and that is where the public is allowed to recreate, it will be open for public use, there's a lot of important recreational sites, important sites that the Nez Perce Tribe uses, and those sites and those uses were established in our standing declarations that were submitted before the Office of Administrative Hearings.

Outside that, again, like I said, the public is allowed to recreate, to use the public lands, and outside that ambient air boundary the air quality must be consistent with the NAAQS or it must meet the NAAQS, and it must meet the state's toxic air pollution standards.

So we're concerned -- so going through -- let me back up.

So looking inside that ambient air boundary, the gray color is -- are the proposed mining sites, some of the pits that will be mined. And I want to draw your attention to that green line that kind of goes from the north, where it says north entry, all the way through the

mine site and to -- if we can scroll down a little bit, there's -- that road goes to the south entry where it exits the mine site and exits the ambient air boundary. So that is called the Stibnite Road access route. It is a proposed route.

Currently there is a route called the Stibnite Road that is being used by the public to go through this area. That road, as I said, exists. Under the proposed mine plan, that road will be reconstructed so that it can be separated a little bit more from mining activities and provide a safer route to the public.

As I said, the public access is important for recreation sites on public land, both from the north entry and the south entry.

Currently the only way to get from -- to recreational sites at the south entry is to go through this road from the north entry to the south entry. And there's some sites, Thunder Mountain, Monumental Summit that you'll see that we referenced, both in our standing declarations and also in our briefing. And those are all recreational sites that are on Forest Service land.

The road that appears there at the south entry is a proposed road called the Burntlog Road. If you scroll down a little bit, I think you can see the name of it there. But that -- it says main access road to the

Cascade log route. That currently does not exist. That is a road that is proposed as one of the alternatives under the mine plan that the Forest Service is considering in its National Environmental Policy Act or NEPA analysis.

So I just wanted to give you kind of a lay of the land. Hopefully that will make it a little more -- make a little more sense of what our issue is here.

So as I said, inside the ambient air boundary there aren't -- the air doesn't need to meet the NAAQS or the state's caps criteria outside of the, we might call that the point of compliance, the air needs to meet both of those standards.

So in this issue when I'm talking about the access road, we are mainly concerned about access through the mine inside of that ambient air boundary.

Now, we raised two issues, one that sort of goes to the same problem here.

One is the legal control of the road. So under the Clean Air Act -- and the Idaho state rules have adopted the regulatory definition of ambient air -- the issue is whether that road can be excluded from ambient air protections, meaning that it can have polluted air that exceeds healthy standards set by the EPA and set by the state for toxic air pollutants. The threshold

question in whether a facility, an applicant can exclude any portions of the facility, outside of the building, can exclude that from ambient air protection is whether it has legal control and practical control.

So if we look at EPA's policy on ambient air -- and just for your reference, that is REC 1138, and we don't need to go to that up on the screen.

But EPA says that in order to exclude an area from ambient air, you have to have two things: You have to have the legal power to control, and exclude the public. Not just control the public, but exclude the public, and the physical ability to exclude the public. So think about fences, maybe surveillance, that kind of thing.

The issue here is that DEQ is arguing -- and the hearing officer accepted this argument -- that they were reasonable in relying on the single statement and certification provided by Perpetua in the application that Perpetua has the legal control to exclude the public. And the reason this is important is because they're allowing the public through there.

So, you know, one of the problems is -- and, you know, if you look at the record, is there is evidence that Perpetua does have legal control to control access to a certain extent, but not to preclude public access.

So legal control can be just, you know, from their plain old simple ownership of land and they can keep people out. It can also be controlled as given to them through a different entity, from, for instance, the Forest Service. So there's a mix of land ownership patterns here, some of it on patented lands Perpetua owns, the rest of it, most of that ambient air boundary, inside that ambient air boundary the Forest Service owns, and that's public land.

The Forest Service, under the current mine plan -- which is not approved yet by the Forest Service, they're still going through the NEPA process. The Forest Service will give Perpetua the legal ability to control access to the extent that they can control the public's access for safety reasons. But there's evidence in the record that shows that Perpetua does not have the legal access to preclude the public. And some of those statements are related to the Forest Service's process here.

That process, the mine plan, currently there was a proposal to close that road, but comments from the public to the Forest Service had made it clear that that is an important road for the public to have open to access these recreational sites. And so the Forest Service, under both alternatives that are being

considered for the mine plan, that road is going to be open to public access. Perpetua cannot, if those two -- if one of those two alternatives -- it doesn't matter which one, as I said, it's the same thing.

If one of those two alternatives gets approved, Perpetua will have the ability to control access to the extent that it needs to to make sure that people can travel safely through there, but it will not be able to close the road to public access.

And so based on that, we don't believe that Perpetua can exclude this road from ambient air protection. It just doesn't meet the two requirements under EPA's policy on ambient air to be able to do that. Again, that's the legal power to exclude the public and the physical ability to also do so.

BOARD MEMBER STEELE: So real quick on that. I mean, we're talking about controlling access or excluding access?

MS. THROWER: Right.

BOARD MEMBER STEELE: I mean, that's what the argument is here?

MS. THROWER: Right. And, I mean, in order to be able to exclude an area from ambient air protections, meaning you don't have -- basically this is -- the whole idea of ambient air is to protect public health; right?

I mean, you have standards, the NAAQS standards, how much particulate matter can be in the air, the state standards for toxic air pollutants, how much can be in the air; that does not create a public risk, a public risk large enough for us to really worry about.

Particulate matters or respiratory irritants particularly, you know, affecting children, older people, people that have pre-existing conditions, but also it does affect, you know, healthy people if there's enough in the air. Same thing with arsenic, it's a carcinogen.

BOARD MEMBER PURDY: But isn't exposure time -- excuse me.

But exposure time is a critical part of that; right? If an individual is allowed to go into the area and camp for two or three days versus only allowed to pass through, and they only spend a half an hour or an hour inside of that bubble, that makes a big difference, doesn't it, the amount of the exposure time?

MS. THROWER: Well, yes and no.

BOARD MEMBER PURDUE: Okay.

MS. THROWER: Under the National Ambient Air Quality Standards which, you know, the state needs to meet, there's criteria set, levels of pollution that you can't go above --

BOARD MEMBER PURDY: Period?

MS. THROWER: -- to the ambient air. Yeah. It doesn't matter if, you know, people are just passing through or if they're going to be camping or if they're living there, you know. You just can't -- it's just a threshold. You're either meeting ambient air qualities standards or you're not.

BOARD MEMBER PURDY: So you don't -- obviously you don't accept Perpetua's guest of the mine --

MS. THROWER: Yes. Right.

BOARD MEMBER PURDY: -- process where it would either escort or control or monitor that access to make sure the people were moving through and not stopping and hanging out in that area, that they would move through the mine area safely as an escorted guest or a monitored guest.

MS. THROWER: That's right. Yeah. And it makes sense in terms of safety. Obviously they don't want people straying off the path, you know.

But in terms of air quality, it -- yeah, that doesn't matter. And it, you know, this is, you know, on paper it's a recreation area; a lot of people are traveling there, are going to travel there in the summer in open air vehicles, like Razors, ATV's or whatever, you know, people who pass in cars and supposedly they can close up their windows and turn their air off and

everything like that. But that still doesn't matter in terms of compliance with the National Ambient Air Quality Standards.

And that's really the threshold that we're talking about here. The state caps that we talk a lot about that, that kind of comes into the arsenic air issue and outside the ambient air boundary, but really for the access road it's the NAAQS and the particulate matter.

And so yeah -- oh, go ahead.

BOARD MEMBER STEELE: I've got a follow-up. So right now is the general public going from the north through the south, or is that whole area controlled right now?

MS. THROWER: It is open to public use. I think that I'll defer that question to Perpetua in terms of whether they have any, you know, if they're doing any activities. There are exploration activities out there. Whether -- they probably do have the ability to control access, maybe even temporarily shut down if they're going to be doing something that would create too much of a safety hazard for the public to pass through. But those are temporary closures, not a complete closure for 16 years, you know, the life of the mine.

BOARD MEMBER STEELE: Okay.

MS. THROWER: If you -- and yeah, if you enter

that south -- if you exit on that south entry, there are Forest Service roads that continue on into, as I said, the important recreational areas --

BOARD MEMBER STEELE: Okay. Thanks.

MS. THROWER: -- that are pretty heavily accessed through summer. Yeah.

So I do want to -- I'm taking a lot of time on this issue, and I do want to go ahead and move to the issue that you mentioned in terms of the guest of the mine.

We don't think that this --

We don't believe that that is consistent with EPA's policy, and it's not consistent with DEQ's guidance on ambient air boundaries.

I think I'll just, in the interest of time, I will just point out one of the glaring inconsistencies is with DEQ's guidance. And I'm going to note a typographical error in our motion in terms of the number, the record number. So I talked --

In our brief we talked about how the guest of the mine issue, which is really the public going through, they don't want to visit the mine, they just want to get to public land. So to call them guests of the mine to take away these ambient air protections is really inconsistent and really against the law and the purpose

and intent of the Clean Air Act.

But even DEQ's guidance says, and I quote,

"For the purpose of defining ambient air, the general public is considered anyone not directly associated with the facility. In general, if someone present at the site would not be subject to OSHA or other worker exposure regulations, then they are considered as the general public."

And that is at REC 1109.

I don't think anybody here can credibly claim that people traveling on this road to access public lands are going to be covered under OSHA or worker exposure laws.

So, you know, allowing people to do this and calling them guests of the mine because they sign a waiver I think is inconsistent with this DEQ guidance, it is against EPA's ambient air policy, and it creates a huge public health risk for the public traveling that, you know, isn't going to understand that when they sign this waiver that they're necessarily going to be exposed to air quality that doesn't meet EPA's standards for public to be able to breathe.

I want to move on to the second issue with

arsenic unless there are any further questions on that?

BOARD MEMBER STEELE: Well, I guess, you know, you talk about DEQ basically not using their guidance appropriately and same with EPA. But DEQ has had correspondence with EPA on that.

MS. THROWER: Right.

BOARD MEMBER STEELE: And they have decided that the road is likely exempt from ambient air protection.

MS. THROWER: Yeah.

BOARD MEMBER STEELE: So would you talk a little bit about that?

MS. THROWER: Yeah. We can go to this recent EPA letter that was just submitted into the record this morning.

And in that case EPA does still have concerns about the road and whether Perpetua has -- has the legal right to exclude the public. So at the top of page 2 it says,

> "With respect to ambient air boundary designation, the EPA continues to have concerns with IDEQ's acceptance of Perpetua's assertion that members of the general public do not have the legal rights of access to areas within the operations area boundary."

So I wouldn't say that that is completely resolved.

There were other issues that EPA had brought up about general access around the ambient air boundary in terms of there being a lot of trails, rivers going through there and everything like that.

But the EPA goes on in that letter, and I think there they are saying that, okay, we are okay with that. The access management plan provides those physical barriers for other areas around the ambient air boundary, and they believe that that is consistent with the policy.

But I think that this road access is still an issue, even after all these communications with EPA.

Okay. So I'll move on to arsenic. So we're moving outside of the ambient air boundary. There's still a lot of dust that's going to be flying around, and what I'm going to go through is the state's rules on this.

Because I think what is clear here is that there's certain prescribed ways to assess toxic air pollutants -- and now I'm shifting to arsenic and more away from particulate matter.

But there are specific state rules on how you calculate your toxic air pollutant emissions, and there's specific thresholds that you have to be under. There are

ways to -- different ways to calculate that and everything and, but this isn't a free-for-all, there's no availability to do project specific adjustments as Perpetua and DEQ have suggested.

So if you look at the state's rule, Section 203 says that,

> "No permit to construct shall be granted unless an applicant can show that emissions of TAPs will not injure or unreasonably affect human health or animal life or vegetation as required by Section 161."

So 161 basically says that toxic air pollutant must not be admitted in quantities or concentrations up to, alone or with other contaminants, injure or unreasonably affect human life -- excuse me -- human health or animal life or vegetation.

Section 203 also states that you can -- that,

> "An applicant can demonstrate compliance with Section 161 by meeting the emission increments in section 586."

Don't you love regulations, right? I'm sure you'll be pulling all of these up at some point.

Section 586 is basically a table of toxic air pollutants emission limits. The one that we're focused

on here is the called the Acceptable Ambient Air Concentrations for carcinogen or AACC. And arsenic has a number, an AACC number.

The regulations also state that AACC's are annual averages. So you figure, like with the mine, 16 years, maybe emissions aren't exactly the same every year. You add up 16 years of emissions, you divide by 16, that's your annual average.

Section 203 requires an applicant to, "Use methods under Section 210 to demonstrate compliance with Section 203."

So if we go to Section 210, it prescribes standard methods an applicant can use in sections .05 and .08 or specialized methods in Sections .09 and .12.

So the one that Perpetua and DEQ used is Section 210.12. And we're all good here, this is all working fine. It says that you can use a method called T-RACT, which is Reasonably Available Control Technology, to demonstrate compliance with the TAP increments in Section 586. So if you do that, if you can't meet the TAP increments in 586, you can meet them by applying this reasonably available control technology. And the regulations give you a little bit of a bonus. They -- instead of having to meet the thresholds in 586, they allow you a ten-fold increase in that threshold.

Okay. So let's say you can emit one unit under 586. Well, now if you use reasonably controlled technology, they're going to let you emit 10 units and you'll still be in compliance. Okay. You're still not going to injure human health unreasonably.

So Section 210.12(B) again states this ten-fold bonus as the cancer risk probability of less than 1 to 100,000. So before with the TAPs increments it was one to a million, now, we're at 1 to 100,000. And the regulation states, "Which is equivalent to ten times the applicable AACC listed under 586." That's where we get that ten-fold bonus.

Now, Section 210.12(C) says that you can demonstrate that you meet the T-RACT AACC, the ten-fold increased AACC, if you -- if you can meet that -- excuse me. If you can meet that amount, then you don't have to do any further demonstration of compliance with Section 161 which is, you know, that's not unreasonably injuring human health.

There are other methods. 210 says that you can use -- or excuse me -- 212 -- 210.12 says there are a couple of other methods you can use: 212.09, I think, net emissions or whatever in addition to T-RACT, but that's not what we're talking about here.

What DEQ and Perpetua did is they did a project

specific adjustment factor is what they called it. And what they did was they took the annual arsenic -- they took the arsenic emissions, the total emissions, and instead of dividing by the life of the mine, which would be your annual emissions as required under the regulations, they divided by a 70-year human lifetime.

So what that essentially does is it lessens the emissions significantly. They were able to comply with the ten-fold AACC level if they did that.

But deleting the emissions that way does not comply with the fact that you need to be comparing your annual emissions, and not, you know, including another 54 years of nothing to derive that figure for your annual emissions. So we don't believe what Perpetua did here complies with the state's rules.

We also don't believe, to the extent that they're arguing that, oh, you can do other things to demonstrate compliance, to demonstrate that there's not an unreasonable risk to human health, we don't see that anywhere in the record.

There's a declaration by Kevin Schilling, who is an atmospheric scientist not a cancer risk assessment scientist, who tried to justify their use of this 70-year dilution factor. We just don't see the evidence that -- again, even if you read the rules to allow something like

that, we just don't see the rationale or the justification or the support in the record to demonstrate that this was a reasonable decision based on the record, and not arbitrary and capricious.

I have taken a lot of Bryan's time. I'm going to stop for questions. But I'm sorry, Bryan, and I hope they'll be a little lenient on the time understanding that, of course, the other parties should have the same amount of time as well.

BOARD MEMBER STEELE: So I just have a couple of questions.

BOARD CHAIR BOWEN: Go ahead.

BOARD MEMBER STEELE: So is there any human habitation that's being impacted, you know, like for 16 years of this project? Or are we mainly talking about the access road?

MS. THROWER: Well, the access road is really just regarding the particulate matter.

Outside the ambient air boundary where the arsenic issue comes in, Yellow Pine is the closest community. I mean, we don't know. We can do a dilution factor and everything, we don't know how far out you would have to go to actually comply with the TAPs increments, the ten-fold TAPs increments.

I think Yellow Pine is about 10 miles west of

the mine site. There are -- there's a population there that lives there year-round. It's not huge, but, you know, rural people are afforded the same protections --

BOARD MEMBER STEELE: Yeah.

MS. THROWER: -- under the Clean Air Act as anybody else.

BOARD MEMBER STEELE: For sure.

MS. THROWER: The Nez Perce Tribe that uses the fishing and gathering and hunting -- I can't attest to the amount of time they spend there -- they're not my client. But in terms of, you know, it's not just an area that people pass through on their way to somewhere else.

BOARD CHAIR BOWEN: Any other questions?

BOARD MEMBER MCELROY: Mr. Chairman.

BOARD CHAIR BOWEN: Yes.

BOARD MEMBER MCELROY: I have a quick question. So the 70-year dilution factor that you're calling out, does DEQ have any guidance documents that walks through how to use that type of factor? Or has this approach been used in other air permits that the DEQ has issued in the past?

MS. THROWER: Not that we are aware of. During discovery we asked DEQ if they could provide us with any other permits that used this type of dilution factor, and we did not get any documents from that. They simply do

not have that.

So we are assuming that this is really the first time in a very precedential move to use this kind of project-specific dilution factor for this permit.

BOARD CHAIR BOWEN: Any other questions?

(No response.)

BOARD BOARD BOWEN: Okay. Mr. Hurlbutt, you've got 30 minutes. We were prepared for 30 each, so 30 minutes, you've got 30 minutes.

MR. HURLBUTT: Appreciate it.

MS. THROWER: Thank you. I definitely appreciate that. I'll have a better lunch with my colleague.

MR. HURLBUTT: Yeah. All right. So I'm going to turn to the issue of DEQ allowing Perpetua to submit a number of plans later, after the permit was already approved, after public comment period had already happened. Those plans still haven't been submitted, they're required to be submitted 30 days before operations might start.

So the permit allows for Perpetua to submit these four plans -- the fugitive dust control plan, the haul road capping plan, the access management plan, and the operation and maintenance manual -- later.

But the Air Rules require, as I'll walk through,

that plans and other information about the project be submitted by the applicant, be evaluated by DEQ, and be subjected to public comment before DEQ issues a permit or makes a final decision on a permit.

And I'll also walk through how relevant case law on meaningful public involvement supports this, and shows that important project details like those that will be included in these plans cannot be shielded from public comment, as was done here.

So starting with the Air Rules -- and this is not nearly as in-depth or as confusing as the arsenic standard stuff that Julie just walked through -- but I'm going to talk about Air Rules.

Let's start with Section 202 of the Air Rules. This is what talks about what needs to be in an application, required information for an application. And this is in Air Rule 202.01.A(i). Required -- applicants must provide, quote,

> "Site information, plans, descriptions, specifications, and drawings showing the design of the stationary source facility or modification, the nature and amount of emissions, including secondary emissions, and the manner in which it

will be operated and controlled." End quote.

Air Rule Section 209 also requires public comment. And it states there that required information for public comment is, quote,

"The department's proposed action together with the information submitted by the applicant and the department's analysis of that information will be made available to the public," end quote. That's 209.01(c)(1).

The four plans that haven't been submitted include:

The type of required information from Air Rule Section 202;

Information about how the site's going -- the facility is going to be operated and how emissions are goings to be controlled;

And it includes the kind of information that the Section 209 requires to be made available during the public comment period;

And the analyses that DEQ is going to perform in the future when it reviews these plans that Perpetua is supposed to submit is the kind of analysis that Section 209 requires to be put forth before the public to review

and comment on before a permit is approved.

Two of the plans have to do with dust control, that's the fugitive dust control plan and the haul road capping plan.

The fugitive dust control plan, that's permit condition 2.6. You can see that at REC 0375, 376.

The haul road capping plan, that's permit condition 3.13 at RAC 0385 through 86.

And the fugitive dust control plan requires, among other things, quote,

> "Specific criteria to determine what frequency and type, water and/or chemical, of dust suppressant must be applied, and appropriate suppressant application rates," end quote.

So the fugitive dust control plan is going to include information about how often Perpetua is going to use dust controls, what types of dust controls they're going to use, and the rates at which they're going to apply them. And this is super important information, as Julia already mentioned.

While there are other sources of fugitive dust from blasting and other operations at the site, the main source is from the haul roads. And how dust is going to be controlled on those haul roads goes straight to the

heart of whether this project can comply with the National Ambient Air Quality Standards.

Similarly, the haul road capping plan, it requires a silt content sampling plan; it requires an arsenic rock sampling plan; and it also requires specifications for how Perpetua is going to inspect and maintain the haul roads.

These plans, these do indeed -- well, first of all, they are plans. They have plans in the name of them. And remember, the required information the applicant must submit includes plans. And it also includes information, specifications, descriptions related to how the site will operate, and how pollution will be controlled. And that's exactly what these plans are and what they include. They describe how Perpetua will operate and control the roads, and how they will try and control dust at the site.

So instead of deferring them to the future, they should have been developed now. There's no reason not to develop them now and submit them to the public for comment before making a decision on the final permit.

And this isn't just kind of a technical gotcha thing. Again, this is really important as the record shows in the air modeling that's included with the Statement of Basis -- I have it right here.

Appendix B to the Statement of Basis has the ambient air quality impact analysis. And as we pointed out in our briefing, DEQ and Perpetua model, what would happen if instead of achieving 93.3 percent dust control, which is what Perpetua is targeting to achieve, what would happen if they instead achieved slightly less dust control and only controlled 90 percent of the dust?

In that modeling they also said, and let's suppose that Perpetua cut its emissions by a lot instead of a -- or cut its operations by a lot. Instead of producing 180,000 tons per day of materials, what if those were scaled back to just two-thirds, so 120,000 tons per day?

When this modeling was performed, a huge cut of the amount of operations -- so there's going to be a lot less driving around and a lot less dust potentially being generated -- and then just a tiny reduction in the effectiveness of controlling dust from those roads, again dropping from 93.3 percent dust control to 90 percent dust control.

That modeling that's in the records shows that the project would not comply with the NAAQS for coarse particulate matter. That's not in dispute. That's in the record. That's at REC 0691 through 0692 where DEQ describes this, and then there's 0693, further

information about that for a couple of pages.

So again, just a small reduction in how effectively they control dust in the roads, even coupled with a huge drop in production going on at the mine will result in the NAAQS being violated.

So this is a super important issue. And the idea that the details in these plans could just be developed later, after the project's been approved by DEQ, after the public's already submitted public comments, does not comport with the Air Rules, Sections 202 and 209.

These are the type of required information that the applicant needs to provide before a permit is issued, and the type of information that needs to go before the public, and DEQ's analysis of what's in those plans and whether it's good enough also needs to go before the public, and that was not done here.

The same is true of the access management plan. This is permit condition 2.7. Like the other plans, this is a plan, again it's the accent management plan -- access management plan. And Rule 202 requires plans to be submitted by the applicant during the permitting process.

And that plan includes information, specifications, and descriptions of how Perpetua will

operate and control the Stibnite Road project with respect to access management.

Access management is another important issue; it relates to what Ms. Thrower just discussed about the appropriate ambient air boundary. Instead of whether and how the public access is being managed, does bear on whether DEQ used the appropriate ambient air boundary for this project.

In the permit the access management plan is required to:

1. Identify the boundary and access points, and specify measures to discourage public access.

And 2. It's also supposed to identify access points that will be monitoring -- that will be monitored, the frequency they'll be patrolled, and the methods that will be used to discourage access.

Again, these are descriptions and specifications and plans about the project that have not yet been developed, not submitted for public comment, but DEQ approved the permit anyway without having that information.

And again, that's not in accordance with the Air Rules of Section 202 that clearly require that kind of information to be provided by the applicant, and Air Rules 209 which require the public to be able to comment

about that information and DEQ's analysis of it before the permit is issued.

BOARD MEMBER STEELE: So I've got a comment. So, you know, IDAPA has rules for fugitive dust. And within those rules, you know, you have to comply with that. And there is a permit condition for that in the permit to comply with the fugitive dust rules. It could also be looked at that these plans are in addition to that to help ensure that those fugitive dust rules are complied with. Have you looked at it that way?

Because this is a very common practice for DEQ to issue a permit and require a plan to be developed at a later date to help ensure compliance with other permit conditions.

MR. HURLBUTT: And so that may or may not be appropriate with complying with the IDAPA provisions that are specific to fugitive dust control.

But whether or not that's true, it's not appropriate to do this when you've got an issue, such as compliance with the National Ambient Air Quality Standards.

And again, that part of Statement of Basis that I pointed out with the modeling where just a tiny increase in fugitive dust control could mean that the NAAQS are violated shows that this is the kind of

situation where you need to have that kind of information considered before and evaluated by the Board.

And that's supported by two cases that we've cited in our briefing and discussed. These are two Federal Court of Appeals cases, Clean Water Act cases dealing with what's required to have meaningful public comment when a pollution permit is being issued, what things need to be put before the public, or which things could be saved for later.

This is the Environmental Defense Fund case that had to do with small municipal storm water discharges and permits for those. The EPA set up a program where instead of setting forth criteria for each small municipality to meet that would be subject to public comment, they were going to let the municipalities develop their own plans to meet six criteria EPA had identified later as to how they would reduce discharges.

That got challenged in court. The Ninth Circuit Court of Appeals held that the plans that those communities were going to come up with were the kind of substantive information about how the facilities would be operated to reduce discharges that's required to be subject to public comment and can't be shielded from public comment

BOARD MEMBER PURDY: So your issue is

specifically around your fear that there will be a lack of public comment opportunity during the development of these four plans? Has DEQ established that they're not going to allow public comment on those plans?

MR. HURLBUTT: The permit as currently written does not allow for public comment on those plans. It calls for Perpetua to submit those plans to DEQ, and it says DEQ will review and then approve them. There's no period afforded for public comment.

But I will also note that public comment after the permit has already been issued, while I suppose slightly better than no public comment, would still not comply with the Air Rules requirements under Section 202 and Section 209 that we discussed. Meaningful public comment has to happen before the final decision's been made on the permit.

BOARD MEMBER PURDY: But they're not allowed to begin operation until those plans are in place and fully approved.

MR. HURLBUTT: Correct. And in the 2nd Circuit in the Waterkeeper case that we cite, similar to the Environmental Defense Fund case, this involved large CAFOs. The EPA proposed that nutrient management plans that specified how pollution was going to be managed on these sites could be submitted later without public

review.

The 2nd Circuit disagreed with that and said that without meaningful public comment, those need to be submitted to the public before issuing those permits.

The same situation here: the fugitive dust control plan, the haul road capping plan, and the access management plan, they all contain substantive and important details about how Perpetua will control dust and manage access at the site, so they cannot be shielded from public review prior to DEQ issuing -- and need to be available prior to DEQ issuing any permit.

And the last thing I'll note on this issue about the plans being deferred: The recent EPA letter from March 12th -- which I don't know if you've all had a chance to review -- but it raises some serious concerns about things that have yet to be put forth to the public for comment.

On page 2 of the letter EPA notes that -- yeah, requests that certain plans do be made available to the public, and I'll just quote here. Near the end of the letter EPA says, quote,

> "Moving forward, we expect that all information relied upon to issue permits by the State of Idaho's permitting program be made available for public

review at the time that draft permits are made available for public comment," end quote.

For whatever reason, EPA seems to be willing to give DEQ a pass here and let DEQ to move forward with these late plans without public comment for Perpetua's permit.

But EPA is signaling here, I think, that it's in alignment with what we're saying that the rules actually require this information to be put forth earlier in the process to allow for meaningful public comment, and that it expects Idaho to do so in the future.

So we would ask you to set aside and remand the permit with directions that DEQ require these plans to be submitted; that they be subjected to public comment along with DEQ's analysis of those plans and their adequacy before making any final decision on the permit.

Any other questions about the plans before I move on to dust control?

So the last issue -- I think this is the third of four issues in our brief. But the last issue being argued now is DEQ's assumption that Perpetua will achieve 93.3 percent dust control. And our argument to that is that it's arbitrary and capricious.

Again, I'm going to say this again, and I

already talked about it, but this Appendix B, the modeling report and the analysis that was done shows that just a tiny reduction in dust control, Perpetua doesn't meet that 93.3. Even if they scale back their operations a ton and they are generating way less dust, they would be violating the NAAQS for particulate matter. So only slightly less dust control to cause NAAQS violations.

The target is for Perpetua to meet this 93.3 percent, but the permit lacks any enforceable conditions to ensure Perpetua will actually achieve such a high level of dust control.

The permit does have some conditions related to dust control. And DEQ might be able to reasonably assume that the project will result in a, you know, pretty good dust control based on that, but there's nothing in there that's really tied to achieving 93.3 percent as opposed to say 90 percent or 85 percent.

Again, just getting back to the Air Rules, Air Rules Section 203 provides that DEQ can't issue a PTC unless it first determines that the facility, quote, "...would not cause or significantly contribute to a violation of any Ambient Air Quality Standards."

Here DEQ acknowledged that throughout the record -- and we cite this a lot in our briefing -- that achieving this 93.3 percent is critical to achieving

NAAQS compliance; that it's a very high and aggressive level standard, and it will automatically require quote -- well, yeah, DEQ states in the record that it will be, quote, "Challenging to consistently and continuously achieve the targeted level of fugitive dust control," end quote. That's REC 0431.

DEQ modeling staff said, quote, that they, "Recommend the permit requiring aggressive implementation of measures to achieve above 93 -- to control 93 percent control efficiency," end quote. That's at REC 0691.

Elsewhere in the record they say that, "Vigilant inspection and monitoring will be required to achieve that."

But again, the permit doesn't actually require meeting 93.3 percent or greater dust control. There's no requirement in the permit itself to meet that.

There are two tables in the permit that have the number 93.3 in it, those are not emission limits or enforceable conditions of the permits, those are just listed targets and talking about the different things going on at the facility.

And even if those listing of 93.3 in those tables were to be considered some kind of limit in the permit, there's nothing enforceable about it. There is no monitoring to see what level of dust control is

actually being achieved, or there is no testing to see at startup kind of what dust control levels are being achieved.

If there were those things, then you might be able to have some kind of actual limit on 93.3 percent. It's not in there.

What the permit does have is the facility dust control plan and haul road capping plan that we've already talked about a little bit, and some other provisions related to fugitive dust.

But none of those things are tied specifically to meeting 93.3 percent as opposed to, say again, 90 percent, which is a pretty high level of control and would not satisfy the NAAQS.

BOARD MEMBER STEELE: So you say that it's arbitrary and capricious, yet there's quite a bit of record for where that 93.3 percent came from.

And, you know, the range, you know, from a conservative standpoint, 90 percent was used for dust, for the dust suppressant; it could have been 94, 95, it could be up to like 98 percent just for the dust suppressant alone. And with the water, the control efficiency could be 75 to 95 percent. So, I mean, in theory there could be up to a 99 percent control, 99.1, something like that.

So to say that it's arbitrary and capricious, I mean -- I mean, I guess I'd like you to elaborate about why.

MR. HURLBUTT: Sure.

BOARD MEMBER STEELE: Like what -- where's the better information that DEQ could rely on to make this decision?

MR. HURLBUTT: So we're not saying that it was arbitrary and capricious for DEQ to conclude that it might be possible to achieve 93.3 percent control. And I think a lot of information in the record you're talking about shows that DEQ, in its technical expertise, can decide that that is an achievable level of control that could be accomplished here.

What is arbitrary and capricious is to conclude that that will be controlled here, because the permit lacks specific conditions tied to actually achieving that as opposed to, say again, 90 percent, which is still a really high level of control, but it's not actually adequate to comply with Ambient Air Quality Standards. None of the things in the permit are tied to that.

There's been mention of this 10 percent opacity monitoring; looking around, seeing with your eyes what it looks like; if it looks like it's a little too dusty, then corrective actions need to be taken. That's great

and that's fine, but there's nothing in the record that shows how that relates to achieving 93.3 percent as opposed to 92 or 91 or 80 percent dust control.

It's a good practice -- that's great that they're doing it -- but our key point is that even if Perpetua comes up with some pretty good plans; submits them to DEQ; DEQ thinks they look pretty good; signs off on them; moves forward with the project; achieves a high level of dust control; that high level of dust control might be 93.3 percent, it might be 88 percent, it might be 95 percent.

DEQ can't approve a project though unless it determines that the project, based on its operations and the limits in the permit, will comply with the air quality standards. And so it was arbitrary and capricious to do that here.

DEQ can say this has a shot at achieving 93.3 percent, and might meet it, but that's not what's required. DEQ has to find that it will not cause a violation of air quality standards.

There might be a lot of other situations where a permit is for a facility and it's not teetering on the edge of non-compliance like this one is. In other situations having a ballpark target for dust control might be fine because there's more wiggle room.

But again -- and I know I've already mentioned this four times, I'm going to mention it a fifth time -- the modeling that's in the record shows that just even if they cut their operations by a whole third, this tiny change in dust control efficiency is modeled to cause NAAQS violations.

And the permit doesn't have anything that precisely leads to 93.3 percent dust control. The project could move forward and be operating and causing NAAQS violations every day, and no one would know any better, and they'd be in perfect compliance with their project, potentially achieving 90 percent dust control.

VICE CHAIR MACMILLAN: So, Bryan, I was just wondering if anybody -- do miners have an idea just how much -- without any control, how much dust would actually be generated? I didn't see that in any of the documents. And the reason I ask that, unless you know how much you begin with, how do you know if there's a 10 percent reduction or zero percent reduction?

MR. HURLBUTT: I think they do know or they have estimates. This modeling starts from, assuming they're driving around this much and generating this much dust, then they say okay, if we control different things by different amounts, then what are the results? And I don't -- yeah. So they do start with that.

VICE CHAIR MACMILLAN: Okay.

MR. HURLBUTT: Yeah.

BOARD MEMBER STEELE: So this might be a question I'll need to ask the DEQ. But Schilling in his declaration, he did, there's a quote in here that he said that the permit -- that the modeling group recommended that the permit require aggressive implementation measures to achieve above 93 percent control efficiency for fugitive particulates from the roadways.

You're saying it's your belief the permit does not require that, it does not require that compliance?

MR. HURLBUTT: It does not. I mean, the fugitive dust control plan requires Perpetua to come up with a plan for how they're going to determine how often to apply materials, which types, and what amounts. And again -- and I'm happy to assume that they'll do a pretty good job of that, but again, how they're going to achieve 93.3 instead of some other lesser amount.

BOARD MEMBER STEELE: Okay.

MR. HURLBUTT: I guess the one last thing I'd say on the 93.3 percent control is that, again, the reason I think the recent EPA letter helps support this, on the first page, the bottom paragraph, EPA raises concerns about the fugitive dust control plan and says at one point, quote,

"The EPA understands that not all details of an approvable plan can be known in advance. But without permit conditions requiring the source to demonstrate that the plan will achieve the required level of control, IDEQ may have limited ability to reject or require improvements to a plan that falls short."

And this matches our main point that even if they submit a pretty good plan and DEQ signs off on it and they follow that plan to a T, IDEQ is not going to actually have the ability to enforce a 93.3 percent dust control because they're never going to know whether Perpetua is actually achieving that, and there is nothing in the permit to ensure that it is.

So with that, we would ask that you set aside, remand the permit for DEQ to either add additional permit conditions, modify the amount of operations that are allowed, or otherwise take action to ensure that the PM 10 NAAQS will be complied with before issuing any permit.

BOARD CHAIR BOWEN: Thank you. Any other questions?

(No response.)

BOARD CHAIR BOWEN: Okay. Thank you very much.

MR. HURLBUTT: Thank you.

BOARD CHAIR BOWEN: We appreciate it.

Now, with the hour, what's the will of the Board? Are you willing to move into the respondents' arguments, or do you want to take a break?

All right. Do we need a motion to take a break?

MS. YRIBAR: Yeah.

BOARD CHAIR BOWEN: All right. I'll entertain a motion to break for lunch.

VICE CHAIR MACMILLAN: I move we break for lunch.

BOARD MEMBER SIGLER: I second it.

BOARD CHAIR BOWEN: Everyone in agreement say aye.

BOARD MEMBER PURDY: How long?

BOARD CHAIR BOWEN: Half an hour.

It's been moved and seconded. All in favor?

(AYES.)

BOARD CHAIR BOWEN: Any opposed?

(No response.)

BOARD CHAIR BOWEN: Thank you. We're adjourned for lunch.

(Thereupon the luncheon recess was taken at 11:55 a.m.)

AFTERNOON SESSION

--oOo--

(Thereupon the afternoon session resumed at 12:32 p.m.)

BOARD CHAIR BOWEN: Okay. We'll call the meeting back to order and we're now on record.

Carol, can you hear us?

BOARD SECRETARY MASCARENAS: Yes, I can.

BOARD CHAIR BOWEN: Great. Thank you.

Now, let's hear from the respondents DEQ and then Perpetua. You've each got 30 minutes.

MS. YOUNG: You ready for me?

BOARD CHAIR BOWEN: We're all ready. The floor is yours.

MS. YOUNG: And thank you for taking a lunch. I'm sure nobody wanted to listen to me while hungry, so I appreciate that.

Again, thank you for hearing this appeal today. My name is Hannah Young. I represent the Department of Environmental Quality. I'm their lead DAG and I'm representing DEQ today.

I do again just want to underscore that it really is an exceptional effort by the Board to read all of the materials and spend the time preparing, so we really appreciate your efforts here today.

I want to begin by discussing this permit from a really high level. As you're now aware from reading the voluminous record and the many, many filings, this permit has been highly scrutinized internally and externally. And, as a result, the permitting process has been complex and lengthy. In fact, it took nearly three years. Development of this permit also included three public comment periods, two public informational meetings, four permit iterations and, in general, just a level of examination that has been unmatched.

The efforts by DEQ demonstrate its desire to not only engage with the public but to issue a permit that is protective and legally defensible.

Now, if you were to only hear from the petitioners today or only read their briefing in the matter, you would be left with a disingenuous impression of this permit. They use words in their brief like rushed, partial, incomplete, vague, to describe the permit and the process, and they also make claims that DEQ is precluding the public from participating and from viewing the permit, and nothing could be farther from the truth. In fact, DEQ has engaged with these same petitioners during all three public comment periods and during the informational meetings, responding to the same claims they've made today if you look at the response to

comments documents. And early in the process, DEQ even made changes to the permit based on their comments that were reasonable and made sense. So we're listening.

As I said, the record relating to this permit is large: It contains emails, correspondence, guidance documents, public comments, public response to comments document. In fact, just the last response to comment document was 85 pages alone. There are three draft permits. Of course the -- I forget if it's 400- or 500-page Statement of Basis and the permit itself.

Upon review of the record you will find, I am confident, that there is not a single part of this permit this has not been considered, studied, and examined by DEQ. And the parts that are not in the permit that the petitioners would like to be there have similarly been studied, examined, and debated.

You know, ultimately DEQ is here defending its decision to issue that permit, just like they've done to the public; to the EPA as we've seen through these letters being introduced; to the hearing officer, and now, of course, to you all at the Board.

Issuing permits is DEQ's job, and DEQ continues defending this permit it issued because it's a good permit written by the experts at DEQ.

Many of the permitting decisions are discussed

in the declarations of bureau chief Mike Simon and atmospheric scientist Kevin Schilling which I know those declarations have already been referenced so far. Together those two gentlemen have a combined 60 years of experience in the air permitting and air quality world. There are a lot of other highly skilled, highly qualified DEQ staff persons that were involved in this permit, including Ms. Floyd, the air quality division administrator who's been at DEQ for 24 years.

Now, petitioners don't like some of DEQ's decisions, and that's fine. I would say that not liking some of our decisions is inevitable, quite frankly. But dislike is not the legal standard, and rightfully so.

The important legal standard is that DEQ was reasonable, acted in accordance with the law, used lawful procedure, and acted in a way that was not arbitrary, capricious, or an abuse of discretion. And clearly DEQ has met that standard.

Finally, one last aspect I'd like to discuss from a high level, and then I promise I'll turn to the discrete issues. And that is that if the Board today finds that DEQ erred on any of the issues raised, then the Board would be changing how the DEQ does business and how DEQ writes permits.

Mr. Steele has sort of taken the wind out of my

sails a little bit to this point in that he raised that there are a lot of customary practices here that DEQ used in writing this permit. And I don't bring this up to say that, you know, this is the way it's always been done so this is the way we should do it, no.

What I'm saying is that DEQ made no exceptions for Perpetua; they cut no corners; they used their standard, custom permitting practices that they relied upon their professional judgment in making, and in adhering to those professional judgments in issuing the permit today.

So with that, I will now turn to the four specific issues brought forward in this petition: The Stibnite Access Road, the submission of project plans, the 93.3 dust control, and arsenic emissions from the roads.

As to all four of those issues, the hearing officer who first heard this matter found that DEQ -- found in DEQ and Perpetua's favor, and determined that we acted reasonably and in accordance with law.

And I recognize that today you are reviewing this matter de novo; in other words, you don't have to defer to what the hearing officer decided.

That being said, the hearing officer thoroughly considered this matter for over a year, and he issued a

very thoughtful, very well written decision that covers all of the issues that you're hearing today. And so I would urge you to rely on the hearing officer's decision which, of course, is in the record, and to also uphold his decision that DEQ acted reasonably and in accordance with the law.

I know these arguments have been fully briefed, you've heard about them, I'll do my best not to belabor them. And, of course, please ask, you know, any questions.

So the first issue is the access route. Petitioners obviously do not agree with DEQ's decision to preclude the Stibnite access route from the ambient air boundary.

There are two points I want to emphasize here:

And the first is that DEQ was absolutely reasonable and acted within its authority when it relied upon Perpetua's assertion that it will have the authority to exclude the general public and only allow guests of the mine.

Section 123 of the Air Rules provides,

> "All documents, including applications for permits to construct, must contain a certification by a responsible official, and that

certification must state that based on information and belief, the statements and information in the document are true, accurate, and complete."

In the permit application Perpetua stated it will have full control over the mine site and the ability to not just control, but exclude, the general public.

Here again is an example of DEQ following its typical process in relying on the assertions made by a permittee, and that makes, I think, particular sense in light of the certification requirement that's in the rules.

To decide that DEQ was unreasonable here is to now say that DEQ is required to investigate or fact check every assertion made by a permittee. And I think it's obvious that they simply do not have the time or resources for that sort of undertaking.

I would also add that this scenario, wherein a permittee does not own the entire facility/property, is not uncommon. We often see facilities (sic) that do not own their entire property but lease neighboring property, maybe they need an easement or an access agreement to part of the property. And all DEQ does in those situations, just like it did here, was get a representation that the permittee does or will have

control over that property. We cannot possibly look at those lease agreements or look at those access agreements and make a claim that that's valid. We're not going to insert ourselves in that type of examination, and we're not a third-party arbitrator, like a court ultimately, or a Board. And so we're not going to involve ourselves. So this is, like I said, it's very common practice.

And here, despite what petitioners have said -- and I know Perpetua will speak at this more at length -- but we have not been presented with any actual evidence that Perpetua will not have control of the mine site and the ability to preclude access at the time the mine is operational. Until and unless DEQ is presented with that evidence, DEQ continues to reasonably rely on Perpetua's assertions.

The permit itself also contains numerous conditions actually requiring Perpetua to have control over the route and the ability to preclude access, which I know was brought up earlier. So condition 2.7 requires a host of things like security escort vehicles, guardhouses, locked gates, warning signs, registration of guests, et cetera, which -- in the access management plan, which must include specific measures Perpetua will use to discourage public access.

If Perpetua does not meet those permit

conditions and, in other words, does not exclude the general public, they will be violating their permit, and their permit will need to be modified or they can be subject to an enforcement action.

The second point I want to make is that DEQ properly used its discretion and did act in conformance with both DEQ and EPA guidance. Both guidances state, "It's appropriate to exclude areas from ambient air where there are measures in place to exclude the general public."

Now, petitioners claim, as you just heard, that DEQ did not act in conformance with that guidance, and they seem to, I would say, oversimplify the guidance and say there are only general public and those directly associated with the facility, and that's just not true.

So I'd like to give you an example, if you'll indulge me. If I visit a facility, which I am often to do in this role, say the Idaho National Lab, because I'm on a guided tour, which happens frequently, or perhaps in my role as representing DEQ. When I am not -- when I am on-site, I am not a member of the general public, but I did receive permission -- right? -- to be on-site. I'm there for a limited purpose; I cannot go anywhere I please; I'm expected to meet safety requirements while I'm on-site; I can only be in certain locations; I often

have to wear a dosimeter; I need to sign a release or liability form; I need to wear a hard hat and the right type of shoes in certain areas. But I'm certainly not an INL employee or one of their contractors.

And to unpack this even further. If I'm driving down Highway 20, which I often do, I'm a member of the general public driving on Highway 20. But the moment I turn onto their facility, I become a guest of that facility. And if I wasn't a guest and I was not allowed to be there, I would certainly be asked to leave. And if I didn't, I would be subject to both civil and criminal trespass. And if I didn't follow the required protocols while on-site, I would also be required to leave. This would be true if the Board were to visit INL; this would be true if a group of school children were visiting the INL.

And I only provide this as an example that it's very common for DEQ to permit a facility knowing that there may be guests allowed on-site. And those guests are not considered members of the general public. So when they're on-site, just like when I'm at INL, I'm not being protected as if I'm within the ambient air; I'm not being protected from potential -- I mean, INL has a Title 5, or I don't know if it's a Title 5, they have an air permit of some sort -- I would not be receiving the NAAQS

protections while I'm on-site that I would be if I left. I'm not a member of the public, but I'm not associated with the facility.

So again, this example is just to highlight that this is not uncommon, and it's absolutely in conformance with guidance.

So in summary, DEQ has thoroughly considered this issue, and while petitioners don't agree with this decision, it is supported by the record and it is reasonable.

BOARD SECRETARY MASCARENAS: Mr. Chair, I have a question.

BOARD CHAIR BOWEN: Yes, Carol.

BOARD SECRETARY MASCARENAS: I, not being familiar with the INL myself, I have thought about that scenario and how we control things, how things are controlled there.

But what about the aspect of, at the INL they can restrict access and control. It goes to the plaintiff's argument, there's two parts that need to be met, control and then the exclusion of access, and surely INL can also prevent access to the facility. Could you respond to that aspect of the argument?

MS. YOUNG: Yes, Chairman and Ms. Mascarenas. I hope I'm understanding your question correctly.

But yes, just like INL, Perpetua will be required to not only control access while it's on site, but preclude the general public, which I would say they do.

And if you've been to the national lab you know that it's a highly secure site with, you know, guards, et cetera, at guard towers when you enter. And if you're not allowed to be there for that specific purpose, if you do not do things like sign the liability waiver, et cetera, then you're not allowed on-site.

So it's not just controlling what you're doing while you're there, but it's also precluding you from entering the site period unless you've met whatever requirements.

And I understand it's not a perfect analogy. No site will be perfectly analogous to another because INL has all sorts of national security concerns and other things. But it's, again, just to highlight that this is not an uncommon situation for there to be more than just general public at the facility.

BOARD CHAIR BOWEN: So just a follow-up question to that. So if a member of the public rolls up to the gate and says, "I want to pass through," are they going to be able to pass through if they desire as a guest of the facility, or are they restricted from entering the

site?

MS. YOUNG: I think that question is probably best answered by Perpetua, so I'll defer to them if that's all right, but --

BOARD CHAIR BOWEN: Okay.

MS. YOUNG: -- my understanding is that they will be allowed to enter if they meet the various requirements, and they will no longer be a member of the general public. I hope that answers your question.

BOARD CHAIR BOWEN: So the assumption is that control will be granted to Perpetua?

MS. YOUNG: Oh, absolutely. Perpetua has to have that level of control and that ability, otherwise they're violating their permit.

BOARD CHAIR BOWEN: Okay.

BOARD SECRETARY MASCARENAS: Thank you.

MS. YOUNG: Yes. Thank you.

BOARD MEMBER STEELE: So to follow up on that a little bit. The petitioners refer to the EPA letter that there was mention that EPA still has some concerns, but then they go on to say in the last sentence of that first paragraph on the second page, whatever approved plan that gets developed, there should be something in that plan that maintains, you know, basically control.

MS. FLOYD: Right.

BOARD MEMBER STEELE: Is it DEQ's intention to do that?

MS. YOUNG: Oh, absolutely. Absolutely. And I would also take issue to some extent with some of the language in this letter. For example, they say that, "There must be measures to maintain continuous monitoring of the public's movement"; they're not the public, they're not the general public.

EPA is not as familiar with this site, this facility as DEQ is, so that's fine. But they're not considered the public. The plan will require, as well as I'd say the permit itself requires that their -- that their movements be monitored and tracked. So absolutely that's the requirement.

And now that you've mentioned it, Mr. Steele, their letter also notes that DEQ's decision here was, as quoted, "Generally consistent with EPA's revised policy on exclusions from ambient air."

BOARD CHAIR BOWEN: And just one follow-up. Let's say the permit goes through the NEPA process with U.S. Forest Service, and they determine or their stipulation is that you must provide public access through the site. What happens to the permit if they make a general ruling like that? What's the status of the permit?

MS. YOUNG: Yes, that would be a change in circumstances; right? And not to throw Perpetua under the bus here, but that's a little bit of the risk that they took by applying for the process while the NEPA process was still ongoing.

You know, but the bottom line -- and I don't want to -- Mr. Pooser will talk about this much more eloquently than I -- but the importance of the mine plan and why a lot, not just this piece, is riding on the mine plan. If the mine plan's not approved, then there's no project anyway so then they don't need an air permit anyways, right?

But if it were to be approved with that caveat that they would have to be -- general public on that road, for example, that would change the analysis, and we'd probably have to go back to the drawing board on the permit.

VICE CHAIR MACMILLAN: Mr. Chairman.

BOARD CHAIR BOWEN: Yes.

VICE CHAIR MACMILLAN: What kind of inspections or monitoring does DEQ typically provide or have happen at mines? I can speak to fish farms, I know something about that. But a mine that's as big as this one, how do you measure compliance with the permit?

MS. YOUNG: Sure. I think with any facility

there's sort of the standard ways that you measure compliance.

One of them is that the permit itself contains a number of quite rigorous reporting and recordkeeping requirements for things specific to access. So DEQ needs to see those records and they need to, you know, see that Perpetua is keeping track of that information.

The other standard way is that DEQ learns, for example, that these permit conditions aren't being followed is when DEQ is on site conducting inspections, which they will be. We often get complaints from folks notifying us, which then DEQ has a requirement to follow-up on those complaints and verify the veracity of those.

And then we often see a lot of self-reports where the facility is letting us know, you know, they've had a -- not a good example here -- but an exceedance or whatever the case may be.

Here the Forest Service, for example, being a, you know, land manager, and keeping us well apprised of the NEPA process, I think DEQ feels also comfortable that that party is going to be keeping us informed about what's going on on-site as well.

But I think the two primary ways that DEQ will be checking on compliance here are those robust

recordkeeping requirements and the inspections that occur.

And just like with any facility, DEQ simply does not have the resources to be on-site 100 percent of the time, that's just an impossibility. But when they are on-site, which happens frequently, they find, you know -- if they find violations -- which they do -- then those would need to be dealt with accordingly

VICE CHAIR MACMILLAN: So as follow-up then, I guess the key point is there's a routine inspection process that DEQ has --

MS. YOUNG: Absolutely.

VICE CHAIR MACMILLAN: -- of mines, and so there's some confidence that you would catch misdeeds, for example -- and maybe misdeeds is not the right word.

MS. YOUNG: Sure.

VICE CHAIR MACMILLAN: But errors in judgment or something.

MS. YOUNG: Absolutely, and that happens regularly.

VICE CHAIR MACMILLAN: All right. Thank you.

MS. YOUNG: Yes. Thank you.

The second topic for consideration by the Board is the decision to allow Perpetua to submit permit

required plans after permit issuance.

And again I want to start by noting that this is common practice for DEQ, as I think Mr. Steele actually already mentioned that this was common practice. And again, if the Board were to find that that was not an allowed practice, every single permitting program at DEQ would have to change how it does business. And this practice really does make sense given the complex realities of permitting various industries.

As Mike Simon testified in his declaration, which is in the record,

> "It is common for the permit program to require certain plans, such as an O&M manual or fugitive dust control plan, to be prepared by the permittee post-permit issuance. This allows the permittee to prepare a specific plan or manual based on the actual equipment purchased and installed, the manufacturer's instructions and recommendations, as well as the operational characteristics of the facility after construction is completed."

And I want to note that it's not just common practice, but it is common practice because the permit

itself contains the conditions and details necessary to ensure compliance with the rules. The plans do not do that. The plans are not what -- are not what are telling us that the rules are met; the permit does that. But the plans provide those operational details that flush out -- flesh out how those permit conditions may be met. I like to think of it as the permit is the what, and the plans are a little bit of the how.

So an example: Section 2 of the permit contains eight separate conditions related to the control of fugitive dust. Condition 2.1 describes the reasonable precautions Perpetua must take. And 2.1 alone contains six substantive requirements.

Condition 2.6 then requires Perpetua to develop a fugitive dust control plan. And condition 2.6 itself contains 12 substantive requirements of what must be further addressed in the plan.

So it's -- you know, it was brought up earlier of whether this was, whether things might have been arbitrary or capricious by DEQ. I think an obvious way DEQ might have been arbitrary and capricious is if they said prepare a fugitive dust plan that will control fugitive dust period. That's not what happened here. There's a lot of specificity in the permit that dictates what must be in that plan, and that's, I think, very

critical here.

BOARD MEMBER PURDY: Does that -- sorry to interrupt.

Does that include the 93 plus percent control?

MS. YOUNG: Absolutely. And I can turn to that now or I can address --

BOARD MEMBER PURDY: No, it's okay.

VICE CHAIR MACMILLAN: So Mr. Chairman. I will anyway.

So the petitioner has pointed out that the DEQ rule requires plan submission --

MS. YOUNG: Right.

VICE CHAIR MACMILLAN: -- as part of the permit application.

MS. YOUNG: Right.

VICE CHAIR MACMILLAN: So how -- how do we get around that?

MS. YOUNG: And I know that Perpetua was going to speak to this too, but I'll address it also.

And I would say that the language that they're relying upon, 402.01, I disagree with their reading of the rule, for one. The rule section states:

"Required information. Site information, plans, descriptions, specifications, and drawings showing the

design of the stationary source facility or modification, the nature of the amount of emissions, and the manner in which it will be operated and controlled."

It seems to me that that list of what's required site information, plans, descriptions, specifications, and drawings is regarding to showing the design of the stationary source, which the plans and specifications for the design of the source are absolutely required early on.

I also want to note a little bit of inconsistency in petitioners' argument in that their latest reply that they filed they say that they understand that the operation and maintenance manual that DEQ is requiring -- which is a plan -- is okay; it's okay that that comes later, they just don't like the other plan. That's a very inconsistent approach and application of the rule in my mind. And --

I'm sorry, I thought I saw a hand raised.

But the last point I want to make a point of is the EPA letter, to the extent that they're relying upon that, also signals that it's fine to use plans, and they talk about information being made available to the public after those plans are approved by DEQ.

The hearing officer -- I lied, sorry, this is my last point.

The hearing officer in his decision also stated that there is no prohibition in the rules that would not allow DEQ to require plans to be submitted later, and in fact, the permit -- the rule language gives DEQ wide discretion in what types of information can be in a permit, and what types of permit conditions, such as the condition to submit a plan. So there's wide discretion there too.

BOARD MEMBER PURDY: I made a note during the petitioners' presentation that they referenced Section 202 multiple times.

MS. YOUNG: Yes.

BOARD MEMBER PURDY: And I don't remember if that was an EPA or an Idaho Code section?

MS. YOUNG: Yeah, that's the rule. And I think that that 202 section is about the permit conditions that DEQ has discretion to include, though I could be misremembering.

BOARD MEMBER STEELE: It's the application.

MS. YOUNG: Yeah.

(Unreportable simultaneous cross-talk.)

BOARD MEMBER PURDY: It's that the application had to be all open to public comment and --

MS. YOUNG: Oh, okay. Sorry, the 209 section was public comment. Thank you.

So I'm happy to turn to that too. So actually, thank you for that lovely segueway, because my second point is that petitioners are claiming that this practice of having plans being submitted later deprives the public from meaningful involvement which, again, I take serious issue with. And that section of the rule 209 simply says that, "The public should be allowed an opportunity to comment on the draft permit." An opportunity.

Here they have had three, because there have been three draft permits that have all gone out for public comment, so that obviously has been met. And there's nothing in there saying that those plans need to be required to be set out for public comment, which, again, EPA seems to agree with in that they're saying that information like a plan should be available to the public. Which, since we're subject to the Public Records Act anyways, are absolutely available to the public at any time.

But all that's to say that what Section 209 of the Air Rules requires is that the permit, the draft permit be allowed to be commented on. That's what occurred here.

And I would further argue that there's nothing

in the plans that the petitioners haven't already had the opportunity to comment on because, like I said, the true substantive requirements are in the permit, and they've had an opportunity to engage with DEQ on that.

The permit says that they're going to use a chemical suppressant. We've talked about the control for the chemical suppressant. We've talked about the need for it to be applied. There's a plethora of conditions related to that. The plan might say the exact hours that the chemical suppressant needs to be applied; based on the manufacturer's label will give you an actual application rate, say every four hours, whatever, but the plan -- the facility hasn't been constructed yet, so they haven't purchased that chemical. That's the kind of detail.

And so as far as what the rules are requiring, and the rules wanting the public to be able to engage with the permit, I would say that's absolutely being satisfied here.

BOARD MEMBER PURDY: Thank you.

MS. YOUNG: Thank you.

So I think I've covered this issue well, I'll move on to the -- and I will note that there were a couple of cases that the petitioners referenced, and I'm going to defer to my esteemed counsel to address those

for you.

The third issue is that petitioners contend DEQ lacked a reasonable basis in determining that the project can achieve 93.3 dust control from the haul road.

And again, if you hear only from the petitioners here or read only their brief, you would be left with a disingenuous impression that DEQ is not confident that this level of control will be met based on the permit conditions. And as we heard from petitioners, you may even be left with the impression that dust control is difficult or outdated. Again, not true. And, in fact, as was brought up, DEQ has rules for the reasonable control of dust.

This is nothing new. There are a lot of facilities that DEQ requires a fugitive dust plan, and that require that, you know, this type of issue be dealt with.

So I want to briefly note that in petitioners' reply, and it was sort of brought out during the conversation earlier, that petitioners agree at this point that the 93.3 control is achievable. So I won't get into the calculation of how that was done. But they seem to take issue with the adequacy of the permit conditions for meeting the 93.3 percent control.

So there are several permit conditions that are

relevant here and that speak to this level of control, which, again, the 93.3 is not an emissions limit, it's a control efficiency. So measuring it and saying 93.3 percent is going to be met is asking for an absolute; it's asking for something that DEQ simply could not provide. If you remanded the permit to DEQ and said we need confirmation that 93.3 percent is going to be met based on, you know, something that the petitioners are asking for, that's an absolute. But absent some sort of long-term study on-site, that information is not going to be able to be provided.

But the permit condition, if those are met, then DEQ has a very high level of confidence that the 93.3 will be met because that 93.3 percent was not pulled from a hat, but is based on the method, standards, and data relied upon by EPA. And you'll see it referenced in the record at AP 42, that's the name of the guidance document that determines the control efficiency.

But back to the permit conditions. So conditions 2.1, 2.2, and 2.6, amongst others, require Perpetua to apply water and chemicals to the roads to control dust.

And as noted earlier in the conversation, DEQ chose a very conservative number of 90 percent in the range, the most conservative number that comes from AP 42

in the 90 to 99 percent control efficiency for the chemicals.

Condition 2.2 requires Perpetua to monitor the frequency and methods used to control fugitive dust at least once every 12 hours.

2.4 requires daily, facility-wide inspections and hauling activities to ensure that the control efficiency is achieved. There is corollary recordkeeping requirements related to that, which DEQ will, of course, be reviewing.

And condition 2.5 mandates that fugitive dust control measures be applied to haul roads on a frequency such that visible emissions from vehicle traffic do not exceed 10 percent opacity. And if emissions do exceed that level, Perpetua must take immediate corrective action until fugitive dust is achieved.

And I think it was Mr. Simon who noted in his declaration that these daily inspection and haul road opacity requirements are more stringent than any other permit DEQ has issued.

So petitioners have used the term aggressive when it comes to these conditions, and we can call it aggressive if you will, that's fine, but it's certainly not a novel approach.

DEQ is well versed in controlling fugitive dust.

I talked about the AP 42 that they used and relied upon in determining that if these permit conditions are met, then this control efficiency will be achieved.

And again, you know, those conditions may seem stringent or they may seem aggressive, but DEQ only puts permit conditions in a permit with the expectation that the permittee will comply. So if the permittee does what it's required to do, complies with the permit, then confidence by the experts at DEQ who have analyzed all of this information is very, very high that the 93.3 percent will be met.

BOARD CHAIR BOWEN: Hannah, a follow-up question here. I think one of the claims that petitioners made is that the permit lacks enforceable criteria. One of the things that I read in the record is this issue of opacity.

Can you translate for the lay folks of us what that actually looks like on the ground as far as what enforcement looks like relative to the criteria?

MS. YOUNG: Yeah. Absolutely. And as a former -- or also a layperson to layperson, I'll do my best. Again, the experts at DEQ, their declarations and their Statements of Basis are really critical here.

But my understanding is that DEQ will also be on-site to do these, you know, when they're doing their

inspections and determining opacity, just like Perpetua will be required to do.

And DEQ staff have actually been trained on determining opacity. So they have a level of training that says this is -- this is 10 percent, you know, this is that threshold. And they have to go to training -- I think the training is done by EPA -- and they look at different dusty conditions, and they actually get trained on how to do that. And so they have a level of confidence with the 10 percent number that, you know, they could identify that.

It's actually, in my mind, a pretty low threshold in that if you're seeing dust, you need to do something about it.

And I also want to note that all of this is actually quite conservative when you consider the winter months when there shouldn't be any dust and, you know, the rainy days. And just the consistent application of water and chemicals, you shouldn't really be seeing dust.

BOARD CHAIR BOWEN: So what -- overall what's the general response to the assertion that there's no enforceability to the 93.3? There's nothing in the permit that's enforceable? What's your response to that, in general?

MS. YOUNG: I mean, again --

BOARD SECRETARY MASCARENAS: Mr. Chair, if I can add to that question?

BOARD CHAIR BOWEN: Sure.

BOARD SECRETARY MASCARENAS: In particular, seeing that the fact that the criteria or the 93.3 percent within our table lacks enforceability.

MS. YOUNG: So I'm hoping I heard the question right; it sounds like you're sort of asking the same thing.

Again, it's not an emission limit, it's a control efficiency. And DEQ will determine that that 93.3 percent has been met if the permit conditions have been met.

All of the permit conditions, including the ones which are just an example of what's in the permit, if those are not met, then DEQ does not have confidence and would consider the control efficiency of 93.3 percent to not have been met.

So it's imperative on Perpetua to meet these conditions. And if they meet these conditions, confidence is very high, again based on AP 42, the data, the studies, et cetera, that the 93.3 percent is being met.

BOARD MEMBER PURDY: So mathematically maybe it's a they must do A plus B plus C, and if they do those

things, it will equal 93.3 greater air control efficiency. So they're not measuring the right side of the equation, they are measuring the, Are you doing A? Are you doing B? Are you doing C?

MS. YOUNG: I couldn't have said it better myself.

BOARD MEMBER PURDY: Within the permit conditions --

MS. YOUNG: Absolutely.

BOARD MEMBER PURDY: -- you would do that.

MS. YOUNG: Absolutely.

BOARD MEMBER STEELE: Another analogy would be like if you have a dust scrubber, and you have particulates coming in, you can't pay money to always have that be measured at the outlet, but you can monitor flow and pressure drop. And if those are always being met, you're going to be --

BOARD MEMBER PURDY: You have confidence in the reading.

MS. YOUNG: Exactly. It's a control efficiency, right, and so it's a perfect example. Okay.

So I have no idea where I'm at on time, my apologies, but I will move onto my final issue, if I may.

BOARD CHAIR BOWEN: You have about five minutes.

MS. YOUNG: Perfect. Right on track.

Lastly, petitioners have alleged that DEQ created a project-specific adjustment factor to artificially dilute the ambient arsenic concentrations attributable to the project. And ultimately here petitioners are claiming that DEQ acted outside the scope of the rules.

And I really only have one point to make here and that is that DEQ did act in conformance with the rules.

You know, I think ultimately petitioners misunderstand DEQ's analysis. And to be fair, it is a technical analysis and it relies on a number of rule sections. And again, as I just said, you know, I am not an atmospheric scientist, I'm not a scientist of any sort, so I will do my best to sort of emphasize the points I would like you all to be thinking about. But I would encourage you to read the section of Kevin Schilling's declaration where he talks about this analysis for, you know, really the best authority as to this point.

But again I want to emphasize that DEQ's approach does fit squarely within the Air Rules, and I would absolutely take issue with the claim that there's been an artificial dilution.

So first DEQ started with the AACC, the applicable acceptable ambient concentration, in 586 which provides that lifetime cancer risk of one in one million for arsenic.

DEQ then performed a T-RACT analysis that's specifically allowed in the rules, Section 210.12.C. And that further refined the acceptable health risk to one in 100,000.

Now, what petitioners dislike is that during that modeling and analysis, DEQ used specific information -- which they don't normally have -- which is the 16-year life of the mine to refine its analysis, as the AACC assumes that the project will be going for 70 years. And that's fine.

When most facilities are constructed you think it's permanent, you have no idea how long it's going to operate, so you're just assuming it's going to operate for someone's lifetime. Here we know that it's not going to operate for more than 16 years. And, in fact, if they were to change their mind, they would run into issues with what has been permitted here.

And that 16 years, that 16-year life of mine was the most relevant data, and it was the best information, and it was inputted to come up with the most accurate projections.

Now, petitioners would like that specific process to be set forth in rule; that's an impossibility. The point of modeling and the point of these engineering analyses are to use the methods and data that are relevant to that specific project, and that's what DEQ did. That's all they did. They didn't further divide by 70 the life of the mine. They further refined the AACC to a calculation of 16 over 70, and they applied that. Which essentially all that's doing is saying we know it's not going to operate for 70 years, we know it's going to operate for 16.

And built into that there are a lot of conservative assumptions, which is very common in modeling and those analyses, or so I'm told.

And ultimately DEQ was required to demonstrate that the project's arsenic emissions would not injure or unreasonably affect human health or animal life or vegetation as required by the rules in Section 161 and 203.

And DEQ feels very confident that they met that standard based on the rules and based on their modeling analyses.

And again, I am happy to do my best to answer questions as to that point, but I would again point you to the experts at DEQ who are much more well versed in

this, and also to point out that the hearing officer found that as to this point DEQ provided unrebutted expert testimony, and the petitioners have not done that. They have not brought forward any experts who have taken specific issue with how that modeling was done and with how those various inputs were set forth in the analysis.

So with that, I would simply like to reemphasize that petitioners simply dislike or disagree, as a matter of opinion, the decisions made by DEQ, but they have failed to prove at every turn that DEQ committed any errors in its thorough and diligent preparation of this permit; they failed to demonstrate that DEQ acted unreasonably; that they violated any Constitutional or statutory provision or an excess of authority or used unlawful procedure or were arbitrary or capricious or an abuse of discretion.

And, in fact, the opposite. I hope what I've demonstrated here to you today is that with every single issue DEQ has a thoughtful and reasoned basis for the decision that it made.

So again, I would thank you for your thoughtful consideration of this matter. And if there are any questions, I'm happy to do my best to answer those.

BOARD MEMBER MCELROY: Mr. Chairman.

Thank you for walking us through those four

points. I do have a question on the second point, and I apologize for not asking it when you were talking through it, we just moved so quickly to the third one.

MS. YOUNG: Yeah. Sorry. Yeah. Absolutely.

BOARD MEMBER MCELROY: The point regarding the submittal of plans in the application, and in Section 2.02 it talks about the site information plans, da da da, showing the design of the stationary source -- which makes sense. But then the back half of that sentence ends with, "...and the manner in which it will be operated and controlled."

And so help us understand, in this case the fugitive dust control plan would be the method that you control those, the fugitive emissions. So how do we not meet that back half of the sentence in the application by not submitting the fugitive dust plan?

MS. YOUNG: Yeah. Absolutely. And I don't want to get too technical in statutory analysis here, but I would read that final comma and "and" as a standalone provision, "The manner in which it will be operated and controlled" as a stand-alone requirement, which DEQ absolutely has in the permit, "the manner in which it will be operated and controlled."

And a lot of those permit conditions we haven't talked about today because they're not being challenged.

There's a lot of operational requirements in the permit. But I think that the word "plan" doesn't necessarily relate to that final "and."

BOARD MEMBER MCELROY: I'm asking -- that's the application procedures.

MS. YOUNG: Oh, right, of the application.

BOARD MEMBER MCELROY: Yeah, in that section it's talking about what's required in the application.

MS. YOUNG: Right. I'm sorry.

BOARD MEMBER MCELROY: And in the back half of that statement, "And the manner in which it will be operated and controlled --"

MS. YOUNG: Yes, I'm --

BOARD MEMBER MCELROY: -- in the application. So that's what I'm trying to resolve, if that's in the plan that's not submitted.

MS. YOUNG: Yeah. And I apologize for speaking over you, but I understand your question better now.

And similarly, I think the same thing applies that what they're required to demonstrate in that section that you've just read, that piece in the application that needs to be met, which is "The manner in which it will be operated and controlled," not the plans related to that sort of final phrase, you know.

So it's a little bit of a matter of

interpretation of how DEQ would interpret that rule section, which DEQ is afforded great deference in interpreting its own rules.

But I don't see that as requiring the -- Perpetua to submit the plans at that point in time related to the manner in which it will be operated and controlled. I think they do need to demonstrate, obviously, the manner in which it will be operated and controlled, but requiring them to have a lot of those details that we talked about during the application is just an impossibility.

BOARD CHAIR BOWEN: Thank you. Okay. Any questions?

BOARD MEMBER STEELE: Yeah, one.

So with respect to arsenic, you know, petitioners talked about the unreasonable risks to public health and Yellow Pine was mentioned. In the modeling analysis, was there any demonstration that the arsenic concentrations all the way, 10 miles out to like a Yellow Pine, would impact like a human habitation?

MS. YOUNG: Right. So what the modeling was required to demonstrate is that there would not be an unacceptable risk to human health at the boundary of the mine and beyond. And that was demonstrated.

BOARD MEMBER STEELE: Okay. Thanks.

BOARD CHAIR BOWEN: Okay. Thank you.

MR. POOSER: Would it be possible to take a little break, just a little five-minute break?

BOARD CHAIR BOWEN: Oh, sure.

(Thereupon there was a brief recess.)

BOARD CHAIR BOWEN: Okay. Ready to reconvene.

We'll now hear from Perpetua. You've got 30 minutes. If you'd state your name again for the record, please?

MR. POOSER: Yeah, Christopher Pooser representing Perpetua.

Thank you, Mr. Chairman and members of the Board.

I don't intend to repeat what Ms. Young has so eloquently stated. Obviously we agree with DEQ, we agree with her defense of the permit, but I will be kind of covering some of the same ground, and I wanted to give you the perspective from Perpetua as well as answer any questions that you may have.

So I asked Paula to pull up this map just so you can kind of get an idea of kind of where the project is.

Can you turn that, Paula?

MS. WILSON: Well, yes.

MR. POOSER: One more. Getting there.

MS. WILSON: Is this still the right document?

MR. POOSER: Yeah, it is, it just needs to be turned. And then scroll. There you go.

MS. YOUNG: There you go.

MR. POOSER: So I wanted to give the Board, I think everybody knows generally where the location is. You can see kind of McCall kind of in the upper left; Cascade is kind of in the lower left, and then you can see Yellow Pine which is about 10 miles to the west of the project at the top. And just to kind of give you an idea of kind of where the project sits. And it's in a very remote-like location.

And this project is a combination of a patented mine claims, which Perpetua owns and controls, and it also includes unpatented mine claims which are on public lands, National Forest Service lands.

And this is a good project. I mean, it's going to produce precious metals; it's going to produce antimony -- if I can say that word right -- and it's, antimony is, domestically is very rare, and it's used for the country's national security, it's important for our country's national security.

And this site was mined for decades. People may be familiar with it. It was abandoned. And Perpetua has been pursuing this project for many years, and Perpetua is actually already on-site and is doing pre-permitting

work primarily related to cleaning up the water quality that's on the site.

And Perpetua's ultimate goal is to leave this project and the site better, better than how it found it.

And so the permit that's before you today is one of many permits that Perpetua has to obtain for the site. There's already been, you know, discussion about the mine plan. Perpetua needs approval from the Forest Service for the mine plan for it to actually have the project.

Perpetua is required to get Clean Water Act permits.

It's required to get permits related to kind of financial assurances.

It's required to get dam safety permits.

And that's just to kind of name a few of the regulatory processes that Perpetua is required to go through to make this project a reality.

Ms. Young kind of touched on the timeline as far as the permit development here, and it was nearly three years. And I only kind of point that out because this was a rigorous and thorough process over that three-year period.

Ms. Floyd talked about, in her declaration, how the typical permit to construct of a mine or source like this one that has public comment takes 150 days. This

permit process took 1,032 days.

So the result -- I mean, the result of this rigorous and thorough process was a rigorous and thorough permit.

And so I'll go ahead and take the issues in the order that Ms. Young spoke to: So starting with the access road, moving onto the operational work plan, talking about the 93.3 percent, and then finally the arsenic averaging.

With respect to the access road, this concerns the ambient air boundary for the facility. And the question that's really been posed to the Board is whether or not DEQ abused its discretion in finding that Perpetua had the legal right to control the site and to preclude the general public, and also kind of the practical ability to exclude the general public access.

And with respect to the legal control, petitioners allege that Perpetua does not have the legal right to exclude the general public to the -- over the access road. And that is an assumption that is based on their assumption that the Forest Service is requiring public access through the site under the mine plan, and that Perpetua can't close this road. And that is just simply not the case. It's untrue and it's not supported by the record that's before you today.

And I'd like to give you just a little bit of context behind the mine plan. As I mentioned, this project is a kind of patchwork of patented and unpatented mining claims. And to control the site, Perpetua has to have Forest Service approval of its mine plan.

And once Perpetua obtains approval from the Forest Service for the mine plan, it will be authorized to operate in accordance to the mine plan.

And one of the key aspects of this mine plan is the creation of the operational boundary for the project. And the operational boundary, which is essentially established for safety and operational reasons, but Perpetua will have the authority, once that operational boundary is established, to control access to that operational boundary, and it will give Perpetua the legal right to exclude public access to their operational boundary, and that includes the access road.

So let me back up a little bit kind of on the timeline with respect to the mine plan. So Perpetua initially submitted the mine plan to the Forest Service in 2016. And that -- in the proposal that it submitted, there was no access road. Perpetua has no need for this road. It has no purpose whatsoever to its operations. And some residents, particularly Yellow Pine residents, voiced concerns about that, because traditionally they

had been able to go past the site.

And Perpetua was asked to consider whether there was some accommodation that could be made with respect to the concerns that the Yellow Pine residents had made. And so what Perpetua did is propose this access road. It wants to be a good neighbor; it wanted to be responsive to some of the concerns of the residents.

And as proposed in the mine plan, Perpetua will have legal authority to control and to exclude the public over the access road. We'll have full control and the ability to preclude public access on this road.

And so, in essence, I mean, the access would be provided to only those who kind of wish to take a shortcut kind of through the project, so they're going through for a limited reason. And they have to agree to the conditions of access.

And so Perpetua is, you know, setting those conditions for safety concerns, for operational concerns. And the people that want to move across the site, which is not the general public but this very kind of select, this select few, are going through at Perpetua's discretion. Perpetua can exclude access to the site. In fact, it can actually close the site for years during construction, during operations; it can close the site for, you know, any kind of concerns about inclement

weather, safety concerns; it has that ability to shut off access to the access road.

BOARD CHAIR BOWEN: We have a question. Go ahead.

BOARD MEMBER STEELE: So if that control road is shut off, how do folks access those areas? How do they get to Yellow Pine and things like that?

MR. POOSER: So if you see Yellow Pine, so just to the, you know, just to the west.

BOARD MEMBER STEELE: Yeah.

MR. POOSER: If you drop down and you come down and there's a black road that kind of goes, it's marked in black that kind of goes to the right, that road kind of ties into the existing Burntlog Road, and then people can pass through that way.

BOARD MEMBER STEELE: Okay.

MS. FLOYD: Can you see that?

BOARD MEMBER STEELE: Yes.

MR. POOSER: So again, kind of under the mine plan that Perpetua has proposed to the Forest Service, it is trying to establish this operational boundary. And the importance of that operational boundary is that it is an ambient air boundary for the purposes of a permit. So Perpetua needs to get that -- needs to get that approved, needs to get that approval. And it is obviously vital to

the project itself.

And so the petitioners, their assumption that the Forest Service is requiring this public access is just simply not true.

Perpetua has proposed this access as part of the mine plan, and once it has approval of the mine plan, it will have that ability to control that operational boundary and exclude the public from the operational boundary, and that includes the access road.

And another point I'd like to make is that ultimately this is the petitioner's burden of proof in this proceeding. And the only factual support that they've actually raised that Perpetua will not have legal control, will not be able to preclude access are two memos that are in the record that were prepared for the Forest Service. And they actually state exactly the opposite. And I kind of point those out.

One is called the Stantec memo, and it's at record 2558.

And there's another more lengthy air quality report that also references the access road, and that is at record 2684.

And both of these documents just simply report what is in the mine plan. And they --

Both of these documents acknowledge that

Perpetua will have legal control of its operational boundary under the mine plan.

Both of these documents acknowledge that the access road can be justifiably excluded from the project's ambient air.

And both documents also acknowledge that EPA has agreed that the access road is excluded from the ambient air.

And I'd like to point out that, you know, there's been some discussion about the EPA letter and the EPA reference to still having kind of concern about whether or not Perpetua has a legal right to exclude access. And I would encourage you to look at those pages because they refer -- because -- back up just a second.

Again, this ambient air boundary was extremely important to the project. Perpetua needed to know early on that that access road was not going to be considered ambient air. And so once it was asked to kind of consider the access road in the mine plan, it approached DEQ and it asked DEQ early on if they could reach some kind of understanding of how this access road could be accommodated under the Air Rules. And that, in turn, led DEQ to communicate with EPA.

And so when you look at those documents, they're specifically referencing EPA's statement that it was good

with DEQ's evaluation of the access road, and that it would not be included in ambient air.

So it's a little disingenuous for EPA to kind of come back at this late time and raise this issue based on its prior representation.

VICE CHAIR MACMILLAN: So will the hauling trucks be using the access road?

MR. POOSER: No. The access road's, it's a completely different thing. Again, Perpetua doesn't need the road. It has no operational value whatsoever.

And so they'll be building this road, you know, for this limited, for this limited purpose, but it's complete separate from the mine operations itself.

VICE CHAIR MACMILLAN: Well I can just imagine somebody in a pickup or something meeting one of those big, huge, gigantic --

MR. POOSER: Yeah, that's not the case. Yeah, not the case.

And so I think kind of at the end of the day this is more like a challenge in sequencing. I mean, Perpetua needs to get Forest Service approval for the mine plan; it needs to get approval from DEQ for its air quality permit; it needs to go through all the other regulatory processes that it's required to go through in order to permit the project. And the fact of the matter

is is that Perpetua can't begin construction until it has the mine plan. And it's expecting the mine plan to be issued in the last quarter of this year. And once it has the mine plan, then it will have the authority that it needs to undergo the project, and it will have the authority that it needs to begin construction.

The second aspect of the access road that Ms. Young handled very, very well, Perpetua does have obviously the practical ability to control access and to exclude the general public. And the permit is quite clear about what Perpetua has to do to actually exclude the general public. And it will have, you know, guard shacks, it will have boundaries. Nobody is going to just drive through the project. That simply cannot happen.

What happens is if people do choose to kind of go through the project, they have to come up, they have to stop, they're going to have to go through a safety briefing, they're going to have to agree to kind of the conditions of passing the site. And then Perpetua will monitor this entire process. It's required to have surveillance, and so it -- and then the travelers that are going through, they have to check in and they also have to check out, and they can't stop. There's -- it's just a pass-thru. All it is is just a pass-thru.

So ultimately DEQ's decision here was it's in

compliance with EPA guidance, and Perpetua has the legal right to control, Perpetua has the legal right to exclude the general public, and the access is actually controlled, and unsupervised access is prohibited.

I can take any questions you have on the access road.

BOARD MEMBER STEELE: So real quick on that memo on the REC 2558, the memo from -- to Brenda with the Forest Service, is that correct, from Eric Clark?

MR. POOSER: Correct.

BOARD MEMBER STEELE: So you said that the operational boundary would be the ambient air boundary?

MR. POOSER: Correct.

BOARD MEMBER STEELE: So the understanding is DEQ has an ambient air boundary, but the Forest Service plans, whatever that operational boundary is, is going to be the ambient air boundary?

MR. POOSER: Yes.

BOARD MEMBER STEELE: Could that change from what it is right now?

MR. POOSER: Well, let me understand that question. So everything that DEQ did to evaluate the air impacts from the facility and whether or not they were NAAQS compliance was based on operational boundary, which is the ambient air boundary. And so if there was some

change to that ambient air boundary, there would have to be, most likely, a different analysis done.

BOARD MEMBER STEELE: But the operational boundary itself has been set and is currently what the ambient air boundary is?

MR. POOSER: So the operational boundary will be set, so it will be established by the mine plan once the Forest Service approves the mine plan.

BOARD MEMBER STEELE: Okay.

MR. POOSER: And that will set the operational boundary, which is what Perpetua relied on for its application for the permit.

And, you know, to reiterate, Perpetua was very clear in application materials that it, that it will have approval, and that it was basing its analysis of the air quality impacts in the compliance with the NAAQS based on the mine plan being approved and the operational boundary being set.

BOARD MEMBER STEELE: So if for some reason that operational boundary is different, Perpetua will have to come back to the DEQ?

MR. POOSER: I think theoretically. I mean, theoretically. Because, again, the operational -- the operational boundary is the ambient air boundary.

BOARD MEMBER STEELE: Yeah.

MR. POOSER: So if somehow it expanded, I would say they probably would not have to, you know, undergo any permit changes; I can't speak if it somehow shrinks.

But the mine plan that is in front of the Forest Service right now, which is -- again which Perpetua expects to be approved later this year, that is what the air ambient boundary and operational boundary is.

BOARD MEMBER STEELE: Okay. Thank you.

MR. POOSER: Let me address the work plan. These are operational work plans. And petitioners argue that DEQ has violated the Air Rules with these operational work plans, and they kind of -- there's talk -- they talk about three different rule violations.

One, they're talking about how these plans should have been submitted with Perpetua's application materials -- and I'd like to get to Ms. Elroy's question in a second.

And they've also argued that these plans need to be fully developed at the time the permit is issued.

And then they also have arguments that these permits or these plans have to be subject to public comment.

And I think this begins at Rule 202 as was discussed earlier. And again, this is talking about a new stationary source and what the application materials

are for a new stationary source such as the project. And I think it's important to read the, kind of the introductory language that's in 202. And it talks about:

> "The applications for permit to construct must be made using forms furnished by the department.
>
> "The application shall be certified by the responsible official in accordance with Section 123 -- 123, and shall be accompanied by all information necessary to perform any analysis and to make any determinations required by Sections 200 to 228."

And that language is very important there because DEQ is actually determining what information is necessary as, you know, per the rules.

And I think if you look back at the permit chronology, you will note that DEQ actually deemed the application incomplete a number of times, and Perpetua was required to submit some supplemental information and updated information with respect to the permit. And so DEQ is exercising its authority fully under Rule 202 to ensure that the, that the permit and application was fully complete.

And then when you move on to the required

information. Again, we've -- Ms. Elroy's talked about sort of the three -- the three different categories, if I'm reading this right.

So I think what the petitioners have really kind of sort of focused on is the first provision which talks about the site information, the plans, descriptions, specifications, and drawings showing the design of the stationary source facility, their modification. And, you know, its opposition to these operational work plans are not plans under this rule. They are not plans that are showing the design of the stationary source; they are operational work plans.

And then the other -- the other components of the application is the nature and amount of emissions, and then the manner in which it will be operated and controlled.

And that was the question that you had, Ms. Elroy. And I think there's kind of two responses to that:

One is what I mentioned earlier, that it's DEQ that's using its discretion on determining what is actually necessary in the permit application so it can actually develop the permit.

And kind of aligned with that point is that DEQ is developing a permit. These work plans are permit

conditions. So it's kind of difficult to understand how a permit condition should be part of the original application materials.

And so Perpetua would surely have, you know, identified the roads as fugitive dust sources, and it would have proposed, you know, controls, and how those would be operated and how those would be controlled, but there's no permit -- there's no permit conditions yet. And again, these plans were all permit conditions. And so there's no requirement whatsoever that these plans be submitted as part of the application materials.

BOARD MEMBER STEELE: Is there a requirement for them to even be developed?

MR. POOSER: I think that's up to DEQ's discretion. I mean, they have the ability -- they have obviously the discretion and ability to build out this permit and determine what the conditions are.

And you'll see in our permit that there are four plans that have to be developed based on the actual operation of the facility.

Does that answer your question?

BOARD MEMBER STEELE: Yeah. I mean, I guess where I'm going with it is there's really no regulatory requirement for each one of those specific plans to be developed, it's really been up to DEQ's discretion to

help determine compliance with the permit that these plans will help ensure compliance with?

MR. POOSER: I'm not familiar with an Air Rule that specifically requires the development of a particular plan. I think it's a case-by-case, permit specific. But clearly DEQ has the discretion to develop these permit requirements and to put these plans in the permit.

BOARD MEMBER STEELE: Okay.

BOARD MEMBER MCELROY: Thank you for walking through that. And just to make it clear in my head. As I look at those three buckets, that third bucket and the manner in which it will be operated and controlled, if I understand you correctly, Perpetua, they included in their air application when they identified the fugitive emissions associated with, for example, the road, they concluded that they would control it with the dust suppressant, or they included some reference in their air application what they were going or what they were proposing to do to operate and control it? Is that how you close the whole loop?

MR. POOSER: Yes, I think that's correct. It's been a while since I looked at the application itself to see if that's specifically in there. I would assume it was because, you know, the haul roads are a big emissions

source on the project, and so DEQ would -- I mean, I'm sorry, Perpetua -- and I'm assuming, it's been a while since I read the application -- would propose how these are going to be controlled.

And it's very common, as we already kind of talked about, for chemical dust suppressant and water to be used together to control fugitive dust. And it's actually in the rules itself.

BOARD MEMBER MCELROY: Okay.

MR. POOSER: And so I think Perpetua would have proposed that.

BOARD MEMBER MCELROY: So that's exceptionally helpful considering that there are four issues that we're talking about on these plans, and it's one of the four. And I'm hearing you use words like "I think" and "I assume."

Is there any way, Mr. Chairman, that we can get validation, yes, that was part of the application? Because then to me it's one of the four issues that checks the box.

BOARD CHAIR BOWEN: I'm assuming we'd have to go back to the record ourselves unless we can ask somebody to research that.

MS. YRIBAR: I can provide a reference for you.

BOARD CHAIR BOWEN: You can provide us a

reference for it.

BOARD MEMBER MCELROY: Thank you, Mr. Pooser, that was very helpful.

MR. POOSER: So that kind of leads to the next allegation that petitioners have made with respect to that these have to be -- these plans have to be submitted to public comment.

And when you look at Rule 209 specifically it talks about, it says,

> "The department's proposed action, together with information submitted by the applicant, and the DEQ's analysis of the information."

And as Ms. Young aptly explained, the content of these plans is very detailed within the permit itself, and those were subject to public comment.

And as far as any concern about public comment, Ms. Young addressed that from DEQ's perspective. And I think this -- the way DEQ's policy kind of treats these operational work plans, it makes complete sense. And as --

One of the examples she gave was that the fugitive dust control plan, for example, requires this chemical dust suppressants, and it requires the chemical dust suppressants be used and applied consistent with

manufacturer's instructions and recommendations.

And when Perpetua is developing its permit application, it doesn't know what chemical dust suppressant it's going to use. It's not that far in the process. Even when the permit is actually issued, it doesn't know what chemical dust suppressant it's going to use. And so -- and that is -- and that is important because there's many, many manufacturers of chemical dust suppressant, and they have different instructions and different recommendations.

And what Perpetua is required to do under the permit is to kind of put that detail into the fugitive dust plan, you know, explain how it is to be mixed; how it is to be applied; what are the application rates; when to apply it; how to use it in different weather conditions. All of that will depend on the particular chemical dust suppressant that it uses.

Another example, like in the fugitive dust plan, is the speed limits. Perpetua is supposed to post and limit maximum speeds on the haul roads. And that is dependent upon the actual construction of the haul roads. It depends on the grade, how many turns are there?

So things like this cannot be -- cannot be submitted as part of the application, they're not even known when the permit is issued before they even have

permission to construct, they only come later. And so it is completely reasonable to have some of the detail, have the framework and the permit is subject to public comment, and then have the detail kind of come in later.

And so I think, you know, at the end there's just nothing in the Air Rules themselves that required these pre-construction operating plans to be fully developed at the application stage or at the permit issuance stage.

VICE CHAIR MACMILLAN: Question.

MR. POOSER: Yes.

VICE CHAIR MACMILLAN: And this doesn't pertain to PTC, but when you use those dust suppressants, so it tamps down the dust, where does the dust go then? My question really pertains to water quality. Does DEQ then, when they are considering -- and I have no -- it's not a point source, I don't think.

But from a water quality perspective, do those suppressants go into the water and potentially affect water quality?

MR. POOSER: I don't know the answer to that question.

VICE CHAIR MACMILLAN: But DEQ, I would assume, would?

MS. YOUNG: If I may, Mr. Chairman, answer the

question. I don't know that --

VICE CHAIR MACMILLAN: Sure.

MS. YOUNG: I know that this was something that has been discussed. It's certainly not in front of the Board today, however, but it's -- it is certainly something that DEQ is aware of.

I'm barely an air attorney, I'm definitely not a Clean Water Act attorney, and so I don't know the details of that, but I do know it's on the agency's radar.

VICE CHAIR MACMILLAN: Thank you.

MR. POOSER: Yeah. And I would assume that this is part of the manufacturer's, you know, recommendations and specifications.

VICE CHAIR MACMILLAN: Right. Right.

MR. POOSER: That's going to address that issue as well.

BOARD MEMBER PURDY: Yes. Those products are going to have directions for use and application rates and application timing and what are going to be required to control --

VICE CHAIR MACMILLAN: I would imagine so.

BOARD MEMBER PURDY: -- their run-off.

MR. POOSER: Yeah. Yeah. And how you apply it, if you apply it in certain weather conditions, et cetera.

BOARD MEMBER PURDY: When you can and cannot apply it.

MR. POOSER: Yes. Right. Yes. So let me turn to the fugitive dust emissions on the unpaved haul roads which is the issue with respect to the 93.3 percent.

So as has been discussed, the permit establishes a 93.3 percent control efficiency for fugitive dust. And this is specific to the haul roads. These unpaved haul roads.

And it's important to note -- I think Ms. Young kind of -- and I just want to reiterate what she said -- is this is control efficiency, it's not a permit limit. I mean, haul roads are not emissions sources that can be measured. You can't put a stack on a road. You can't measure the fugitive dust that's coming off a road.

And so the way that DEQ has dealt with this is established a control efficiency which it used for its modeling, and then it needs to ensure that the permit can achieve that 93.3 percent.

And so there's really kind of two questions that the petitioners initially brought up in this contested case petition:

And they were whether or not DEQ had kind of abused its discretion, number 1, in its choice of 93.3 percent.

And then the second question was really kind of the determination of the control analyses that were in the permit were sufficient to actually achieve the 93.3 percent.

The first question about DEQ's sort of choice of the 93.3 percent has already been addressed as Mr. Hurlbutt kind of acknowledged that they're not contesting that any longer.

And again, there's been previous discussion about the EPA documentation that shows below, like on chemical dust suppressant between 90 and 98 percent, and water between 75 and a hundred percent.

And so there really is no question that 93.3 percent is achievable for a project like this, and that DEQ was completely reasonable in making that determination.

And then that leads to the next question, and I think this has been addressed enough already. But it really is kind of like, you know, all of these permit conditions, as they add up in DEQ's determination, its decision that all of these different permit conditions add up to ensure that this 93.3 percent control efficiency can be achieved if all those conditions are met.

And so the petitioners seem to want to look at

each one of these permit conditions in isolation, individually, and you just simply can't do that. I mean, and there was some mention during the argument that there's just -- that none of the conditions in the permit tied to the 93.3 percent, and that's just not -- that's just not true.

When you look at the fugitive dust plan in particular, and the requirements for the control of fugitive dust with chemical dust suppressants, water, et cetera, and then you also have -- and you also have a lot of different dust -- fugitive dust control that Ms. Young kind of highlighted. And then you even have --

The permit even goes further than that in something that hasn't been talked too much thus far is the production limits that are in the permit. There are life of mine production limits that limit how much daily hauling and excavation can be done at the site.

And that is another way that DEQ limited the fugitive dust emissions coming from the haul roads is by limiting how many, you know, essentially trucks can be on these roads at any one time in its production.

In addition, there's been a discussion about the haul road capping plan, and it has silt limits. The DEQ required that the road material has to have a maximum of 4 percent silt. And Perpetua is required to monitor that

sample and to ensure that the roads meet that -- meet that requirement.

And then you have all the many monitoring and daily monitoring and daily recordkeeping requirements of the permit.

How am I doing on time?

BOARD CHAIR BOWEN: Right about 10 minutes to wrap up.

MR. POOSER: Okay. I'm doing good then.

So the last issue is this arsenic averaging. And I don't have a ton to say about this. I think that Ms. Young said it very, very well. I think it's addressed very eloquently in the hearing officer's determination and Mr. Schilling's declaration. But I think there's some important points that I think need to be considered here.

And we're talking about the AACC. And from my own education, the acceptable ambient concentration for carcinogen with respect to arsenic, and that is based on -- that number that is in Section 586 is based on a one in one million determination. It's a determination that one in a million is an acceptable risk based on a lifetime exposure of arsenic. And so what that means is that there's a continuous exposure for 70 years; so every minute of every day for 70 years there is exposure there.

And I was in the back and couldn't see who made the comment, but there was a comment made about exposure time is kind of critical for TAPs -- and it is. And this is a 70-year -- this is a 70-year exposure time is kind of what we're dealing with.

And so when you look at the Air Rules, they allow for that adjustment that Ms. Young talked about. When there's T-RACT and that risk, and that acceptable risk comes in, it's kind of lowered to one in 100,000. And again based on a 70-year continuous exposure, chronic exposure.

And so, you know, DEQ, we think they were completely appropriate in evaluating if this risk was acceptable here. And it refined its analysis based on the 16-year life of the mine.

And, as I mentioned, there's production limits in the permit, and those are based on the life of the map -- they're based on the life of the mine. Perpetua only has so much ore to produce. And so regardless if the mine operates for 16 years or 70 years, the production limit caps the amount of arsenic emissions because there's only so much ore to be had.

And so in that sense this does not dilute emissions at all; the emissions are what -- the emissions are based on the available ore on the site.

And so in looking at the 70-year exposure DEQ model, the highest annual arsenic emissions from the project for the 16 years, and then it took into account the fact that there was going to be 54 years of no arsenic emissions, and we thought that was completely reasonable under the analysis and the rules that DEQ used.

And there was a question about the impact, kind of how far out the arsenic exposure goes. And there's a -- I'd like to give you a site so you can actually see kind of on the map what the impacts of the arsenic is from the modeling that was done.

And Paula, I don't know if you can pull this up, but it's number, document number 36.

MS. WILSON: Okay. Hang on a sec. Okay. There is document 36.

MR. POOSER: And then if you go to page 353 of the PDF.

MS. WILSON: Is this the page you want?

MR. POOSER: Yeah, that's it.

So this kind of, just sort of illustrates where there was one sort of problem area that DEQ is evaluating the risk for. But you can kind of see how far out the arsenic goes based on the maximum -- the maximum risk they were using for this analysis.

BOARD MEMBER STEELE: So where is Yellow Pine compared to this?

MR. POOSER: So it would be --

BOARD MEMBER STEELE: The upper left corner?

MR. POOSER: Yeah, it would be 10 miles to the west.

BOARD MEMBER MCELROY: What was the AACC for arsenic? Just to put the table into perspective.

MR. POOSER: 2.0002. It's one in a million so I think it's .002, or .002 --

UNIDENTIFIED SPEAKER: Yeah.

MR. POOSER: Yeah, for the one in 100,000. So I just wanted to provide that because I know the question had been asked twice.

So with that, I'll conclude my remarks.

BOARD CHAIR BOWEN: Okay. Any other comments, questions?

(No response.)

BOARD CHAIR BOWEN: Okay. Thank you very much. We are prepared for a 10-minute rebuttal if you'd like to take that?

MS. THROWER: All right. Thank you, Mr. Chairman. I think we'll follow the same format as we did the first go-round.

So I'll address the ambient air issues. You

know, DEQ said that it's reasonable to rely on Perpetua's assertions, application certified, they signed it and everything, that they're excluding the public, general public and only allowing guests of the mines. It's because they've labeled everybody as guests of the mine. I mean, it is -- it's, you know, unreasonable. And anybody that goes there for any reason, even if they, to go through that road to access public land, even if they went there not even knowing they were going to pass through an active mine site, they're supposed to be considered guests of the mine?

I mean, this is -- this is Perpetua's way of getting around not being able to exclude that road or to exclude that road from ambient air protections because it is a road that is to remain open for public use to access public land.

You know, these people don't have any intent on visiting the mine; they won't be allowed to visit the mine. As I said, they might not even know that they were going to be passing through an active mine site.

You know, we're not asking DEQ to go out necessarily and do investigations of Perpetua's legal authority to exclude the public from here, but we are asking them to look at the entire record and all the evidence in there.

And there are statements about how this road is going to be open, it is part of the -- inconsistent with the U.S. Forest Service travel management plan as a public road to access public recreation site.

You know, to the extent that DEQ just ignored all of that, that is unreasonable, that's arbitrary and capricious.

If we look at the Administrative Procedures Act, an agency is supposed to make decisions based on all the evidence in the record. Again, we're not saying go out and get titles to this or that or whatever, but there's evidence in the record that this road is to remain open for public use. So, you know, they couldn't close it; they couldn't exclude the public completely, so they labeled everyone as guests of the mine.

I don't think that the INL example is really -- you know, it's not really relevant here. And I understand situations, there's probably not an exact situation like this, every situation is going to be, have to be evaluated on a case-by-case basis. But Ms. Young, you know, talks about visiting INL on-site wearing a hard hat, wearing a dosimeter.

You know, as far as we know, as far as we understand from the access management plan or what was, you know, in the record regarding a potential access

management plan, all we know is people are going to sign a paper saying they're guests of the mine. I don't even know if they're going to really understand and realize that they are going to be breathing in a lot of particulate matter and a lot of arsenic.

You know, I think there's a, you know, sort of a sense, I think, from the DEQ and Perpetua about, well, you know, people are just going to be passing through here, you're not going to breathe this for a long time. But the Clean Air Act, I mean, you know, it -- that's the purpose of the Clean Air Act is to provide these protections to the public even if you're just passing through a road.

I mean, there's facilities where there's -- and I'm not super familiar with INL but, you know, there's facilities, and I assume this is one, that, you know, there's a highway and maybe there's facilities on both sides, and both of those facilities have an ambient air boundary, but the highway is excluded from the ambient air boundary, it has ambient air protections. So I don't think the INL example is quite on point here.

I wanted to go back a little bit. I'm not going to have Ms. Wilson pull up the map, but there's a lot of -- even Google gets it wrong so, you know, it's a complicated area. There's, you know, it's not paved

roads; it's a, you know, it's public land; there's a lot of rivers and mountains and all sorts of things going around there, so it's hard to get the layout of the roads and the access and everything there. So I'm going to refer you to our opening brief that we filed before this Board on page 17 and 18 which is REC 3476 and 3477. And then I'm going to go through some of the statements from the hearing officer's decision about access to that site and sort of the layout of the land.

Currently this is not a shortcut; this is the only way to get from the north entry to the south entry to public lands to recreational sites for people. That is -- well, sorry. I take that back. That is -- that will be the only way for people to get to that area if you exclude them from the rest of the ambient air boundary. There is a road on the north side of the ambient air boundary that is a circuitous route that can get to these recreational sites, but that would go through the ambient air boundary and that will be closed to the public. So, you know, it's not a shortcut. This is the only way that people in Yellow Pine can and will be able to get to these other recreational sites is going straight through the mine site.

Again, it was mentioned that these people are there for a limited reason; yes, they are there for a

limited reason to pass through to use the public land. They're not there as a guest of the mine; they're not there to visit the mine; they're not there to, you know, eat lunch at the mine; they're not there to, you know --

I mean, you know, I think EPA's policies and DEQ's guidance recognizes that there are certain people that would normally maybe be part of the public that aren't the public that are visiting the mine, like invitees, people bringing deliveries, you know, contract workers, things like that. Sure, those people are excluded from the general public. But people passing on this road just to get to public lands are not guests of the mine.

There's been discussion about, you know, there's not a lot of people out here; you know, the general public is very few. Well, I mean, if you consider everyone as guests of the mine, there is no general public, this is true. But, you know -- and Yellow Pine is far away.

But I want to make the point that this is an important recreational area for people. People go there and they spend a lot of time there in the summer. They spend -- our standing declarations, I'll refer you back to those -- some people spend a lot of time hiking, backpacking, fishing, camping with their kids, at just in

areas that are right outside of that ambient air boundary.

So, you know, when we start talking about, oh, well, you know, it doesn't matter that there's not a lot of people there; it does to them and it does to the Clean Air Act. The Clean Air Act doesn't distinguish, like, well, okay, we can apply these rules if we're in the city versus these rules; we'll have a little bit laxer rules if we only think, you know, a hundred people live there or something like that. That's not how the Clean Air Act works. The Clean Air Act is there to provide protection to everybody in the public, whether you're in a rural area, whether you're in the city.

And not to mention all the Nez Perce Tribe members that routinely use that area for hunting, fishing and gathering and spiritual activities.

I wanted to mention the EPA letter. It was mentioned, I believe, by Perpetua that, hey, this discusses that they're okay with the access road.

But if you look at their letter, they're talking about the ambient air boundary. So I discussed this about how, you know, that Perpetua has to have physical or some sort of other barriers to preclude people from the ambient air boundary. And that is what EPA is discussing that they are okay with, and they are --- and

they think that that meets the policy, but that is not including the access route.

BOARD CHAIR BOWEN: Two minutes.

MS. THROWER: Okay. So arsenic. Ms. Young said the permit is customary. This is -- it's customary for them to dilute arsenic emissions. There was page 42 of our brief, footnote 6, there's references there to memos between DEQ staff about their concerns, about looking for legal counsel on this issue of whether they can dilute the arsenic by seven years instead of doing a real average annual emission standard.

There was talk about specific information, that they have specific information that this mine is only going to occur for 16 years for emissions, rather than the AACC assumes that a facility is going to operate for 70 or more years.

There are specific processes set out in the rules for specific information. For example, the rules have a short-term exception. Section 210.15 allows a facility to have a 10-foot bump, just like with T-RACT, but a 10-foot bump in the AACC if your facility is operating for less than five years.

The other option is that you use annual average emissions. There's no other rule for project-specific adjustments.

BOARD CHAIR BOWEN: Would you wrap up?

MS. THROWER: Okay. When DEQ passed these rules, they made that cancer assessment, you know. What DEQ here is saying is that they think that being exposed to a high concentration of emissions for 16 years is the same as low concentrations of emissions for 70 years.

They haven't made that cancer risk assessment. This was an atmospheric scientist declaration by Kevin Schilling that basically just provided the same rationale for the project-specific adjustment that was in the response to comments that we don't agree with. And there's no additional cancer risk assessment that says that that was appropriate for them to do.

And with that, I will turn it over to my colleague.

BOARD CHAIR BOWEN: Okay. Thank you.

MR. HURLBUTT: Thank you. All right. So first on allowing Perpetua to submit plans later after the permit has been approved, I just want to touch on a few things that came up.

The first one is I think I heard both DEQ and Perpetua suggest, how could they possibly come up with these plans now? That would be ridiculous, it's just too much detailed information and it's too burdensome.

The whole permit, the permit application, the

Statement of Basis is full of all kinds of complicated, complex, technical, specific details about tons of aspects about this mine, and the idea that they couldn't come up with how frequently and in what amounts they're going to apply dust controls, or how they're going to actually access -- manage access at the site is just absurd, and the operational boundary is a good example of that.

During Mr. Pooser's talk the operational boundary was up there. Perpetua explained how they decided on this operational boundary a long time ago. I think deciding on that boundary was probably way more complicated than coming up with plans for how they're going to control dust, how they're going to control access management and things like that that are in these required plans that have not yet been submitted.

Related to that, the EPA letter talks about the access management plan. And I heard Ms. Young say that absolutely the access management plan is going to track public access through the site.

EPA in its letter recommended that the plan include some kind of continuous monitoring, "Maintain continuous monitoring of the public's movements through the site," and DEQ is saying absolutely that will be in the plan. I don't know what basis there is for saying

that absolutely that will be in the plan.

If you look at permit condition 2.7 which lays out what needs to be in the access management plan, it says, among other things, "Public access to the facility may be monitored by the use of security escort vehicles or other things."

And this gets to the underlying problem here. We don't yet know what's in the access management plan. Our clients, other members of the public, EPA have not been able to comment on what's actually in the access management plan because it hasn't been developed yet, and it's not going to be submitted for public comment. This permit has already been approved without these kinds of important details being before the public and being subject to their comments.

Again, there could be the kind of monitoring of public through the site, but there's no requirement in the permit that that actually be included.

Next is interpreting Section 202 about what needs to be required in an application. Ms. Elroy had a good point about 202 saying site information, plans, descriptions, specifications, and drawings, and that those relate to the facility; they also relate to the nature and amount of emissions; they also relate to the manner in which things will be controlled; you can't weed

those out of there. And of course not every single detailed specification can reasonably be included in an application; it's what are the important ones that need to be in there.

And that's where, as Mr. Pooser pointed out, at the beginning of Section 202 it says that the application must include, quote, "All information necessary to perform any analysis or make any determination required under Sections 200 through 227."

So those are the determinations that DEQ has to make that this project will comply with National Ambient Air Quality Standard; will comply with arsenic TAPs; will comply with other standards.

So no, unimportant details that don't go towards whether this is going to comply with air quality standards might not need to be part of the plan's information, description, specifications.

But if that information is important and actually goes towards whether this permit will comply with air standards, they absolutely need to be included. And so that would include here dust control.

I'm going to mention this for the sixth time in the record, if they do not meet their dust control by just a tiny bit, the project will violate the NAAQ. And until we see application rates and timing and frequency

of dust control measures, there's no way DEQ could have done the analysis it needed to do to make its determination that this project will comply with the PM 10 NAAQ. That's the kind of information that needs to be put before the public. That's what those two federal appellate court decisions that I referenced support.

I guess with that I'll turn to the 93.3 percent issue unless anyone has questions about the plan? I sense that everyone is pretty ready to get out of here.

Just two points on meeting the 93.3 percent dust control target. As I pointed out, there is nothing that specifically ties any of these permit conditions to actually achieving 93.3 as opposed to some slightly lesser amount like 90 percent or 85 percent. I didn't hear DEQ's attorney or Perpetua's attorney point to anything that does that. There's sort of the sense that, well, there's a lot of things in here, and if you consider them all together, that's enough to hit 93.3 percent. And that's just, that's not true.

Those things are enough to think that this is probably going to do a pretty good job at dust control, it's not going to come in at, you know, 5 percent dust control or something terrible like that. But there's just no basis for saying that, well, yeah, this will hit 93.3.

What provisions in the permit are any different than if they were trying to hit 90 percent dust control, or 85 percent dust control, or 98 percent dust control? Everything that's in the permit is just pretty good practices for pretty good dust control that will probably do a pretty good job. But this idea that they're going to hit 93 and barely meet the NAAQS is not supported by what's in the permit or anything in the record.

And then the final thing on 93.3 percent. DEQ suggested that, gosh, there's just nothing we could do about this, they're asking for something impossible here. But there are things that could be done about it.

Source testing is something that's commonly done to see how a particular pollution control might work.

There could be ways to test at initial operations how the dust control is actually going, to see if it's coming in at 93.3 percent.

And then there's also the available practice in the Air Rules of having ambient air boundary monitoring. This is in Section 211 of the rules. DEQ can require ambient air boundary monitoring. That would be a backstop that could confirm that based on everything DEQ and Perpetua says will happen will achieve 93.3 percent and would not cause a NAAQS violation, that will confirm that that is actually happening if there was ambient air

boundary monitoring around the site.

Additionally, there could just be changes to what's done. There are other sources of fugitive dust that could be limited. The operations could be limited. There's not -- there are things that could be done to ensure that the project will comply with the NAAQS that have not been done now.

And unless there's any further questions, I thank you.

BOARD CHAIR BOWEN: Thank you.

Thank you to everybody that's presented. Appreciate it.

Is it the desire of the Board to enter into executive session? I'll entertain a motion.

VICE CHAIR MACMILLAN: Yes, sir. Mr. Chairman, I move the Board enter into an executive session pursuant to Idaho Code 74-206(1)(f) to communicate with legal counsel for the public agency to discuss the legal ramifications of and legal options for pending litigation or controversies not yet being litigated but imminently likely to be litigated.

I request that a roll call vote be taken and that the vote -- and that vote be recorded in the minutes of this meeting.

BOARD CHAIR BOWEN: Thank you. Do I hear a

second?

BOARD MEMBER MCELROY: Second.

BOARD CHAIR BOWEN: Elaine, would you take a roll call vote, please?

BOARD CLERK GANINO: Yes, Mr. Chairman.

Mark Bowen.

BOARD CHAIR BOWEN: Aye.

BOARD CLERK GANINO: Dr. Randy MacMillan.

VICE CHAIR MACMILLAN: Aye.

BOARD CLERK GANINO: Carol Mascarenas.

BOARD MEMBER MASCARENAS: Aye.

BOARD CLERK GANINO: Beth Elroy.

BOARD MEMBER ELROY: Aye.

BOARD CLERK GANINO: John Sigler.

BOARD MEMBER SIGLER: Aye.

BOARD CLERK GANINO: Clayton Steele.

BOARD MEMBER STEELE: Aye.

BOARD CLERK GANINO: Pat Purdy.

BOARD MEMBER PURDY: Aye.

BOARD CHAIR BOWEN: Motion carries. We adjourn to executive session. Thank you.

Thanks, everybody.

(Thereupon the Board convened into executive session off the record.)

BOARD CHAIR BOWEN: Randy, do we have a motion?

VICE CHAIR MACMILLAN: Mr. Chairman, I move that the Board resolve out of the executive session and that the meeting of the minutes reflect that no action was taken during executive session.

BOARD CHAIR BOWEN: Thank you.

We have a motion, do we have a second?

BOARD MEMBER SIGLER: Second.

BOARD CHAIR BOWEN: We have a motion and a second.

Elaine, would you take a roll call vote, please?

BOARD CLERK GANINO: Yes, Mr. Chairman.

Mark Bowen.

BOARD CHAIR BOWEN: Aye.

BOARD CLERK GANINO: Dr. Randy MacMillan.

VICE CHAIR MACMILLAN: Aye.

BOARD CLERK GANINO: Carol Mascarenas.

BOARD MEMBER MASCARENAS: Aye.

BOARD CLERK GANINO: Beth Elroy.

BOARD MEMBER ELROY: Aye.

BOARD CLERK GANINO: John Sigler.

BOARD MEMBER SIGLER: Aye.

BOARD CLERK GANINO: Clayton Steele.

BOARD MEMBER STEELE: Aye.

BOARD CLERK GANINO: Pat Purdy.

BOARD MEMBER PURDY: Aye.

BOARD CHAIR BOWEN: Motion carries. We're back in session.

The first order of business is a five-minute break. We'll be right back.

(Thereupon there was a brief recess.)

BOARD CHAIR BOWEN: Okay. Call this meeting back to order. I want to certainly thank everybody for the effort that's been put into this. We have -- as a Board we've heard a lot, there's a lot to consider.

Any comments from the Board?

(No response)

BOARD CHAIR BOWEN: Without that, I will entertain a motion.

VICE CHAIR MACMILLAN: Mr. Chairman, I move the Board take the issue as presented, the amended petition for review of preliminary order, under advisement, and issue a written final order within 56 days of today's hearing.

BOARD CHAIR BOWEN: We have a motion. Do we have a second?

BOARD MEMBER MCELROY: Second.

BOARD CHAIR BOWEN: We have a motion and a second.

Elaine, will you take a roll call vote, please?

BOARD CLERK GANINO: Yes, Mr. Chairman.

Mark Bowen.
BOARD CHAIR BOWEN: Aye.
BOARD CLERK GANINO: Dr. Randy MacMillan.
VICE CHAIR MACMILLAN: Aye.
BOARD CLERK GANINO: Carol Mascarenas.
BOARD MEMBER MASCARENAS: Aye.
BOARD CLERK GANINO: Beth Elroy.
BOARD MEMBER ELROY: Aye.
BOARD CLERK GANINO: John Sigler.
BOARD MEMBER SIGLER: Aye.
BOARD CLERK GANINO: Clayton Steele.
BOARD MEMBER STEELE: Aye.
BOARD CLERK GANINO: Pat Purdy.
BOARD MEMBER PURDY: Aye.
BOARD CHAIR BOWEN: The motion is carried.
With that, we're ready to adjourn. Do we have a motion to adjourn?
VICE CHAIR MACMILLAN: So moved.
BOARD CHAIR BOWEN: Do we have a second?
BOARD MEMBER SIGLER: Second.
BOARD CHAIR BOWEN: All in favor?
(AYES.)
BOARD CHAIR BOWEN: Thank you. We are adjourned. Thank you very much.
(Proceedings concluded at 3:43 p.m.)

CERTIFICATE OF CERTIFIED SHORTHAND REPORTER

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I, DORIS M. BAILEY, CSR NO. SRL-1074, a Certified Shorthand Reporter, certify:

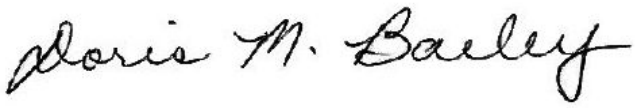
That the proceedings were transcribed by me or under my direction, to the best of my ability;

That the foregoing is a true and correct transcription of all proceedings, to the best of my ability;

That I am not a relative or employee of any attorney or party;

I further certify that I am not financially interested in the action.

IN WITNESS WHEREOF, I set my hand and seal this 19th day of March 2024.



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My Commission Expires: June 12, 2028

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BEFORE THE BOARD OF ENVIRONMENTAL QUALITY
STATE OF IDAHO

IN THE MATTER OF AIR QUALITY PERMIT TO CONSTRUCT P-2019.0047	Agency Case No. 0101-22-01
NEZ PERCE TRIBE, IDAHO CONSERVATION LEAGUE, and SAVE THE SOUTHFORK SALMON, Petitioners, vs. IDAHO DEPARTMENT OF ENVIRONMENTAL QUALITY, Respondent, and PERPETUA RESOURCES IDAHO, INC., Intervenor-Respondent.	OAH Case No. 23-245-01

SPECIAL MEETING
MAY 1, 2024
BOISE, IDAHO

REPORTED BY: DORIS M. BAILEY, CSR, RPR, CRR
Idaho CSR License Number SRL-1074

A P P E A R A N C E S

BOARD MEMBERS:

MIKE BOWEN, Chair

BETH ELROY

JOHN R. MACMILLAN, Vice Chair (Remote)

JOHN SIGLER (Remote)

CLAYTON STEELE (Remote)

PAT PURDY (Remote)

ALSO PRESENT:

ANN YRIBAR, ESQ.
Deputy Attorney General

ELAINE GANINO
Board Clerk
PAULA WILSON
Board Coordinator

--oOo--

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P R O C E E D I N G S

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BOARD CHAIR BOWEN: It's Monday, May 1st, 2024, 9:00 AM. This is Mark Bowen, Chairman of the Idaho Board of Environmental Quality.

I call to order this special meeting of the Idaho Board of Environmental Quality. In addition to being a public meeting, we are also on the record on the matter of Air Quality Permit to Construct Issued to Perpetua Resources Idaho, Inc., agency case number 0101-22-01, OAH case number 23-245-01.

This special meeting is being held in the state office of the Department of Environmental Quality.

For those present in the meeting room, please sign in on the sheet provided at the entrance.

There won't be an opportunity for public comment today.

Elaine, could you please take roll?

BOARD CLERK GANINO: Yes, Mr. Chairman.

Mark Bowen.

BOARD CHAIR BOWEN: Here.

BOARD CLERK GANINO: Dr. Randy MacMillan.

Randy? He's there, I see him there. Randy? He's not responding. I'll go back and try him again.

Beth Elroy.

BOARD MEMBER ELROY: Here.
BOARD CLERK GANINO: John Sigler.
BOARD MEMBER SIGLER: Here.
BOARD CLERK GANINO: Clayton Steele.
He's online also.
BOARD MEMBER STEELE: Here.
BOARD CHAIR BOWEN: There we go.
BOARD CLERK GANINO: Pat Purdy.
BOARD MEMBER PURDY: Here.
BOARD CLERK GANINO: We'll go back to Randy MacMillan.
VICE CHAIR MACMILLAN: Here.
BOARD MEMBER BOWEN: There we go.
VICE CHAIR MACMILLAN: I'm here.
BOARD CHAIR BOWEN: We got you, Randy. Thanks.
VICE CHAIR MACMILLAN: All right.
BOARD CHAIR BOWEN: And Carol's not joining us; correct?
BOARD CLERK GANINO: Correct.
BOARD CHAIR BOWEN: Okay. All right. So the Board --
BOARD MEMBER STEELE: Clayton Steele here.
BOARD CHAIR BOWEN: Clayton, we've got everybody. Thank you.
BOARD MEMBER STEELE: Okay. Thanks.

BOARD CHAIR BOWEN: The Board intends to take action at this meeting. No additional statements or oral argument will be taken at this meeting. A court reporter is present to record the Board's discussion.

We will now move on to the agenda items. Agenda number 1 is the option for the Board to go into executive session. I will entertain a motion.

BOARD MEMBER ELROY: I move the Board enter into executive session pursuant to IC 74-206(1)(f) to communicate with legal counsel for the public agency to discuss the legal ramifications of and legal options for pending litigation, or controversies not yet being litigated but imminently likely to be litigated.

I request that a roll call vote be taken and that vote be recorded in the minutes of this meeting.

BOARD CHAIR BOWEN: We have a motion. Is there a second?

VICE CHAIR MACMILLAN: Second.

(Reporter clarification.)

BOARD CHAIR BOWEN: Randy, Dr. MacMillan.

We have a motion and a second. We'll now call a roll vote.

Elaine.

BOARD CLERK GANINO: Yes, Mr. Chairman.

Mark Bowen.

BOARD CHAIR BOWEN: Aye.
BOARD CLERK GANINO: Dr. Randy MacMillan.
VICE CHAIR MACMILLAN: Aye.
BOARD CLERK GANINO: Beth Elroy.
BOARD MEMBER ELROY: Aye.
BOARD CLERK GANINO: John Sigler.
BOARD MEMBER SIGLER: Aye.
BOARD CLERK GANINO: Clayton Steele.
He's online also.
BOARD MEMBER STEELE: Aye.
BOARD CHAIR BOWEN: There we go.
BOARD CLERK GANINO: Pat Purdy.
BOARD MEMBER PURDY: Aye.
BOARD CHAIR BOWEN: The motion has carried. We will now move to executive session.
Thank you.
(Thereupon there was a brief recess.)
BOARD CHAIR BOWEN: All right. I'll entertain a motion.
BOARD MEMBER ELROY: I move that the Board resolve out of executive session and that the meeting of the minutes reflect that no action was taken during the executive session.
BOARD CHAIR BOWEN: We have a motion.
MS. YRIBAR: Clayton.

BOARD CHAIR BOWEN: Do we have a second?
BOARD MEMBER STEELE: Second.
BOARD CHAIR BOWEN: We have a motion and a second. All in favor? I guess we'll take a roll call vote.
Elaine, will you take a roll call, please?
BOARD CLERK GANINO: Yes, Mr. Chairman.
Mark Bowen.
BOARD CHAIR BOWEN: Aye.
BOARD CLERK GANINO: Dr. Randy MacMillan.
VICE CHAIR MACMILLAN: Aye.
BOARD CLERK GANINO: Beth Elroy.
BOARD MEMBER ELROY: Aye.
BOARD CLERK GANINO: John Sigler.
BOARD MEMBER SIGLER: Aye.
BOARD CLERK GANINO: Clayton Steele.
BOARD MEMBER STEELE: Aye.
BOARD CLERK GANINO: Pat Purdy.
BOARD MEMBER PURDY: Aye.
BOARD CHAIR BOWEN: Motion carries. So we are back on the record after executive session.
We're now on agenda item number 2, Amended Petition for Review of Preliminary Orders Filed in the Matter of Air Quality Permit to Consent -- Construct Issued to Perpetua Resources Idaho, Inc., Agency Case

number 0101-22-01, OAH case number 23-245.

This is an action item to discuss and adopt a final order prior to service of a written order within 56 days of the March 14th, 2024 oral argument.

I'll entertain a motion.

BOARD MEMBER ELROY: I move based on the foregoing, the DEQ Board finds:

Number one. DEQ acted responsibly in determining that Perpetua will have legal control of the Stibnite Road access route such that it could properly be excluded from consideration as ambient air.

Number 2. DEQ acted responsibly in determining that Perpetua what will have physical and practical control of the Stibnite Road access route such that it could properly be excluded from the consideration as ambient air.

Number 3. DEQ did not violate the air rules by allowing Perpetua to submit some plans after the PTC was issued.

Number 4. The PTC includes enforceable conditions that will achieve 93.3 percent dust control.

Number 5. There was insufficient evidence to support DEQ's evaluation of the ambient air concentration.

The DEQ Board moves to remand this matter to the

hearing officer for further factual development in accordance with the terms of this order.

We further direct our legal counsel to draft a final order in accordance with the terms of our decision, and to serve it on the parties by Thursday, May 9th.

BOARD CHAIR BOWEN: We have a motion. Do we have a second?

BOARD MEMBER PURDY: Second by Pat Purdy.

BOARD CHAIR BOWEN: We have a motion and a second. We will now have a general discussion. I'd open it to Board members to discuss any of the items, 1 through 5.

MS. YRIBAR: You want to just call on people?

BOARD CHAIR BOWEN: Yeah, let's start.

Dr. MacMillan, I'll start with you.

VICE CHAIR MACMILLAN: Mr. Chairman, I do not believe DEQ's creation and application of a project-specific adjustment factor can be supported by Idaho's air quality rules. I believe DEQ has misinterpreted how the acceptable ambient concentration for carcinogens, the AACC, must be applied if it is to comply with our air quality rules.

Further, and most disturbing to me, is that the creation of a project-specific adjustment factor suggests that there is a significant ignorance about cancer,

carcinogens, and carcinogenosis.

While DEQ experts correctly identified the AACC as the gold standard for minimizing cancer risk, they failed to recognize that the ACC -- the AACC fundamentally functions to limit the initiation of cancer, not only after 70 years, but every day of a person's life, starting at birth.

By applying the, what I would call short-sighted project-specific adjustment factor to the Stibnite Gold Project, DEQ created a misleading risk analysis that greatly underestimates the actual cancer risk.

With your permission, Mr. Chairman, I would like to explain further.

BOARD CHAIR BOWEN: Go ahead, Dr. MacMillan.

BOARD MEMBER MCMAHON: Mr. Chairman?

BOARD CHAIR BOWEN: Yes, go ahead.

BOARD MEMBER MCMAHON: By way of background, the Board should know that I have received considerable graduate education, was a senior research fellow conducting post-doctoral research, and spent considerable part of my career as a research comparative pathologist. Prior to entering a private enterprise here in Idaho, I was a professor of veterinary and aquatic animal medicine.

During my training, teaching, and research, I

became well versed in numerous aspects of cancer biology, including how cancer is initiated, how it -- how cancer is promoted, and how it progresses.

The biological processes associated with cancer are the same whether the cancer occurs in humans, other mammals, fish, or mollusks.

The AACCs that we see in Section 586 of our air quality rules are air emission concentration limits exclusively intended to minimize the risk of starting cancer. Cancer starts when a carcinogen such as arsenic is inhaled and causes mutation in cellular DNA. That mutation is inheritable, meaning it is passed from the mutate cell to daughter cells.

Also, depending on various physiological variables, cancer can quickly or slowly lead to uncontrolled, neoplastic cell growth that is cancerous cell growth, and development of a tumor grossly recognized as cancer.

One of the challenges of cancer as a human disease is that it is not readily recognized in its early stages. This should not be surprising when you consider that humans contain 10 to 100 trillion cells.

Often it is only after considerable growth that a grossly or histologically recognizable cancer becomes evident. Sometimes it's not detected until a person

feels ill, seeks medical attention, or dies.

To reiterate, once cancer is initiated, neoplastic, uncontrolled cellular replication may occur relatively quickly, or it may take many years, perhaps more than 70 years for detection of a recognizable cancer.

The take-home message is the cancer starts well before it is recognized. You don't need 70 years for it to appear. There are multiple variables that impact the initiation, promotion, and progression of cancer, such as age, immune status, comorbidities, and co-factors.

The co-factor with the Stibnite Gold Project would be dust, particularly pm 2.5 or smaller particles, all of which contain arsenic.

Inhaled dust can linger for extended periods in our lungs. Such dust is associated with a variety of pathologic processes that can amplify or enhance the development.

But most germane in this contested case are carcinogen dose and duration. The greater the dose of carcinogen exposure, the greater is the chance of cancer initiation; the longer the duration of carcinogen exposure, the greater is the risk of developing cancer.

Low dose exposure, as embodied in the AACC and applied daily for up to 70 years, would be expected to

limit cancer to only a one in one million chance.

The higher dose, such as associated with this short-term project in a T-RACT acceptable concentrations, would be expected to limit cancer to one in 100,000 chances, even after 70 years.

DEQ concluded that the Stibnite gold project cancer risk exceeds the AACC associated risk and exceeds the T-RACT associated risk.

The Idaho rules are not ambiguous. There is an acceptable risk associated with the AACC standard. There is an an acceptable risk associated with DEQ-approved T-RACT projects, and there is an acceptable risk associated with the short-term project that is five years or less. There are no other acceptable risks identified in Idaho's air quality rules.

DEQ's project-specific adjustment factor creates a new, higher level of cancer risk for 16 years. DEQ assumes 70 years is required for cancer to develop. That is an incorrect assumption.

The AACC, the T-RACT, and short-term AACC emission exposure limits are actually daily limits that apply over a person's entire lifetime, regardless of how long they live. The acceptable cancer risk remains one in one million or one in 100,000. Higher carcinogen doses increase the cancer risk every day of a person's

life. A higher daily dose for 16 years elevates the cancer risk even more.

Application of the project-specific adjustment factor allows DEQ to ignore 16 years of higher cancer initiation risk. The PTC proposes to allow 16 years higher daily carcinogen doses, and disguises such doses using a non-rules-based mathematics. Use of the project-specific adjustment factor ignores 16 years of cancer initiation due to higher carcinogenic arsenic dose that is otherwise allowed by rule. The AACC, the T-RACT, and short-term project AACCs dictate an annual average compliance.

DEQ further violates this compliance point by instituting a five-year rolling average compliance. Such a creative compliance point allows even further departure from our air quality goals, and specifically compliance with Section 161 of our air quality rules.

And personally it grieves me to disagree with DEQ. I regard DEQ staff as a team of environmental heroes. They have a daunting task to protect our environment and, in particular, help the people, animals, and plants, while fostering financial success. But even heroes make mistakes.

In my opinion, DEQ has misapplied the Idaho air quality rule, and they do not have authority to create

new cancer risks.

Thank you.

BOARD CHAIR BOWEN: Thank you, Dr. MacMillan.

Ms. Elroy, any comments?

BOARD MEMBER ELROY: Yes. Dr. MacMillan very eloquently expressed my opinion as well.

I will share with all of the parties of this case that the Board has extensive technical knowledge and experience associated with, as Randy explained, as well as decades of air permitting experience on this Board. So we do feel like due to the Board's expertise, it greatly helped us navigate through a very challenging contested case.

I do want to call out the legal support that we received by the Deputy Attorney General Ann Yribar. Her legal expertise absolutely helped us also navigate through this case, and I do want to just say thank you to Ann and recognize her for her expertise and support in navigating us through this case.

Thank you.

BOARD CHAIR BOWEN: Thank you.

Mr. Sigler, any comments?

BOARD MEMBER SIGLER: Yes, this is John Sigler.

I concur with Dr. MacMillan's summary and added comments. I think that very adequately and accurately

puts forward not only the review that's been done by the Board, but technical experts and the legal staff, that going forward we will have a solid foundation for providing the instructions that we're going to do here shortly.

BOARD CHAIR BOWEN: Thank you.

BOARD MEMBER SIGLER: That's all.

BOARD CHAIR BOWEN: Thank you.

Mr. Steele, any comments?

BOARD MEMBER STEELE: No, I do not have any comments.

BOARD CHAIR BOWEN: Thank you.

Mr. Purdy, any comment? discussion?

BOARD MEMBER PURDY: Sorry. Trying to find the unmute button.

No, I do not have any comments. Thank you.

BOARD CHAIR BOWEN: Thank you. I'd just like to add a general discussion to just --

The Board would like to acknowledge the effort of all participants. There's been a tremendous amount of work on everybody's behalf on this. We understand how complicated and how much work has gone into this. We want to express gratitude for everybody's participation. I think everybody here is interested in the safety and health of the citizens of Idaho.

And I also would like to acknowledge and thank the work of our Attorney General, Ms. Yribar, her assistance.

So with that, we have a motion and a second. Elaine, will you take the roll, please?

BOARD CLERK GANINO: Yes, Mr. Chairman.

Mark Bowen.

BOARD CHAIR BOWEN: Aye.

BOARD CLERK GANINO: Dr. Randy MacMillan.

BOARD CHAIR BOWEN: Randy, you need to unmute.

VICE CHAIR MACMILLAN: I was, but aye.

BOARD CHAIR BOWEN: Thank you.

BOARD CLERK GANINO: Beth Elroy.

BOARD MEMBER ELROY: Aye.

BOARD CLERK GANINO: John Sigler.

BOARD MEMBER SIGLER: Aye.

BOARD CLERK GANINO: Clayton Steele.

BOARD MEMBER STEELE: Aye.

BOARD CLERK GANINO: Pat Purdy.

BOARD MEMBER PURDY: Aye.

BOARD CHAIR BOWEN: Motion carried.

We've reached the end of our agenda today. I'd entertain a motion to adjourn.

BOARD MEMBER ELROY: So moved.

BOARD CHAIR BOWEN: Do I have a second?

BOARD MEMBER SIGLER: This is John. I second.
BOARD CHAIR BOWEN: We have a motion and a second. All in favor say Aye.
(AYES.)
BOARD CHAIR BOWEN: Any opposed?
(NO RESPONSE.)
BOARD CHAIR BOWEN: Hearing none, we stand adjourned.
(Proceedings concluded at 11:35 a.m.)

CERTIFICATE OF CERTIFIED SHORTHAND REPORTER

STATE OF IDAHO }
} ss.
COUNTY OF ADA }

I, DORIS M. BAILEY, CSR NO. SRL-1074, a Certified Shorthand Reporter, certify:

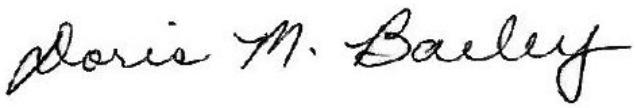
That the proceedings were transcribed by me or under my direction, to the best of my ability;

That the foregoing is a true and correct transcription of all proceedings, to the best of my ability;

That I am not a relative or employee of any attorney or party;

I further certify that I am not financially interested in the action.

IN WITNESS WHEREOF, I set my hand and seal this 9th day of May, 2024.



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My Commission Expires: June 12, 2028

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Idaho Rules of Civil Procedure

Rule 30

(e) Review by the Witness; Changes.

(1) Unless waived by the deponent and the parties, the deponent must be allowed 30 days after being notified by the officer that the transcript or recording is available in which (A) to review the transcript or recording; and (B) if there are changes in form or substance, to sign a statement listing the changes and the reasons for making them. (2) Changes indicated in the Officer's Certificate. The officer must note in the certificate prescribed by Rule 30 (f)(1) whether a review was requested and, if so, must attach any changes the deponent makes during the 30-day period. (3) Witness Failure to Sign. (A) In General, If the deposition is not signed by the witness within the 30-day period, the officer must sign it and state on the record the fact of the waiver of signature, or of the illness or absence

of the witness or the fact of the refusal to sign the deposition together with any reason given for not signing. (B) Use of Unsigned Deposition. The deposition may be used as if it were signed, unless pursuant to Rule 32 (d)(4) the court determines that the reasons given for the refusal to sign require rejection of the deposition in whole or in part.

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BEFORE THE BOARD OF ENVIRONMENTAL QUALITY
STATE OF IDAHO

IN THE MATTER OF AIR QUALITY PERMIT TO CONSTRUCT P-2019.0047	)	
NEZ PERCE TRIBE, IDAHO CONSERVATION LEAGUE, and SAVE THE SOUTH FORK SALMON,	)	Agency Case No. 0101-22-01
Petitioners,	)	OAH Case No. 23-245-01
vs.	)	
IDAHO DEPARTMENT OF ENVIRONMENTAL QUALITY,	)	
Respondent,	)	
and	)	
PERPETUA RESOURCES, IDAHO, INC.,	)	
Intervenor-Respondent.	)	

BOARD OF ENVIRONMENTAL QUALITY MEETING

June 12, 2024

IDAHO DEPARTMENT OF ENVIRONMENTAL QUALITY
1410 NORTH HILTON STREET
BOISE, IDAHO

Reported by:
Misti L. Alcalde, ID CSR #1137, CA CSR #13338, RPR

BOARD OF ENVIRONMENTAL QUALITY MEETING

BOARD MEMBERS APPEARING IN PERSON:
MARK BOWEN, Chair
DR. JOHN RANDY MACMILLAN, Vice Chair
BOARD MEMBERS APPEARING REMOTELY:
CAROL MASCAREÑAS, Secretary
CLAYTON STEELE
PAT PURDY
ALSO PRESENT: PAULA WILSON, Paralegal, DEQ
ELAINE GANINO, Clerk to the Board

P R O C E E D I N G S

BOARD CHAIR BOWEN: Okay. We'll call this meeting to order. It's Wednesday, June 12th, 2024, 9:00 [sic] a.m.

My name is Mark Bowen, chairman of the Idaho Board of Environmental Quality. I call to order the special meeting of the Idaho Board of Environmental Quality.

In addition to being a public meeting, we're also on record in the matter of Air Quality Permit to Construct issued to Perpetua Resources Idaho, Inc., agency case no. 0101-22-01, OAH case no. 23-245-01.

This special meeting is being held in the state office of The Department of Environmental Quality. For those present in the meeting room, please sign in on the sheet provided by the entrance, but there won't be an opportunity today for public comment.

Elaine, could you please take the roll.

BOARD CLERK GANINO: Yes, Mr. Chairman.

Mark Bowen.

BOARD CHAIR BOWEN: Here.

BOARD CLERK GANINO: Dr. Randy Macmillan.

VICE CHAIR MACMILLAN: Here.

BOARD CLERK GANINO: Carol Mascareñas.
BOARD MEMBER MASCAREÑAS: Here.
BOARD CLERK GANINO: Clayton Steele.
BOARD MEMBER STEELE: Here.
BOARD CLERK GANINO: Pat Purdy.
Pat, I think you're still on mute.
BOARD MEMBER STEELE: Pat, are you here?
Pat, are you here for roll?
BOARD MEMBER PURDY: Yes. I'm sorry, I thought I said "here."
BOARD CHAIR BOWEN: Okay. Thank you.
The board attempts to take action at this meeting. No additional statements or oral arguments will be taken at this meeting. The court reporter is present to record the board's decision.
We'll now move on to agenda items. Agenda item no. 1, executive session pursuant to Idaho Code 74-206(1)(f).
I'll entertain a motion.
VICE CHAIR MACMILLAN: Mr. Chairman, I move the board enter into an executive session pursuant to Idaho Code 74-206(1)(f) to communicate with legal counsel for the public agency to discuss the legal ramifications of and legal options for pending litigation or controversies not yet being

litigated but imminently likely to be litigated. I request that a roll call vote be taken and that vote be recorded in the minutes of this meeting.

BOARD CHAIR BOWEN: We have a motion. Do we have a second?

BOARD MEMBER STEELE: Second.

BOARD CHAIR BOWEN: We have a motion and a second.

Is there any discussion?

Hearing none, we have a motion and a second. We'll now conduct a roll call vote.

Elaine.

BOARD CLERK GANINO: Mark Bowen.

BOARD CHAIR BOWEN: Aye.

BOARD CLERK GANINO: Dr. Randy MacMillan.

VICE CHAIR MACMILLAN: Aye.

BOARD CLERK GANINO: Carol Mascareñas.

CAROL MASCAREÑAS: Aye.

BOARD CLERK GANINO: Clayton Steele.

BOARD MEMBER STEELE: Aye.

BOARD CLERK GANINO: Pat Purdy.

BOARD MEMBER PURDY: Aye.

BOARD CHAIR BOWEN: The motion is carried.

We'll now move into executive session.

(EXECUTIVE SESSION COMMENCED.)

BOARD CHAIR BOWEN: I'll now entertain a motion to get out of executive session.

VICE CHAIR MACMILLAN: Mr. Chairman, I move that the board resolve out of executive session and that the meeting of the minutes reflect that no action was taken during the executive session.

BOARD CHAIR BOWEN: We have a motion.

Do we have a second?

BOARD MEMBER MASCAREÑAS: I second.

BOARD CHAIR BOWEN: We have a motion and a second.

Elaine, will you take the roll, please.

BOARD CLERK GANINO: Yes, Mr. Chairman.

Mark Bowen.

BOARD CHAIR BOWEN: Aye.

BOARD CLERK GANINO: Dr. Randy MacMillan.

VICE CHAIR MACMILLAN: Aye.

BOARD CLERK GANINO: Carol Mascareñas.

BOARD MEMBER MASCAREÑAS: Aye.

BOARD CLERK GANINO: Clayton Steele.

BOARD MEMBER STEELE: Aye.

BOARD CLERK GANINO: Pat Purdy.

BOARD MEMBER PURDY: Aye.

BOARD CHAIR BOWEN: Motion carries. We're now back on record after executive session. We're

moving to agenda item no. 2, discuss and adopt order relative to motions filed on May 23rd, 2024. Petitioners motion for clarification and/or reconsideration and respondent's and intervener respondent's joint motion for reconsideration and/or clarification of final order.

This is an action item to discuss and make a decision prior to service of the written order. I'll entertain a motion.

VICE CHAIR MACMILLAN: Mr. Chairman, I move that the board order the following:

Petitioner's motion for clarification and/or reconsideration is denied. The joint motion for reconsideration and/or clarification of final order is granted in part and denied in part.

The Board of Environmental Quality clarifies its decision as to the effective date of the final order. The Board of Environmental Quality denies the request to reconsider its decision on the ambient arsenic concentration issue.

The Board of Environmental Quality denies the request to reopen the proceedings or hold additional hearing before the board.

The Board of Environmental Quality

denies the request for additional clarification or instructions to the hearing officer.

BOARD CHAIR BOWEN: We have a motion.

Do we have a second?

BOARD MEMBER STEELE: Second.

BOARD CHAIR BOWEN: We have a motion and a second. That was Clayton who seconded.

Is there any discussion? I'm going to go through the roster for any discussion.

Dr. MacMillan, any discussion?

VICE CHAIR MACMILLAN: None.

BOARD CHAIR BOWEN: Carol Mascareñas, any discussion?

BOARD MEMBER MASCAREÑAS: No comments.

BOARD CHAIR BOWEN: Clayton Steele, any discussion?

BOARD MEMBER STEELE: No.

BOARD CHAIR BOWEN: Pat Purdy, any comments?

BOARD MEMBER PURDY: No.

BOARD CHAIR BOWEN: We will call for a vote.

Elaine, would you call for a vote, please.

BOARD CLERK GANINO: Yes, Mr. Chairman.

Mark Bowen.

BOARD CHAIR BOWEN: Aye.

BOARD CLERK GANINO: Dr. Randy MacMillan.
VICE CHAIR MACMILLAN: Aye.
BOARD CLERK GANINO: Carol Mascareñas.
BOARD MEMBER MASCAREÑAS: Aye.
BOARD CLERK GANINO: Clayton Steele.
BOARD MEMBER STEELE: Aye.
BOARD CLERK GANINO: Pat Purdy.
BOARD MEMBER PURDY: Aye.
BOARD CHAIR BOWEN: The motion is carried.

The board will issue our final written final order either today or tomorrow depending on signatures.

We've reached the end of our agenda. I'll entertain a motion to a adjourn.

VICE CHAIR MACMILLAN: So moved.
BOARD MEMBER STEELE: Second.
BOARD CHAIR BOWEN: We have a motion and a second.

Will you call roll call vote, Elaine.

BOARD CLERK GANINO: Yes, Mr. Chairman.

Mark Bowen.

BOARD CHAIR BOWEN: Aye.
BOARD CLERK GANINO: Dr. Randy MacMillan.
VICE CHAIR MACMILLAN: Aye.
BOARD CLERK GANINO: Carol Mascareñas.

BOARD MEMBER MASCAREÑAS: Aye.
BOARD CLERK GANINO: Clayton Steele.
BOARD MEMBER STEELE: Aye.
BOARD CLERK GANINO: Pat Purdy.
BOARD MEMBER PURDY: Aye.
BOARD CHAIR BOWEN: We stand adjourned. Thank you everybody. Thanks for your participation.
(Meeting adjourned.)

CERTIFICATE OF CERTIFIED SHORTHAND REPORTER

STATE OF IDAHO)
) ss.
COUNTY OF ADA)

I, MISTI L. ALCALDE, Certified Shorthand Reporter and Notary Public in and for the State of Idaho, do hereby certify:

That the proceedings were transcribed by me or under my direction, to the best of my ability;

That the foregoing is a true and correct transcription of all proceedings, to the best of my ability;

That I am not a relative or employee of any attorney or party;

I further certify that I have no financial interest in the event of the action.

WITNESS my hand and seal this 20th day of June, 2024.



MISTI L. ALCALDE
RPR and Notary
Public in and for the
State of Idaho.

My Commission Expires: 7-7-27

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BEFORE THE BOARD OF THE ENVIRONMENTAL QUALITY
STATE OF IDAHO

IN THE MATTER OF AIR QUALITY PERMIT TO CONSTRUCT P-2019.0047	
NEZ PERCE TRIBE, IDAHO CONSERVATION LEAGUE, and SAVE THE SOUTH FORK SALMON, Petitioners,	BEQ Case No. 0101-22-01 OAH Case No. 23-245-01
vs.	
DEPARTMENT OF ENVIRONMENTAL QUALITY, Respondent.	
and	
PERPETUA RESOURCES IDAHO, INC., Intervenor.	

REPORTER'S TRANSCRIPT OF PROCEEDINGS:

HEARING DAY 1

9:00 a.m. at 1109 South Main Street, Suite 220,

Boise, Idaho

On October 17, 2024, before

Hearing Officer Dylan Lawrence

Reported by:
Vanessa S. Gosney, CSR #752, RPR

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Also Present: Tiffany Floyd
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Michael Bogert
Mike Simon
Will Tiedemann
Ian von Lindern
Emily Schilling
Kevin Lewis
Faith Quigley
Marie Kellner
John Robison
Lynn Lewinski

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P R O C E E D I N G S

HEARING OFFICER LAWRENCE: We are here in the matter of the air quality permit to construct P-2019-0047. It is OAH case number 23-245-01 and DEQ case number 01-01-22-01.

My name is Dylan Lawrence. I am acting as a hearing officer in this matter. We obviously have lots of people in attendance. Vanessa, the court reporter, has already taken down everybody. So just in terms of introductions, I am thinking if counsel who are actually questioning witnesses in the hearing can introduce themselves and I will start with DEQ.

MS. YOUNG: Hannah Young, representing the Department of Environmental Quality. I am with the attorney general's office.

HEARING OFFICER LAWRENCE: And how about Perpetua?

MS. HANCOCK: Nicole Hancock with Stole Rives.

HEARING OFFICER LAWRENCE: How about for the petitioners? And I realize we have a few different petitioners. We will start with the ones in the room and then move to Zoom.

MS. THROWER: Julia Thrower for Save the South Fork Salmon.

MR. HURLBUTT: Bryan Hurlbutt for Nez Perce Tribe and Idaho Conservation League.

HEARING OFFICER LAWRENCE: Thank you. Again, my name is Dylan Lawrence. I am acting as the hearing officer here.

Any stipulations that the parties have come to that we need to talk about on the record before we get started?

MS. YOUNG: Yes. The parties did stipulate that Kevin Schilling, who is our first witness that we will be asking questions of, has been stipulated to be an expert witness in this matter.

HEARING OFFICER LAWRENCE: And counsel for the other parties, do we agree with that?

MR. HURLBUTT: Yes.

MS. HANCOCK: Yes.

MS. THROWER: Yes.

HEARING OFFICER LAWRENCE: Thank you.

So this hearing is being recorded by the court reporter, Vanessa, at the front. And we are recording it on Zoom as well.

And we also agreed that because the parties are doing prehearing statements and

post-hearing written statements that we don't need to open up with opening statements or anything like that.

So are there any other preliminary administrative matters we need to talk about before we let DEQ go? We did talk about order of presentation. It will be DEQ, then Perpetua, and then the petitioners in order of presentation. Anything else we need to talk about before we begin the questioning?

MS. YOUNG: Hearing officer, I would just confirm that DEQ is going to start with Exhibit No. 100 per the parties' discussions.

HEARING OFFICER LAWRENCE: Okay.

MS. YOUNG: So that's my plan.

HEARING OFFICER LAWRENCE: Okay. All right. Anything else?

Okay. I think DEQ is ready. We can swear the witness now.

KEVIN SCHILLING,

a witness having been first duly sworn to tell the truth, the whole truth and nothing but the truth, was examined and testified as follows:

DIRECT EXAMINATION

BY MS. YOUNG:

Q. Again for the record, my name is Hannah Young, and I represent the Department of Environmental Quality.

MS. YOUNG: I know we don't have any microphones so if folks can't hear me, or Bryan, if you can't hear me please let me know and I am happy to try and speak up.

Q. BY MS. YOUNG: Good morning.

A. Good morning.

Q. Kevin, can you start by just stating your name and, again, spelling your last name for the record?

A. Kevin Schilling, S-C-H-I-L-L-I-N-G.

Q. Thank you. Where are you currently employed?

A. The Idaho Department of Environmental Quality.

Q. And what is your current title?

A. Stationary source air modeling supervisor.

Q. Great. How long have you been in that role?

A. Approximately 20 years.

Q. Okay. Now, I know this may be hard to give me an exact number, but in your time at DEQ, do you think you could give me your best guess as to how many air quality permits you have been involved in developing?

A. There will be some large air bars on that, but I would say hundreds, maybe closer to a thousand. It's really difficult to tell because I'm involved in both supervising over review of those as well as actively involved in other projects.

Q. Right. So hundreds would be at least a fair guess, a good guess?

A. Yes.

Q. Great. So you've touched on this a bit, but in your opinion, what does it mean to develop a permit?

A. What it involves is we receive an application. It is reviewed and emission estimates are reviewed and regulatory review as well to see

what regulations apply to the proposed project. And then we have -- it kind of goes in two different directions to both the permit writer and to a modeling review analyst.

The modeling review analyst, his or her job is to evaluate whether the proposed project will cause or contribute to a violation of a standard or a TAPs increment. They write a modeling review memorandum to the permit writer.

The permit writer is in charge of reviewing emission estimates. And then the modeler will also make recommendations on important permit limits that are needed to ensure compliance ultimately. And then the permit writer drafts the permit. And sometimes it goes through public comment and then final permit issuance.

Q. Perfect. Thank you.

So it sounds like the development of a permit can be quite the task.

A. Sometimes. It highly depends. It is highly variable.

Q. Sure.

A. Some are easy and some are very complex.

Q. Fair enough. Thank you.

And again, just a ballpark, but of the

hundreds of permits you have been involved in developing, how many included a TAPs analysis? And just moving forward, when I say "TAPs" or "TAP," I am referring to a toxic air pollutant.

A. I would say most all of them. So again, TAPs, if absolutely nothing else, there's applicability of whether we need to do modeling for the TAPs. And given the large number of TAPs, most of the projects do involve modeling.

Q. Great. So again, it would be hundreds of permits?

A. Yes.

Q. Thank you.

Do you consider yourself a toxicologist?

A. Not at all.

Q. Okay. And why not?

A. My educational background is not in toxicology, although I have taken some course work that touches on toxicology. Nor does my work role involve toxicology work.

Q. Perfect. Thank you.

Are you familiar with the DEQ's rules for the control of air pollution in Idaho?

A. Yes.

Q. Describe your familiarity.

A. I would say I'm very familiar with them. Starting all the way back in graduate school where we had a project that required putting together a permit application and involved contacting the Idaho air quality bureau at that particular time. So that was kind of my first introduction to Idaho rules.

My first job right out of grad school was with DEQ as a program development specialist. That involved working on a large public comment project that involved going through some PSD regulations, so I became quite familiar there.

I was a short timer the first time at DEQ and left for Morrison Knudsen Corporation in their environmental group, which was basically consulting work. Shortly after I took that position, we were hired by the Department of Energy, at that time called the IMEL, to produce an air permitting handbook, which I was one of the principal authors of that. We also did some permitting work for, of course, the MK rail shop at that time. So we did their permitting work and some other permitting work as well. And that was all before -- well, then in -- I almost forgot about this.

In the early 1990s, while I was at MK, DEQ started down the path of taking their toxics policy and promulgating that into regulation. And I was on the Idaho Association of Commerce and Industry. And being familiar with the rules and policy fairly well, I was put on the chairman of the air toxic subcommittee at that time, and we met with DEQ and others in developing those regulations. Unfortunately, I had to leave that position for other project obligations, so I wasn't able to be an intimate part of that process through -- all the way through promulgation.

Q. Sure. So it sounds like, based on everything you have described, you're very familiar with the air rules?

A. Yeah.

Q. Would that be a fair assessment?

A. I believe so.

Q. Great. And did you prepare an expert declaration in this matter?

A. Yes.

Q. And did you review it before it was filed?

A. Yes.

Q. I would like to hand you a copy of your

declaration, which I have marked as Exhibit 100. And then I have a copy for the other parties.

Is this a true and accurate copy of the declaration you submitted? And feel free to take a look at it.

A. To the best of my knowledge.

Q. Great. Thank you.

MS. YOUNG: Hearing officer, I would move to admit Mr. Schilling's declaration into the record as expert testimony and mark it as Exhibit 100.

HEARING OFFICER LAWRENCE: Approved.

(Hearing Exhibit No. 100 admitted.)

MS. YOUNG: Thank you.

Q. BY MS. YOUNG: In advance of today's hearing, Kevin, did you review the other expert declarations submitted by the parties?

A. Yes, I did.

Q. And have you previously been qualified as an expert in this contested case?

A. Yes.

MS. YOUNG: So again, I know there has been a stipulation, but just formally for the record I would move to formally qualify Mr. Schilling as an expert in this matter.

HEARING OFFICER LAWRENCE: Any objections

from any of the parties?

MS. HANCOCK: No objection.

MS. THROWER: No.

HEARING OFFICER LAWRENCE: Okay. Granted.

Q. BY MS. YOUNG: Okay. Thanks for all of that background information.

Let's talk a little bit about the rulemaking history which you have already alluded to. But in your declaration you stated that you participated in the development of Idaho's TAP permitting regulations in the mid '90s; is that correct?

A. Yes.

Q. And you spoke a little bit about this, but could you just again reiterate what the purpose of that rulemaking effort was?

A. Primarily to transform a policy which the regulated community and probably other stakeholders as well saw as not nailed down well enough; wanted something more concrete that could be consistent, predictable.

Q. Great.

A. And focusing on something that would be both easy for industry to use as well as protective of public health.

Q. Great. As the regulations were being developed at that time in the '90s, can you describe the thought process about relying on EPA's unit risk factors?

A. Yes. Going all the way back to the toxics policy that was used in permitting, the cornerstone of that was focused on project risk. In other words, any particular project, whether it is a new facility or a modification, not causing a risk to exceed one in a million or one in 100,000, some things changed with T-RACT going from policy to regulation. And I am just focusing on the carcinogenic parts of it today.

Q. Great. So you mentioned that sort of the cornerstone would be this project cancer risk.

What was the regulated community's reaction to that threshold?

A. Well, you know, there's always a little bit of pushback. One in a million cancer risk is a very small increment of risk, and on the IACI subcommittee I recall having all sorts of nice little demonstrations of how operation of a wood stove over the whole year would cause a risk to the neighbors of a certain level. So there was some struggles in establishing that one in a million

cancer risk. And then that moved into the one in 100,000 provided you use T-RACT.

Of course the URF establishes that link between the risk factor and developing an easy-to-use representation of that being a concentration that represents a one in a million risk given a 70-year exposure.

HEARING OFFICER LAWRENCE: Counsel, can I jump in with a question real quick?

MS. YOUNG: Absolutely.

HEARING OFFICER LAWRENCE: Since it has come up, can you just explain generally for me what unit risk factors are?

THE WITNESS: It would probably be best explained by our toxicologist, but it is basically, and make sure I get this right, the risk associated with exposure of one microgram per cubic meter over a 70-year lifetime.

HEARING OFFICER LAWRENCE: So the 70-year lifetime is sort of built into the unit risk factor?

THE WITNESS: Yeah. Yeah. That's the lifetime, not necessarily the exposure duration.

HEARING OFFICER LAWRENCE: Okay. Thank you.

MS. YOUNG: That's great. Thank you.

Q. BY MS. YOUNG: So just to recap there, it sounds like, based on your experience, the regulated community saw that threshold as stringent?

A. Yes.

Q. Does reliance on the URFs remain a central piece of the TAPs regulations today?

A. Yes. I believe it is really the cornerstone of the whole TAPs program for regulating carcinogenic compounds. You know, maintaining that project risk under one in a million or one in 100,000 when T-RACT is used.

And even in the 2019 rules, the definition of toxic air pollutant carcinogenic increments, it, in fact, references the hundred in a million cancer risk being the criteria, and that the AACCs are an expression of that for a continuation exposure over the lifetime.

Q. And you alluded to this, but in your example of a wood stove, you know, I guess through that example you are sort of illustrating, if I'm understanding you, that there's a lot of inherent risk out there. And when you compare that inherent risk to one in 1 million, one in 1 million would be really small.

Is that an accurate assessment of what you were explaining?

A. Yes, that's my interpretation.

Q. Perfect. Great.

But in most cases or the majority of applications that you see at DEQ, are you analyzing the URF?

A. We're not analyzing the URF. It is in there as a link between the AACC and -- it essentially documents how we came up with the AACC.

Q. Sure.

A. Now, in the regulated community during the development of these regulations, especially the IACI group, it is primarily larger Idaho industries. We have sugar beet factories, potato processors, pulp mills, phosphate fertilizer facilities. All of these facilities we tend to permit on a permanent basis. And they also have relatively consistent operations and consistent emissions from year to year. They may vary within each year, but year one is going to look -- usually look pretty close to year two and year three and et cetera. So the easiest way to regulate that and handle it is to have an increment that's expressed as an annual value.

That way industry goes back -- and the rest of our permitting actions are focused on -- annual is a very nice nugget of time to look at because we have annual PM10 -- well, at that time we had annual PM10 standards, and we have annual PM2.5 standards and NAAQ standards, so we tend to regulate on an annual basis a lot of things. So it becomes easy to use to regulate carcinogenic TAPs on that annual basis.

Q. Sure. Thank you for that explanation.

You stated earlier, I suppose, that you reviewed Mr. Tiedemann's declaration in this matter; is that correct?

A. Yes.

Q. Exposure duration adjustments were both considered and rejected during this 1990s rulemaking process that we were just discussing.

Do you recall him saying that?

A. Yes, I do.

Q. As someone who participated in the rulemaking process, is that in line with your recollection?

A. Not exactly. I think it demands some further explanation. There was a lot of talk about short term, the less than five years, and debate

about that. And there was certainly some statements made about not imposing a whole 70 years' worth of emissions into a less than five-year period. And of course we now have the short-term allowance within the air toxics rules for that.

However, given the nature of the regulated community and what DEQ typically saw, no one foresaw the idea of a temporary project of, like, 16 years or 50 years or 25 years. It's like short-term projects were remediation projects, pilot plants, those type of things. So the regulators didn't -- we didn't really foresee a need for a 16-year duration project. So it just wasn't evaluated, wasn't discussed.

But the cornerstone of the rule still remained a project-imposed risk of one in a million or one in 100,000 with T-RACT.

Q. Thank you.

So that one in 1 million was just assumed to be for a 70-year lifetime?

A. Yes.

Q. Because the project was permanent?

A. Yes.

Q. Thank you.

So again, just to clarify, it sounds like what you're saying is that it wasn't a rejection, it just wasn't really discussed or anticipated?

A. Yes, to the best of my recollection.

Q. And did you review Dr. von Lindern's declaration?

A. Yes, I did.

Q. And in his declaration he also discusses the development of the TAPs rules. And he discusses that the rules were intended to be easy to apply but prescriptive and strict enough to protect public health.

Do you recall him saying that?

A. Yes.

Q. And what is your reaction to that statement?

A. Some agreement. There was a big focus on easy to use, and of course a big focus on needing to be adequately protective of public health. And of course a fair amount of debate amongst everyone about what that means.

I really believe that the intention and the record shows that, again, we come back to project-imposed risk of one in a million for a

project being the primary criteria rather than an annual value never to be exceeded.

Q. Great. Thank you.

Okay. Let's move on and discuss the analysis that DEQ and Perpetua performed for the arsenic emissions for this project.

But I want to start by having you walk us through your typical permitting process. And I recognize you did a little bit of this earlier, but if you will humor me and do it again a little bit more where TAPs modeling is involved. So just how a typical permit comes in and how you review it.

A. Uh-huh. Well, first of all, when it first comes in, our overriding requirement is, is in the rules, that we must -- the application must demonstrate to the satisfaction of the department that operation of the proposed project won't cause or contribute to a violation of a National Ambient Air Quality Standard or TAPs increment. So that's the overriding thing.

And for permitting purposes, we go to Section 210, which addresses the TAPs pre-construction compliance demonstration requirements. And if an applicant uses Section 210, it's determined that they comply with Section

161, which is the overriding rules for control of toxic substance to a point that you won't unreasonably cause adverse health impacts.

Sorry for the butchering of the exact language.

Q. I'm sorry to interrupt, but if it would be helpful, we are also happy to pull up the rules if that would be helpful for either the hearing officer or the witness to have the rules.

HEARING OFFICER LAWRENCE: It is up to the witness. I have my own copy here.

THE WITNESS: I think I have summarized.

Q. BY MS. YOUNG: I think you have accurately summarized them.

A. Yeah. So within Section 210, the application has estimated emissions for the toxic air pollutant associated with their proposed project. They've also submitted like a modeling analysis of those emissions that then demonstrate that they'll be under those AACCs. And we review those analyses, the inputs, how the model has been run. Often that involves an iterative process going back to the applicant because there's deficiencies or we didn't feel their take on it was conservative enough, so we may go back and request

that they do something different. And they may need to completely rework their application in order to address those deficiencies. And we may call it incomplete, and then when it comes back we will reassess their revised submittal.

Q. Great. So it sounds like, based on what you're describing there, a lot of refinements that can occur.

Is that true?

A. Yes. There can be -- they can be as simple as providing just additional justification for something to where, you know, it just gets us to that extra confidence level where we go, okay, that's good enough.

Or it can be a complete reworking to where they have to go back and add additional controls somewhere or move something to a different location to where it has a different impact or fundamentally change their process in extreme cases.

Q. Do these refinements become permit conditions?

A. Yes. What the facility needs to do to demonstrate compliance, what they model has to be using emissions that are either design capacity,

something that is inherently limited by the nature of the process, or specifically limited by a permit condition.

Q. Okay. So with that in mind, now considering the permit application that came in for this Stibnite Gold Project, can you briefly walk us through how that process occurred?

A. Yeah. I will use a bit of an abbreviated part.

Q. I think everybody would appreciate that.

A. We will start at the initial application that came in that had -- I'll also focus on the carcinogenic TAP since that is why we are here.

When the permit initially came in it had the TAPs modeling demonstration that showed compliance with the AACCs -- using the AACCs as an annual benchmark for compliance. So everything was fine there. We drafted, we did a modeling review memorandum, went to the permit writer, the permit was drafted, went out for public comment. There were some concerns they expressed about applicability of certain sources that were not included in the analysis, so there was a whole lot of regulatory uncertainties. And both DEQ and Perpetua took a deep dive back into that and

decided, well, yeah, we should -- we need to include those other emission sources in the analyses.

Q. So just to pause right there to make sure I'm understanding this. Sorry to interrupt. It sounds like based on that first application and the first sort of refinement was to be more conservative and include additional sources?

A. Well, yeah. There was debate about whether it's just being more conservative or whether we're addressing a deficiency in the rules.

Q. Sure. That's fair.

A. And I'm not the permit writer. And luckily I was able to stay out of the details of that particular issue. But anyway --

Q. Yes. Go ahead.

A. -- it involved a need to rework things. And there were several options Perpetua could take. They could take a refined look at how it's being regulated, how emissions are being controlled and a number of different things.

So through a lot of work, Perpetua landed on bringing up the fact that, well, this is going to be a less-than-permanent source, a 16-year life of project source rather than a full 70-year

or permanent project.

So then in looking at our rules, it definitely was something we have not seen very often before. So in looking at that, because the one in a million cancer risk is the cornerstone, addressing for the exposure duration was appropriate given my understanding of how the URF and risk assessment calculations would be conducted.

Q. Perfect. Thank you.

So again, this would be a typical situation wherein you start with an application and the analysis gets refined over time?

A. In that way it's typical.

Q. Sure. I understand there's a lot that was atypical about this particular project.

A. Yes. But making refinements during the process is unfortunately more typical than atypical.

Q. Sure. Thank you.

So you've talked about how the air rules work related to a TAPs analysis. But in your declaration you specifically discuss how the rules support DEQ's analysis and Perpetua's analysis in this permit.

So can you just walk us through or touch on any of the rules that you think are really relevant to the analysis that was performed for the project?

A. Well, one of the big ones in the 2019 rules, and maybe this is one worth bringing up --

Q. Yeah. So just to take a pause then really quick, Kevin, because I think I know where you are going with this. I'm going to ask Michael to share his screen on the Zoom and pull up the 2019 version of the air rules, which I believe you could just take judicial notice of the rules and they don't need to be entered into the record. And I also think they're just demonstrative at the point.

HEARING OFFICER LAWRENCE: Any other parties have concerns or objections?

MS. THROWER: No objection.

Q. BY MS. YOUNG: So if I was following where you were going?

A. Yeah, 125. Ambient air quality increments based on the probability of developing excess cancers over a 70-year lifetime exposure to one microgram per cubic meter, again a carcinogen, and expressed in terms of a screening emission

level or an acceptable ambient concentration for a carcinogenic toxic air pollutant. They're listed in 586.

Q. Perfect. So what is important about this definition?

A. I think one of the -- well, two things, the identification of one in a million cancer risk. The other thing I believe that's important is the link that says this is expressed in terms of the screening emission limit or the acceptable ambient concentration of a carcinogen.

So in my view, this again makes it clear that it focuses on a total project-imposed cancer risk rather than a specific year by year.

Q. Okay.

HEARING OFFICER LAWRENCE: Counsel, can I ask a quick question?

So the rules we have up on the screen now are rules that are not in effect right now?

MS. YOUNG: Yes. Thank you for that. If you would like me to answer or I can draw it from the witness.

HEARING OFFICER LAWRENCE: Please proceed, I just wanted to clarify.

Q. BY MS. YOUNG: So, yes, the hearing

officer just asked if we are looking at the 2019 rules; is that correct?

A. Yes.

Q. And so were these the rules that were in effect at the time the permit was issued in 2019?

A. Yes, I believe so.

Q. If I am doing my math right?

HEARING OFFICER LAWRENCE: I think the permit was issued in 2022.

Q. BY MS. YOUNG: Thank you. The application came in in 2019, but this was also in effect when the permit was issued in 2022?

A. I believe so, yes.

Q. Thank you for that.

HEARING OFFICER LAWRENCE: Thank you.

THE WITNESS: I am trying to remember when CBR.

Q. BY MS. YOUNG: Yes. 2019 and 2022 are sort of the major dispositive time periods, these were the rules that were in effect?

A. Yeah. They weren't remove -- this section wasn't removed because it was no longer -- because there was a fundamental change. We had a rule cleanup.

Q. Yes. And you don't have to worry about

explaining that.

HEARING OFFICER LAWRENCE: Just for my, was that part of the zero-based regulation effort?

THE WITNESS: Yes, it was.

HEARING OFFICER LAWRENCE: Okay.

Q. BY MS. YOUNG: Thank you.

Let's see here, so I interrupted you to bring this up. But you said in your review of the project you sort of started with this definition.

Are there any other rules you want to walk through in terms of the projects -- you know, the permit for this project?

A. We have all of Section 2010, which basically governs how the permit was evaluated from toxic air pollutant standpoint. And that contains the provisions for T-RACT given the factor of ten adjustment if more rigorous controls are used. It also contains the exclusion for sources that are regulated by specific federal rules, the NESHAP and NSPS. And then has some prescriptions of how the analyses are performed and then links back to Section 586, which contains both the screening emission levels, the unit risk factors, and the acceptable ambient concentrations for carcinogens which are expressed as annual averages.

So in Perpetua's case, in order to develop an appropriate factor to compare or an appropriate concentration to compare to the AACC, we needed to account for the exposure duration. So that's essentially all we're doing there, is it was a 16-year exposure duration rather than a 70-year exposure duration, which is the origin of the 16 over 70 factor.

Q. Thank you.

So based on the definition of 586 that you just read, would it be your opinion that the TAPs rules are increment based?

A. Yes.

HEARING OFFICER LAWRENCE: It might be helpful to explain that concept generally for me, what increments are and the relevance here.

MS. YOUNG: Yeah. Thank you.

THE WITNESS: The standards tend to be a limit that -- a total limit of what's in air quality, like we have the PM2.5 annual standard. And that accounts for what you would get if you took a monitor out there and monitored over the same period. So we have the impacts of everything there. We have the project, the whole rest of the facility, any neighboring facilities, and a

background that would need to be included in that.

So it's a standard. You have to figure out a way to be below that one way or another.

Q. BY MS. YOUNG: So just to pause right there. It is taking into account background, for one?

A. Yes.

Q. And for two, it is an annual limit that gets placed on the facility or the project?

A. Yeah. In the case of the annual standard we would have limits to the facility that would control their annual emissions.

Q. Perfect. Thank you. Versus an increment to the hearing officer's question, how does that differ?

A. An increment is just a base-allowed impact for that project. So it doesn't concern itself with what goes on at the whole rest of the facility or what goes at the neighboring facility or what is already there for background. It says you can do this no matter what.

Q. And for 586 and the TAPs rules, the increment is the lifetime, the one in 1 million over a lifetime?

A. One in 1 million over a lifetime of

exposure.

Q. 70 years?

A. Yeah. It can get confusing of going between what's the duration of the exposure versus the lifetime of the receptor.

Q. Perfect. Thank you.

I feel like I've really spent a lot of time on the rules, so thanks for humoring me on that.

In Section 586 you reference that it uses and references the URFs, correct?

A. Yes.

Q. Now, I know this is not the case, but the rules could have used only the AACCs potentially, correct?

A. Yes, they could have. There would have been, in my opinion, no need to put in the URFs on that or draw out such a focus of project risk being limited to one in a million.

Q. If the rules only contained the AACC and did not reference the URFs, correct?

A. Yeah. It would be less clear that it's project risk we're concerned about. I wouldn't say it would be clear that the intent would be just an annual standard because through the rulemaking

process and that entire thing and background, project risk was always sort of the cornerstone focus.

Q. Perfect. Thank you.

So in your opinion, inclusion of the URF demonstrates what?

A. That it's a project cancer risk that is the focus rather than an annual strict increment.

Q. Perfect. Thank you.

HEARING OFFICER LAWRENCE: Apologies, if you have already said. Can you explain why that is? Why the presence of the URF in Rule 586 makes it a project-based risk analysis?

THE WITNESS: It is the combination of that and the definition of the toxic air pollutant carcinogenic increments that we just read through earlier that really says it is cancer risk that is the important thing. The URF provides the vehicle that identifies the relationship between an exposure and cancer risk. So it's kind of a tool that you can use to generate cancer risks for an alternate exposure duration.

HEARING OFFICER LAWRENCE: Okay. Thank you.

Q. BY MS. YOUNG: So in your expert opinion, why is an adjustment based on project

duration appropriate?

A. If you didn't account for such an adjustment, you would be overstating the total amount of emissions that would come from the project. And if you overaccount for the total emissions coming from the project, you would overaccount for the carcinogenic risks.

Q. So to make sure I am understanding, duration then is directly related to the risk?

A. Yes.

Q. Okay. So regarding the five-year rolling average contained in the permit, can you explain why this was an appropriate measure?

A. It goes back to the same cornerstone of the rules being project-imposed risk. As long as project-imposed risk is the criteria and we have a duration of the project of 16 years, what really matters for demonstrating, whether it complies or not, is where are we at after 16 years.

Now, we use something less than 16 years as a responsible vehicle to identify when things might -- you know, if they might be going wrong at an earlier time.

So often for industries that have consistent year-to-year operations, we, again,

center in on that one-hour period.

For something such as Perpetua that has highly variable operations and highly variable emissions, it is not appropriate and is overly constraining to use that one-hour interval. So it was decided that a five-year interval would be much more appropriate for regulating the facility.

Q. So in a completely different context, if the standard was annual, then five-year rolling average wouldn't make sense, right?

A. No, it wouldn't.

Q. But here it is not annual, it is a 16-year project life standard, for lack of a better word, correct?

A. Correct.

Q. So five years is less than that actual standard?

A. Yes.

Q. And it provides you, you said -- I think you used the word "responsible," it is sort of the responsible way of making sure that compliance is being achieved during the project and not at the end when it is sort of too late to make any adjustments.

A. Yes. Exactly.

Q. Perfect.

And you mentioned the variability that this project has, so I guess I will just ask you. Is it your understanding that the mining project -- this particular mining project has a lot of variability year to year?

A. Yes, much more than we see in the vast majority of our permitting projects.

Q. And you don't have to get into the weeds here, but what is some of that variability that you would see at this project?

A. As they open up, and again, Perpetua's team would be better able to describe that, but as they open up new areas of a mine you have something in one area that is being opened up and then a different year a different area opens up. So in opening up those areas it involves different stages of excavation and hauling and different processing. So it's just there's a lot of moving parts there.

Q. Okay. So what impact does this year-to-year variability have on ultimate compliance?

A. Really, the year-to-year variability doesn't affect ultimate compliance. And perhaps a good way to think of that might be is if we have a

pitcher of water. And let's say that the water contained in the pitcher represents ore to be processed. And because of the direct proportionality of things, it also represents the emissions associated with processing that ore. And again, the direct proportionality also would represent the impacts and ultimately the cancer risk.

Now, to the side of that let's have a pan that contains the amount that's processed and all the way up to allowable cancer risk.

So as I take that picture of water I can pour it into the pan in different ways. I can pour it in fairly fast, or intermittently, a little bit now, a little bit later. Slow and continuously. Jerky. That doesn't matter. What matters is that the pan that limits the risk that all the water that's poured is contained in the pan, if that makes sense.

Q. It does make sense. So the way you're pouring it represents the variability from year to year.

A. Yes.

Q. But the pan represents the ultimate risk.

A. Yeah.
Q. Perfect. Thank you.
So in this context, and especially in light of the analogy you just provided, the five-year rolling average makes sense?
A. Yes, it does. Because a little bit of jerks through that is immaterial in ultimate compliance.
Q. And just to double down on your analogy here. The permit does create some side boards as far as limits of ore to be processed?
A. Yes.
Q. So it is not like you can pour it all on day one, for example?
A. Right. I didn't get into making a perfect analogy there.
Q. It is a good analogy, I just wanted to create those side boards or have you discuss those side boards from the permit.
A. Yeah. There are shorter-term processing limits in there that, in fact, were needed not just for TAPs compliance but were primarily needed to assure compliance with the other standards, such as the 24-hour PM10.
Q. Perfect. Thank you.

And just one last question on this rolling average. It is a rolling average, correct?

A. Yes. Basically each year it shifts and drops off the later year and adds on the newer year.

Q. Perfect. Thank you for that clarification.

HEARING OFFICER LAWRENCE: How does that work in the first five years of the project life?

THE WITNESS: Well, at year five is when you then start evaluating that.

HEARING OFFICER LAWRENCE: Okay.

THE WITNESS: I'm not the permit compliance person, so I may be able to be corrected there some. But that's my understanding.

HEARING OFFICER LAWRENCE: Okay. Thank you.

Q. BY MS. YOUNG: But it's not like it's at year five, at year ten, and at year 15?

A. No. It's at year five, and then year six, seven, eight, nine, and then moving on from there.

Q. And I imagine the first five years could have quite a bit of variability as the mine is just becoming operational?

A. I would suspect.

Q. Thanks.

Let's move on to the west end pit issue. And if you want to reference it, it starts on Page 10 of your declaration when you start discussing the west end pit.

A. Page what?

Q. Ten, which is record number 3926. This is Exhibit 100.

Can you explain how the permit limited, let's start with west end pit production?

A. Yes. There's sort of two main limits. There's a total mine limit in there of 788.4 million tons. And then there is a west end pit-specific limit of 50 percent of that, which is 394.2 million tons.

Q. And then how about a limit to non-west end pit production?

A. A limit to the non-west end pit production sources was not needed because even if 100 percent of the production is from non-west end pit sources, we're still in compliance.

Q. Perfect.

Can you explain further why a 50 percent limit wasn't explicitly included for the non-west end pit?

A. Yeah. Maybe if you will entertain me a little bit to make a little bit of an example. I was trying to think of a way to explain this beyond mining. Given that it is Halloween season and we go trick or treating, little Timmy has a basket of candy he got from trick or treating.

HEARING OFFICER LAWRENCE: I think I will need to sample those.

Q. BY MS. YOUNG: Go ahead, Kevin.

A. Timmy's mom is concerned about how he eats, so she said you can only have eight pieces of candy.

Q. Excuse me, eight pieces of candy over how long of a duration? Or I guess it doesn't matter.

A. Well, in this case we'll bring it closer even though she's a really strict mom, just said that's all he can have is just eight pieces.

Q. Perfect.

A. So that's the whole project.

Timmy's mom is also concerned about Timmy getting a little bit overweight so she is concerned about his calories. These Snickers, let's just say they are 100 calories a piece. And then we have sugar-free Werther's Originals. They

are a lot less, let's say 25.

So of course Timmy wants to have all eight Snickers, but that isn't going to work. That violates his calorie intake. So if we wants mainly just Snickers --

Q. And I don't think you told us what the calorie limit was?

A. 500 calories.

Q. Okay.

A. I am having to use math in my head right now.

Q. So just to make sure I'm understanding. If he had eight Snickers that would blow through his 500-calorie limit?

A. Yeah. He would be at 1,000 calories and he would be in violation and sent to his room.

So he can have four Snickers and a collection of Werther's Originals with it and be fine. Or if he just has nothing but Werther's Originals he is still well below his 500-calorie limit.

So it's kind of the same way with the west end pit and the non-west end pit sources. They are kind of sugar free with regard to the impact. So we really don't need to set a limit,

although we have an overall limit of Timmy still can't have more than eight pieces total. So there is still that limit. And if all eight pieces are Werther's Originals, he can't have any Snickers.

So it is kind of the same thing with the west end pit. If all the of the production is non-west end pit production, that leaves no room for any west end pit production.

Q. So the west end pit has the explicit limit in the permit, correct?

A. Yes.

Q. And there is also, as you mentioned, just to underline this, an overarching limit?

A. Yes. The total.

Q. The total limit, thank you. And it is your opinion that between those two limits, that's sufficient?

A. Yes. This still keys in on the fact that the important criteria is project imposed risk rather than treating the AACC as an annual limit in itself.

Q. Perfect.

HEARING OFFICER LAWRENCE: Can I ask a quick question, Counsel?

Is the reason the west end pit is sort

of the limiting factor, is it -- what are the factors that make that? Is it geography? Wind? Is it like the nature of the deposit in that particular location?

THE WITNESS: I think really the Perpetua crew would be best to address that. But the way it works out through the modeling is that those west end pit sources have a driver to the analysis given the location of where they are to ambient air locations. How the ore plays into that, I don't recall explicitly.

But both, yeah, wind, location of where the pits are at, the concentration of arsenic in it. All of those things play into where you have the maximum locations.

And through the analysis, air isn't as homogenous as a lot of people think about it. When we run our models, we have thousands of receptors and it is highly dynamic the way impacts are. So in other words, these impacts aren't all over the entire ambient air surrounding the plant, they are at specific areas.

MR. SHORT: Do you want to --

THE WITNESS: That would be useful.

So as you see there, where the west end

pit is, and the way the prevailing winds are, you can see how the west end pit is positioned to heavily impact that area just northeast.

HEARING OFFICER LAWRENCE: Do we know why the west end pit is more on the east side of the project?

THE WITNESS: Well, that, I can't speak to that one.

MS. YOUNG: So I can formally admit this. This is obviously a demonstrative of an exhibit in Kevin Lewis's declaration. So I could go ahead and move to admit Kevin Lewis's declaration as Exhibit 200?

MS. HANCOCK: 201.

MS. YOUNG: As 201. And we have copies of that which I can pass around. And I believe this is attached to his declaration.

HEARING OFFICER LAWRENCE: Any objections from any party?

MS. THROWER: I don't have any objection, but for Brian's purposes, do you have an REC number you can let him know?

MS. HANCOCK: I do.

MS. YOUNG: Thank you.

HEARING OFFICER LAWRENCE: It definitely

looks familiar to me, but I don't know if I can put my finger on it right now.

MS. YOUNG: It is 4145. So for the transcript it is record number 4145, Exhibit 201.

HEARING OFFICER LAWRENCE: To the extent you need a ruling from me, it is admitted.

(Hearing Exhibit No. 200 admitted.)

MS. HANCOCK: We already provided the record copy. I think we agreed we wouldn't exchange around the declaration.

MS. YOUNG: I'm sorry, for the record, the counsel previously discussed that anything contained in the electronic record doesn't necessarily need to be provided in hard copy if everybody has it.

Q. BY MS. YOUNG: Thank you for that tasty analogy.

In Dr. von Lindern's declaration, I'm looking specifically at Paragraph 19, he states that "DEQ misinterprets the purpose and function of the maximum one-year annual average ambient carcinogen concentration in implementing the TAPs rule."

MS. YOUNG: And again for counsel, that's on Paragraph 19 of his declaration.

THE WITNESS: Yes, I recall that.

Q. BY MS. YOUNG: In your recollection, do the air rules use the word "maximum" when referring to the AACCs?

A. No. The term used in the AACCs are an annual average.

Q. So is the term "one year" used in the rules?

A. No, I don't believe so.

Q. Does the addition of the word "maximum" make sense to you related to the AACCs?

A. I believe the term "maximum" misrepresents the intent of having the rules be applicable for a project total risk. I believe, again, treating the AACCs in this instance as the maximum allowable in any one year is overly restrictive for the facility.

Q. Perfect. Thank you.

In his declaration, in Dr. von Lindern's declaration, Paragraph 21, he also uses the phrase "margin of safety."

Do you recall reading that in his declaration?

A. Yes.

Q. Are you familiar with that term, "margin

of safety"?

A. Somewhat familiar with it. Not so familiar with it in the terms he was using, I believe. I am more familiar with margin of safety being used in the context of regulatory development. As an agency develops a rule you must impart a margin of safety. So in that regard I'm not real clear on understanding of the use of his margin of safety discussion.

Q. So to clarify, tell me if I have this correct. You're familiar with this terminology when it comes to building a regulation?

A. Yes.

Q. But not familiar when it comes to implementing a regulation?

A. Yes.

Q. Why would it be more appropriately discussed or used in the first context of developing a regulation?

A. Well, because you want to develop something that is -- has that margin of safety built into it, and then you design the rule around it so you don't have to reevaluate margin of safety when implementing the rule.

Q. Thank you. So in that same vein, do the

TAPs rules already contain that maybe margin of safety, for lack of a better word, or the conservative pieces that would be needed to create a margin of safety?

A. I believe they would have. Of course, it's always up for debate whether they did that to the satisfaction of various parties. But for example, some of the conservatisms within the rules are that we consider areas of applicability being any area external to the boundary of the mine. In other words, we are not just looking at where someone lives or where someone might live, it is anything that's not under the direct control of the mine.

And then beyond that, we're not making any adjustments for how long -- how many hours per day someone might be there or how many days per year. We're assuming 24 hours a day, 365 days a week [sic] for the entire duration of the exposure, which in this case is 16 years.

Q. So the 16 years, once you know what the project is going to be, you're not then also adjusting any of the other factors like, for example, if you knew it was only operating for eight hours, it is just 24 hours a day, 365 days a

year.

Is that accurate?

A. Right. It can get a little bit confusing because if Perpetua took a limit to limit their emissions to so many hours per day, that would be captured in their permit if they chose to take a permit limit for it.

Q. Sure.

A. And that would be accounted for in their emissions. But the exposure, that assumes that someone is at that receptor 24 hours a day, 365 days a year.

Q. Perfect. Thank you.

A. The assumption is, and the toxicologist would be better able to talk to this, but a conservatism built into the URF as well.

Q. Right. So let's see here, Dr. von Lindern opines that the five-year rolling average reduces arsenic concentrations making or creating an excess cancer risk by 45 percent.

Do you recall that statement?

A. Yes.

Q. Is that something that you would feel comfortable opining about as not a toxicologist?

A. Only to the extent of what I've been

talking about before that our whole position here, and this is the key of everything, is that it's a project risk rather than an annual risk. And if you buy that's what it is and we're not dealing with a year-by-year allowable impact, then all of these other things fall into place. The five-year averaging period, west end versus non-west end pit discussions one way or another there.

So everything hinges on that one concept of whether we're dealing with a project-imposed risk or an annual limit.

Q. So what you've been sort of referring to as the cornerstone of the rules, that's the piece of this analysis that you're comfortable opining on?

A. Yes.

Q. Perfect. Thank you.

So given the claim by Dr. von Lindern and Mr. Tiedemann that DEQ should take a stringent or a strict interpretation of the rules, what's your reaction to that statement or those assumptions?

A. I believe we take a stance with the rules that implements the rules to our best understanding and reasonable understanding of what

they are. We have a case where a lot of different stakeholders wish the rules were either more stringent or less stringent and would like to see them account for co-contributing sources, additive carcinogenic effects, other things that may have just come out in the last 30 years since the rules have been promulgated that deal with new toxicological concepts and whatever else. But we are dealing with the rules we have and we implement them to what we believe is a reasonable and fair assessment to our regulated community. And sometimes we face challenging things that don't completely fit in the box we anticipated them to fit in. And we look at the rules and interpret them accordingly. We firmly believe that making this assessment based on what's in the rules as defining project risk as the cornerstone. We feel it is appropriate to make that exposure duration adjustment.

Q. Thank you.

So based on what you just described, how would you specifically characterize Dr. von Lindern's assessment of the TAPs rules?

A. I believe it's overly restrictive in that it focuses on treating the allowable

carcinogenic impacts as a one-year limit as opposed to a total-project limit.

Q. Thank you.

So I have just two last questions for you.

In your opinion, based on everything we've just discussed, your experience implementing the rules, your personal knowledge of the rule history, et cetera, was the analysis for arsenic emissions performed by DEQ for the project a reasonable approach?

A. Yes. I believe it was not only reasonable, I believe it was the best interpretation of the rules for that. Again, focusing on the project cancer risk.

Q. Did you use sound science?

A. I believe so.

Q. And lastly, based on your experience and expertise, does the permit create an unreasonable -- excuse me, an unacceptable cancer risk?

A. Not as defined by -- not as acceptability is defined by our regulations. And the reasonableness as interpreted by our rules and regulations.

MS. YOUNG: With that I would just reserve time for any necessary redirect.

HEARING OFFICER LAWRENCE: Okay.

MS. HANCOCK: I have one clarification. I said that Mr. Lewis's exhibit was marked as 201. His was actually marked as 200. So if we can make that correction in the record.

MS. YOUNG: I don't have any further questions for Mr. Schilling at this time.

Thanks, Kevin.

HEARING OFFICER LAWRENCE: Okay. Thank you.

Do we want to take a quick break before we go into Perpetua?

MS. HANCOCK: I think a quick break would be great.

HEARING OFFICER LAWRENCE: Okay.

MS. YOUNG: I think 20 minutes to be conservative.

HEARING OFFICER LAWRENCE: Okay. So at about 10:25 we will start reconvening.

(Break taken from 10:07 a.m. to 10:31 a.m.)

HEARING OFFICER LAWRENCE: I think DEQ finished its direct examination of Schilling and next up we have Perpetua. Any other procedural matters we need to address before we do that?

MS. YOUNG: None from DEQ.

HEARING OFFICER LAWRENCE: All right. Please proceed.

CROSS-EXAMINATION

BY MS. HANCOCK:

Q. Thank you for your testimony already this morning, Mr. Schilling. I just wanted to cover a couple of points. The hearing officer had asked you a question about when that five-year rolling average period, what happens in the first five years.

Do you recall that?

A. Yes, I do.

Q. During that first five years under the permit, there are still conditions that would restrict the production limits that would be imposed on Perpetua; is that right?

A. Yes. Additional restrictions were needed to demonstrate compliance with the shorter term air quality standards such as the 24-hour PM10, the 24-hour PM2.5.

Q. And so just in simple terms, on a daily basis, do you recall what the production limit was under the permit on the operations?

A. Was it something around 188,000 tons per day, something around there. And with using the five-year rolling average I believe came out to be around 130-something-thousand tons per day. So there's a difference, but not -- it's not as though they could dump all five years into the first year.

Q. Okay. So just to be clear, if we just round off at 180,000 as the daily limit and 135,000 as the five-year rolling average daily limit for purposes of our discussion, they could produce up to 180,000 tons per day out of the mine, but they would have to operate in a manner that would allow them to average no more than 135,000 tons per day on that five-year rolling average basis; is that right?

A. Yes. Yes.

MS. HANCOCK: Mr. Foster, can you pull up the Rule 210, please?

Q. BY MS. HANCOCK: I want to just first start with subsection 12 of this rule. You're familiar with Section 210 that we're looking at here?

A. Yes.

HEARING OFFICER LAWRENCE: Quick clarification. Which version of these rules do we

have up?

MS. HANCOCK: This would be the 2022 rules.

Q. BY MS. HANCOCK: Under subsection 12B, as in boy, are you familiar with that section there where it says "Compare the source's or modification's approved T-RACT ambient concentration at the point of compliance for the toxic air pollutant to the amount of the toxic air pollutant that would contribute to an ambient air cancer risk probability of less than one to 100,000 (1:100,000)(which amount is equivalent to ten (10) times the applicable acceptable ambient concentration listed in Section 586)"?

Do you see that?

A. Yes.

Q. So once Perpetua opted for the T-RACT control provisions, the cancer risk probability analysis that you performed was to ensure that it operated below a risk probability of one in 100,000?

A. Yes, for a total project-imposed risk.

Q. And is this section in 210 subsection 12(b) what you applied when you were looking at Perpetua's permit?

A. Yes.

Q. Is there anywhere in here that you can see where it talks about annual emissions?
A. No.
Q. In fact, this section doesn't even say anything about an annual amount at all, does it?
A. No.
MS. HANCOCK: Mr. Foster, if we can go up to Section 210 under the title, "Demonstration of Preconstruction Compliance."
Q. BY MS. HANCOCK: Was it your understanding that under Rule 210 that DEQ could consider the production limits of the project as part of its evaluation and analysis?
A. Yes.
Q. And that's because the rule specifically allows you to look at the project design, equipment, work practice, and the operational requirements or any combination thereof?
A. Yes.
Q. Okay. And if we could look under 210.02 subsection D.
Did you understand that under this section DEQ could take into account the physical and operational limits that were described in the application from Perpetua?

A. Yes.
Q. Okay. And if we look at 210 subsection 04.
And under subsection 04 it allows you to also use and consider the applicable specialized methods that were described in subsections 09 through 12; is that right?
A. Correct.
Q. And then if we look at under 12 subsection D.
Did you understand that as part of DEQ's allowances under Section 210.12(d) that you were allowed to take into account and consider the emission limits from the project?
A. Yes.
Q. Thank you.
MS. HANCOCK: I have no further questions.
HEARING OFFICER LAWRENCE: I actually do have a quick question while we have the rule in front of us there.
So Mr. Schilling, my question is about C under subsection 12 there, where it says basically if you comply -- I think paraphrasing it is like if you comply with 586 then you've satisfied -- or maybe it is B. "If the source's or modification's

approved T-RACT" -- so "no further procedures for demonstrating preconstruction compliance will be required."

So my question, just out of curiosity, is what if you don't meet that condition in C? If you reference 586 and you're not showing that you're within 586's confines, what's the next step for compliance in that scenario.

THE WITNESS: If I am understanding the question correctly, they would basically be unable to meet 586 with the implementation of T-RACT, if they can't do that, the permit would be denied. Or if we discovered there was an error that would result in them not meeting that one in 100,000 risk, it may be kicked back to the applicant to rework the entire analysis. Because we can't issue the permit unless they can demonstrate to our satisfaction that it's met.

HEARING OFFICER LAWRENCE: So it is not like there is an alternative route. It is either you meet C in 586 or you don't.

THE WITNESS: Yeah.

HEARING OFFICER LAWRENCE: Okay. Thank you. That's helpful.

Okay. So time for cross-examination,

correct?

Bryan, are you handling this?

MR. HURLBUTT: Yes, I am.

HEARING OFFICER LAWRENCE: Okay. You may proceed.

CROSS-EXAMINATION

BY MR. HURLBUTT:

Q. Mr. Schilling, can you hear me okay?

A. Yes.

Q. Okay. Mr. Schilling, in your experience, prior to the Stibnite Gold Project, did DEQ ever use a project-specific adjustment factor like the one used here to address TAPs compliance where the duration of the project and the seven-year lifetime are factored in?

A. Are you asking -- I didn't hear part of the question, but I believe you were asking outside of this project, have we ever used that 16 over 70 adjustment factor?

Q. Correct.

A. No, we had not.

Q. Okay. And that's in the estimated hundreds of permits that you have been involved at the DEQ, you have never seen that before?

A. Yes. We have never -- we have not encountered applications that were over five years, but less than 70. So the project is unique in that regard that it was of limited duration. So surprisingly enough, we had not seen that happen before.

We have, however, over the years the emission factors have been honed in on and DEQ has been more thorough in assessment of a lot of the emission sources. Way back when I was first starting the modeling of fugitive emission sources was a whole lot more uncertain. Fugitives were sometimes not included in the analyses because models weren't handling them well.

So it's not as though we just dreamed something up. We hadn't encountered the situation before.

Q. Mr. Schilling, have you been involved in any air permits for any other mines in Idaho?

A. Yes. I don't recall the specifics of them, but there's been some phosphate mines. And we will be in the process of evaluating some more. We have one mining project in the door right now.

Q. Do you know if any of those mines were seeking a permit to operate for more than 70 years

or 70 years or more?

A. All of those projects to my knowledge have involved permitting on a permanent basis. So they are not accounting for a shorter lifetime duration of the mine.

Q. Okay. Are applicants required to indicate how long they plan to operate?

A. Only if they want to take credit for a shorter than permanent duration in their permitting -- in their permit itself. If they can demonstrate compliance on a permanent basis, that's the route they go to get their permit.

Q. Okay. I'd like to introduce a hearing exhibit here. This is already in the record at REC1191 through 94. It's titled, "DEQ Position on Arsenic Modeling Addendum" and it goes on from there.

Mr. Schilling, are you familiar with this?

A. Yes, I am.

Q. What is it?

A. This is basically a summary of our approach for the Stibnite project.

MS. HANCOCK: Did you clarify that that is Exhibit 300 for the record?

MR. HURLBUTT: Yes, thank you. Exhibit 300 for the record.

(Hearing Exhibit No. 300 admitted.)

Q. BY MR. HURLBUTT: Mr. Schilling, can you turn to the last page of that, Section 3.4, that's titled, "Substantial Change in Regulatory Approach"?

A. Yes.

Q. And did you write this, Mr. Schilling?

A. Yes, I did.

Q. Do you mind reading that Section 3.4?

A. Sure. "The arsenic modeling addendum is a complete change in the regulatory approaches to demonstrate compliance with toxics. It abandons the Section 210 approach used in the application for an arsenic Section 161-210 hybrid analysis. The methods used in this unique analysis should be thoroughly vetted by DEQ well before permit application is submitted. Month before permit issuance is not time for developing a creative permitting approach with new emission inventory approaches, new modeling analyses and challenges for crafting enforceable permit provisions/limits."

Q. Thank you.

Is it the 16/70 exposure duration

adjustment, is that the substantial change in regulatory approach that you're referencing here?

A. Yes, it is.

Q. Okay. You may have already covered this in your direct testimony, but could you explain what the normal approach is that DEQ would use and how the 16/70 is different?

A. The typical approach that DEQ uses with most of the permit applications is that we -- the annual average is a nice nugget to regulate on. And it's easiest to calculate emissions for an annual -- a maximum annual impact. And when those demonstrate compliance, that's the easiest path to permitting.

Q. Sorry to interrupt, but when you say "when those demonstrate compliance," do you mean comparing them --

A. Yes. Thank you for the question. When they can demonstrate compliance, assuming a repeatable annual impact in treating the AACC as an annual limit. And most of the projects we get, even some of the older mine projects, they permitted it in a way that allowed for consistent operations -- there wasn't the variability component in there. Or what they often did was

overestimated their emissions to where they could get a permit and it just involved year-to-year compliance and not a need to do a five-year averaging period.

So when this first came in to us, you know, we were -- our certainty level -- my certainty level was not so high. And I was concerned about the regulatory applicability of this method. I had put this together expressing my concerns about that.

Follow up to this involved extensive interaction with my permitting team as well as our deputy attorney general at the time and discussions with Perpetua's as well.

So this is kind of the beginning point of a process used to kind of say, hey, we may encounter some rocky points with this approach. Maybe we need to round up the team and we need to talk about it a little bit more.

Obviously I was not wrong in assuming we have some things to discuss.

Q. Thank you.

Mr. Schilling, you testified earlier about the TAPs rulemaking and testified that your recollection is that the TAPs rules were intended

to be consistent, predictable, and easy to use; is that right?

A. Yes.

Q. You also testified about Section 586, that has the carcinogens, URFs, ELs, AACCs. Can you explain again how one, instead of just comparing to the AACC listed in Section 586, can somehow use the URF to come up with a different comparison point?

A. Yes. What we're mainly doing is not so much -- the AACC is an annual representation of one in a million cancer risk. So we're then going to one in 100,000. You use -- the total exposure concentration allows for adjustment for the exposure duration. So the URF defines your basically risk for a unit amount of contaminated exposure. And then using the exposure duration you come up with an exposure concentration, which then can be compared to the AACC, which is that one in a million cancer risk representative of a 70-year lifetime.

Q. Would it be simpler to just compare the annual average AACC listed there to the annual average concentration that was modeled?

A. It would certainly be simpler. I don't

believe it would be more appropriate. Again, what's most appropriate is --

Q. I was just asking if it was simpler.

A. Oh.

Q. Thank you.

MS. YOUNG: Mr. Hearing Officer, I'm sorry to interrupt. But since he was asked a question, can the witness be allowed to finish his answer?

HEARING OFFICER LAWRENCE: I'll allow it.

Go ahead. If you felt like you needed to clarify something, please proceed.

THE WITNESS: It's simpler. I don't believe it is appropriate though. Because we still center on the fact that what matters is project-imposed cancer risk and not a year-by-year evaluation.

Q. BY MR. HURLBUTT: Is it appropriate to use this kind of exposure duration adjustment for any and all of the carcinogens that are listed as TAPs? Here it was used for arsenic, right? But would it be applicable to any TAPs?

A. My understanding would be that it could, but that would be best answered by the toxicologists.

Q. Okay. Do you still have a copy of your declaration in front of you, Mr. Schilling?

A. Yes.
Q. Would you please turn to Paragraph 19 of your declaration?
There you discuss air rule Section 210.15. That applies to short-term --
HEARING OFFICER LAWRENCE: Hold on one second. Bryan, can you let me catch up? Where were you going?
MR. HURLBUTT: Paragraph 19 of Mr. Schilling's declaration.
HEARING OFFICER LAWRENCE: Okay. Thank you.
Q. BY MR. HURLBUTT: Which discusses air rule Section 210.15.
A. Yes. I didn't get the full part of your question.
Q. Yeah. The question was just, the short-term source rule there, does that apply to sources that operate for five years or less?
A. Yes. As defined.
Q. Okay. And does that section grant a ten time increase in the applicable qualifying short-term sources?
A. It allows for a factor of ten adjustment to the allowed carcinogenic risk.
Q. Okay. In your opinion, Mr. Schilling,

could a five-year source get a project-specific adjustment factor like was granted to Perpetua? So five over 70?

A. I think that would demand some more careful evaluation. Since we have a prescriptive rule that addresses a short-term project of five years or less, I am not -- I would need to consult with people. My initial thought would be well, we have a rule that says what you do when you're a project of five years or less duration. I would need to evaluate. My initial thought is that we would have to work within the constraints of that provision if they wanted to use the five-year adjustment.

Now, if you're saying they don't want to use the five-year adjustment rule but just want to use the existing framework of the exposure duration adjustment and use five years under that rather than the specific five-year adjustment allowance in the rule, is that kind of what you're asking?

Q. Sure. Yeah, what do you think about that? I guess I was asking about either. Could you use both approaches?

A. I think there again it would need to be evaluated since the rules did identify a project of

duration less than five years falling in a certain defined bucket of the rules. So my initial thought is that the five-year period kind of caps how much you can really account for things, especially given some of the discussions within rulemaking about addressing these short-term projects defined of as five years or less.

Q. Mr. Schilling --

HEARING OFFICER LAWRENCE: Mr. Hurlbutt, can I jump in? I have a question that would be ridiculous for me not to ask now rather than wait later because it is so related.

Mr. Schilling, I am going to preface this question with a disclaimer that my dad was a hardcore scientist. The STEM gene skipped not only one generation but two, my kids don't have it either. But for all of the expert witnesses, please keep that in mind.

But with respect to this five-year rule that's hard-coded into the rules. My question on that is, like, if that five-year sort of flexibility rule that is in the rules now, if it didn't exist at all and we just had the rest of the rules the same way they are now and someone walked in and applied for a project for just a five-year

duration, how do those two different paths differ? Application of the hard-coded five-year rule versus going through the process that you did to get to 16 over 70, which in this case my hypothetical would be five over 70. I know that is a long question, but I don't know how else to approach it.

THE WITNESS: Yeah. Kind of the hypothetical of -- if I understand this correctly, you're asking what if we did not have the five-year provision within the TAPs rule but an applicant came in with a project of five years limited lifetime.

HEARING OFFICER LAWRENCE: Right, exactly.

Maybe part of it is describing what goes into the math of the hard-coded five-year rule versus the math that you used to get to the 16 over 70 adjustment factor?

THE WITNESS: The 16 over 70 adjustment factor kind of focuses on the URF and the calculation of an exposure concentration that allows consideration of exposure duration. At some point -- and I'm kind of starting to wade into an area of toxicology that is not the most comfortable waters for me.

My initial feeling would be as we get

into five years we start getting into a concern about well, are we dealing with carcinogenic risk versus -- well, chronic risk versus acute. That's one consideration.

I think we also start getting into the case of, well, do we have some concerns over dosing, which I believe is why the five-year thing was put in there to begin with, is that -- long-term exposure is the criteria here and there's not a magical point at which all the sudden it's too much in a short period of time. And there's debate about where that should be and where you should no longer be able to throw a bunch of contaminant on someone.

My interpretation is that the rules have said that is five years, when it is a five-year project this is the path you need to take.

And beyond five years my interpretation is that well, we're now into a carcinogenic long-term exposure and it would be more appropriate to account for that actual duration of dose. And not doing that would be assuming you're actually subjecting a receptor to more pollutant than what they are actually going to be exposed to over their lifetime.

HEARING OFFICER LAWRENCE: Okay. And if I understood the background correctly, am I remembering correctly that there's not really any particular magic to the five years itself, but DEQ receives sort of a regular stream of applications for these remediation projects and other types of projects that are shorter in duration so that is what the rule is there for.

THE WITNESS: Yeah. Regulatory bodies don't always work with perfect science because there's a lot of discrepancy in the scientific community. What ends up in regulation is sometimes something that no one completely agrees upon, but it's sort of the best way to move forward. The factor of ten, well, did it just happen that that's the magical factor that really works? I'm sure you can talk to a bunch of toxicologists and it should be five or 12 or some other number. Maybe it should be ten years instead of five years.

So I think we have some -- explaining it away is like trying to get in the heads of a whole bunch of lawmakers and people involved in negotiated rulemaking. Sometimes it just comes down to this is what we have to deal with it. And we do our absolute best job trying to interpret

what's the intent of the rule, what was the intent of the rulemakers, and is this a reasonable interpretation? Does it make some kind of sense and do we feel it is reasonably protective of public health as prescribed by the intent of the rule.

HEARING OFFICER LAWRENCE: Okay. Thank you.

Mr. Hurlbutt, sorry to interrupt. While you were on that topic I figured I would ask my question on that.

MR. HURLBUTT: That's okay.

Q. BY MR. HURLBUTT: So Mr. Schilling again, you testified earlier that the intent of the rule is to be simple and consistently applied.

Wouldn't it be simplest to have this short-term five-year exception that gets multiplied by ten and no other exceptions based on the duration of a project?

A. Again, it would be definitely simplest. But there's another component of the rules that's important and that is the rules also need to afford reasonable flexibility to the regulated community to conduct business accordingly. I know there's a lot of debate that can be made, you know, where do you cross a line of operational flexibility?

In this case I really think there's a lot of evidence in the record in past rulemaking and the way the rules are written that really corners in on the project-imposed risk is the criteria and not an arbitrary, annual, hardcore cast-in-stone limit that you can't ever exceed.

Q. Mr. Schilling, in this same Paragraph 19 of your declaration, if you still have that there?

A. Yes.

Q. You state, "in general, DEQ determined it would not be appropriate to subject individuals to a lifetime allowable cancer risk within a duration of less than five years."

Why did DEQ think that's not appropriate?

A. Well, there's -- let's see, this is Paragraph 19?

Q. Yes.

A. Excuse me just a minute while I make sure what I was referring to.

Q. Sure.

A. What I am trying to recall is, I am talking about the historical perspective of DEQ to the best of my recollection in that at the time of rule promulgation, DEQ determined it would not be

appropriate to subject a lifetime of cancer risk in a five-year period, therefore the development of that five-year provision for the factor of ten rather than a factor of I think it would be 14 or something like that.

So in other words, my interpretation is that DEQ felt that subjecting that entire slug of carcinogenic exposure or carcinogenic dose into a five-year or less period would not be reasonable.

So I'm interpreting that as an establishment of five years being that -- kind of that cutoff point, the cap to you can no longer put more into things for something less than five years.

Q. Okay. Do you agree that it would not be appropriate to subject an individual to a full lifetime allowable cancer risk for a five-year or less project?

A. I would not be the person to answer that question, again, because I'm not a toxicologist.

Q. Okay. Under your view of the air rules, Mr. Schilling, could a six-year source get a project-specific adjustment factor of six over 70?

A. It would seem so. I would want to confer with the rest of staff and see if there

would be some overriding reason not to.

Q. Okay. And I know you said you're not a toxicologist, but you have worked with the rules a lot and clearly think about human health and said that you have some training in things relating to toxicology.

Do you think it would be appropriate to subject an individual to a full lifetime allowable cancer risk in six years?

A. Well, my thoughts on what I personally feel might be appropriate -- we're kind of getting into a case of going what do I feel about something versus what's allowed under the rules. So I'm struggling a little bit with that.

Right now I am looking at within the regulatory framework we used here, what I'm seeing is the five years is being the bright line, very well known that in the science of things there's usually not very bright lines. We deal a lot with shades of gray. Certainly six years is looking a lot more gray to me than 16 years. I know you're asking a yes-or-no question and I'm maybe answering it more like a -- sounding like a politician.

Before I personally, if I received an application that used an adjustment for six years,

I would want to consult with both my legal team, my management team, and our toxicologist before saying yeah, you're good to go.

Q. Okay. Mr. Schilling, when DEQ assesses TAPs compliance for a new source, does DEQ consider toxic air pollutants from other sources that individuals may be exposed to, earlier sources, later sources, at the same time?

A. No. Going back to your question on simplicity of the rules. There was some discussion of those kind of things during rulemaking. It was decided that the TAPs would be regulated on an increment basis only, that being for the project. So in other words, not just on a facility basis.

You know, in this particular case the project is the entire facility. In a lot of cases we have facilities that have been around for multiple decades and where their emissions have occurred prior to development of the TAPs rules, we don't look at those. They came in with a project, they are given the increment that's allowed by the TAPs rules.

Q. So for TAPs compliance purposes, it's put on a bit of a blinder as to whether there's exposures people might be experiencing before or

after that project; is that correct?

A. That is correct.

Q. Okay. If DEQ received an air permit application for a second mine or an expanded mine or something at this Stibnite project site after this first 16-year project occurs, would DEQ have to consider the amount of cancer risk already eaten up by this 16-year Stibnite Gold Project that's at issue here?

A. You had kind of two options there and it is important to distinguish between them, I believe.

The first option, let's take a hypothetical example that a Perpetua 2 came in and was a completely new plant right next door to Perpetua 1. To the best of my knowledge, we would be looking at that Perpetua 2 plant and they would have the same incremental risk allowance in the --

Q. Sorry to interrupt, when you say "incremental risk allowance," you mean they would have their own new fresh?

A. Exactly. They would have a new one in a million. Their project would be able to impose an additional one in a million or one in 100,000 with T-RACT allowance for that.

Q. Okay.

A. If Perpetua was to modify in some way, and it was determined that it is an actual modification, they would also get another increment just like any other facility that modifies their operations argument given another increment.

Q. And I guess we have been talking about filling up pans or eating up cancer risk, but do you remember, Mr. Schilling, what the amount of the allowable lifetime cancer risk the Stibnite Gold Mine Project was modeled to eat up, if you will?

A. Well, at the maximum receptor, which is a very limited place, I would have to look, but it was less than 50 percent of the T-RACT allowable AACC.

You know, one of the things to consider is that if another mining company went in right next door, it's highly unlikely that they would impact the same receptors. That's not to say it's not a concern, but that was used as one example of why an increment approach was reasonably protective. And I'm not saying whether that's right or wrong, and I have my own opinions, personal opinions about it, but that's the way the rule was developed.

Q. Okay. So if someone lived somewhere else near a highly industrialized area, if multiple sources came in there that were short term, is there -- do you have concerns that one short-term source could eat up a bunch of somebody's cancer risk and then a second source that operates after that first one fills up that full bucket and it overflows eventually?

A. I kind of have --

MS. YOUNG: I just would object to the question as being beyond the scope of what we're talking about for purposes of this project at this hearing.

HEARING OFFICER LAWRENCE: I am going to sustain that. I tend to agree.

MR. HURLBUTT: Okay.

Julia, do you have the copies to share with everyone? I guess this is Exhibit 301. This in the TAPs modeling addendum the statement of basis at record 0710. If you could share that with them, Julie, I would like to introduce that as a hearing exhibit.

MS. THROWER: Yeah. So "Arsenic Modeling Addendum Review, Identify Questions and Concerns"?

MR. HURLBUTT: Yes, please.

MS. THROWER: 301. And for the record it also starts at REC1183.

Q. BY MR. HURLBUTT: Mr. Schilling, are you familiar with this?

A. Yes, I am familiar with it.

Q. I am bringing this up to draw your attention to Table 6, which is in the last page.

A. Table 6? Mine doesn't have tables in it.

Q. So I am looking at REC0714.

MS. THROWER: Okay. I apologize. I gave the wrong exhibit. So I will take those back. I apologize. This will be Exhibit 301 starting at REC0710.

MR. HURLBUTT: Yes.

(Hearing Exhibit No. 301 admitted.)

Q. BY MR. HURLBUTT: I just wanted to draw attention to, again, Table 6, which is the last page of this.

MS. HANCOCK: If we can wait one second, we don't have our copies yet.

THE WITNESS: Just to clarify, this is from the modeling review memorandum that -- or the modeling review of the TAPs addendum; is that correct?

Q. BY MR. HURLBUTT: Yeah. Thank you.

In the arsenic column in that table, the far-right column, that 41.30 percent, is that the number that's the sort of modeled amount of lifetime cancer risk that this project would eat up if somebody was exposed to that?

A. Yeah, the 41.3 percent? Yeah, the maximum modeled adjusted the exposure concentration is the .00095 micrograms per cubic meter. And that ends up being 41.3 percent of the T-RACT adjusted AACC.

Q. And to make sure I understand what you said earlier, if, say, at year 17 some new source came up, whether it was at the Stibnite site or right next door or whatever, they don't have to factor that 41.3 percent of cancer risk that's been eaten up?

A. That is correct.

MS. YOUNG: Same objection as far as outside the scope and calls for speculation.

HEARING OFFICER LAWRENCE: I actually do kind of want to hear the answer real quick.

So please go ahead and answer.

THE WITNESS: Yes, they could. It would be a new source and, again, it's project-specific

increment so it's a different source and we look just at the project.

Q. BY MR. HURLBUTT: Okay. I would like to ask now about this issue with increments versus standards or limits.

Because something is an increment, does that necessarily mean it cannot be an enforceable limit, Mr. Schilling?

A. Well, I'm not sure I'm completely following all of the confusion between the differences between increments and standards. We have here an increment, which is a one in a million cancer risk or one in 100,000 cancer risk, and that is certainly going to be regulated on and made enforceable.

The difference between a standard and an increment is that, you know, a standard accounts for all others -- like an air quality standard. That would be where we need to include all other sources and background and need to stay below a certain threshold.

An increment either allows for just that, an incremental amount of pollution. In some cases like PSD increments, it allows for all other sources beyond a certain point can chew up so much

air quality provided they still stay -- everything still stays below the national air quality standards.

In the case of our TAPs rules, it is a project-specific increment. So the project is -- that's the most the project can chew up is that is their pocket of pollution they're allowed to contribute.

HEARING OFFICER LAWRENCE: Can I jump in real quick? Bryan, I have a quick follow-up question.

Mr. Schilling, that framework that we're talking about right now in terms of like the difference between the ambient standards for the NAAQS, N-A-A-Q-S, versus toxics, does that general framework, does that derive from the Clean Air Act itself or as opposed to is it the State of Idaho that made the determination that toxics are going to be on this project-specific basis versus treated like the National Ambient Quality Air Standards?

THE WITNESS: The toxics are not addressed by the Clean Air Act. That is an Idaho-specific program. So it was negotiated with the regulated community back in the early '90s to develop the rules. So it's Idaho-specific. EPA does not

oversee our toxics program directly.

HEARING OFFICER LAWRENCE: Thank you. Sorry to interrupt.

THE WITNESS: Can you repeat your question again?

Q. BY MR. HURLBUTT: I don't remember exactly where we were.

A. I don't either.

Q. The TAPs rules use increments, but isn't it true that those still are enforceable limits in a permit? You can't go above, as you argue, the acceptable cancer risk. That is a limit, an enforceable limit?

A. Yes.

Q. Okay. Thank you.

Moving on to the five-year rolling average issue.

In your experience at DEQ have you used multiyear averages for assessing emissions for TAPs compliance?

A. I don't believe we have because permit applicants have not submitted something requesting that. They chose to demonstrate compliance using their worst case annual emissions. So that's what we -- we don't go out of our way to do something

that the applicant doesn't request.

Q. Okay. Mr. Schilling, do you know if DEQ or Perpetua ever calculated the maximum annual average arsenic emission for the Stibnite Gold Project?

A. I don't know. I'm not sure whether they did or not nor would we have requested them to if they're proposing to use a five-year rolling average. That is what we're going to analyze and that's what we're going to regulate on.

Q. Okay. So you don't know how much higher the maximum annual average the Stibnite Gold Project is compared to the maximum five-year rolling average that was used?

A. I don't off the top of my head. It could probably be calculated out. Bear in mind, they are also constrained with various production limits to assure compliance with the 24-hour PM10 and PM2.5 as well as annual PM2.5.

Q. Okay. I'm going to pull up Section 210 of the air rules, which you did just discuss with Ms. Hancock.

You are familiar with Section 210 of the air rules, Mr. Schilling?

A. Yes.

Q. I have done some highlighting here, but these are the 2022 rules. In green is Section 2, "Quantification of Emission Rates."

Do you mind reading the highlighted part B underneath there, Mr. Schilling, if you can read it?

A. "The uncontrolled emissions rate of a toxic air pollutant from a source or modification is calculated using the maximum capacity of the source or modification under its physical and operational design without the effect of any physical or operational limitations."

Q. Okay. Thank you. I am going to scroll down still within Part 2 within Section 210.

Do you see that part C and D here also talk about the maximum capacity of the source?

A. Okay. Section C, yes, I see that. Were you wanting me to read that?

Q. Well, yeah, why don't you read part D for T-RACT source, please.

A. "The T-RACT emissions rate of a toxic air pollutant from a source or modification is calculated using the maximum capacity of the source or modification under its physical and operational design with the effect of:"

MS. HANCOCK: Just remember there is a court reporter writing down what you say.

THE WITNESS: I'm sorry.

Q. BY MR. HURLBUTT: So this Section 210.02 is referring to maximum emission rates during this step of the TAPs process; is that right?

A. It's also important to have -- to consider part I and double I in there as well. But yeah, that's the maximum capacity of the source.

Q. Okay. So if this step of the process for emissions looks at the maximum or the maximum subject to be controlled, why don't you need to look at the maximum annual average for comparing TAPs compliance later on? Can you disregard the maximum and use a five-year rolling average later in the TAPs process?

A. We are kind of dealing with two different things here. Let me take just a second here.

Q. Do you guys want me to keep sharing this or stop sharing? I don't know if this is helpful or distracting.

MS. HANCOCK: Maybe until you're done.

THE WITNESS: We have done that. We calculated the maximum emission rate under its

physical and operational design. That doesn't mean that we make assumptions that it operates in a way that it doesn't. But this just says how we need to calculate those emissions, not how we need to assess them in the impact analysis. And using the five-year average allows you to account for how the facility will actually be operated.

I think this seems to be playing sort of a little bit of -- the only term that comes to mind, and pardon me for using it, but it is kind of verbal gymnastics in my mind to be using that. It's like, well, we calculate the maximum emissions that are going to occur under the physical and operational design of the equipment considering how it's being used. And then we assess impacts accordingly.

The fact that it may operate at this maximum hourly rate doesn't mean that we have to assume that it operates that way for five years continuously. That's not the purpose of what we're dealing with in Section D.

Q. So is there some use for these maximum rates in the TAPs compliance process?

A. Yes, most definitely. We want to make sure that what's calculated for the piece of

equipment or the operation is representative of the maximum emissions that occur within the unit of time defined for that source. Like, if we're looking at an hour, it's like, well, yeah, we want to make sure that the generator's running at its maximum load so that we're not underestimating those particular emissions.

Q. But then you don't need to use those later to look at actual compliance --

A. We do use them, we just also account for the duration of their use, which is put in as an enforceable permit limit.

Q. Okay.

A. And this we do for every permit we write regardless of whether we're dealing with this T-RACT or we're dealing with any other industry coming in. We never assume that the thing is going to operate at their maximum for 8,760.

With a caveat to that, an applicant can take that approach to make their permitting simpler and they can avoid getting burdensome permit limits if they make the overly conservative assumption that they can operate at 8,760 at full bore and that meets the rules, we're happy. It reduces the amount of time we have to review the permit. It

makes their permit simpler. You know, even though it is a gross overestimation of the emissions and impacts of the source.

Q. Okay. Thank you.

MR. HURLBUTT: I don't have any further questions. I don't know if Ms. Thrower does.

MS. THROWER: Yeah, I do.

HEARING OFFICER LAWRENCE: Counsel, does anyone have any preferences on whether we take a quick break now or plow through.

MS. YOUNG: I don't have a preference if we plow through or not, but if they go until 12:30, that's an hour. And given that Bryan was the primary on cross, that seems like a lot of time.

MS. THROWER: We represent different clients.

MR. HURLBUTT: You guys were afforded one hour.

MS. THROWER: But we had discussed these weren't hard and fast time limits. We are here at a hearing at the board's request to get information about these issues. If you guys want to cut me off, I will make an objection on the record that I did not have the opportunity to cross-examine this witness.

MS. YOUNG: I just wanted to note is all that I would like -- I tried my best to reserve a little time for redirect, and I just want to make sure I still get that.

HEARING OFFICER LAWRENCE: Right.

And Mr. Schilling, how are you doing? Do you need a break before --

THE WITNESS: I am still good.

HEARING OFFICER LAWRENCE: Okay. You may proceed, Ms. Thrower, but please be cognizant of time.

MS. THROWER: I will try to be as brief as I can.

CROSS-EXAMINATION

BY MS. THROWER:

Q. I think I can still say good morning?

A. Yes, good morning.

Q. All right. Thank you for being here.

I did want to ask a few follow-up questions. You had testified that when you were talking about the 16/70 adjustment factor that you said that duration is directly related to risk.

Do you remember saying that?

A. Yes.

Q. Okay. So in your opinion, is a lower

concentration of a carcinogenic pollutant over a longer period of time always equivalent to a higher carcinogenic pollutant for a lower time in terms of cancer risk?

A. By the methods we use to calculate risk, by the equations we use that involve the exposure duration. Yeah. I think the question you're getting at is if you take the same -- I am wading into toxicology again and I'm not the best person for that. But the way the equation we used works is what matters is the exposure concentration is linked to the actual quantity of material breathed in. And that that's what governs it. So if it is a little more in 16 years versus less than that over 70 provided it's the same quantity, that is an equivalent risk by the equation.

Q. And you would say that's the case for all carcinogenic pollutants?

A. That's the --

MS. HANCOCK: I would object to the scope of this. We're limited to just the arsenic issue here.

HEARING OFFICER LAWRENCE: Can you repeat your question, Ms. Thrower?

MS. THROWER: Yeah. I said, do you think

that that applies to all carcinogenic pollutants?

MS. YOUNG: I would also note an additional objection that Mr. Schilling hasn't been qualified as a toxicologist. It seems like we're wading really deeply into that.

MS. THROWER: But he testified as far as duration is directly related to risk so I am trying to figure out what his basis for that testimony is.

MS. YOUNG: Sure, again, but related to the arsenic, the piece he did the modeling for.

MS. THROWER: So I will rephrase my question.

Q. BY MS. THROWER: So you believe that this exposure duration, which we've been calling, applies to arsenic as a carcinogenic pollutant in all cases?

A. I always get nervous hearing the words "all" or "never." But to the best of my knowledge the equations to calculate the exposure concentration are linear, which would mean yes.

Q. Okay. So when Mr. Hurlbutt was asking you about six over 70, you testified you were a little nervous about doing it in that case; is that correct?

A. Yes.

Q. Okay. Did you consult with a toxicologist for the Stibnite Gold Project prior to this contested case?

A. Not to the extent we have now. I don't believe so.

Q. Okay. I will move on from the toxicology area.

So Mr. Hurlbutt had talked about the five-year short-term source rule. And that is in 210.15 is what we cited to.

So just to have it on the transcript that this rule basically says that if your source is going to operate for five years or less, you can use this rule which gives you a ten-fold adjustment factor to the AACC?

A. Yes.

Q. So you testified that if a five-year source, five-year or less source didn't want to use that rule, but go under the regular rule, what would happen -- or Mr. Hurlbutt asked you if a five-year source or less went under -- wanted to go under the regular rule, what would happen? And I am paraphrasing your testimony, but you said that you have a rule and they would go under the five-year rule.

A. I believe so.

Q. Is that a fair assessment?

MS. HANCOCK: I would object to the extent that we are just restating what has previously been testified to. So it is cumulative in nature, but it also is misrepresenting the full extent of his answer previously. This goes back to the last question as well.

MS. THROWER: Do you want me to go back and ask the court reporter to read his testimony?

MS. HANCOCK: The record stands for what it stands for. You can ask your questions however you want. I am just lodging an objection because I don't know having him reconfirm what he's already testified to in a way that paraphrases it differently than his testimony is the proper way to do it.

MS. THROWER: If you're worried about the differences --

HEARING OFFICER LAWRENCE: I'm going to jump in here. I will sustain the objection. It feels like we are revisiting a lot of testimony that we have already talked about.

Q. BY MS. THROWER: Mr. Schilling, you testified if a source coming in five years or less

would go under a five-year rule?

A. Yes.

Q. And that's the rule that they would use because that rule is there?

A. Uh-huh.

Q. Now, do you have a rule that says what you do if you are more than five years, expected to operate for more than five years?

A. Yeah, it is the standard one in a million cancer risk or one in 100,000 for T-RACT being the increment. So we would use our equation to make an adjustment for the exposure duration in the calculation of the exposure concentration.

Q. Is that what the rule says?

MS. HANCOCK: I am not trying to be obnoxious with this, but the rules say what the rules say, and asking a witness what the rules say, it doesn't --

HEARING OFFICER LAWRENCE: Let me ask a question that I was going to ask anyway that I think may get at this.

Mr. Schilling, I know we have been in the rules a lot. But just taking a step back and just high level, what is the primary textual basis in the air rules themselves for the 16/70

adjustment factor?

THE WITNESS: The rules say, again, what matters is the project-imposed cancer risk. What matters there is total risk. And so we have to properly account for the exposure for that duration rather than 70 years.

The rules don't tell me in my analysis when I'm analyzing NAAQS emissions, how I'm supposed to account for the NO to NO2 conversion that happens in the stack and may happen in the atmosphere prior to monitoring, but that's what we do in the analyses.

The rules don't -- you know, if the rules had everything in them prescribed -- you know, the rules don't preclude what we do, but we believe we took a reasonable assessment of the intent of the rules.

And if the rules had everything, every scenario in there, we wouldn't need scientists and engineers at the agency to implement these. We would have a software program that could just crank through it and issue the permit out and check through does it meet this.

So the fact that the rules don't specifically allow that adjustment doesn't mean we

shouldn't do it or that -- I believe it would be inappropriate not to do it.

HEARING OFFICER LAWRENCE: It was helpful for me.

Ms. Thrower, you may resume, but please try to minimize sort of revisiting prior testimony.

MS. THROWER: Just to this because, Mr. Hearing Officer, you had asked for the textual basis for his testimony.

Mr. Hurlbutt, I hate to put you on the spot, but can you pull up the IDAPA rules 210.12.B.

MR. HURLBUTT: Yes.

MS. THROWER: Thank you. .12.B.

Q. BY MS. THROWER: Okay. So 210.12.B says, "Compare the source's or modification's approved T-RACT ambient concentration at the point of compliance for the toxic air pollutant to the amount of the toxic air pollutant that would contribute an ambient air cancer risk probability of less than one to 100,000."

Is there anything in that rule that you read that allows for an exposure adjustment or that provides textual basis for using an exposure adjustment?

A. I don't see anything that precludes its

use, and it's -- in order to calculate the ambient concentration at the point of compliance for assessment of a one to 100,000 cancer risk. The models we use only generate at most an annual impact, so if we want to assess a 16-year impact, which is the life of the mine or the project duration, we need to use an adjustment factor outside of the model to account for that proper exposure concentration. I can't put in my model for it to generate a project -- a concentration that's representative of the concentration requested here, the T-RACT ambient concentration at the point of compliance, which is the concentration resulting from the entirety of the project, which would be the 16 years.

Q. Well, this is just asking the agency, or whoever is administering the application for the permit, to compare the T-RACT ambient concentration at the point of compliance to the amount of the toxic air pollutant contributing to the cancer probability of less than one to 100,000 which is equivalent to ten times the applicable acceptable ambient air concentration listed in Section 586.

So reading that, isn't this just the simple comparison? You have the ambient air

arsenic concentration that presumably the applicant gave you, and you compare that to the amount of toxic air pollutant listed in Section 586?

A. Yes, but in order to get to the proper averaged concentration, we have to multiply the model out by a factor of 16 over 70 to calculate the correct concentration.

Q. Okay. So I'll warn you, as I said, we are going to get into a little math. But just to go back, you testified that you were the air modeling supervisor.

Did you supervise or were you actively involved in the Stibnite Gold Project permit to construct?

A. A little bit of both. I was more involved in the framework of how we're demonstrating compliance with arsenic and how that is working in the five-year averages and those, and not so much in the direct checking of the model inputs and verifying those. So it was more supervisory and less nuts and bolts.

Q. Okay. So I may go out of the scope of what you know, so just tell me. But you reviewed Dr. von Lindern's declaration, correct?

A. Yes.

Q. And you reviewed the section where it talks about an averaging of the WEP and non-WEP models, being the west end pit and the non-west end pit models?

A. Yes.

Q. So this is the area I want to explore with you. And I also want to talk about this as you've obviously reviewed your toxicologist, Dr. Paden's declaration, right?

A. Yes.

Q. And she calculates her risk assessment based on a certain number of arsenic concentration, correct?

A. I believe so.

HEARING OFFICER LAWRENCE: Is this something we should be asking her when she's a witness?

MS. THROWER: Well, this is sort of more on the basis of where that number came from. I don't believe her declaration went -- from her declaration it looks like she was given this number and she would not know where it was calculated. I can certainly ask her that. But if she says, no, I don't know, and I have lost this witness for the remainder of the hearing.

HEARING OFFICER LAWRENCE: Okay. Go ahead.

Q. BY MS. THROWER: So Mr. Schilling, I am going to hand you Exhibit 303. This is also in the record documents at REC6888.

Can you read what the title of this table is?

A. "TAP Maximum Model Concentrations in AACs."

(Hearing Exhibit No. 303 admitted.)

Q. BY MS. THROWER: Do you have any familiarity or recollection of this table?

A. It is looking familiar of being -- this would actually be best described by --

MS. YOUNG: Sorry, I don't have a copy of this exhibit.

THE WITNESS: Yes, I am familiar with it. Details on it would probably be best answered by Perpetua's consultant, Kevin Lewis.

Q. BY MS. THROWER: To your knowledge, he is the most likely one that would understand where the numbers came from?

A. He would have the best understanding, but I may also.

Q. Okay. Do you have knowledge of the basis of how that number -- I'm sorry. Let me go back.

So if we look at the row for arsenic --
A. Uh-huh.
Q. -- and we look at W2, there's a value there. What is that value?
A. .00095.
Q. Okay. And that's in micrograms per cubic meter?
A. Uh-huh.
Q. So that number, what does that number represent?
A. That is the adjusted impact for the W2 scenario assuming that 100 percent of the production at the mine occurs from that source only.
Q. Okay. Just to get some clarifying questions. What did you mean by "adjusted impact"?
A. I believe the impact of -- again, I would have to go back and assess this more to be absolutely sure, but this could be verified certainly by any questions to Kevin Lewis, but I believe that has been adjusted for the 16 over 70 duration.
HEARING OFFICER LAWRENCE: And just so I know, since this is an appendix, what document did this come from? What does it live in?

MS. THROWER: Yeah. This came from Stibnite Gold Project Permit to Construct TAP Addendum Appendix C.

HEARING OFFICER LAWRENCE: Okay. Thank you.

MS. THROWER: That was REC6088.

Q. BY MS. THROWER: Mr. Schilling, I think maybe more of my questions are going to be directed towards Mr. Lewis, but I just wanted to have one more clarification.

A. Certainly.

Q. One more question here. You said it is the adjusted impact for W2 scenario assuming 100 percent production of that source only.

Do you know what source the W2 model scenario is talking about?

A. I believe -- I would have to go back to the key and see. It's been a while since I have reviewed this, and outside of the context of the entire document it's a little bit difficult for me.

HEARING OFFICER LAWRENCE: Ms. Thrower, if I can jump in.

So ultimately the test here is what I am going to find helpful for resolving and this feels like a line of questioning that is not going to help me out.

MS. THROWER: This does go to Dr. von Lindern's last part of his declaration in terms of WEP and non-WEP averaging. However, as I said, it appears that Mr. Lewis might be the more appropriate person to ask. So I'm fine, if Mr. Schilling doesn't have a recollection right now without reviewing other documents, I'm happy to leave it at that.

HEARING OFFICER LAWRENCE: I think we should.

MS. THROWER: Okay. I have no further questions then.

HEARING OFFICER LAWRENCE: Okay. Thank you.

I do have some questions, and I know you want redirect.

Do you have any idea how much time you need for redirect?

MS. YOUNG: Maybe ten minutes. But I prefer you go first so you can ask them in the way they make sense to you in case there is overlap.

HEARING OFFICER LAWRENCE: Is everyone okay? I am probably in the same ballpark, ten minutes likely. Something like that.

Are we okay to proceed?

Okay. These won't be in any particular

logical order. I apologize in advance. I'm trying to accomplish a few things here.

EXAMINATION

BY HEARING OFFICER LAWRENCE:

Q. So when I read back through the DEQ order and some of the transcripts when this was before the board, I got the sense that there was some discomfort with the fact that there was this 135,000-ton per day figure, right?

Can you remind me what the significance of that figure is? Do you remember that number?

A. The 135,000 tons per day, that number?

Q. Right.

A. I believe that was the five-year rolling average daily production limit.

Q. Right. So what I was sensing, there was discomfort on the board between the fact that -- as I recall, and maybe I am articulating this not correctly, but the 135,000-tons per day, is that what the modeling was assuming was the emissions rate?

A. That's what would go into the long-term modeling for the carcinogenic impacts. It's kind of the same discussion again about the pitcher full

of water and on a daily basis for other reasons we have that higher limit. But for a five-year period, that daily limit is ratcheted down to better reflect a five-year period, which we believe is more representative of long-term chronic impact rather than a short-term limit.

Q. So just kind of paraphrasing. And I don't know if they ever went this far, but it seemed like where somebody was going, with that 135,000-tons per day, why isn't that also like an annual limit in the permit? What I think I'm hearing is that's not necessary because we have fluctuations over time.

A. Yeah. I think again where the whole crux of all of this comes down to is we contend we are dealing with a total project risk evaluation rather than needing to hold to an annual -- each year needing to assume each year is the same year after year after year.

So I think that -- that is basically the question for all of the different points of contention is whether we can use what matters in that whole life-of-mine period, which we have kind of broken out into this five-year rolling average.

Or, as I understand the petitioner

saying, no, you need to look at each year and you need to identify the absolute maximum that each year could emit and evaluate the impacts for that worst case year. And that must be less than this increment that's based on a 70-year exposure.

Q. All right. Thank you.

So another question I have. I think your declaration and the DEQ's hearing statement when it is talking about the 16/70 adjustment factor, it uses the term that essentially this all works, this is all okay when there's an enforceable limit on the duration of operation.

So what is the enforceable limit in the permit for the 16 years?

A. That would be there's the total life-of-mine production limit, going back to my candy example, that sort of governs the whole project over the life of the mine. So by limiting that total production and specifically limiting the west end pit production, that assures that the total amount emitted and the average concentration that that causes, won't cause an excess cancer rate in excess of one in 100,000 as allowed by T-RACT.

Q. Is there any ability under the way the permit is currently worded that they could operate

for more than 16 years or is that baked into the conditions of approval is there is no way they could exceed 16 years?

A. That gets into a bit of an evaluation and there's been hypothetical questions of what would happen if after 16 years they simply requested to go another 16 years.

And we would need to evaluate whether such a request is actually a modification of the permit, which would enable the facility to get another increment, or if essentially they're asking for a permit violation.

We have things that are referred to as sham permits, and that means someone asks for a little bit less right now to be below something and then they later come in and go oh, well, we're going to do something -- we're changing something, we want to do this other thing.

And if it's shown that well, it really wasn't a modification, but you all along wanted to do something else, but you asked for something lesser just in order to get it approved, that's referred to as a sham permit.

Q. Is there any particular reason? Am I correct that there is not an actual permit term

currently that says this is limited to 16 years of operation?

A. It is limited by the total production. So by our risk calculations, you know, you would have the same risk whether that took 16 years or if they took 70 years to produce that same amount.

Q. And even if there's, like, not a practical implication in terms of cancer risk, is there any particular reason that the permit couldn't say, because we are basing all of this on this 16-year assumption and what they are telling us that we will only operate for 16 years, is there some reason that couldn't be baked into the permit as a condition? Does that mess something up?

A. Oh, if the 16 years were actually put in there?

Q. Yeah. Correct.

A. I don't know specifically. There again, I am going to kind of punt a little bit on that. I am the modeling review supervisor and analyst. That kind of goes into more of a permitting question --

Q. And I do mean the question more in terms of is there a permitting reason why that wouldn't work? That would mess up some other aspect of the

permit or something like that?

A. I don't know would be my answer. I don't see where it would mess up something.

Q. Okay.

A. It isn't in the permit and certainly Perpetua would want to weigh in on that.

HEARING OFFICER LAWRENCE: Thank you. Those are all my questions.

Ms. Young.

MS. YOUNG: Okay.

REDIRECT EXAMINATION

BY MS. YOUNG:

Q. I will start, Kevin, with what we were just talking about. And if you, again, don't feel comfortable because this is a little bit outside juror scope, just let me know.

Isn't it true that condition 3.6 of the permit to construct says that the permitee shall haul no more than 788.4 million tons of ore and creates an additional limit from the west end deposit. So I realize that was a confusing question, so let me rephrase.

Isn't it true that Section 3.6 -- or condition 3.6 of the permit contains both an

overarching limit as well as a limit from west end pit production?

A. That's correct.

Q. And isn't it true that the permit also creates an ongoing daily limit?

A. Yes.

Q. So through those two limits, isn't it true that the life of mine is limited to 16 years as the permit is currently written? And if Kevin Lewis needs to answer this as has been alluded to, that's fine too.

A. The production limit, you're talking in terms of limits of production. They are not forced to produce that much. That caps their production. So in the absence of a time limit in there, they could actually extend operations longer. And actually, if they went at a slower pace they would need to extend it longer.

But by extending it longer, since our emissions are proportional on production and concentrations are proportional on emissions and risk is dependent upon the total exposure, you're going to arrive at the same risk whether it would be 16 years or 70 years.

And in fact, I think if they say well,

instead of 16 years we're going to process this ore over 70 years, then we would just be -- we wouldn't have the adjustment factor.

Q. Sure. I was going to ask a follow-up to that and I lost my question. Apologies. I think maybe I'll reserve some additional clarification here for the other Kevin. I appreciate that additional explanation.

I just have a few more questions for you.

It was asked, I believe by the hearing officer, you know, if you have 586 to demonstrate compliance and you have the T-RACT one in 100,000 to demonstrate compliance, what would occur if the -- you couldn't meet either? And you had indicated that the permit would be denied, correct?

A. Yeah. Or they would have to go back and rework it. We couldn't issue a permit without demonstrating compliance.

Q. Perfect. Thank you. So that was going to be my question.

Wouldn't it also be an option for the permit applicant to go back and consider their analysis and make additional refinements, which we talked about earlier is a normal part of the

iterative process?

A. Yes.

Q. Perfect. Thank you.

You were asked by the petitioners if you had ever been involved with a permit where there was this type of adjustment.

Do you recall that question?

A. Yes.

Q. Isn't it true you have never been approached by an applicant to have this type of adjustment before?

A. Yes, that's correct. We wouldn't normally say, hey, use this. We deal with what is requested for their project.

Q. So in the other permits that you've been involved in developing, they simply didn't know at the time of the application what their duration was going to be. They were assuming they would be operating permanently?

A. Yes.

Q. And that's true for the phosphate mines that were referenced earlier; isn't that true?

A. Yes. They were permitted on a permanent basis.

Q. Because they don't know how long they

are going to be operating and they could be operating for many, many years, correct?

A. Yes.

Q. And isn't it true that some of those mines have been operating for many, many years?

A. Yes.

Q. Perfect. Thank you very much.

A. And they have had numerous modifications because they found new areas.

Q. Perfect. Thank you.

Let's see. As to this Exhibit 300 that you were shown, which is your position paper. I noted it doesn't have a date on it, and you might not recall, but do you know approximately when this paper was written? And if you don't know, that's okay.

A. I don't. I know it was prior to permit issuance.

Q. Okay. Thank you.

In the Section 3.4 that Mr. Hurlbutt asked you to read from, which is on the final page, Page 4, you said that the analysis should be thoroughly vetted; is that correct?

A. Yes.

Q. Was it thoroughly vetted?

A. Yes, it was.
Q. Perfect. It also was asked if this was a normal approach.
Do you recall?
A. Yeah, I believe so.
Q. And again, is that because you've never had a permit applicant come to you with a known duration of project from the get-go?
A. That's correct.
Q. So it wasn't creative in that you were trying to necessarily get around the rules, it's just you have never been presented with this problem before.
Would that be a fair assessment? I don't want to use the word "problem," but this type of project?
A. Yeah. It kind of gets into a little bit of semantics as far as how do you interpret the word "creative." And I may have actually even used the term. And it's looking at it, analyzing it, digging into it and figuring out, well, what is the intent of the rule? Okay. Oh, we believe this is what we're trying to control. This is a way to get at it. Oh, this is what really matters. Gee, we never thought about it that way before. Okay.

Let's move forward. Let's check on it, make sure it's a reasonable approach to our interpretation, which we did, and then moved forward with it.

Q. Perfect. Thank you.

Let's see, I think that's the only questions I have as to that exhibit.

Moving on. You were presented with a number of potential hypotheticals, including the possibility that a source would operate for six years.

Is that the situation we're in today?

A. No, it's not.

Q. You were also given some hypotheticals where you responded that you would be entering into more of a gray area.

Do you recall?

A. Uh-huh.

Q. Do you feel like you're in that gray area here with the 16-year duration?

A. I don't believe so. We had thought about that and it seemed like a reasonable estimate of a chronic exposure.

Q. So you don't feel like your judgment and the sound science you used crossed any line here. I believe crossing the line was referenced earlier.

A. No, I don't believe so.
Q. Thank you.
There were also some questions from the petitioners as well as the hearing officer about the rules that were relied on. And you indicated that the rules don't preclude this analysis, correct?
A. Yes.
Q. Isn't it also true that Section 586 supports the analysis that you performed?
A. Yes, in that the relationship between the URFs and the AACCs which are an expression of the one in a million cancer risk for 70-year exposure.
Q. Perfect.
And isn't it true that the definition that we read of the toxic air pollutant carcinogen supports the analysis that you performed?
A. Yes.
Q. And isn't it true that Section 203.03, which requires this analysis be demonstrated to the satisfaction of the department, supports the analysis that you performed?
A. Yes.
Q. And isn't it true that Section 210

supports the analysis that you performed?

A. Yeah. We performed the analyses according to the prescriptive nature of 210.

Q. Perfect.

And the specific section that allows you to perform the T-RACT adjustment is specifically and explicitly stated in the rules, correct?

A. Yes.

Q. There were some questions that I think confused the issue a little bit between the emissions being calculated versus the adjustment after the modeling of the emissions had occurred.

Do you recall that conversation?

A. Yes.

Q. Is there anything that you want the opportunity to explain there as far as the difference between calculating the emissions on the front end versus looking at the actual risk being created on the back end?

A. Only just a concluding statement that what went into the model was maximum emissions as the facility is allowed to operate under its design or the constraints of the permit issued. So that's what went into the model.

MS. YOUNG: Perfect. Let's see here. I

think those are all the questions I have. Thank you, Kevin.

HEARING OFFICER LAWRENCE: Thank you, Mr. Schilling.

MS. HANCOCK: Can I reserve the right to maybe do a brief redirect after lunch?

HEARING OFFICER LAWRENCE: You can reserve the right.

MS. HANCOCK: Would you permit me to do a brief redirect after lunch?

HEARING OFFICER LAWRENCE: On what topic?

MS. HANCOCK: On the topics that was covered by the petitioners.

HEARING OFFICER LAWRENCE: Can you be more specific?

MS. HANCOCK: I just need to make sure -- I want to look at my notes and just make sure, but I want to do a double check to make sure we didn't have something on the record that was incorrect. It wouldn't be longer than ten minutes.

HEARING OFFICER LAWRENCE: Okay. Mr. Schilling, would you prefer to do that now or do you want to wait until after lunch?

THE WITNESS: I don't have a preference. I would defer to anyone who has a pressing issue or a

desire.

MS. HANCOCK: My understanding is he is going to be here throughout the course of the hearing.

HEARING OFFICER LAWRENCE: Unless someone wants to take a break I would be inclined to just go ahead and do it now.

MR. SHORT: I could use a break.

HEARING OFFICER LAWRENCE: Why don't we take a lunch break and do that after lunch.

MS. HANCOCK: Thank you.

(Break taken from 12:21 p.m. to 1:28 p.m.)

HEARING OFFICER LAWRENCE: Okay. We are reconvening in the Perpetua air permit matter. As we left it before lunch, Perpetua had asked to reserve some time for a few follow-up questions for Mr. Schilling, but just informed everybody they don't need to do that any longer. So we're just going to proceed to DEQ's next witness.

MS. YOUNG: Yes. Thank you, Hearing Officer.

HEARING OFFICER LAWRENCE: So we need to swear the witness.

NORKA PADEN,

a witness having been first duly sworn to tell the truth, the whole truth and nothing but the truth, was examined and testified as follows:

DIRECT EXAMINATION

BY MS. YOUNG:

Q. Can you please state your name and spell your last name for the record.

A. Norka Eliana Paden, P-A-D-E-N.

Q. Thank you, Dr. Paden.

Where are you currently employed?

A. I work for the Idaho Department of Environmental Quality.

Q. Perfect.

How long have you been with DEQ?

A. I have been with DEQ for eight years.

Q. For eight years. Thank you.

What is your current title?

A. My title is toxicologist risk assessor.

Q. All right. How long have you been in that role?

A. I have been in that role for eight years.

Q. And where did you work prior to DEQ?

A. In Idaho I worked for the Idaho Department of Environmental Quality for five years.
Q. I'm sorry, before DEQ.
A. I worked for the Idaho Department of Health and Welfare for five years.
Q. What degrees do you have?
A. Perfect.
I have a master's in human ecology. I went to the Free University of Brussels in Belgium. And I graduated with a degree of environmental toxicology, a Ph.D., from Texas Tech University.
Q. So you consider yourself a toxicologist, correct?
A. Yes, I am a toxicologist.
Q. What about your education and background qualifies you as such?
A. I have vast experience doing risk assessments. I have been a toxicologist and practicing for 16 years. Prior to that, overseas also I did over nine years. So I have been doing risk assessments for close to 25 years. That is not in my declaration, but I am just adding that.
Q. Okay. So in your declaration you mention the 16 years, but you're saying that you didn't include those previous nine years when you

were overseas?
A. Yes.
Q. So you are adding that to the record now?
A. Exactly.
Q. Perfect. Thank you.
Let's see, and does your education also go into consideration as far as considering yourself a toxicologist?
A. Yes. That's correct.
Q. Thank you. This might be difficult to give me an exact number, but could you come up with a best guess of how many risk assessments you've performed in your career as a toxicologist?
A. My best guess would be over 50.
Q. Over 50, 5-0?
A. 5-0.
Q. Perfect. Thank you.
And did you prepare an expert declaration in this matter?
A. Yes, I did.
Q. I am going to hand you a copy of your declaration. You can take a minute to review it. After you do, can you tell me if this is a true and accurate copy of what you submitted?

A. Yes, it is.

MS. YOUNG: We've marked that as Exhibit 101.

(Hearing Exhibit No. 101 admitted.)

Q. BY MS. YOUNG: In advance of today's hearing did you review the other expert declarations that were submitted?

A. Yes, I did.

MS. YOUNG: Hearing officer, I would move to first qualify Dr. Paden as an expert witness, and specifically as a toxicologist.

HEARING OFFICER LAWRENCE: Any parties opposed?

MS. HANCOCK: No.

MS. THROWER: No.

HEARING OFFICER LAWRENCE: Approved.

MS. YOUNG: Thank you. I would also move to admit Exhibit 101, Dr. Paden's declaration, into the record as expert testimony.

HEARING OFFICER LAWRENCE: Granted.

Q. BY MS. YOUNG: Thank you.

Okay. Dr. Paden, in your declaration on Paragraph 5 you stated that you reviewed the transcript from the May 1st, 2024, special board of environmental quality meeting in this matter; is

that correct?

A. That is correct.

Q. So you are familiar with the oral comments that board member Dr. McMillan made individually at that meeting?

A. Yes.

Q. Thank you.

In his comments he stated that "DEQ's project-specific adjustment factor creates a new higher level of cancer risk for 16 years."

Do you recall that statement?

A. Yes, I do.

Q. Based on your expertise as a toxicologist, do you agree?

A. I disagree with that. As you can see in my declaration, Table 2, you can see that actually the excess cancer risk for 16 years is lower than at 70 years.

Q. Thank you.

So in your opinion the adjustment factor that DEQ used does not create a higher level of cancer risk?

A. No, it doesn't.

HEARING OFFICER LAWRENCE: Can you speak up a little bit?

THE WITNESS: No, it doesn't.

Q. BY MS. YOUNG: He also stated that "DEQ is making the assumption that 70 years is required for cancer to develop."

Do you recall that statement?

A. Yes, I do.

Q. And do you agree with that statement, and that statement being that "DEQ is making an assumption that 70 years is required"?

A. I don't think DEQ is making that assumption. That 70 year comes from EPA life risk assessment and that's taking into account how long somebody is going to live, for 70 years.

Q. Perfect. Thank you.

So in your declaration, and I'm looking specifically at Paragraph 22, you concluded that DEQ's analysis followed EPA guidelines; is that correct?

A. Yes, that's correct.

Q. And you also conclude that it resulted in an acceptable cancer risk; is that correct?

A. That is correct.

Q. Can you expand on why you came to that conclusion?

A. My declaration, you can see some of the

results that I have on Table 2. But most importantly, the 16 years that we are discussing in this hearing, and that is four in 1 million cancer risk. So that is the below the T-RACT which is below our rule standard for cancer risk.

Q. Great. So you state in your declaration that DEQ followed EPA guidelines. And can you explain why DEQ's reliance on EPA's guidelines is appropriate?

A. If we go to section -- Paragraph 11 in my declaration, I don't know if you have that equation.

Q. Yes.

A. So what I did, I tried to interpret -- so the formula is not stated in the rule, however parts of the formula are in that table. So I tried to --

Q. I'm sorry, I'm going to stop you right there for clarity. When you are talking about that table, per your Paragraph 11, you are talking about Section 586 in the rules?

A. Yes, that's correct.

Q. Thank you.

A. And so I tried to derive or calculate the ACC specifically for arsenic using the values

that you have in that table.

And so when I did that, I compared that and it's the same formula that EPA uses to calculate excess cancer risk. So I conclude that DEQ has in the rules that ACC uses the inhalation unit risk which comes from EPA. And then there is a footnote there that indicates that value is taken from EPA. And so usually when we perform risk assessments we use that approach that I outline in Paragraph 11.

And then Paragraph 12, what I did there, is basically it's an expanded formula of what I have in Paragraph 10.

Q. That's perfect. I actually am going to ask my co-counsel here to share his screen and bring up these formulas that are in the declaration and we'll walk through them a little bit.

MS. YOUNG: Of course, as always, I would certainly welcome you to interrupt me at any time and ask the questions that you need.

HEARING OFFICER LAWRENCE: Are you sure you want to open that door?

MS. YOUNG: I think I am. Famous last words maybe.

HEARING OFFICER LAWRENCE: Real quick.

Could we, just for the record, sort of define what you guys mean by the phrase "risk assessment"? I think it would be helpful to have an elevator risk definition out there.

MS. YOUNG: Sure. I appreciate that.

Q. BY MS. YOUNG: Norka, could you define what it means to conduct a risk assessment?

A. Yeah. A risk assessment, when there is any contaminate in the environment you want to ensure that the concentrations that are going to be in the environment are not going to cause any human health effects, and you usually use the most conservative scenario for a sensitive population. So that is how risk assessments are carried out.

Q. Okay. So you raised a good point, that there is the consideration of sensitive populations.

And does the URF already take into account sensitive populations?

A. Yes, that's correct. So EPA derives those unit risk factors for a wide variety of contaminates, carcinogens, in this case for arsenic. And that value comes from -- usually from experiments they do with animals and that they extrapolate that to humans. And so they use

updated scientific information to come up with a value that is the upper level, the most conservative value that somebody can get exposed through a lifetime and it is not going to cause any cancer risk.

Q. Any excess cancer risk?

A. Any excess cancer risk is at the levels that are permissible, but EPA which is ten amount of four to ten amount of six.

Q. Which is 10,000 to a million? One in 10,000 or to one in 1 million; is that correct?

A. One in 10,000 to one in 1 million, so that's the range.

Q. Thank you.

So here is on Paragraph 10, under Paragraph 10 of your declaration, the formula that you said you had used, which is a formula for the maximum modeled concentrations for carcinogenic TAPs accounting for life of mine production limits.

Is that correct?

A. Yes, that's correct.

Q. And if you go to Paragraph 12. This is, you had stated, an expanded version of that formula on 10; is that correct?

A. That's correct.

Q. Okay. And I'm going to walk us through the formula a little bit. I'm sorry if this is really at the most basic level, but as someone who also does not have any math or science real experience I think it is helpful.

So looking at Paragraph 12, which we can see right now, the ED, the exposure duration.

Do you see that in there?

A. Yes.

Q. Okay. And if you compare that exposure duration, that ED number, to the formula under Paragraph 10, is that where you inputted the 16?

A. Yeah. That's what DEQ used to calculate the permit, and then they used the value of 16 as an exposure duration.

Q. So that 16 represents the exposure duration from EPA?

A. Exactly.

Q. So for Paragraph 12, you have the ET, the exposure time, and that's assumed to be 24 hours a day, correct?

A. Yes. Based on the information, that's on Table 1 of my declaration, that's 24 hours per day.

Q. Thank you.

And then the exposure frequency is 365 days a year, correct?

A. Yes, that's correct. 365.

Q. So we just covered the ET and the EF which is 24 hours per day and 365 days a year, right?

A. Correct.

Q. Now if you look back at the formula on 10, the ET and the EF, again, the 24 hours and the 365 days a year, is it true that it is being represented in this formula under Paragraph 10 as highest annual concentration, which is the 24 times 365?

A. That highest annual concentration is the CA, which is the highest annual concentration. Is that what you were asking?

Q. Let's see here. So maybe I'll just ask you to explain it. Maybe we'll keep 12 up, if you could keep 12 up and then explain how those different pieces of the formula relate to what we're looking at on Paragraph 10.

A. Yeah. If you have both, if you have it side by side so it will be easier to understand. So you have on the left-hand side of the formula the lifetime exposure concentration, which is in

micrograms per cubic meter. And that represents the exposure concentration on the EC on that formula from EPA.

And then that equals to -- on 10 we have the highest amount of a concentration, and that will be equivalent to the CA in Paragraph 12, which is the contaminate concentration in air.

Now, the exposure time and exposure frequency, as you see in Table 1, it's exposure time is 24 and exposure frequency is 365. And then you're going to have exposure duration. But in the denominator, you have AT, AT defined as the lifetime in years, which is 70, times 365, times 24.

So as you can see, if you have a numerator, that 365, that comes from exposure frequency and the 24 that comes from the exposure time, they are going to be canceling out. Meaning that you are dividing the same number -- you have the same number numerator and denominator, so that is going to be one.

So that's the reason I conclude that that's the same formula that comes from EPA and what we use -- what our permit writers use to calculate the 16 years of duration. And the 70, it

is coming from the lifetime exposure of 70 years.

Q. Okay. Thank you for that. And thank you for walking us through that a little more artfully than I was able to.

You reference Table 1 under Paragraph 13. And that's where you see the averaging time, which is the denominator is 70 times 365 times 24. And the reason you don't see -- I'm sorry, let me pause there.

Is that correct?

A. Yes, that is correct.

Q. And the reason you don't see the 365 and the 24 on Paragraph 10 is because they would be on both the numerator and the denominator essentially canceling each other out, correct?

A. Yes, that's correct.

Q. Looking at the simpler formula under Paragraph 10, we see that the 16 has been entered in for exposure duration, correct?

A. Correct.

Q. And in your experience of conducting risk assessments, have you ever put a different site-specific number there?

A. Yes, I did. In fact, usually when we are talking about residential exposures you can use

different values from EPA, 26. Or when you are evaluating a receptor that could be -- a receptor who is going to be exposed, a recreational person who is going to go to the site only for a short amount of time, you can use that exposure duration, that way you don't overestimate the risk.

So if you have information that is provided to me as a risk assessor and they tell me I am going to look at the risk here, to be more accurate I can use that information and put the 26, the 16, 15, whatever number the person is going to get exposed to get an accurate calculation of the cancer risk.

Q. So can you put numbers that are lower 16?

A. Lower than 16? Yes.

Q. So again, just to reiterate, when DEQ provided you with that 16 number, that wasn't atypical in your experience in doing risk assessments to put in a specific number for that exposure duration?

A. Yeah. For the record, I did not calculate this permit, I am just evaluating the permit. So I did not calculate. But I am just evaluating what I was provided. So they did use

the 16 and that's an accurate value and it's conforming with what EPA has in the guidelines.

Q. Perfect. Thank you.

So this would be an adjustment based on the actual exposure duration.

Can you explain why duration is so important?

A. When somebody is exposed to any contaminate, you have to evaluate what are the different -- the time, because that is very important. So if you are getting exposed to a chronic exposure, you know more than one year, that's going to be different than if you are going to get exposed for 24 to 48 hours, which would be an acute exposure. So that is very important.

Q. And it's important in the cancer risk analysis, correct?

A. Definitely. You usually see that a chronic exposure will cause cancer where as acute exposures, at least in toxicology, we don't consider that. We just evaluate if it is emergency, acute exposure. We do not evaluate cancer risk for an acute exposure, but for chronic exposure.

Q. So obviously the 16 years at issue here

would be considered a chronic exposure?

A. Exactly.

Q. And you sort of explained this, but if you could just discuss this again, sort of understanding the difference between the exposure being chronic versus an amount of exposure?

A. Yeah. Exposure being chronic, that's the definition. You expose somebody for more than a year, several months. And sub chronic could be 30 to 90 days. And then acute, 24 to 48 hours. The amount the person is exposed, that also influences what are going to be the outcomes from risk.

Q. Perfect.

So we covered this a little bit about the URF considering sensitive populations, but is it your experience that these risk assessments bake into them a lot of conservatism?

A. They do. In fact, if you go to my exhibit that I put there for my declaration, Exhibit B, it has the original screening levels. So if somebody at DEQ will ask me to do a risk assessment, and that's the screening values that we are going to use.

And you can see I changed the values,

but on the right-hand side I wanted to concentrate on those numbers that they have for first, second, third phase. So there is different age adjustments that EPA uses to be very conservative in the analysis.

HEARING OFFICER LAWRENCE: I'm sorry, I don't think I have the right document in front of me.

MS. YOUNG: Exhibit C, I believe.

And to also let you know, Dr. Paden, Michael has put it up on the screen to confirm we are looking at the same thing.

THE WITNESS: Yeah. We already consider all those. The age adjustments, they mention that in the analysis.

Q. BY MS. YOUNG: And you said earlier that the risk assessment also considers sort of the worst case scenarios for a number of the factors; is that correct?

A. Exactly. When we are looking at any risk assessment we want to look at values that are the worst case scenarios. So we are trying to be conservative so that way we are using a population that is going to be at most risk. So when you are talking about children, like in this case, or

pregnant women, which are the most sensitive, or the elderly, they are sensitive populations. They are already considered in the analysis on that URF and also, as you can see, in the original screening levels.

MS. YOUNG: Great. Thank you, Dr. Paden. I don't have any further questions at this time. Though I would reserve some time for any necessary redirect.

HEARING OFFICER LAWRENCE: Okay.

Perpetua, are you ready to ask Dr. Paden some questions?

MS. HANCOCK: I am.

CROSS-EXAMINATION

BY MS. HANCOCK:

Q. I just have one question. On your Exhibit C that we were just looking at, if we can go to the next page.

Can you tell me what this page reflects?

A. Yeah. These are some calculations for resident risk screening levels for arsenic in air using the highest concentration that I was provided by our permit writer. So that's what we have the screening level. What is highlighted in red,

that's the screening level that we used to say whether or not there is any cancer risk.

Q. Does arsenic have a mutagenic mode of action?

A. No. And that is what we have there. There is a lot of studies, but there is not strong evidence. So to my understanding, EPA has told me, and you can see in their most updated original screening levels value that it is not mutagenic.

MS. HANCOCK: That is all I have. Thank you.

HEARING OFFICER LAWRENCE: Okay. Mr. Hurlbutt, Ms. Thrower, how are you guys breaking up your cross-examination of the witness?

MS. THROWER: I think I will go first.

HEARING OFFICER LAWRENCE: It would be helpful for me to know how you are splitting it up. Are you guys covering particular subject matters?

MS. THROWER: I think I am doing most of it. I will cover everything in her declaration, I believe.

HEARING OFFICER LAWRENCE: And are there any issues here where there's a different analysis or outcome based on your representation of Save the South Fork Salmon versus Nez Perce Tribe and ICL?

Are those different parties relevant to any of this?

MS. THROWER: I don't want to speak for Mr. Hurlbutt, but his clients have different levels of use of the area so I don't know if in terms of talking about risk assessment if there's anything he may follow up in that respect or something like that. So I don't want to -- I think I intend to cover everything for all the petitioners, but I'm not going to say he's not going to want to ask a few questions afterward.

HEARING OFFICER LAWRENCE: That is helpful for me.

MR. HURLBUTT: That's fair. If I have any additional questions, it won't be very many.

HEARING OFFICER LAWRENCE: Thank you, guys.

CROSS-EXAMINATION

BY MS. THROWER:

Q. Good afternoon, Dr. Paden.

A. Good afternoon.

Q. So I want to start with just going through some of your experience as a toxicologist. From your qualifications statement it looks like you have been -- you said you have been an

environmental toxicologist with DEQ for 16 years?

A. For DEQ eight years.

Q. And then another eight years would be the predecessor agency; is that right?

A. For Health and Welfare I worked for five years.

Q. Okay.

A. So 13 years.

Q. Okay. So 13 years with IDWH and DEQ together?

A. Yeah. In total, yes. For the state, 13 years.

Q. And both those agencies, the focus of your work was to provide risk assessments analyses for contaminated sites or superfund sites; is that correct?

A. That's correct.

Q. It sounds like you also provided comments to policymakers and negotiated rulemaking?

A. That's correct.

Q. Were you at DEQ when the TAPs rules were negotiated?

A. No, I haven't. That's before my time.

Q. Okay. And you've done many risk assessments, as you have testified, at least 50 or

so, for contaminated sites.

Do you do any risk assessments for individual permit applications, like the Stibnite Gold Mine Project?

A. Well, that is not considered a risk assessment because that doesn't fall under a superfund site, so CERCLA requires risk assessments for sites that are contaminated. So even if I wanted to, that doesn't fall within the scope of my work.

Q. Okay. Have any of your risk assessments involved analysis of air quality --

A. Yes.

Q. Exposure to air quality?

A. Yes, several. Several.

Q. I wanted to talk about the public health consultations that you mentioned in your declaration. It says you authored six of those public health consultations for the agency for toxic substances and disease registry.

Again, were all those public health consultations on contaminated sites? Or existing contamination versus potential future releases of contaminants?

A. Some of them were petitioned by

nonprofit organizations that was not necessarily a contaminated site, they just wanted to know whether or not exposures to particular contaminates will harm public health and not necessarily superfund sites.

Q. When you say not contaminated sites, you are saying not an officially recognized --

A. Superfund site.

Q. But these nonprofits thought the site might be contaminated, so they wanted you to look into that?

A. Yeah. Correct.

Q. So I want to go back to those risk assessments again. How did you go about calculating a receptor's exposure to a contaminate? And by "receptor," I think that is a new term we have thrown out here. But that would be a human that may be in contact with the contaminate.

So again, how would you go about calculating a receptor's exposure to a contaminate?

A. Usually risk assessments, like I explained before, we evaluate and we take into consideration the most sensitive populations which are children, pregnant women.

Q. Okay. And those risk assessments, do

you typically calculate a different risk, cancer risk, for an adult versus a child?

A. Like I mentioned here for the original screening levels, both are considered together, adults and children. So that's already incorporated in the approach that EPA uses.

Q. Okay. Have you ever separated out cancer risk based on life stages in your public health assessments?

A. In public health assessments, yes. Because I follow ATSDR approach, which is quite different from what EPA requires.

Q. Okay. So I am going to move on to the actual permit application.

The first time you were asked to evaluate the cancer risk from the Stibnite Gold Project was for this contested case, right?

A. Yes.

Q. Okay. And just to make clear, and when I mean the contested case, I mean after the permit was issued.

A. That is correct.

Q. So I want to turn to Page 8 of your declaration. I'm sorry, not Page 8, but Paragraph 8.

Okay. You state here that the cancer risk estimates were accurately calculated.

Do you see that?

A. Yes.

Q. And do you still agree with that statement?

A. Yes, I do.

Q. In Paragraph 10 you show the equation that purports to calculate the lifetime exposure risk. That's what you have testified to what that equation is with Ms. Young?

A. Correct.

Q. So just to back up a little bit. In order to calculate the excess cancer risk by your method you need to calculate the lifetime exposure, correct?

A. Yes.

Q. Okay. And as you said, that's done with the equation in Paragraph 10.

A. Uh-huh.

Q. So I want to focus on this term "highest annual concentration." In this case we're talking about arsenic.

In Paragraph 9, you state that you used the number for the highest annual concentration,

which you called the maximum model annual concentration, as 0.00416 micrograms per cubic meter; is that correct?

A. That is correct.

Q. And the number and the value of the first column in Table 1 is that same number, right, .00416 micrograms per cubic meter?

A. Yes, that's correct.

Q. And you said that you were given a number by DEQ.

Were you referring to the 16 years or were you referring to the highest -- this .00416 number?

A. I consulted with our permit writer and I asked what was the worst case scenario in this case and I used that number to calculate the risk.

Q. Okay.

A. And now in this contested case I was asked whether or not the use of the 16 years is accurate or not. And that's what I used the 16 years to indicate that that was something that is allowed by EPA.

Q. Okay. So the 0.00416 number, you were also just given by DEQ?

A. Yeah. I reviewed documents that went

into the calculation. Usually when you do risk assessments we use a wide variety of data and then you calculate your 95th percentile which is the highest value we can have or an average or a GME. In this case it was this value, which I understand from reading the summary of the permit that that was the worst case scenario from the modeling.

Q. Right. Okay.

Does the accuracy of your cancer risk calculation depend on the accuracy of that number given to you for the highest annual concentration?

A. Yes.

Q. Okay. Would you be concerned about your conclusion that this permit meets that T-RACT cancer risk if you knew that number that DEQ gave you was lower than the higher annual concentration?

A. I am not concerned because I consulted with the permit writers and I trusted that they did the calculations to the best of their ability, therefore my calculation is also accurate.

Q. But if they gave you a number that was lower than the highest annual concentration, would you feel like you would need to redo your analysis?

A. I would sit with them and I would ask them to explain to me why this concentration is

lower. And if I feel that there's some miscalculation, then we will have to have a conversation.

Q. Okay. So Mr. Schilling said that this number was a five-year rolling average and not the highest annual concentration.

Does that give you any concern?

A. I'm not familiar because I am not a permit writer, so I cannot answer that question.

Q. Well, if someone gave you -- as a hypothetical, if someone gave you an average of five numbers and didn't give you the individual numbers, but said, hey, I calculated the contaminate concentration over an average of five years, would you consider that a good analysis in terms of that is the highest annual concentration?

MS. YOUNG: I am just going to object and say asked and answered. I feel like Dr. Paden's already testified that that's more in the realm of a permit writer and that she's already answered the question, essentially.

HEARING OFFICER LAWRENCE: I will give you one more shot Ms. Thrower, and then move on.

Q. BY MS. THROWER: Okay. If someone came to you and said do a risk assessment like you did

here, and I'm giving you for your highest maximum -- or for the maximum annual concentration, I'm giving you a five-year rolling average that I've calculated. Would you be concerned that your cancer risk calculation may not be accurate?

A. In my position as a toxicologist I cannot just be given a number. I need to make sure that the numbers that I'm going to use are reliable. So I consult with the people that I have at DEQ, the manager, the permit writers, and say how did you come up with this concentration so I cannot just, okay, this is a number and you are going to calculate.

And my role as a toxicologist and the model for DEQ is to take care of the environment and human health, so I am not going to put at risk the population that are going to be exposed. So that is my role and I take that to heart.

So I probably won't just take any number that anybody will give me to do a calculation. I will have to double check and make sure that the numbers I am using are accurate.

Q. Okay. Thank you. And I don't mean to suggest you don't take your job seriously.

So let's turn to Paragraph 12 of your

declaration. Again, this is EPA's methodology that Ms. Young had questioned you about.

So this methodology, this equation comes from the risk assessment guidance from EPA for superfund sites; is that correct?

A. That is correct.

Q. And this is the same guidelines or guidance that DEQ is claiming that it is relying on for this 16/70 adjustment factor; is that correct?

A. That is correct.

Q. Does the superfund risk assessment guidance consider incremental sources?

A. Incremental cancer risk?

Q. Yes. Incremental, yeah, so from multiple sources.

A. From multiple sources, I don't think I am understanding the question.

Q. Let me try and rephrase that.

Does the superfund risk assessment guidance ignore other sources of exposure?

A. When you are doing a full-blown risk assessment you have to consider all the exposures from all the media for arsenic: water, soil, air. In this case we are talking about permit and you are talking about something specific which is air

emissions. So I was told that this is what we are using.

And what I am trying to say is that DEQ used a formula that comes from EPA and that the permit writer used to change the exposure duration just as I would do for any other risk assessment.

Q. Right. So I understand you would be looking at different routes of exposure like from air and water for the same contaminant for a risk assessment, but would you be looking at other sources? So for instance, if you were doing a risk assessment on a superfund site, you are looking at contaminant A and whether people can be exposed to that.

Are you looking at other sources of contaminate A that might be around that superfund site?

A. Yeah. This is outside the scope of this discussion, but if you are just curious of the work that I do, yeah, if there are any other sources around a particular superfund site that had to do with arsenic, yes, I would say, yeah, is there any background? Is there any mine over here? But usually we are concerned with a superfund site, we are just evaluating this particular mining area, we

are just going to look at that.

And you can add lines of evidence, whether or not there is background natural occurring arsenic to compare to your project. But I am just going to do my analysis based on that particular superfund site.

Q. Okay. And that analysis involves a lot of different factors, not just exposure duration; is that right?

A. Yes. It is a wide variety of factors.

Q. And you didn't consider any of those factors in your cancer risk calculations for this permit; is that correct?

A. I did not do the calculation myself. I am just trying to demonstrate what the permit writer did and that it aligned with what EPA allows.

Q. Okay. Thank you.

So I want to go to Table 2 of your declaration. In Paragraph 14, Table 2, you use the equation that you had in your earlier part of your declaration to calculate the excess cancer risk probability using the inhalation unit risk for arsenic derived by the EPA. This is getting to be a long question. Let me start that over.

So let's just say Table 2 shows the results of your calculations using those equations you have above in your declaration, correct?

A. Yes, that's correct.

Q. Okay. And it shows in the first row, it shows that if you use the exposure concentration using the 16/70 adjustment factor, your cancer risk is four in 1 million; is that correct?

A. That's correct.

Q. And that is equivalent to one in 250,000? Four in 1 million is equivalent to one in 250,000?

A. No, it is not equivalent. I don't understand what you're trying to say.

Q. I was just trying to see if we can compare it -- well, it's okay.

So again, in Table 2, the second row, it shows if you don't use the 16/70 adjustment factor you calculate the excess to be two in 100,000; is that correct?

A. That is correct.

Q. So in Paragraph 17, in the last sentence of that paragraph you state that "this analysis shows at maximum arsenic levels modeled 0.00416 micrograms per cubic meter for exposure of

16 or 70 years are within the public health guidelines."

Do you see that in your declaration?

A. Yes.

Q. And by "public health guidelines," you mean EPA's guidelines, correct?

A. EPA and also ATSDR's.

Q. Okay. And you conclude that the two in 100,000 cancer risk is within the EPA's recommended range of one in 1 million to one in 10,000, correct?

A. Correct.

Q. But is this two in 100,000 the cancer risk that we're talking about for the T-RACT cancer risk in this case?

A. This is above the T-RACT, but what I was trying to demonstrate, even if it is above the T-RACT it is still within what EPA recommends.

Q. But not what the Idaho rules require?

A. Not the 70, but the 16.

Q. Let's move down to Paragraph 21.

So in Paragraph 21 you mention other sources of recommendations for arsenic concentration ranges, for example, from the Texas Commission on Environmental Quality and the World

Health Organization. And you state, "the maximum modeled air concentration in this case is below those established thresholds," correct?

A. Correct.

Q. Do you agree those thresholds don't really bear on whether this permit application meets the Idaho air rules?

A. These are additional lines of evidence that any toxicologist would use to substantiate that really there is no risk.

MS. THROWER: Okay. I have no further questions.

THE WITNESS: Thank you.

HEARING OFFICER LAWRENCE: Mr. Hurlbutt, do you have anything else?

MR. HURLBUTT: I just have one line of questioning, I don't think it will take long.

HEARING OFFICER LAWRENCE: Okay.

CROSS-EXAMINATION

BY MR. HURLBUTT:

Q. Can you hear me okay?

A. Yes.

Q. You said at the beginning of your testimony that you disagree with Board Member McMillan's statement that this 16/70 approach creates a new cancer risk; is that right?

A. That is correct.

Q. The 16/70 approach allows the project to emit more arsenic over 16 years than if it had to meet the annual AACC every year, right?

A. I am not aware that they are going to emit more. I don't think that is the discussion. It is my understanding that there is a concentration, and that's the value I used. That is the maximum concentration and that's what I used for my calculations.

Q. Okay. You're not aware that the reason the 16/70 approach was used was because if the project's arsenic concentrations were compared to the T-RACT adjusted annual values it would have exceeded those?

A. Yeah. What I was trying to demonstrate here is that if you use -- number one is that you

are allowed to change the exposure duration. So that's the primary role with my declaration. So you are allowed to not use the 70, but 16, and that's what I am trying to demonstrate.

And even if you go farther with the 70, still the risk is not -- is within what EPA recommends. So that is what I am trying to demonstrate in my declaration.

Q. Okay. Even if you think that the project's arsenic emissions create an acceptable risk, they're still higher than what would be allowed if Perpetua had to meet the applicable AACC every year; isn't that right?

A. I don't agree with that statement.

Q. Okay. So you don't think there is a higher risk from arsenic exposure under this project compared to if they had to meet the annual AACC each year?

A. I would have to defer that to Kevin or the permit writer with the AACC or the rolling average, which I am not competent to answer that question.

Q. Okay. So how you can say Board Member McMillan was wrong in saying that this creates a higher cancer risk than what was traditionally done

by DEQ?

A. Because you are talking about 70 years. Dr. McMillan was saying it is creating a new higher cancer risk and I don't see that in my evaluation. I still find that even if you do 70, you're still within what EPA allows.

Q. Okay. But you don't think that this approach is allowing higher levels of arsenic exposure than the normal approach that DEQ has employed that Mr. Schilling testified about?

A. No, I don't think so.

Q. Okay.

MR. HURLBUTT: Thank you.

THE WITNESS: You're welcome.

HEARING OFFICER LAWRENCE: I have a couple of questions.

EXAMINATION

BY HEARING OFFICER LAWRENCE:

Q. So at the conclusion of Mr. Schilling's testimony I asked him a question about the 16-year -- all the modeling is based on 16 years life of mine, so why isn't that actually like a permit condition?

And if I understood his answer

correctly, part of it was essentially that even if they don't produce a lot every year and they stay under their production limits, if they go past 16 years, as long as they're still within their overall production limits, it doesn't change the cancer risk.

Does it sound like I am accurately describing what he testified to?

A. Could you rephrase your question?

Q. Yeah. What I was asking Mr. Schilling was this whole issue of 16 years. So if all of the modeling is based on the assumption that the mine is only going to operate for 16 years, my question is why not have a permit condition that actually says that, that says the mine is limited to 16 years? Do you follow me so far?

A. Yes. Yes.

Q. Okay. And so as I understood his response, it was -- part of it was, well, the first thing is there are production limits in the permit, so that's one thing that kind of takes care of this issue of the length of the mine. And even if Perpetua ramped down its production so that it was going beyond 16 years, but still staying within its overall production limits, the fact that it is

going beyond 16 years doesn't change the overall cancer risk. That's at least what I understood. And I was just curious as to whether you had an opinion about that one way or the other.

A. Yeah. That's accurate. We are doing this average in time and that is what you call lifetime exposure. You are considering -- already when you are doing 16 you are considering somebody being exposed for 16 -- that is the exposure duration, but you are doing it throughout the 70 years somebody will live.

So there is still some -- you are taking into consideration the concentrations that will last and will have that cancer risk over a lifetime.

So just because you are not going beyond 70, the cancer risk concentrations are still being taken into consideration. So just because I didn't say it is going to beyond that, it is not going to stop there. So you've been for 16 years there, so your cancer risk has been evaluated if you would be living for 70 or having your lifetime exposure. So I don't know if you are following me.

Q. I don't mean to be annoying, but to me it seemed like one of the big concerns by the board

is just the whole difference between higher exposures for shorter amounts of time and lower exposures for longer amounts of time. And what I am just trying to figure out is, let's just hypothetically say that Perpetua operates beyond 16 years but they're still staying under all of the other production limits in the permit. How does that change the excess cancer risk?

A. Yeah. This is a very controversial topic, because as I state in my declaration, cancer just has a wide variety of factors. You are not just going to treat the arsenic. Somebody can already have cancer and I go and live by the mine, I cannot blame the mine to be causing my cancer because I already had previous exposure. So it is a very difficult topic to discuss. I'm sure Theresa will have a little better understanding to explain specifically knowing the project and how is it going to operate and when is it going to stop.

Q. Okay. And another question I have, obviously the petitioners haven't gone yet and they will get into their case more specifically, but in my review of the materials they filed. As I understand it, one argument they are making is that DEQ's approach in the application of the 16/70

factor doesn't take into account different cancer risks at different life stages. And I am just wondering what your overall reaction is to that argument from a high level.

A. Yeah. As I explained to Hannah when she asked that question regarding the URF, when you are evaluating cancer risk for any carcinogen, there is that unit risk factor that EPA provides. And when we use that factor, that already takes into account a very conservative approach in which all the most sensitive populations are being evaluated when you are using that factor. And to do that EPA goes through years and years of review. That number is vetted. So we as toxicologists we rely on that to do our risk assessments.

Q. Okay. So specifically, that issue of different risks at different stages, like pregnant women, children, that's baked in, for lack of a better phrase, into the unit risk factor specifically? That's where that occurs?

A. Yes, that's correct.

Q. Thank you. I apologize if you said all that and I just needed to hear it again. Sometimes it helps to hear things multiple times.

Those are all my questions.

Do we have any redirect from DEQ?

MS. YOUNG: Just a few questions. It shouldn't take too long.

REDIRECT EXAMINATION

BY MS. YOUNG:

Q. I don't want to belabor this, maybe this is just something you haven't had the time to think through, but part of what the hearing officer was asking, so let's say that the mine was operated, hypothetically, which is dangerous, but for 17 years. So it took an extra year, but that reduced the year-by-year exposure because they were producing less. That I think is one possible scenario that has been floated.

Would that create a major change to your analysis or do you think it would create a major excess risk at that point if it was one year over but because of the production limit there was less being -- you know, exposure?

A. If you are having an emission or exposure, a concentration that is less, you know, theoretically when you do the calculations, it is going to give you less risk because you are plugging in the lower number.

Q. Right. So the one question I wanted to ask was looking at Paragraph 12, this formula. Under Paragraph 12, the formula, petitioners were asking you about using the annual average versus the five-year rolling average.

Do you recall that?

A. Yes.

Q. Isn't it true that this CA, contaminate concentration and air value, is supposed to be a representative period of emissions; is that correct?

A. Yes. It is a continuous exposure, it is a chronic exposure.

Q. So it is representative of the exposure, not necessarily the maximum exposure at any given point in time?

A. No. It is the continuous exposure, not the maximum.

Q. It is the continuous and not the max?

A. Yes.

Q. Okay. Thank you.

So if a five-year rolling average was actually more representative because of the variability of the project, would that actually be the best number to use as the representative

number?

A. Yeah. That's correct.

Q. Okay.

MS. YOUNG: I don't have any other questions.

HEARING OFFICER LAWRENCE: Okay. Thank you.

Perpetua, anything?

MS. HANCOCK: Nothing further. Thank you.

HEARING OFFICER LAWRENCE: Okay. So this concludes DEQ's case in chief, correct?

MS. YOUNG: Correct.

HEARING OFFICER LAWRENCE: Okay. Well, thank you.

Do we want to proceed to Perpetua or take a break?

MS. HANCOCK: Maybe just a five-minute switch-it-up break and then start again.

(Break taken from 2:31 p.m. to 2:39 p.m.)

HEARING OFFICER LAWRENCE: We are ready to proceed with Perpetua's case in chief.

MS. HANCOCK: Thank you.

THERESA LOPEZ,

a witness having been first duly sworn to tell the truth, the whole truth and nothing but the truth, was examined and testified as follows:

DIRECT EXAMINATION

BY MS. HANCOCK:

Q. Good afternoon, Ms. Lopez. Would you mind starting by giving us an overview of your education background?

A. Yes. I earned a Bachelor's of Science in nutritional science with a minor in zoology from the University of Florida. And I received a Master's in Public Health degree from the University of Colorado Health Sciences Center.

Q. And just because the TV is the microphone, if you make sure you keep your voice up.

What is your role today?

A. Today I am a principal toxicologist with Tetra Tech.

Q. Can you help me understand with your Master's in Public Health and your BS in nutritional science how that translates into a toxicology expert?

A. When I was in college, toxicology was not a major at my university, but nutritional science is the prevla of toxicology. You use the same types of studies to do an analysis of the effects of nutrients on the body as opposed to other chemicals. And in nutrition you have ill effects on both ends, too little or too much. So the science translates directly.

Q. And how long have you worked as a toxicologist?

A. 32 years.

Q. Where are you employed?

A. At Tetra Tech.

Q. And what is Tetra Tech?

A. Tetra Tech is multifaceted environmental engineering company.

Q. In your time there for 32 years, have you always served as a toxicologist?

A. Yes.

Q. Can you describe your role at Tetra Tech, what kinds of things you do as a toxicologist?

A. I have a wide range of projects that I work on. I have government clients, I have private clients. I provide consultation in risk assessment

in toxicology and in public health.

Q. Specifically have you been engaged in cancer risk assessment?

A. Yes. Cancer risk assessments are generally part of any risk assessment that we do depending on the chemicals we are working with.

Q. And throughout the course of your career, do you see chemical engineers performing this type of analysis that you do?

A. No.

Q. Do you have any memberships that you belong to in your role as a toxicologist?

A. I am a member of the Society For Environmental Toxicology and Chemistry as well as for the Society For Risk Analysis which are two professional organizations.

Q. And are they as what it sounds, both specializing one in toxicology, one in risk assessments?

A. Yes.

Q. How long have you been a member of the Society For Risk Analysis?

A. More than 30 years. I started out with the Rocky Mountain chapter about 30 years ago. And I am still a member today.

Q. Okay. And then do you serve in any leadership roles at the Society of Toxicology?

A. At SETC, yes. Well, at the moment I am going to be a session chair for them at their next annual meeting.

Q. And then do you present on toxicology at that annual meeting as well?

A. There are several presentations that are going on that are my work. I am not presenting them, I am having other people present them, but I am there as a session chair and as an attendee. The last presentation I did was for SETC in 2019 at the world conference.

Q. Okay. And then do you hold any certifications?

A. I am considered a qualified person for risk assessments by the government of Saskatchewan.

Q. In Canada?

A. Canada.

MS. HANCOCK: At this time we would ask to have her recognized as an expert toxicologist specializing in exposure and risk assessment.

HEARING OFFICER LAWRENCE: Any parties object or oppose that?

MS. THROWER: No objection.

MS. YOUNG: No.

HEARING OFFICER LAWRENCE: Okay. Granted.

Q. BY MS. HANCOCK: And we previously circulated Exhibit 201, which is her expert declaration, and provided the hearing officer with a record copy of that. At this time we would move to admit that as an exhibit.

HEARING OFFICER LAWRENCE: Any objections to that?

MS. THROWER: No objection.

HEARING OFFICER LAWRENCE: Granted.

(Hearing Exhibit No. 201 admitted.)

Q. BY MS. YOUNG: You are free to reference that at any time. Just at a high-level summary, your expert declaration here covers three main areas, as I've summarized it, and tell me if I'm correct.

The first area you verify that DEQ conducted a proper risk assessment using a methodology that is scientifically proven by adjusting the lifetime arsenic emissions for the operational life of the mine to be the 16 years; is that correct?

A. Yes. They did a proper analysis by EPA methodologies.

Q. And the second area is that you verified that DEQ properly calculated the cancer risk emissions from this permit using that 16 out of 70 calculation and comparing it to the T-RACT AACC of one in 100,000; is that right?

A. Yes.

Q. And the third area you verified that DEQ's use of the five-year rolling average production limits did not exceed that T-RACT cancer limitation of one in 100,000?

A. Yes.

Q. I want to go a little bit through the background of what we heard today but just to make sure we are tacking on the same way.

Can you tell us what an IUR is?

A. An IUR is an inhalation unit risk and it is developed by EPA and published by them.

Q. And what does it measure?

A. It is a risk probability of exposure to a chemical for a lifetime at one microgram per cubic meter that carries an excess lifetime cancer risk of one in 1 million.

Q. So it is measuring a cancer risk in excess of the cancer risk that we see in our everyday lives?

A. Yes.
Q. And were the IURs adopted by DEQ?
A. Yes.
Q. And what do they call it?
A. They call them URFs.
Q. And do you know what URF stands for?
A. Unit risk factor.
Q. The unit risk factor.
How do you know that the unit risk factor is the same as the IUR and adopted by DEQ?
A. You can look at the IURs published by the US EPA and they right down the line compare exactly with the URFs. And I believe that there is one table that, actually in the statute, that noted that that's where they came from.
Q. Okay. Is it commonly accepted within the industry that the IURs and the URFs are the same?
A. Yes.
Q. Do you know what the formula is for a URF that you use in your calculations?
A. To use a URF in a calculation?
Q. Right.
A. It is the toxicity value that you compare an exposure concentration to to estimate

risk from that exposure.

Q. Okay.

MS. HANCOCK: If we could just, Mr. Foster, if you wouldn't mind pulling up Exhibit 203.

Q. BY MS. HANCOCK: I'm sorry for the bulk of this. Normally we look at it electronically. But you recognize Exhibit 203?

A. Yes. It is EPA's health assessment document for inorganic arsenic.

Q. And what's the year of this publication?

A. 1984. March 1984.

Q. And is this a document upon which you rely in the regular course of your role as a toxicologist?

A. I could go back to these documents, but what they do is summarize the approach taken by US EPA and the experts they hired to develop IURs, in this case for inorganic arsenic. They have matching documents for every chemical that they have evaluated. And it documents what they looked at, what they did, and the conclusions that they came to.

Q. Okay. Is this a guidance document that is used as Mr. Tiedemann describes in his declaration?

A. It is not a guidance document. It is a technical background document to show how they came to the conclusion of the IUR.

Q. Okay.

MS. HANCOCK: Your Honor, I would move for the admission of Exhibit 203.

HEARING OFFICER LAWRENCE: Any objections?

MS. THROWER: No objection.

MS. YOUNG: No.

HEARING OFFICER LAWRENCE: Okay. Granted.

(Hearing Exhibit No. 203 admitted.)

MS. HANCOCK: And if we could, Mr. Foster, go to Page 123 of 354 on the PDF.

Q. BY MS. HANCOCK: I am jumping ahead because we are already in this document so I am going to take one fact point out of context here.

You're familiar with Table 6.1?

A. Yes.

Q. Okay. And is this a document that you've looked at before, especially Table 6.1?

A. Yes, I have looked at these before.

Q. Is arsenic a mutagenic mode of action? Or does arsenic have a mutagenic mode of action?

A. EPA does not consider it to have a mutagenic mode of action. Just like Dr. Paden said

earlier today, if you look at how EPA assesses arsenic, even on their printout it says it is not a mutagenic. It is not considered to have a mutagenic mode of action. And that was considered in this document.

Q. And do you know -- we had heard some questions earlier. Do you know if in setting the IUR, or what has now been adopted as the URF, that was taken into account to protect sensitive subpopulations as well?

A. Yes. That is how EPA develops their toxicity values.

Q. Since this background, this is dated in 1984, since this background, has the IUR risk probabilities for arsenic ever been changed?

A. The IUR for arsenic has not been changed since 1984.

Q. Have there been other chemicals that have been updated or changed with new information?

A. Yes.

Q. Okay. So what does that tell you as a professional toxicologist?

A. It tells me that EPA periodically updates their toxicity values based on any new information that they feel changes the conclusions

they made at an earlier time.

Q. And it tells you that no changes were necessary with respect to arsenic, at least as through today?

A. Yes.

Q. Okay.

MS. HANCOCK: If we could just pull up Exhibit 205.

Q. BY MS. HANCOCK: You're familiar with Exhibit 205?

A. Yes.

Q. And what is this document?

A. It appears to be a memorandum to Orvil Green from Robert Wilkosz and Tim Teater.

Q. And do you know who those individuals are, Robert Wilkosz and Tim Teater?

A. I do not know them personally, no.

Q. And this is from the Department of Health and Welfare?

A. Yes.

Q. And the subject line there says, "Request for layman's explanation of what the URF and the TLV are."

Do you see that?

A. Yes.

Q. Are you familiar with what a TLV is?
A. Yes. It's a threshold limit value.
Q. If we go down to the second paragraph. This explanation you can see there that it talks about -- in the first paragraph it talks about that the URF is used to describe the possibility of developing excess cancers over an average of a 70-year lifetime.
Is that accurate and consistent with your understanding of the URF?
A. Yes.
Q. And if we go down to the second paragraph where it says, "each URF represents months of research and often years of policy process. Teams of toxicologists gathered all the toxicological information for each known or suspected carcinogen that could be found around the world. The available data were then rated or point factored per the quality of the research. A URF then is a probability statement derived from this process."
Do you see that?
A. Yes.
Q. And is that consistent with how you understand the URF is utilized?

A. Yes.

Q. It then goes on to say, "Each URF was proposed by EPA and extensively reviewed and debated in public by scientists, health officials, and industry representatives. Every URF represents a consensus of the best science and health opinion of the potency of a given carcinogen."

Do you see that?

A. Yes.

Q. And is that consistent with what you understand is the science and the kind of beef behind the URF number or value that is adopted by the DEQ?

A. Yes. That is the basis for how EPA develops their IURs. And the IUR was adopted by the DEQ and called a URF.

Q. And they also talk about that it was protective of that sensitive subpopulation, we talked about that. But again, that's consistent with what you understood is captured in that value system; is that right?

A. Yes.

Q. Okay. And again, even since this memo was published and authored, are you aware of any changes that have been made to the arsenic numbers

in the IUR or the URF?

A. I am not aware of any changes that have been made to arsenic.

Q. And then let's do one last one here. This one will be 208.

Okay. Are you familiar with exhibit -- I could back up.

MS. HANCOCK: Can I move to admit Exhibit 205?

HEARING OFFICER LAWRENCE: Any objections?

MS. THROWER: No.

MS. YOUNG: No.

HEARING OFFICER LAWRENCE: Granted.

(Hearing Exhibit No. 205 admitted.)

Q. BY MS. HANCOCK: Exhibit 208 that is in front of you now, are you familiar with this document?

A. Yes.

Q. What is this document?

A. This is part of a series on risk assessment that EPA has published. This one deals specifically with inhalation risk assessment.

Q. Okay. Is this the one where it has the derivation of the IUR?

A. This does not have a derivation of the

IUR, but it has the calculation for exposure concentration that indicates that you do need to take into account exposure duration as well as frequency in time if that is a consideration for your project.

MS. HANCOCK: Mr. Foster, I am going to go to Page 18 of 68.

Q. BY MS. HANCOCK: While he's going there, Ms. Lopez, did the IUR consider the risks and effects to those subpopulation sensitivities even as bolstered by Exhibit 208?

A. Yes. As it states right there, that the default linear extrapolation approach, which is what was used to develop the IUR and the URF for arsenic is generally considered to be conservatively protective of public health including sensitive subpopulations.

Q. Did you read Dr. von Lindern's declaration, and he had raised some concerns about whether those children and pregnant women were factored in to consideration with the risk -- with the cancer risk probabilities?

A. Yes, I read his statements.

Q. Is that accurate given your experience with what the IURs capture and the data sets that

we've just looked at in these documents?

A. It is not accurate.

Q. And do you have any concerns that the IUR or the URF lacks in consideration of any of the subpopulation groups with specific sensitivities?

A. No. As stated by EPA it does not.

Q. Okay.

HEARING OFFICER LAWRENCE: Could you repeat that question and answer.

(The requested record was read.)

HEARING OFFICER LAWRENCE: Thank you.

Q. BY MS. HANCOCK: Okay. Let's look at Page 22 of 68.

Do you see equation six --

A. Yes.

Q. -- in Exhibit 208? Are you familiar with what this equation measures?

A. Yes. This equation directs how to calculate an exposure concentration from a contaminate concentration in air.

Q. And we just heard from the DEQ's expert toxicologist and she performed a calculation. Is that where these value systems come from?

A. Yes. I believe that's exactly the same equation she had in her statements.

Q. Okay. And so this is a valid methodology to use as a toxicologist for evaluating and including consideration of that exposure duration?

A. Yes.

Q. In your experience does the exposure time matter for any kind of carcinogen?

A. Yes, exposure duration always matters. That is why it is in the equation, that you do have to take that into account. And you have to take into account as well the lifetime in years. That is in the denominator of equation six.

Q. And when you say "the denominator," what is the code that is reflected up there that would capture that?

A. AT, average in time.

Q. And the average in time would mean that as a denominator you saying how much actual exposure is in the numerator and then total possible exposure is in the denominator?

A. The averaging time takes into account the lifetime exposure of exposure because that is how the IUR is developed, it is developed to be protective of a lifetime of exposure. So when your exposure duration does not equal 70 years, you have

to adjust for that in the numerator of the equation.

Q. Thank you. So the lifetime exposure goes in the denominator and then the actual exposure time goes in the numerator?

A. That's correct. And as you can see in here, the other adjustments that they direct you to do are 365 days a year, 24 hours a day. That is the standard in the denominator. If you have any variations of those, you could take those into account as well in the numerator.

Q. So we might come back to this in a few minutes when we do our calculations. But it's critical for what you just said that when you're looking at a lifetime exposure, it is lifetime exposure based on 24 hours a day, seven days a week, 365 days a year?

A. Yes.

Q. And so when you're looking at the numerator, the actual exposure, you want to measure the same 24 hours a day, seven days a week, 365 days a year?

A. You do if that is the maximum exposure that you believe will occur in your project. It can be less, obviously.

Q. And maybe we will do the spoiler now.
A. Sure.
Q. If someone was going to have less days of the year, for example, they celebrate holidays, there's weather events that might not let you operate. How would you account for that in both the numerator and the denominator to make sure you are measuring the same?
A. The denominator doesn't change, but the numerator does change. You would have fewer days per year or perhaps fewer hours per day depending on what that difference is. And then the exposure duration is again the length of the exposure, how many years can you be exposed at this project, at this site.
Q. Okay. So we will come back to that when you do your calculations in just a minute.
I want to turn to the AACC. Can you tell me what the AACC is?
A. It stands for ambient annual cancer concentration I believe, or contaminant concentration. It is a term in the statutes of IDEQ.
Q. Under Section 586 in particular to this?
A. Yes.

Q. How does that relate to the IURs or the URFs for purposes of your calculations as a toxicologist?

A. It is a one in a million risk divided by the IUR to come up with an ambient air concentration to which one could be exposed every day for 70 years without exceeding an excess cancer risk of one in 1 million.

Q. And in this case we have -- you understand that we had -- Perpetua had opted for the T-RACT controls that lowered the cancer risk probabilities to one in 100,000.

A. Yes.

Q. So how do you convert -- make that same calculation using the IURs with respect to the T-RACT numbers?

A. You would use the risk of one in 100,000, which is one E to minus five, divided by that same URF. And then you could come up with an AACC concentration that is ten times higher than the AACC concentration at one in 1 million.

Q. Okay. And we just heard the DEQ's toxicologist perform her calculation utilizing the actual exposure as compared to the lifetime risk exposure under the AACC.

Did you perform a similar calculation?

A. I did.

Q. Okay. And is that the right calculation to perform?

A. Well, the right calculation to perform is this one to come up with an exposure concentration to which you can compare a risk-based screening concentration. Or you can use the IUR to multiply by the exposure concentration as it is shown up there, and that will give you the risk, the lifetime risk.

Q. And did you perform that same calculation with respect to Perpetua's mining permit?

A. Yes.

Q. Actually, how many calculations did you perform?

A. I performed at least three. There are several different ways you can rearrange both the published AACC or the exposure concentration calculation and you will arrive at the same conclusion, which is that the risk should be the same.

Q. And so when you say you performed three different calculations, it is not to get three

different results, is it?

A. No. No, it is to confirm that no matter how you look at it you are coming up with the same answer.

Q. And do you perform those three different calculations so you can verify that the other calculations were performed correctly?

A. Yes.

Q. Okay. So tell me about the first calculation that you performed. And if we want to cross reference it, it is on Page 8 of your declaration, which is Exhibit 201, Paragraph 24.

A. Yes. So this calculation took the exposure, the CA, contaminate concentration in air, which was the emissions from the mine, multiplied it by 24 hours a day, 365 days a year, for 16 years, and then divided by the averaging time in years to develop an exposure concentration that is equal to .00095.

Q. Okay. How did you know to use 16 years as the actual exposure duration in this calculation?

A. Well, using the maximum emissions rate that was developed based on the maximum production of the mine, that would deplete the source in

16 years and that's as long as it could happen. It can't happen beyond the source being removed. So at the maximum emissions for 16 years, that's why I used the 16 years. At that point the source is depleted and there could be no more emissions.

Q. Okay. I want to back up and make sure that we have clear on the record each one of those elements.

You understand that this permit contains a condition that limits the total production that could come out of this mine to approximately 788.4 million tons?

A. Yes.

Q. And so no matter what Perpetua wants to do, they can't pull any more ore out of the ground under this permit other than that amount.

A. That is my understanding.

Q. Okay. And then you also understand that there are permit conditions under this permit that limit how much production they can take on a daily basis; is that right?

A. Yes.

Q. And it's approximately 180,000 tons a day; is that right?

A. That's what I understand.

Q. And so no matter how much they want to take out on a daily basis and how many crew members they have or how many tools they have, they can't take out more than what the permit condition allows at approximately 180,000 tons a day?

A. Yes. That is my understanding that the permit has limits in it.

Q. And then you also understand that on a five-year rolling average, that they cannot average more than 135,000 tons per day on that 5-year rolling average basis?

A. Yes.

Q. And so no matter how much they want to take 180,000 tons a day every day, at some point in a five-year period they have to start tapering down in order to make sure they hit those averages; is that right?

A. Yes.

Q. And you calculated if the mine operated 24 hours a day, seven days a week, taking out the maximum capacity that they could take using that five-year rolling average, that they would take 16 years to deplete the production limits that were allowed under that permit; is that right?

A. Yes. Those are the numbers that I

confirmed before doing my calculation.

Q. And you came up with -- if you do that full calculation, if we look ahead to your Paragraph 28, what was the cancer risk that's presented by that total production limit and that total mine operation under the permit?

A. At limit the concentration is .0095, that is the exposure concentration. You can compare that to the T-RACT AACC by dividing it, and that represents a risk that -- well, you multiply it by one in 100,000 to estimate the risk associated with the .00095.

Q. Okay. So if the mine operates around the clock every day of the year for 16 years straight, what is the cancer risk that is being emitted by those mining operations? What's the actual value that you calculated?

A. The actual risk is four in a million or approximately one in 240,000.

Q. Okay. And that is what you have in Paragraph 28 of your declaration?

A. Yes.

Q. And that one in 240,000, we compare that against the T-RACT cancer risk probability of one in 100,000, and the mining operation is less than

that?

A. Yes.

Q. Approximately two and a half times less than that?

A. Yes.

Q. And if we did that on a percentage basis, do we know what that works out to be?

A. I believe we saw earlier that it works out to be about 40 percent.

Q. Okay. And when you say "earlier," that's because the petitioners had put in Exhibit 303 and it showed that there was -- 301, excuse me, it showed it was 41.3 percent; is that right?

A. Yes.

Q. Okay. And so 41.3 percent you understand means of the cancer risk probability that you have to stay under, in the worst case scenario operating every single day for 365 days a year for 16 years straight, you have taken every ounce of ore out of the ground that you are entitled to take under this permit, you have only used up 41 percent of what that cancer risk probability would be; is that right?

A. Yes.

Q. And we did have some questions earlier today, well, what happens if we build in a 16-year limitation into the permit? And obviously under this example that we've looked at, we have looked at kind of worst case scenario where you are operating in the most concentrated, shortest duration of time to evaluate that cancer risk.

Does that mean it is realistic to think you can get all the ore out of the ground in that 16 years?

A. If the exposure -- the concentration in air was calculated using maximum production and maximum everything and that was going to take 16 years, if you're changing the 16 years and you're not taking out as much every year, then the concentration in air goes down, the emissions go down, which would maybe increase how long it would take to pull it out. But that final calculation would still be the same because you would have a certain concentration that accumulates over a certain amount of time and that is tied to the extent of the ore body.

Q. So for example, of that 24/7, 365 days, if they operated at 50 percent of that, you take into account that there is shift work or holidays

or weather events or whatever life happens that allows you to not work every day all day long, if they were working at 50 percent of that, does that mean that the emissions would be proportionately less because your production is proportionately less?

A. Yes.

Q. Okay. So in other words, it doesn't matter if you spent a longer period of time in order to take the same amount of the production limits that are currently in the permit, it doesn't matter if you took longer to get them out, it doesn't change your risk factor or your risk calculation?

A. It does not change the risk because it does not change the cumulative exposure concentration.

Q. At the risk of being a little bit cumulative here, I am wondering if you can use our white board and do a calculation for us to show that. And I know you have worked one up for us, so either you can do it live or you can use the one we've already worked up and walk us through it. Whichever you prefer.

A. I am happy to do either one. If people

want to watch me do math on the fly, I will do it from scratch.

MS. THROWER: Ms. Hancock, I am just wondering how we can have Bryan see this.

MS. HANCOCK: We can take a picture of it and send it to Bryan.

Bryan, can we take a picture of it and e-mail it to you?

MR. HURLBUTT: Yeah, that's fine.

MS. HANCOCK: So Bryan, we will mark that as Exhibit 220.

MR. HURLBUTT: Okay.

Q. BY MS. HANCOCK: Ms. Lopez, do you want to walk us through this calculation?

A. Sure. The one at the top is the T-RACT AACC, .0023 micrograms per cubic meter per year. And it is assumed that there would be a 70-year exposure because this is based on the URF, which is the 70-year lifetime exposure. The total exposure concentration, the cumulative exposure concentration over 70 years would be 0.161 micrograms per cubic meter. And that is represented by the URF and AACC for T-RACT. And this is at one in 100,000 risk level.

So if you took the maximum production of

the mine, which here I put is .00414 micrograms per cubic meter. This is the maximum emission based on the maximum daily production limit which is what is presented in the permit. 16 years is the number of years until the production limit of the mine is reached. That is the 74 -- I'm sorry, I don't have the number off the top of my head. But the limit of production of the mine based on the ore reserves.

This calculation gives you a cumulative dose over that time of .066 micrograms per cubic meter. So you can see this is below this already. If you --

Q. When you say "this," you mean? Just for the record.

A. I'm sorry. The T-RACT AACC cumulative dose is higher than the dose for exposure to the life of the mine based on production limits.

If you were to take .066 divided by .161, which is the T-RACT AACC cumulative dose, you would come up with a risk that is equivalent to four in a million or one in 240,000. That is one other way to check that the calculation was done correctly.

There were earlier questions that were

brought up about well, what happens if the life of the mine goes longer. And this is the interaction between exposure concentration, emissions rate, and the amount of time that it takes.

If you drop down production 50 percent, let's say for whatever reason, that would have a concurrent drop in the concentration, the exposure concentration. And then that would happen for 32 years, at which point you would still end up with a cumulative dose that is the same, .066.

Q. And in that example that you just walked through, that is at 50 percent production rate; is that right?

A. That is. Because if you're 50 percent production for the emissions, it's going to take you twice as long. But the end result is that you still have the same cumulative dose for your lifetime.

Q. So even if you took 32 years, because you have the lower dose, you're still at a risk level of one in 240,000?

A. That's correct. You can't decrease this without increasing this and vice versa.

Q. And this is really kind of the inverse of what you were doing with the 16 over 70

calculation to begin with. You're just looking at the worst case scenario, the most concentrated amount of mining operations that's going to pull out the most emissions in the shortest amount of time; is that right?

A. Yes. It's my understanding that this had to be calculated on the worst case maximum scenario for mine production.

Q. Okay.

MS. HANCOCK: We would move to admit Exhibit 220 into the record.

HEARING OFFICER LAWRENCE: Any objections?

MS. YOUNG: No.

MS. THROWER: No.

HEARING OFFICER LAWRENCE: Admitted.

(Hearing Exhibit No. 220 admitted.)

MS. HANCOCK: I was just going to also move to admit Exhibit 208 as well into the record, which I think is the last exhibit I need to have admitted. This is the risk assessment, the 2009.

HEARING OFFICER LAWRENCE: Any objections to admitting that one?

MS. YOUNG: No objection.

MS. THROWER: No.

HEARING OFFICER LAWRENCE: Okay. It is

admitted too.

(Hearing Exhibit No. 208 admitted.)

HEARING OFFICER LAWRENCE: Can I ask the question while we have this stuff in front of us?

So I totally get the sort of inverse relationship between duration and exposure concentration and how one goes up and the other goes down and you get the same number.

My question is about, can you summarize for me the science behind that mathematical assumption that the cancer risk doesn't change because the lifetime exposure is the same no matter what you are doing with time and concentration?

THE WITNESS: Sure. Exposure to a higher concentration for a shorter amount of time is the risk equivalent of a higher -- lower concentration for a longer period of time. That is stated in one of EPA's documents. I can point that out to you. But that is the relationship. It is the cumulative dose over a lifetime.

HEARING OFFICER LAWRENCE: Right.

THE WITNESS: In this case the cumulative dose is related to how long the source is there. And that would be 16 years at this production rate. It could be longer if it was a lower production

rate, but the end result is that the cumulative dose does not change.

HEARING OFFICER LAWRENCE: That would be helpful, I think, if I can lay eyes on that EPA document that you referenced.

Is that in one of the ones you have already admitted?

THE WITNESS: I don't think you have admitted it. I don't know. EPA 2005.

MS. HANCOCK: We do have the 2005 EPA document. Perhaps what we can do is grab it on a break, and then can we come back to that one?

HEARING OFFICER LAWRENCE: Yes.

MS. YOUNG: I apologize for interrupting. I would request a break here soon. Maybe this is a good time to take a quick break? I apologize it's in the middle of testimony.

MS. HANCOCK: That's okay with me.

HEARING OFFICER LAWRENCE: How long makes sense?

MS. YOUNG: 15 to 20 minutes.

HEARING OFFICER LAWRENCE: Let's do 20.

(Break taken from 3:24 p.m. to 3:49 p.m.)

HEARING OFFICER LAWRENCE: So as we left off, as I recall, we were doing direct of Ms.

Lopez, and then there was this issue that I asked about a particular document that isn't currently attached to any expert declarations.

Is that right?

MS. HANCOCK: That is correct. It is the 2005 EPA document. We are having hard copies brought over so everybody will have a hard copy. But we will mark it as Exhibit 221 and we will just look at it electronically for right now, if that is okay with everyone, and then you will have a hard copy by the end of the day.

Q. BY MS. HANCOCK: Ms. Lopez, you have to tell us which page to go to.

A. It is Page 10 of Appendix A.

Q. What are we looking at here in this document?

A. This is one of several guidance documents from US EPA and this is the guidelines for carcinogen risk assessment, so it lays out the foundation of how you evaluate carcinogens in a risk assessment.

Q. Okay. And earlier when we were looking at Exhibit 203, that was the 1984 document, you specifically said that is not a guidance document;

is that right?

A. That's right.

Q. Is this one an actual guidance document?

A. This is a guidance document, yes.

MS. HANCOCK: I don't remember if I said this on the record, but we will have this as Exhibit 221.

Q. BY MS. HANCOCK: If we can go to Page 10, did you say?

A. I think it is A-10. It is Page 10 of Appendix A.

Q. And the hearing officer had asked for -- you had described the science when we were talking about Exhibit 220 and if there is a lesser dose or exposure over a longer period of time that is the same as having a higher dose on a shorter period of time.

A. Correct, that was the question. And I think this speaks directly to it from US EPA, that absent data to the contrary, the default assumption is that the cumulative dose received over the lifetime, which is what that .066 would be, it is an appropriate measure of dose or exposure. This assumes that a high dose of such an agent reached over a shorter period of time is equivalent to a

low dose spread out over a lifetime.

And this is speaking as to how the IUR can be used in either way but you do need to take into account exposure duration as well as the concentration to which one is exposed.

Q. And so in this situation, once Perpetua had done its modeling work and determined the maximum emission of arsenic from the mining operations, we know what the dosage amount would be; is that right?

A. The maximum emissions concentration based on maximum production limits for 24 hours a day, 365 days a year, would take 16 years to reach production limits and that is how you come to the cumulative dose of .066.

Q. And having a production limit of 788.4 tons in the permit as a condition of the permit, is that what provides the cancer risk protection in this permit to make sure that the emissions from this mine are in conjunction with the daily limitations of productivity, is that what provides the protection to ensure that there 's never a greater cancer risk posed by this mining operation than the one in 100,000?

A. Yes. Because it limits the amount of

emissions cumulatively until you reach the production limit.

Q. So you can produce less on a daily basis and go a longer period of time and still stay within those exact same calculations that you performed, which would mean one in 240,000 risk probabilities for developing excess cancers as compared to the T-RACT controls?

A. Yes, because the cumulative dose would not change.

Q. Based on your math and your analysis of the calculations that the DEQ toxicologist performed, is the adjustment factor creating a misleading risk analysis that would underestimate the actual cancer risk from this project?

A. No. The method used is completely in line with EPA guidance documents that are not specific to this project, they are not specific to Idaho. They are the standard of practice that EPA sets and they were developed completely outside of this particular process.

Q. And just said more basically, is anyone slicing and dicing these numbers or looking at this permit in a fancy way or creative way that is trying to disguise or hide the actual cancer risk

that is being presented here?

A. No. This is how the science is done. This is the methodology that is required under the guidance documents in conjunction with the use of an IUR or URF.

Q. And is this calculation that you performed, is this settled science in the toxicology field?

A. Yes.

Q. Is this unique to Idaho or is it done beyond Idaho?

A. It is done beyond Idaho. It is not unique to Idaho and it is used throughout the United States.

Q. Okay. Would it accurately reflect the cancer risk presented by this mining permit with the conditions that are in the mining permit if this project were evaluated on a 70-year lifetime exposure?

A. The 70-year lifetime exposure is the basis for the IUR, so you do have to adjust the concentration in air by the exposure duration in order to make an appropriate comparison between an exposure concentration and a dose based on what your exposure concentration is.

Q. And if you didn't make that actual exposure duration calculation, would it be an accurate reflection of the cancer risk that is presented by this mining permit?

A. No, it would not.

Q. Do you believe that DEQ accurately and properly considered the risk from the emissions from the SGP mine?

A. Yes.

Q. And you had the opportunity to read Dr. von Lindern's declaration; is that right?

A. Yes.

Q. And is the effect of -- do you have an opinion as to what the effect is that he's advocating in his declaration as to how this should be calculated?

A. There is quite a bit of discussion in there that regards different life stages as to when someone might be exposed to it and that it might have longer reaching effects than if an adult is exposed. All of those goes to something called a mutagenic mode of action.

Arsenic, I think actually as Dr. Paden showed in her calculations, is not considered to have a mutagenic mode of action, so that adjustment

for that early life stage exposure is not necessary.

But even if it were necessary, as it is considered for other chemicals, that is done actually in the exposure duration.

Q. And have you calculated what his methodology would represent in a value form as compared to the one in 100,000 T-RACT controls?

A. I did not reperform whatever he was trying to do.

Q. Okay. In your professional opinion, would his methodology overestimate the cancer risk value system that would be required by the AACC?

A. Yes. His approach overestimates the risk associated with arsenic in air.

Q. And so it would make it more stringent than what's required under the AACC or under the T-RACT as well?

A. It seems to me that his interpretation disregards the fact that there is a lifetime exposure, but -- I'm sorry, there is a lifetime averaging time but there is not a lifetime of exposure duration.

Q. And if we look at Paragraph 39 of your declaration in Exhibit 201. It is on Page 11 of

your declaration. We had talked earlier about the multiple ways in which you performed a calculation. You have one here in Paragraph 39.

Can you describe what you're calculating in Paragraph 39?

A. Yes. If you took the T-RACT AACC of .0023 that is equivalent of lifetime cancer risk of one in 100,000, and you assume that that has to be met every year, you're actually looking at a risk that is equivalent to one in 7 million. And that's because that AACC assumes that you will be exposed at that concentration for 70 years. So if that is not going to be met, then you have to adjust for the exposure duration, which is a shorter amount of time. So that's what I was discussing there.

Q. Okay. So rather than one in 100,000 as required by the T-RACT, it would apply a new incremental benchmark of one in 7 million?

A. Yes.

Q. You say in Paragraph 41 of your report that the T-RACT AACC represents the chemical-specific airborne concentration at which the risk to an individual, if exposed all day every day for a lifetime, would be one in 100,000.

Would any other interpretation define

fundamental toxicological science used by the EPA in the development of the IURs?

A. Yes, it would.

Q. Okay. I want to talk about the five-year rolling average for a moment.

HEARING OFFICER LAWRENCE: Ms. Hancock, can I jump in with a quick question?

MS. HANCOCK: Sure.

HEARING OFFICER LAWRENCE: Ms. Lopez, on the one in 7 million risk in Paragraph 39. Can you for me just sort of articulate in general terms how protective that's considered in the toxicological world? Are there other times when that one in 7 million would be considered too risky or is that considered pretty safe in just about all contexts?

THE WITNESS: That would be considered safe in about all contexts because again it is an incremental risk. And I think as Dr. Paden spoke to earlier, the risk range that you regulate to is between one in 10,000 and one in 1 million. So this is seven times below 1 in 1 million and that is because it is looking at a risk per year. Cumulative risk, cumulative dose, so that is why it is one in 7 million.

HEARING OFFICER LAWRENCE: All right. Thank

you.

Q. BY MS. HANCOCK: So in other words, seven times higher than what even any of the experts would put in the range of risk analysis?

A. Seven times lower. It is one in 7 million as opposed to one in 1 million which is considered the lower end of that range.

Q. Okay. Let me fix that. In other words, it would be seven times more stringent than the most current stringent standard?

A. Yes.

Q. Okay. And in this situation we're actually -- it is even more extreme because we are comparing it to the T-RACT which would be one in 100,000 is the upper limit within which we have to make sure we don't operate to create a cancer risk; is that right?

A. Yes.

Q. If we turn now to the five-year rolling average. Just at a high level, what is your conclusion as to whether a five-year rolling average production limit ensures that the production from the mine will not exceed the cancer risk at any point of time in that five years?

A. The five-year rolling average allows for

production changes that can happen on a daily basis because of I'm sure many numerous work site conditions that would prevent a maximum production from happening.

But whether it is five years or six years or the full 16 years, in the calculation that IDEQ did, they assumed a maximum emission that could happen for 16 years until the production limit is reached, which is a worst case scenario. And the cumulative dose is then .066. And that will carry an incremental lifetime cancer risk of one in 240,000, which is below the T-RACT standard.

Q. If we could pull up Dr. von Lindern's declaration. I don't know if he is -- if we have a number assigned to it?

MS. THROWER: No, not yet.

MS. HANCOCK: Do you want a number assigned to it?

MS. THROWER: Sure.

(Hearing Exhibit No. 302 marked.)

Q. BY MS. HANCOCK: If we look at Dr. von Lindern's declaration, I would like to turn to Figure 1.

HEARING OFFICER LAWRENCE: How many pages in is that?

MS. HANCOCK: It is on Page 12.

Q. BY MS. HANCOCK: You've had an opportunity to look at Dr. von Lindern's Figure 1; is that right?

A. Yes.

Q. And have you been able to make sense of what you understood Figure 1 to be?

A. I don't necessarily agree with his labelings there, but I think what he was trying to do is graph continuous exposure to the AACC for 70 years. That's what that diagonal line would represent. He has it marked as cumulative risk, but it could also be seen as cumulative exposure, cumulative dose.

Q. Okay. And maybe at the most basic level, does duration of exposure matter in your world, duration of exposure to a carcinogen?

A. Yes, it does matter. And I think this figure shows that it does. Because as you can see, although he has it labeled age and years, I would call that exposure duration. That at 16 years of exposure the risk is two in a million. It doesn't continue on if the exposure stops. That's where the risks would stop.

Q. Okay. So if we look at 16 years of

exposure, we can see there's actually arrows that point to where on that line where the risk would be; is that right?

A. Yes.

Q. And the orange line up top, that is what you understood would be representative of that one in 100,000 T-RACT number?

A. Yes.

Q. So we can see that if it is at 41 percent, which we have looked at other numbers in your calculation of one in 240,000 gets us about the same number, we are well under what would actually be the actual cancer risk in the T-RACT; is that right?

A. That is right. Because that one in 100,000 orange line across the top is the limit of risk. And the risk is four in a million, so that would be at that four in a million stage, what he has here is the AACC. But if you were to put the project-specific exposure concentration in, it would be, at 16 years, it would come up to about the 4 E to the minus six line. It then would continue straight across to the end. It would not continue on diagonally, it would end and go straight across.

Q. Because as we just talked about with a limit on the production limits, there is no more emissions and so no more greater risk being presented by this project; is that right?

A. That's right.

Q. So even after the 16-year life of mine, you wouldn't continue up the exposure line?

A. No, you would not.

Q. If we turn to your declaration, at Figure 1. And this is in your attachment, so for electronically it is Page 18 of 42. Or Page 4 of her Attachment A.

Do you have a similar slope that you have reflected here?

A. Yes. This figure came from the EPA 1984 document. It is one of several that they have in there. And this showed how they did the linear extrapolation to develop the IUR. This one is specific to this study that they looked at. But it is that same slope of the line that you can see on the X axis on the bottom, that the cumulative dose increases the risk, which is on the Y axis, over the course of years.

Q. Okay. And what does this figure tell us about the risk that's presented here? How would we

read this in relation to this permit?

A. That the risk increases with dose, but that dose is cumulative. And once you've hit that total cumulative dose that is related to the production limit, that the risk stops and that would be it, so it wouldn't appear on this line.

But this is -- it's the same concept that was in Dr. von Lindern's Figure 1, that it is linear, it is related to exposure duration, and it is related to cumulative dose.

Q. Just in summary of all the things that we've been talking about, does the permit issued by DEQ present an unacceptable risk as governed by the regulations?

A. No. Because the cumulative risk is about four in 1 million, which is below the standard risk that they were using.

Q. And from your professional judgment as recognized toxicologist expert in this matter, does DEQ's permit analysis ensure that the mining operations will operate in a manner that will not present any excess cancer risk as compared to the T-RACT probabilities?

A. Yes. Their analysis shows that the cumulative incremental cancer risk will be below

that specified in the T-RACT.

Q. Okay.

MS. HANCOCK: That's all the questions I have.

HEARING OFFICER LAWRENCE: Okay. Ms. Young, do you have questions?

MS. YOUNG: I don't have any questions, no. Thank you.

HEARING OFFICER LAWRENCE: I'm sorry, I forgot about the issue we were talking about before, about witness tomorrow. Do we need to do anything on that?

MS. YOUNG: We do, but I haven't had a definitive answer.

MS. THROWER: I wanted to confer with Bryan before I decide for both of us.

HEARING OFFICER LAWRENCE: I just wanted to make sure I wasn't forgetting something.

MS. THROWER: I will do that when we are done here.

MS. HANCOCK: I think now that we have the hard copy exhibits, if we can pass those out, and then I would like to formally move to admit Exhibit 221.

HEARING OFFICER LAWRENCE: Okay. Anybody

object to that?

Okay. It is admitted.

(Hearing Exhibit No. 221 admitted.)

MS. THROWER: We are going to deal with cross-exam the same way we did with Dr. Paden. Bryan may have a question or two in follow up.

HEARING OFFICER LAWRENCE: Okay.

CROSS-EXAMINATION

BY MS. THROWER:

Q. I just wanted to go through and start with your background. So are most of your risk assessments for contaminated sites?

A. The risk assessments I have done range from contaminated sites to I have done some permitting. They are all forward-looking in the sense that you have a particular situation and then you project the risk forward.

Q. Okay. And did you say you did some risk assessments for permitting?

A. I have done some, yes.

Q. Was that in Idaho?

A. It was not in Idaho.

Q. And when you say you did risk assessments that are forward-looking, exactly what

do you mean in terms of are there different factors to consider or I guess can you explain that a little better?

A. Sure. You take the chemical concentration in whatever media you are looking at and you estimate what would happen, what would be the risk, what would be the hazard if someone is exposed to that concentration for a certain exposure duration for a certain exposure time, if it is for cancer over a lifetime, and come up with your risk. So it is all looking forward, it is not looking backwards into the population.

Q. Okay. And is it forward-looking in terms of potential other sources for that same carcinogen that that same receptor might experience?

A. Well, no. Most of them don't need to take that into consideration because you are looking at a site and you are looking at full exposure to that site. Some of the risk assessments I have done on consumer products do take that into consideration, but that is a different regulatory framework, if you will.

HEARING OFFICER LAWRENCE: Ms. Lopez, if you could speak up a little. Since you are facing that

way I am having trouble hearing you.

THE WITNESS: Sure, I'm sorry.

Q. BY MS. THROWER: So what other factors aside from exposure duration do you consider in your risk assessments?

A. It depends on the risk assessment. It can be exposure time. It can be exposure frequency. Exposure time is the hours per day. Exposure frequency would be days per year. Exposure duration is the number of years. There can be other considerations in there such as an intake rate for inhalation, it would be the inhalation rate. If you are going to figure out the actual dose you are going to need the body weight as well. So those are some of the factors that could be taken in.

Q. Did you consider any other factors other than this exposure duration for this permit?

A. Well, the calculation assumed a 365-day-per-year exposure frequency and a 24-hour-per-day exposure time, so those were taken into account as directed by EPA to do a risk calculation.

Q. But no body weight. For instance, I assume body weight is taken into account for

exposure to children versus an adult?

A. It would be if we were looking at a different kind of assessment. But IURs are based on exposure concentration and not a dose.

Q. If you could turn to your declaration. I want to go ahead and look at Page 2. Maybe I meant to look at your memorandum.

Let's go to your memorandum that is attached to your declaration, Page 2. That is ERC4292.

So can you read the third bullet point there under -- you have a paragraph that starts, "This memorandum supports my expert opinion on the first two issues." Can you read that third bullet point?

A. Yes. "This memorandum addresses the use of a short-term adjustment factor provided for in IDAPA210.15 of the air rules allowing a ten times adjustment to the AACC for short-term projects. This is an example of the use of exposure duration and risk assessment. And the adjustment for exposure duration in other risk assessments is also appropriate."

Q. Okay. So you state in that bullet point that the use of short-term adjustment factors

provided for in 210.15.

Can you explain where that is in 210.15?

A. Sure. They are discussing an adjustment to the AACC based on a short-term exposure, short term there meaning five years versus 70 years, which is consistent with what the EPA would do to incorporate an exposure duration into an exposure concentration.

Q. So when you say five years, this is what we've been referring to as the short-term source adjustment provision?

A. Yes.

Q. And so your understanding is that that short-term source provision allows a ten times adjustment to the AACC in Section 586; is that correct?

A. No. What I'm saying there is that these regulations do recognize that there is a difference in exposure duration that has to be taken into account when you are evaluating risk.

Q. Okay. And do you see anything in the regulations that take into account doing exposure adjustments to look at risk for anything that is planning to operate for more than five years?

A. It does address, and I'm sorry I don't

know the exact number, but it does address taking into account project-specific considerations. So yes, I do believe it is in there.

Q. But you can't point to anything right now?

A. Section 210.12 maybe. I don't have the regulation in front of me, I'm sorry.

Q. Do you want me to pull that up or do you know if that is the exact provision or you're not sure? I don't want to scroll through the entire rule. I don't think anyone wants it at this point.

Okay. That's fine.

So let's look at the last paragraph on Page 2 of your memorandum. Can you just read that first sentence of that last paragraph, please?

A. The one that starts "Based on my review"?

Q. Yes, thank you.

A. "Based on my review of the relevant documents, in my opinion the foundation of the TAPs rule is consistent with the scientific principles underlying dose response assessments that are established by EPA. IDAPA586 reflects EPA risk assessment methodology that prompts adjustment of the exposure duration to assess the dose response

risk assessment properly."

Q. So what specific documents did you review that established the foundation of the TAP rules for you?

A. Well, the foundation of the TAP rules are the IURs that came from the US EPA. If you were going to use the US EPA, the toxicological values, you have to adopt the EPA guidance documents that regulate how they are to be used.

Q. Okay. Is there any documents that lay the foundation for using exposure duration adjustments that were ultimately incorporated in the rules?

A. Well, by adoption of the IURs you have adopted how they are going to be used. And EPA directs, in EPA 2009, I think, is the one we showed, also in EPA 1989 that was introduced earlier, and several other guidance documents, how they are to be used.

Q. So we've talked about the TAPs being an incremental standard.

What is your understanding of an incremental standard?

A. I don't believe we've agreed that they are an incremental standard. They are an

incremental unit and it is based on risk.

Q. Okay. So what does it mean for you when it's an incremental -- like the term "incremental," what does that mean to you?

A. An incremental risk over that that would be experienced otherwise in life.

HEARING OFFICER LAWRENCE: Ms. Thrower, now I am having trouble hearing you.

Q. BY MS. THROWER: So on Page 5 of your memorandum, you talk about the IRU as an incremental risk considering unrelated risk present over a lifetime.

Do I have the right page?

A. I'm not sure.

HEARING OFFICER LAWRENCE: While she is looking for that, can someone remind me what particular document we are in right now?

MS. HANCOCK: Exhibit 201.

MS. THROWER: It is her declaration. And I am trying to figure out if this is from the declaration itself or if it is in the memorandum that was attached.

Q. BY MS. THROWER: So in Paragraph 22 of your declaration, you start to discuss the same formula from the EPA superfund guidance that

Dr. Paden discussed, correct?

A. Yes.

Q. And again that formula is from the EPA superfund risk guidance?

A. Yes. This is from EPA2009 that is the guidance for the superfund.

Q. And you use the same number, very close to the same number. I think you and Dr. Paden differ by the last digit there, but it's neither here nor there at this point. But you use the same number that Dr. Paden did to calculate your excess risk, cancer risk; is that correct?

A. I used, yes, the same concentration.

Q. And you also call that the highest model annual arsenic concentration; is that correct?

A. Yes.

Q. And did you just obtain that number from Perpetua or DEQ?

A. I was provided it by Perpetua.

Q. So you didn't do any calculations on your own to derive that maximum concentration?

A. No, I am not an air modeler.

Q. And you're not familiar with how the number was derived?

A. I did ask how the number was derived,

and it was derived on maximum production to come up with the maximum emission rate.

Q. Okay. Do you understand it is a five-year rolling average?

A. Yes.

Q. Okay. Obviously from your declaration you talk about that.

Is a five-year rolling average necessarily going to be a maximum emission rate?

A. Under what timeframe?

Q. Annual.

A. No. It is a five-year rolling average.

Q. I want to go to Paragraph 39 of your declaration. And I just want to go through the second sentence where you state, "if the T-RACT AACC of .0023 micrograms per cubic meter for arsenic were based on a one-year exposure then the risk presented by that value was about one in 7 million."

Can you explain how you got that calculation?

A. Yes. You take the .0023, multiply it by one year, and divide it by 70. And the resulting number has to be multiplied by 1 E minus five, sorry, it is one in 100,000, since the T-RACT AACC

of .0023 is based on a one in 100,000 incremental lifetime risk.

Q. So this would be an analysis you would do to get this lifetime risk if your source was only planning to operate at one year?

A. Well, you would take the concentration that the project gives you that they're going to produce. I wouldn't take the AACC. This is the risk associated with that AACC for one year.

Q. I apologize. Let's say they are maximum emissions equalled to that AACC?

A. Yes.

Q. Then your cancer risk assessment or calculation here of one in 7 million this is basically based on if this was a one-year project?

A. Yes.

Q. So under the air rules, again we talked about the short-term sources that operate for five years or less having this exception. For a source operating for six years or more -- and Mr. Hurlbutt asked Dr. Schilling about six-year sources. For a source operating six years or more, would they be able to go through this T-RACT AACC provision under this exposure duration theory using an adjustment of six years over 70?

A. I think that would be up to IDEQ. I think if you do that you have to accept a limit on your project.

Q. So presumably if a source was only operating over six years, all the emissions would occur in that six years. I understand under the exposure duration adjustment you spread those out over 70 years.

But in the case of someone in the area for six years, let's say a child, is loading a lifetime risk of arsenic exposure within six years the same risk for a child as it is for an adolescent or adult?

A. According to EPA's methodology and their toxicity values, yes.

Q. Okay. And Section 586 specifically says that the AACCs are annual averages.

What's your basis in Paragraph 37, why don't you turn to that, where you state "the AACCs are not annual average air concentrations limits or standards."

What is your basis for making that statement?

A. The AACCs are an inverse based on the risk of the IUR, and they are a risk-based

concentration that represents a concentration that a person could be exposed to 24 hours a day 365 days a year for a lifetime without exceeding a risk of one in 1 million if we are talking about the AACCs or one in 100,000 if we are talking about the T-RACT AACCs.

Q. And just above that in Paragraph 35 you said that, in the second sentence in Paragraph 35 you say that "omitting this adjustment," the exposure duration adjustment, "is contrary to common scientific practice and the intent of the air rules as reflected in DEQ documents."

And I added a couple of words there because I think there was just a little bit of typographical error there.

You attach to your memorandum, you attach A, an Idaho DEQ 1992 and 1993 documents. So if we could turn to that document.

MS. THROWER: Bryan, can you pull that one up on the screen? So that's RE4405. And this is not one of the attachments that was directly attached to her declaration, but it was like that big group of attachments that I think you guys sent over separately or something. I don't know.

So Bryan, if you can scroll so we're at

comment 108.

MS. HANCOCK: Do you have hard copies of it?

MS. THROWER: No. This was attached to Ms. Lopez's declaration.

HEARING OFFICER LAWRENCE: 4405, was that the REC number?

MS. THROWER: 4405, yeah.

MR. HURLBUTT: Sorry, the one displayed is the one without the REC number.

MS. HANCOCK: Maybe if we could go up to the title page just so we can orient her?

THE WITNESS: Okay.

HEARING OFFICER LAWRENCE: Title page of 4377.

MS. HANCOCK: What I am trying to figure out is if this is part of what we admitted as an exhibit.

HEARING OFFICER LAWRENCE: It is in the big binder that you guys provided to me.

MS. HANCOCK: Okay.

Q. BY MS. THROWER: So just to go back. So you said that omitting this -- in Paragraph 35 in your declaration, you state that "omitting this adjustment is contrary to the common scientific practice and the intent of the air rules as

reflected in DEQ documents."

In this document that's up on the screen, it appears that this is a response to comments during the rulemaking. And comment 108 is from a commenter from the public about that it is not appropriate for an industrial park situation, there will never be residential application. It talks about a refined analysis that should be liberalized to include different model, actual meteorological data, more appropriate risk factors, actual hours of operation, more accurate emission factors obtained.

Now, if we go down to, Ms. Lopez, if you can see the last paragraph on that page, the last paragraph that is the response to comments, first sentence? Can you read that for me, please?

A. Can you be more specific about what you want me to read?

Q. It starts with "It is not possible."

A. "It is not possible for IDHW to carve out special exemptions or emission factors for potential or hypothetical new or modified industrial sources or exposure scenarios. Our rules must take a balanced approach that is generally applicable and consistently applied."

Q. Okay. That's fine. Thank you.

Is this one of the documents that you reviewed that is the basis for your statement saying that omitting an adjustment factor is contrary to the intent of the air rules?

A. Yes, this is one of the documents.

Q. And this says that IDHW doesn't want to carve out special exemptions; is that correct?

A. That's what it says.

Q. Could those special exemptions be exposure duration scenarios?

A. No. That wouldn't be a special exemption. That would be part of the exposure concentration equation that existed even in 1993.

MS. THROWER: Thank you. I have no further questions.

HEARING OFFICER LAWRENCE: Mr. Hurlbutt, are you going to ask a few?

MR. HURLBUTT: Yes, please. I have just one line of questioning I would like to follow up with.

CROSS-EXAMINATION

BY MR. HURLBUTT:

Q. Ms. Lopez, suppose a person has already been exposed to a source of arsenic air emissions for part of their life and then they are exposed to the Stibnite Gold Project for 16 years.

Would that person's cumulative arsenic exposure be greater than if they had been exposed to just the Stibnite Gold Project?

MS. HANCOCK: I'd object. That is outside the scope of what we are talking about here. We are purely talking about excess cancer rates within the permit limitations here.

HEARING OFFICER LAWRENCE: I appreciate -- I will give a little latitude.

Go ahead, Bryan.

Q. BY MR. HURLBUTT: Do you want me to ask the question again?

HEARING OFFICER LAWRENCE: Yes, please.

Q. BY MR. HURLBUTT: Sorry, do you want me to ask the question again, Ms. Lopez?

A. Yes.

Q. So if somebody was already exposed to arsenic for part of their life and then they were

exposed for the full 16 years of the Stibnite Gold Project, would that person's cumulative arsenic exposure be greater than if they had only been exposed to the Stibnite Gold Project?

A. Their cumulative risk of exposure from the Stibnite Gold Mine Project would be exactly what is estimated. It doesn't change what somebody may or may not have come into it with. That's not what the permits do. That's not what risk assessment science does from the EPA.

Q. But would that person's cumulative arsenic exposure be greater than if they had only been exposed to the Stibnite Gold Project?

A. Are you asking me to hypothesize what their exposure may have been, what they absorbed and what they took in? May or may not be. That is not taken into consideration when EPA put out their risk assessment guidance.

Q. If someone had been exposed to, say, the same amount of airborne arsenic as the Stibnite Gold Project will cause over 16 years and then they were also exposed to the Stibnite Gold Project, their exposure would be higher, right, than if they had not been exposed to anything prior to the Stibnite Gold Project?

A. I think if you are looking at someone's cumulative exposures from every source over a lifetime then yes.

Q. Okay. And that person's risk of cancer would be greater, right?

A. I'm not sure I understand your question. These are population-based risks, so anybody's individual cancer risk depends on their individual factors.

Q. So if somebody's lifetime cumulative exposure is greater than the exposure that would occur from the Stibnite Gold Project, would their cancer risk be higher?

A. Again, that is an individual cancer risk and this is a population-based cancer risk. So their total exposure would be greater, would their individual cancer risk be greater? I can't answer that question.

Q. Okay. What if someone was exposed to the Stibnite Gold Project for 16 years. And then after that for the next 54 years of their 70-year life they were exposed to a source continuously at that AACC annual applicable level.

Would their 70-year exposure exceed the acceptable cancer risk?

MS. HANCOCK: I would continue the same line of objections. We are talking about the hypotheticals that are well outside the bounds of this permit.

HEARING OFFICER LAWRENCE: I am starting to agree, Mr. Hurlbutt. I think we have covered this topic enough, and I kind of agree that it is -- we're looking at project-based risks here.

MR. HURLBUTT: Just one final question.

Q. BY MR. HURLBUTT: The risk analysis you performed did not factor in the possibility of somebody being exposed to another source prior to or after being exposed to the Stibnite Gold Project; is that right?

A. That's right. It is a risk assessment based on the exposures at the mine.

MR. HURLBUTT: Okay. Thank you. No further questions.

HEARING OFFICER LAWRENCE: Any redirect from Perpetua?

MS. HANCOCK: I don't have any further redirect.

HEARING OFFICER LAWRENCE: Anything else with respect to Ms. Lopez we need to talk about?

Okay. Thank you, Ms. Lopez.

So we are at 4:45. Thoughts about what to do for the rest of the day?

MS. HANCOCK: Kevin Lewis is our next witness and I don't know that we are going to get through him. I propose we start him tomorrow. Or I could do his expert qualifications if you want to maximize the minutes, whatever you prefer. But I am not going to get very far with him.

HEARING OFFICER LAWRENCE: Counsel for the other parties, any strong opinions?

I personally would be inclined to go ahead and shut down for the day. My brain is not going to be able to absorb a lot more. That would be my thought.

MS. YOUNG: I still have the same pending question.

HEARING OFFICER LAWRENCE: Let's take a short recess while they discuss.

(Break taken from 4:45 p.m. to 4:47 p.m.)

HEARING OFFICER LAWRENCE: Do you have an update for us?

MS. YOUNG: Yes, thank you. So both counsel, all parties, have graciously agreed to allow Dr. Paden to not return tomorrow. But it is DEQ's intention for Mr. Schilling to be available

and attend the hearing all day tomorrow if there were any questions. But I appreciate everybody's willingness to let her not come back.

HEARING OFFICER LAWRENCE: Okay. Thank you.

Anything else we need to do today before we --

MS. HANCOCK: Nope, I don't think so.

HEARING OFFICER LAWRENCE: All right. We will adjourn for the day.

We will start at 9:00 tomorrow.

(Hearing adjourned to the following day at 4:48 p.m.)

REPORTER'S CERTIFICATE

STATE OF IDAHO)
) ss.
COUNTY OF ADA)

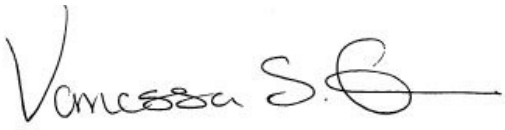
I, VANESSA S. GOSNEY, Certified Shorthand Reporter and Notary Public in and for the State of Idaho, do hereby certify:

That prior to being examined, the witness named in the foregoing deposition was by me duly sworn to testify to the truth, the whole truth and nothing but the truth;

That said deposition was taken down by me in shorthand at the time and place therein named and thereafter reduced to typewriting under my direction, and that the foregoing transcript contains a full, true and verbatim record of said deposition.

I further certify that I have no interest in the event of the action.

WITNESS my hand and seal this 31st day of October, 2024.



VANESSA S. GOSNEY
RPR and Notary
Public in and for the
State of Idaho.

My Commission Expires: 10-29-25

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Idaho Rules of Civil Procedure

Rule 30

(e) Review by the Witness; Changes.

(1) Unless waived by the deponent and the parties, the deponent must be allowed 30 days after being notified by the officer that the transcript or recording is available in which (A) to review the transcript or recording; and (B) if there are changes in form or substance, to sign a statement listing the changes and the reasons for making them. (2) Changes indicated in the Officer's Certificate. The officer must note in the certificate prescribed by Rule 30 (f)(1) whether a review was requested and, if so, must attach any changes the deponent makes during the 30-day period. (3) Witness Failure to Sign. (A) In General, If the deposition is not signed by the witness within the 30-day period, the officer must sign it and state on the record the fact of the waiver of signature, or of the illness or absence

of the witness or the fact of the refusal to sign the deposition together with any reason given for not signing. (B) Use of Unsigned Deposition. The deposition may be used as if it were signed, unless pursuant to Rule 32 (d)(4) the court determines that the reasons given for the refusal to sign require rejection of the deposition in whole or in part.

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BEFORE THE BOARD OF ENVIRONMENTAL QUALITY
STATE OF IDAHO

IN THE MATTER OF AIR QUALITY PERMIT TO CONSTRUCT P-2019.0047

NEZ PERCE TRIBE, IDAHO CONSERVATION LEAGUE, and SAVE THE SOUTH FORK SALMON,

Petitioners,

v.

IDAHO DEPARTMENT OF ENVIRONMENTAL QUALITY,

Respondent,

and

PERPETUA RESOURCES IDAHO, INC.,

Intervenor-Respondent.

Case Docket No. 0101-22-01
OAH Case No. 23-245-01

EXPERT DECLARATION OF KEVIN SCHILLING

I, KEVIN SCHILLING, hereby declare under penalty of perjury and pursuant to the law of the State of Idaho that the foregoing is true and correct:

I. Introduction

1. My name is Kevin Schilling. I am the Stationary Source Air Modeling Supervisor for the Stationary Source Bureau at the State Air Quality Division of the Idaho Department of Environmental Quality (DEQ) in Boise. I have held this position since September of 2004; however, the title of the position and location within the organizational structure of the Air Quality Division has changed over time.

2. Presently, two staff positions, both Air Quality Dispersion Modeling Analysts, report directly to me. Darrin Mehr fills one of those positions and the other is filled by Christina Boulay. Ms. Boulay filled the position vacated by Dr. Pao Baylon, who left DEQ in 2023 for employment with a private environmental consulting company. Dr. Baylon was the lead Air Quality Dispersion Modeling Analyst for review of the Perpetua Resources Idaho, Inc. (PRI) Stibnite Gold Project (SGP) air impact analyses that were submitted with the Permit to Construct (PTC) application.

3. My role in the permitting of the SGP has been both supervisory and technical/policy review and evaluation. As mentioned above, Dr. Baylon was the lead in review and verification of impact analyses submitted with the application, and he also performed supplemental analyses to support DEQ's conclusion that the SGP would not cause or contribute to violation of air quality standards or increments. Where air impact modeling methods used by PRI and presented in the PTC application were atypical or of questionable appropriateness, Dr. Baylon discussed the approach, data, and analyses with me. Prior to permit issuance, Dr. Baylon, DEQ Permit Writer Kelli Wetzel, Permitting Supervisor Darrin Pampaian, Stationary Source Bureau Chief Mike Simon, and I discussed various aspects of the SGP, including proposed operations, emission calculations, permit provisions needed to assure compliance, and monitoring and recordkeeping requirements. This was done to provide a comprehensive assessment of DEQ's confidence of NAAQS and TAP compliance in a weight-of-evidence type approach. At the conclusion, DEQ was highly confident that operation of the SGP, as described in the application and as required by the DEQ PTC, will not cause or contribute to a violation of a National Ambient Air Quality Standard (NAAQS) or exceed an applicable Toxic Air Pollutant (TAP) increment.

A. Assignment

4. The *Final Order in the Matter of Air Quality Permit to Construct P-2019.0045*[1] ("Final Order") indicated there was "insufficient evidence to support DEQ's analysis of the ambient arsenic air concentrations." Three remaining issues were identified by the Board of Environmental Quality (DEQ Board) for resolution. These are:

[1] REC 3706, *Final Order in the Matter of Air Quality Permit to Construct P-2019.0047*, *Nez Perce Tribe, Idaho Conservation League, and Save the South Fork Salmon v. Idaho Department of Environmental Quality*, Case Docket No. 0101-22-01, OAH Case No. 23-245-01 (Final Order at 12).

a. DEQ did not act reasonably in using a five-year rolling average for T-RACT that was not properly supported by permit conditions.

b. There was insufficient evidence to support the T-RACT analysis limiting the non-West End pit production limit.

c. DEQ did not act reasonably and in accordance with law when it applied the 16/70 calculation to the ambient arsenic air concentration analysis.

5. The identified issues pertain to specific requirements for how analyses and developed permit conditions and restrictions must provide for satisfactory assurance that the facility will operate as described in the application and as needed to comply with applicable air quality standards and/or increments. The accuracy, representativeness, and/or conservatism of methods and data used to estimate impacts were described in detail in the PTC application materials submitted by PRI and in DEQ's *Modeling Review Memorandum* and the *TAPs Addendum Modeling Review Attachment* attached thereto.[2] The aspects of methods and data used in the analyses are not in question by any of the three remaining issues, and this report will not revisit or expand on DEQ's confidence in the results of impact analyses. This report will address the above-listed issues by showing how DEQ's regulatory interpretation is appropriate and that the permit conditions adequately assure compliance with the arsenic T-RACT TAP increment.

B. Summary of Opinions

6. This Expert Declaration will show that:

a. Use of a 5-year rolling average production limit for assessing compliance with the T-RACT AACC is appropriate because long-term exposure to a given concentration over the life of the project is the critical parameter for the risk-based AACCs. Short-term fluctuations in impacts do not affect compliance and do not impact long-term exposure concentrations.

b. A specific limit on non-West End Pit production is not necessary to assure compliance with T-RACT AACCs. Since West End Pit production is the risk driver in analyses, the combination of a limit on total production and a limit on the fraction of total production that may occur from West End Pit sources is adequate to assure compliance with the T-RACT AACC.

[2] *See* REC 699, 701-711, 719-720, Idaho Department of Environmental Quality, *TAPs Addendum Modeling Review Attachment* to the PRI SGP *Modeling Review Memorandum* (January 6, 2022) (REC 697-713, Demonstrating Compliance with IDAPA 58.01.01.203.02 (NAAQS) and 203.03 (TAPs) as it relates to air quality impact analyses) ("DEQ's TAPS Modeling Attachment"). For convenience, a true and correct copy of DEQ's TAPS Modeling Attachment is attached hereto as Exhibit A.

c. DEQ acted reasonably and in accordance with law when it applied a 16/70 factor to adjust concentrations for comparison to the T-RACT AACC. The Expert Declaration of DEQ Environmental Toxicologist Dr. Norka Paden [3] shows that the factor is appropriate because cancer risk estimates, as evaluated by the EPA risk model, are conservative and are a function of a combination of concentration, exposure time, exposure frequency, and exposure duration. Dr. Paden's Declaration provides the primary justification for using the 16/70 factor to account for the limited duration SGP, and this Declaration provides a brief description of how that meets the requirements of carcinogenic TAP permitting rules.

C. Qualifications and Experience

7. I received a Bachelor of Science (BS) degree in Environmental Science, with a minor in chemistry, from Washington State University in 1986. After graduation I was employed by Washington State University as a Research Assistant at the Laboratory for Atmospheric Research while attending graduate school. I received a Masters of Science (MS) degree in Environmental Engineering (specializing in atmospheric chemistry, air pollution meteorology, air pollution monitoring, and atmospheric pollutant dispersion) from Washington State University in 1988.

8. I initially began employment with DEQ (at that time the Division of Environmental Quality) in 1989 and then left the agency in 1990 for employment with Morrison Knudsen Company, a large Idaho-based construction company. I worked in Morrison Knudsen's Environmental Group, performing a wide range of air quality related projects where a key focus was air pollutant impact assessment. These projects included permitting, pollutant emissions estimation, atmospheric dispersion modeling, air pollution monitoring, and industrial hygiene functions.

9. In the mid-1990s, I actively participated in the initial development of Idaho's TAP permitting regulations while working at Morrison Knudsen. I provided technical and regulatory assistance to the Idaho Association of Commerce and Industry (IACI). IACI negotiated with DEQ on the development and promulgation of the TAP rules. I held the position of Chair of the Air Toxics Subcommittee during part of the multi-year negotiations. I stepped down from Chair of the subcommittee before final promulgation of the TAP rules because of other project obligations at Morrison Knudsen that required extensive work outside of Idaho. The work on the IACI Air Toxic Subcommittee involved:

a. Evaluation of the basis from which carcinogenic and non-carcinogenic air impact limits would be established.

b. Ensuring that the interests and concerns of the regulated community were considered in the development of regulations.

[3] *Expert Declaration of Dr. Norka Paden* (August 13, 2024) ("Paden Decl."), ¶¶ 11-18.

c. Structuring regulations in a format that is easily used in the context of air permitting for industrial facilities and DEQ.

10. I returned to DEQ in December of 2001, working in the Technical Services Division where I primarily reviewed air impact modeling analyses submitted as part of air permit applications. I transferred to the Air Quality Program Office as the Stationary Source Air Modeling Coordinator in 2004. Later my title was changed from *coordinator* to *supervisor*.

11. My primary responsibilities as Stationary Source Air Modeling Supervisor are both management/administrative and senior level technical and regulatory oversight. A critical component of my position in the Stationary Source Modeling Group is performing, reviewing, and overseeing technical and regulatory aspects of air impact analyses that satisfy regulatory requirements for permit issuance. Where project-specific conditions present unique circumstances, and there is uncertainty in the acceptability of proposed technical and regulatory approaches to address those unique circumstances, DEQ collectively employs its expertise and experience to develop and evaluate the approach.

II. Background Discussion

A. Permitting Requirements for TAPs

12. TAPs were regulated only by *Idaho Air Rules* Section 161[4] prior to the mid-1990s. DEQ developed a permitting TAPs Policy to provide consistency in how TAPs would be addressed in air permitting. The foundation of that policy was to ensure that a proposed project would not cause impacts to ambient air exceeding: 1) non-carcinogenic pollutant concentration levels that are based on occupational exposure limits; and 2) carcinogenic pollutant concentration levels that are based on EPA inhalation Unit Risk Factors (URFs) (as described in more detail in the Expert Declaration of Dr. Norka Paden[5]) and a selected acceptable lifetime cancer risk. The unit risk is lifetime[6] excess cancer risk estimated to result from continuous exposure to a toxic air contaminant at a concentration of 1 microgram/cubic meter of air ($\mu g/m^3$).

13. The regulated community (those applying for and regulated by an air quality permit from DEQ) expressed concerns in the early 1990s regarding DEQ regulation of TAPs by policy. The regulated community, under the representation of IACI, then engaged in regulatory negotiation with DEQ to establish TAP rules for air permitting. The goals of the negotiations were to develop rules that: 1) are reasonably protective of public health, but still afford flexibility to regulated

[4] *Idaho Administrative Procedures Act 58.01.01, Rules for the Control of Air Pollution in Idaho* ("Idaho Air Rules"), Section 161, Toxic Air Pollutants. This Section states: "Any contaminant that is by its nature toxic to human or animal life or vegetation must not be emitted in such quantities or concentrations as to alone, or in combination with other contaminants, injure or unreasonably affect human or animal life or vegetation."

[5] Paden Decl., ¶¶ 12-16.

[6] 70 years was selected as a lifetime.

facilities and projects; 2) are relatively easy to understand and implement; and 3) do not require excessive expenditure of time and resources by DEQ and the permittee during the permitting process.

14. During development of the TAP rules, DEQ's reliance on EPA URFs remained the regulatory approach cornerstone for developing consistent acceptable methods to evaluate impacts to ambient air for carcinogenic TAPs. A DEQ internal memorandum[7] responding to a request for layman's explanation of URF & TLV/100 stated, "Within IAQB (Idaho Air Quality Bureau) New Source Review (NSR) policy, URFs are used to calculate acceptable ambient levels for a given carcinogen. IAQB generally establishes that an ambient concentration which causes no more excess cancers than one in a million (1×10^{-6}) is acceptable." In the early stages of TAP regulation development, DEQ sent IACI a letter that provided a "straw-man" of possible TAP regulatory language.[8] That regulatory straw-man proposal stated the following for procedures to demonstrate compliance for emissions of carcinogenic pollutants:

> "For sources that can demonstrate, using Department-approved methods, that emissions of carcinogens contribute an ambient air cancer risk probability of less than 1:1,000,000 and that emissions of non-carcinogens contribute to an ambient air concentration less than one percent of the Threshold Limit Value, no additional procedures are needed."

15. During development of the TAP rules, DEQ continually asserted that carcinogenic TAPs resulting from a permitting project should be regulated to prevent an unacceptable excess cancer risk based on a 70-year lifetime. Excess inhalation cancer risk probability over a 70-year lifetime is calculated from the EPA Inhalation Unit Risk and the Exposure Concentration, as described in the Expert Declaration of Dr. Norka Paden.[9] The formula is as follows:

Excess Cancer Risk Probability = (IUR)(EC)

Where: IUR = Inhalation Unit Risk per $\mu g/m^3$ of exposure
EC = Exposure Concentration in $\mu g/m^3$

An acceptable arsenic concentration can be calculated by rearranging the formula and solving for EC using an allowable risk of 10^{-6} (1-in-1,000,000) and a IUR of $0.0043/(\mu g/m^3)$ for arsenic. The resulting EC is 2.3 E-4 $\mu g/m^3$, which is the AACC listed in *Idaho Air Rules* Section 586. This clearly shows how the EPA cancer risk model was used to generate AACCs to protect against lifetime cancer risk from long-term exposures.

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[7] State of Idaho Department of Health and Welfare, Division of Environmental Quality. *Request for layman's explanation of URF& TLV/100*. From Robert Wilkosz and Tim Teater. To Orvil [sic] Green. March 7, 1991. A true and correct copy of this memorandum is attached hereto as Exhibit B.

[8] State of Idaho Department of Health and Welfare, Division of Environmental Quality. Letter from Robert Wilkosz, Bureau Chief, Technical Services Bureau, to Dick Rush, Vice President, IACI. July 29, 1992. A true and correct copy of this letter is attached hereto as Exhibit C.

[9] Paden Decl., ¶ 15.

16. Dr. Paden further explains that the Exposure Concentration can be calculated using the contaminant concentration, exposure time, exposure frequency, exposure duration, and applicable averaging time by the following:

$$EC = (CA \times ET \times EF \times ED)/AT$$

Where: EC = Exposure Concentration ($\mu g/m^3$)
CA = Contaminant Concentration ($\mu g/m^3$)
ET = Exposure Time (hours/day)
EF = Exposure Frequency (day/year)
ED = Exposure Duration (years)
AT = Averaging Time (70 years x 365 days/year x 24 hours/day)

17. The above formula is used to calculate an Exposure Concentration for a specified project duration over a 70-year average lifetime. This Exposure Concentration can then be compared to a concentration limit that is protective for lifetime cancer risk, such as the AACC or the T-RACT AACC. Although the AACC is expressed as an annual average, it represents the concentration averaged over a 70-year lifetime, as defined by how it was generated from URFs and how it is intended to limit long-term exposure concentration and limit the associated excess cancer risk to 1-in-1,000,000. When the Exposure Duration is equal to the 70-year Averaging Time, and the Exposure Frequency and Time are conservatively set to 365 day/year and 24 hours/day, then the Exposure Concentration is simply equal to the Contaminant Concentration, which is the annual impact obtained from the model. Since the vast majority of DEQ permitting projects are of permanent operations (70 years), no adjustment of the Contaminant Concentration is required to obtain the Exposure Concentration.

18. The SGP will have an Exposure Duration of 16 years, the applicable Contaminant Concentration (an annual value obtained from modeling results) is 0.00416 $\mu g/m^3$, the Exposure Frequency is 365 days/year, and the Exposure Time is 24 hours/day. The calculated Exposure Concentration is then:

$$EC = \frac{(0.00416\ \mu g/m^3)(24\ \text{hours/day})(365\ \text{days/year})(16\ \text{years})}{(24\ \text{hours/day})(365\ \text{days/year})(70\ \text{years})} = 0.00095\ \mu g/m^3$$

As observed in the equation, with conservative assumptions for exposure time and frequency, the equation reduces to the 16/70 factor that was used in DEQ's analysis to account for the limited life of the mine. This demonstrates how a 16/70 adjustment factor to annual estimated impacts is appropriate.

19. DEQ air permits are issued to facilities primarily for permanent and consistent operations where resulting emissions vary little through time. Rather than develop a carcinogenic TAP rule that provided for a project-specific lifetime in the calculation of allowable carcinogenic TAP concentrations in ambient air, DEQ provided simpler regulatory language that provides a concentration limit based on a 70-year continual exposure and expressed that exposure as an annual

average exposure concentration. TAP permitting regulations in *Idaho Air Rules* Section 210.15 provide a short-term project adjustment factor of 10 to apply to the allowable AAC when a project will have a duration of less than 5 years. This shows: 1) an adjustment in the exposure concentration is appropriate (in this case, the rules adjust the AACC rather than the exposure concentration); 2) an adjustment greater than 10 cannot be used for projects of duration less than 5 years. In general, DEQ determined it would not be appropriate to subject individuals to a life-time allowable cancer risk within a duration of less than 5 years. Therefore, the adjustment was capped at 10, rather than using a higher value or values calculated from exposure durations of 5 years of less (e.g., 70 years/5 years = 14 or 70 years/2 years = 35). These short-term projects were most commonly remediation and pilot-scale projects having a duration of up to several years.

B. Form of the Arsenic AACC

20. *Idaho Air Rules* Section 586 state that the AACCs "in this section are annual averages." The rules also state that the Toxic Air Pollutant Carcinogenic Increments "are based on . . . a seventy (70) year lifetime exposure." The former is the averaging period of the modeling results (CA), and the latter is the average period of the lifetime exposure concentration (EC) used for determining excess cancer risk. Air impact analyses only demonstrate compliance with standards when the analyses use the same averaging period as the applicable standard. An annual average impact concentration does not demonstrate compliance with a 24-hour standard. In the case of carcinogenic TAPs, the applicable standard is a pollutant-specific inhalation cancer risk posed in ambient air that results from allowable emissions from the proposed project for the life of the project. That acceptable cancer risk is either 10^{-6} (1-in-1,000,000) as expressed in the AACC or 10^{-5} (1-in-100,000) when controls meeting T-RACT are used. The listed annual AACCs are an expression of that standard when applied to a permanent project/facility that has no permit restrictions on operating duration. These AACCs were developed using the EPA inhalation Unit Risk Factors (URFs) that existed at the time *Idaho Air Rules* Section 586 was promulgated. The *Idaho Air Rules* do not preclude use of an exposure concentration adjustment for impacts, and the EPA risk model that was used in the development of the AACCs provides for this adjustment to calculate the exposure concentration.

C. Arsenic Compliance Approach for SGP

21. The arsenic TAP compliance demonstration approach used by PRI for the SGP permitting analyses was thoroughly described in DEQ's *TAPs Addendum Modeling Review Attachment* of the DEQ *Modeling Review Memorandum*[10] for the SGP. This Expert Declaration will summarize the regulatory approach used to demonstrate compliance and provide additional justification for that approach. It will not reiterate the conservatism of the data and methods of the modeling approach used to estimate arsenic impacts to ambient air, as that is not an identified issue.

22. During development of final SGP permitting analyses, PRI expressed concern that compliance with AACCs could not be demonstrated with the conservative assumptions used in

[10] REC 698, 710-711; DEQ's TAPS Modeling Attachment at 2, 14-15.

previous analyses, including the assumption that the SGP was a permanent source rather than one of 16-year duration. Rather than revise the analytical approach to provide a less conservative assessment of impacts, I proposed that compliance with carcinogenic TAP increments could be based on cumulative cancer risk of the limited-duration project rather than the worst-case annual impact for a project of limited duration. Since the AACC annual average is an expression of a 1-in-1,000,000 cancer risk limit for permitting projects, modeled impacts (annual contaminant concentration) must be adjusted to an exposure concentration that is appropriately comparable to the annual average AACC. Therefore, annual impacts for a project with a 16-year duration could be multiplied by a 16/70 factor to more appropriately compare to the AACC, which is based on a 70-year exposure duration. Similarly, year-to-year variability in emissions could be distributed over an alternative averaging period, provided there is still an adequate periodic evaluation that long-term risk limits are not exceeded.

23. My justification for the acceptability of using a 16/70 factor to adjust modeled impacts was based on technical/scientific considerations, my personal working-level knowledge of DEQ's TAP rules, and my limited knowledge of carcinogenic risk assessment and its relation to the TAP rules. Because of the unique 16-year project duration of the SGP and because *Idaho Air Rules* only identify AACC values for 70 years and less than 5 years, I discussed the approach with the DEQ permitting team prior to proposing use of the method. The DEQ permitting team concluded that the exposure duration consideration was an appropriate adjustment to the calculation of an exposure concentration (EC) for comparison to the T-RACT AACC, and it was concluded by the team that this approach was consistent with implementation of the URFs and identified acceptable excess cancer risks (1-in-1,000,000 or 1-in-100,000 when T-RACT is used) adopted by DEQ as AACCs into *Idaho Air Rules* Section 586.

III. Response to Remaining Issues Identified by the Board of Environmental Quality

A. DEQ Acted Reasonably in Using a 5-Year Rolling Average for T-RACT and it was Supported by Permit Conditions

24. *Idaho Air Rules* Section 586 state that AACCs are annual averages. The implication of the stated issue is that when a standard or increment is specified for a certain averaging-period, then any limits imposed on operations should be for the same averaging period or a shorter averaging period. For example, an operational limit designed to limit emissions that is based on a 5-year averaging period would not be adequate for assuring compliance with an annual average standard. This is because variability in operational rates within the 5-year period could result in a violation of the annual standard while still complying with the 5-year operational limit in the permit. For short-term 1-hour standards, DEQ uses 1-hour averaged operational limits and 1-hour averaged monitoring requirements. Permit requirements to assure compliance with a 1-hour limit would not be based on longer averaging periods such as daily rates because the 1-hour limit could be exceeded while still complying with the daily rate.

25. As I have established earlier in this declaration, carcinogenic TAP AACCs were established to ensure that impacts of any carcinogenic TAPs from a project or facility would not cause a lifetime cancer risk over 1-in-1,000,000 or 1-in-100,000 when using T-RACT. Cancer risks used to establish AACCs were based on EPA's cancer risk model (using established EPA URFs), where risk is dependent on an exposure for a certain project duration, and the risk varies linearly with exposure duration. Because limiting total project-caused cancer risk is the underlying criteria for carcinogenic TAP regulation, any permit limits must only assure that concentrations in ambient air over the total duration of the project do not cause a potential exposure concentration associated with a 1-in-1,000,000 or 1-in-100,000 cancer risk. Therefore, compliance with the carcinogenic AACCs would still be demonstrated if processing rates were only limited to the 788.4 million tons over the life of the mine (combined with the restriction on West End Pit production as described in the next section). Use of a 5-year averaging period for limiting processing rates easily accomplishes this requirement for a project with a 16-year duration, and it provides for reasonable periodic assurance of compliance with the long-term limit.

26. The *Final Order* from the DEQ Board[11] asserted that, "A five-year rolling average allows considerable daily and annual increases in exposures which are contrary to limits set forth in the Air Rules." Because pollutant-specific total project cancer risk is the blanketing objective of regulating carcinogenic TAPs, and since risks as assessed by the EPA risk model are a function of exposure concentration (accounting for exposure duration over a lifetime), any daily and annual variability is inconsequential to the exposure concentration and resulting risk. For example, assume a processing rate of 200,000 tons/year results in an annual arsenic impact of 3.0 E-4 $\mu g/m^3$, 153,000 tons/year results in 2.3 E-4 $\mu g/m^3$ (equal to the standard), and processing 100,000 tons/year results in an annual impact of 1.5 E-4 $\mu g/m^3$. Then assume a facility processes 200,000 tons during years one and two, 100,000 tons during years three and five, and 153,000 tons during year four. The total material processed over five years is 753,000 tons, and the mean annual processing rate is 150,600 tons/year. The same mean processing rate would result from processing 150,600 tons for each of the five years, and this would result in the same average annual air impact and the same carcinogenic exposure concentration. Since the exposure concentration (a resulting project caused concentration averaged over a lifetime) is a measure of compliance with AACC, the five-year rolling average is consistent with limits in *Idaho Air Rules* for carcinogenic TAPs.

B. DEQ had sufficient Evidence Supporting Limits on non-West End Pit Production

27. Final maximum potential arsenic exposures resulting from the SGP, as limited by permit conditions, were calculated from maximum modeled annual impacts and post-processing of those impacts by the following equation[12,13]:

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[11] REC 3713 (Final Order at 19).

[12] REC 710-711, DEQ's TAPS Modeling Attachment at 14-15.

[13] *See* REC 1947-48, *Stibnite Gold Project Permit to Construct Application TAP Addendum.* Prepared for Perpetua Resources Idaho, Inc., Prepared by Air Sciences Inc., October 5, 2021 (full document at REC 1921-2146).

$$LifeExposure_{Wi,j,n} = \left[\left(WEPExposure_{Wi,n}\right)(50\%) + \left(nonWEPExposure_{Sj,n}\right)(50\%)\right]\left[\frac{16\ year\ LOM}{70\ year\ exposure}\right]$$

Where:

W_i	=	West End Pit scenario, where i = 1 to 4
S_j	=	Non-West End Pit scenario, where j = B1, B2, H1, H2, H3, H4, Y1, Y2, and Y3.
n	=	specific receptor.
$LifeExposure_{Wi,j,n}$	=	lifetime exposure in µg/m^3 for West End Pit scenario i, non-West End Pit scenario j, at receptor n.
$WEPExposure_{Wi,n}$	=	annual maximum modeled impact in µg/m^3 for West End Pit scenario i at receptor n
$nonWEPExposure_{Sj,n}$	=	annual maximum modeled impact in µg/m^3 for non-West End Pit scenario j at receptor n
16 *year LOM*	=	maximum life-of-mine
70 *year exposure*	=	lifetime exposure used for development of AACCs in *Idaho Air Rules*

The issued permit provided a total mine production limit and a production limit for West End Pit operations. The *Final Order* from the DEQ Board[14] stated, "However, the equation listed above shows that the non-West End Pit production was also limited by 50%. The Board of Environmental Quality was unable to determine from the record where this 50% reduction came from or whether it was actually applied when doing the calculation."

28. The DEQ Board, in the *Final Order*, fails to understand how the issued PTC appropriately and effectively limits both West End Pit and non-West End Pit production. The listed equation provides worst-case impacts for the various scenarios, but by itself it does not fully explain how certain sources must be limited by the permit to assure that the SGP operates as described in the application and in compliance with applicable standards and increments. The PTC limits total hauling and excavation from the mine to 788.4 million tons (West End Pit production combined with non-West End Pit production) and limits hauling and excavation from the West End Pit to 394.2 million tons, which is equal to 50% of total allowable production. Impacts to critical receptors (those having impacts that may approach the T-RACT AACC) are far greater for West End Pit sources than for non-West End Pit Sources. Analyses performed by DEQ during review of the application[15] showed that maximum arsenic impacts when 100% of the allowable production is from non-West End Pit sources (0.0023 µg/m^3 before adjusting for the life of the mine and 0.00053 µg/m^3 after adjusting for the life of the mine) are well below the maximum impact when 100% of allowable production is from West End Pit; therefore, with both a limit on total production and West End Pit production, an additional limit on non-West End Pit production is not necessary to assure that the SGP operates as represented in the application and as needed to

[14] REC 3714 (Final Order at 20).

[15] *PERPETUA RESOURCES IDAHO, INC. – P-2019.0047 PROJ 62288 - Lifetime Arsenic Exposure for Scenarios W1-W4 (DEQ's Post Processing Analysis).xlxs*. Excel Workbook. DEQ, 2021. A true and correct copy of this Excel workbook is provided concomitantly with this declaration and identified as Exhibit D.

assure that applicable emissions do not exceed the arsenic T-RACT AACC. Non-West End Pit production is limited to the facility-wide 788.4-million-ton limit for total hauling and excavation at the mine if there were no West End Pit production.

29. Production is effectively limited from non-West End Pit sources because of the following relationship:

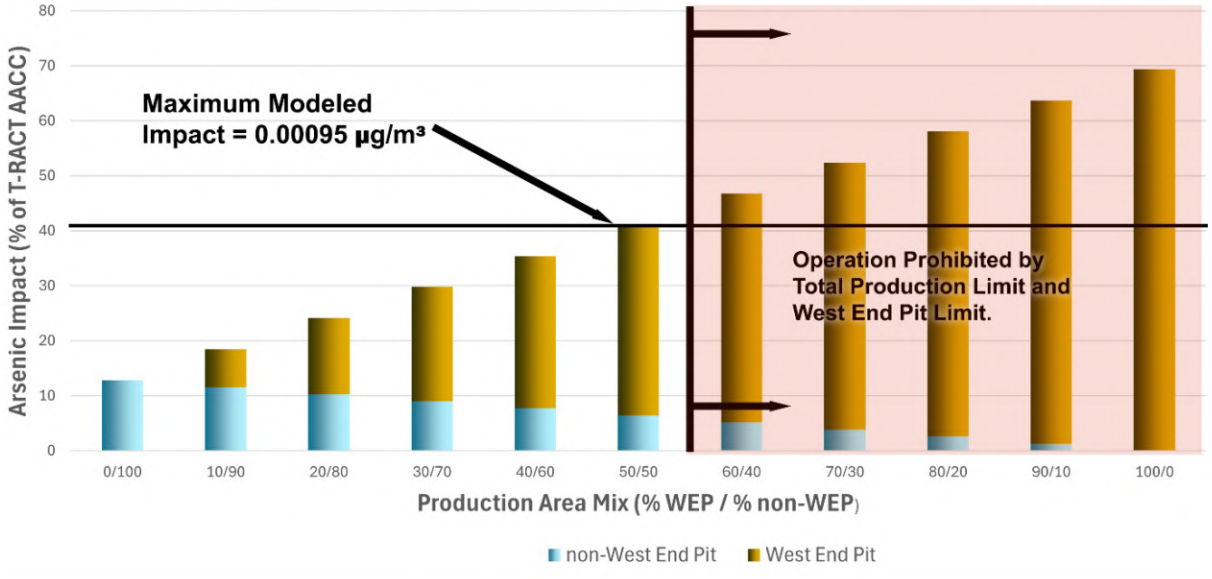
$$Production_{Non\text{-}WEP} = Production_{total} - Production_{WEP}$$

Where:

$Production_{Non\text{-}WEP}$ = production from non-West End Pit Sources
$Production_{total}$ = Total allowable production.
$Production_{WEP}$ = production from West End Pit Sources (not to exceed 50% of $Production_{total}$)

30. The effect of a limit on total production and West End Pit production can be observed by showing how maximum arsenic impacts change with changes in the fraction of total allowable production that occurs from the West End Pit. This was done for the single receptor that had the highest overall exposure concentration. Figure 1 shows how the total adjusted impact is affected by changes in the West End Pit production. The Figure shows how total impacts increase as West End Pit production increases and non-West End Pit production decreases. Figure 1 also shows how impacts would increase above the adjusted combined impact of 0.00095 µg/m^3 for West End Pit allowable production above 50% of the total allowable production from combined West End Pit and non-West End Pit sources.

Figure 1: Maximum Arsenic Impacts as a Function of the Percentage of Total Allowable Production that may Occur from West End Pit Sources



C. DEQ Acted Reasonably and in Accordance with Law when it Applied the 16/70 Calculation to the Ambient Arsenic Air Concentration Analysis

31. The DEQ Board, in the Final Order, misses the point that project-caused pollutant specific cancer risk is the overriding criteria of acceptability and that AACCs, expressed as an annual average, are provided to simplistically apply to permanent sources with emissions of low variability. The Final Order states that "nowhere in the Air Rules does it provide that a project that will operate more than 5 years but less than 70 years may be adjusted in proportion to the amount of time it will operate." Idaho Air Rules do not preclude the use of such a factor within the context of the regulatory intent. *Idaho Air Rules* do not alter EPA's science nor preclude its use, which includes use of a 70-year lifetime exposure duration in calculating AACCs. For projects with an enforceable operational life of less than 70 years, an adjustment for reduced exposure duration is appropriate. Total project-caused carcinogenic risk has been identified as the criteria from which the AACCs were established, as has been described earlier in this Declaration. When specific parameters associated with a project subject to the AACCs are not consistent with the assumptions/conditions that went into development of the AACCs, DEQ staff are compelled to adjust for those in an appropriate and/or conservative manner. DEQ then used its authority to write reasonable permit conditions per IDAPA 58.01.01.211 to limit total production including specific limitations on the West End pit.

32. Additionally, DEQ did not adjust the AACC. DEQ adjusted the applicable modeled impact concentration, which has a duration of 16 years, to an exposure concentration representative of a 70-year lifetime. With this adjustment, the exposure concentration can be compared to the AACC or the T-RACT AACC. The adjustment involved assuming maximum modeled impacts persist for the 16 years of mine life, and then those impacts are evenly distributed over a 70-year period to be consistent with the assumptions of carcinogenic TAP regulations.

33. Apart from the DEQ Board's identified issue with lack of specific allowance in the *Idaho Air Rules* to use an adjustment factor to account for project duration, the *Final Order* also stated that "DEQ did not provide sufficient evidence in the form of an expert opinion from a toxicologist or other qualified expert regarding the cancer risk associated with the 16/70 adjustment." As previously mentioned, outside of DEQ's adjustment factor of 10 specified for short-term sources of less than five years, cancer risk associated with exposures between 5 and 70 years are based on the EPA risk assessment model, using established URFs and exposure concentrations. DEQ's toxicologist, Dr. Norka Paden, demonstrated in her declaration[16] that use of the 16/70 adjustment factor is appropriate to calculate exposure concentration impacts of a 16-year project to be compared to the T-RACT AACC, which is based on a 70-year lifetime.

IV. Conclusions

34. Regarding the three remaining issues identified by the DEQ Board on the arsenic analysis supporting issuance of the DEQ PTC, DEQ concludes:

[16] Paden Decl., ¶ 18.

A. A 5-year rolling average production limit and associated monitoring of production was appropriate and reasonable because the criterion of acceptance is project-caused excess inhalation cancer risk. Short-term variability is inconsequential to the total risk.

B. Limits on total production along with a limit on West End Pit production effectively limits non-West End Pit production. A separate limit on non-West End Pit production is not necessary because compliance with the T-RACT AACC is still demonstrated when 100% of total allowable production is from non-West End Pit sources.

C. DEQ acted reasonably and in accordance with law when applying the 16/70 factor to generate an Exposure Concentration to compare against the T-RACT AACC. As demonstrated, AACCs are an annual representation of the acceptable Exposure Concentration for a permanent project and a 1-in-1,000,000 excess cancer risk. Standard EPA risk assessment methods (the same methods used to develop the AACCs) were used with the modeled annual concentration to calculate an Exposure Concentration representative of the 16-year project duration while conservatively assuming a 24 hour/day Exposure Time and a 365 day/year Exposure Frequency. This reduces to the 16/70 factor applied to the modeled concentration.

DATED August 13, 2024

/s/ Kevin Schilling
KEVIN SCHILLING

CERTIFICATE OF SERVICE

I hereby certify that on August 13, 2024, a true and correct copy of the foregoing ***EXPERT DECLARATION OF KEVIN SCHILLING*** was served on the following:

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EXHIBIT A

TAPs Addendum Modeling Review Attachment

1.0 Introduction and Summary

Perpetua Resources Idaho, Inc. (PRI) submitted the *Stibnite Gold Project (SGP) Permit to Construct Application TAP Addendum* (*TAP Addendum*), prepared by Air Sciences Inc. (Air Sciences) and submitted to DEQ on October 5, 2021. The TAP Addendum reassessed source applicability to Toxic Air Pollutant (TAP) permitting requirements, refined TAPs regulatory methods to demonstrate compliance with applicable TAP increments, revised and/or refined operations and operational parameters affecting TAP emissions, and refined TAP air impact analyses. The revisions and refinements made for the TAP Addendum also reduced PM_{10} and $PM_{2.5}$ emissions, and this effect is presented in this *TAPs Addendum Modeling Review Attachment* (*Modeling Review Attachment*).

2.0 Scope of TAPs Addendum

DEQ reevaluated TAPs compliance regulatory interpretations and impact assessment methods following the second public comment period of February 18, 2021, through March 19, 2021. Areas of revision in response to issues identified after the public comment period included:

- Revising source-specific TAP impact assessment applicability, primarily identifying what sources can be excluded because they are "covered" or "addressed" by a National Emissions Standard for Hazardous Air Pollutants (NESHAP) or New Source Performance Standard (NSPS).
- Refining regulatory methods used to demonstrate compliance with TAP increments.
- Refining TAP emission calculation methods and dispersion-affecting parameters.
- Reassessing TAP impacts resulting from revised and/or refined methods and data.
- Providing a best-estimate of actual TAP emissions that will occur from operation of the mine, and then comparing this to maximum permit-allowable emissions.

PRI and Air Sciences, PRI's permitting consultant, submitted the *TAP Addendum* on October 5, 2021.

3.0 Revised NESHAP/NSPS TAP Exclusion

DEQ and PRI reevaluated TAP source applicability after the second public comment period in response to expressed concerns regarding sources excluded as per *Idaho Air Rules* Section 210.20 (excluding sources that are "covered" or "addressed" by a NESHAP). TAP applicability is explained in greater detail in the main body of the DEQ Statement of Basis. As a result of the reevaluation, some additional sources were included in the TAP impact modeling analyses that were not previously. TAP sources from gold mining that were modeled in the final TAP analyses included: drilling, blasting, excavating, hauling, prill silos, rock dumps and storage piles, and tailings.

Air Sciences consulted with DEQ to refine TAP compliance demonstration methods from what was originally submitted in the application. The refinement was primarily needed to show compliance with the

arsenic Acceptable Ambient Concentration of a Carcinogen (AACC). The revised methods are described in the submitted *TAP Addendum* and this DEQ *Modeling Review Attachment*.

4.0 TAPs Refined Compliance Demonstration Approach

PRI, in consultation with DEQ, used a highly refined TAPs analysis approach to demonstrate compliance with applicable TAP increments. This approach involved the following:

- AACC Adjustment for Toxic Air Pollutant Reasonably Available Control Technology (T-RACT) Utilization.
- TAP Emission Averaging Period.
- AACC Adjustment for the Operational Life of the Mine.

4.1 AACC Adjustment for T-RACT Utilization

Idaho Air Rules Section 210.12 allows TAP impacts of 10 times the AACC if the application demonstrates that T-RACT is used for the TAP emission sources. This represents a life-time cancer risk of 1-in-100,000. An adjustment cannot be made for non-carcinogenic TAPs listed in *Idaho Air Rules* Section 585.

Review of the T-RACT demonstration is performed by the DEQ permit writer and is described in the main body of the DEQ Statement of Basis.

4.2 TAP Emission Averaging Period

Annual average emissions of carcinogenic TAPs are typically used in the dispersion model to estimate maximum annual impacts. PRI refined the analyses by using source-specific emission rates that are representative of a 5-year averaging period. This approach is appropriate because carcinogenic impacts are of concern from a long-term exposure basis.

4.3 AACC Adjustment for the Operational Life of the Mine

AACCs were established based on a 1-in-1,000,000 cancer risk over a 70-year lifetime, as stated in *Idaho Air Rules* Section 006.125:

> ***Toxic Air Pollutant Carcinogenic Increments**. Those ambient air quality increments based on the probability of developing excess cancers over a seventy (70) year lifetime exposure to one (1) microgram per cubic meter (1 ug/m3) of a given carcinogen and expressed in terms of a screening emission level or an acceptable ambient concentration for a carcinogenic toxic air pollutant. They are listed in Section 586.*

PRI indicated the maximum life-of-mine will be 16 years. Life-time exposures to carcinogenic TAPs were refined by multiplying the maximum modeled annual impact by a ratio of 16/70. Section 5.7 of this *Modeling Review Attachment* provides more details on this adjustment for the project.

5.0 Refined TAP Emission Estimates and Modeling Methods/Parameters

This section describes changes made to TAP emission estimates and to methods/parameters used in the impact modeling analyses.

5.1 Operational Adjustments

PRI and Air Sciences proposed and committed to several operational adjustments to reduce actual and estimated TAP emissions:

- Installing and operating dust collection systems on drilling rigs (determined to be T-RACT).
- Capping the haul roads that are outside of the pits and development rock storage facilities (DRSFs) with clean (lower levels of arsenic) development rock (determined to be T-RACT).
- Eliminating the West End Development Rock Storage Facility, which eliminated the highest-emitting operational scenario W5.
- Limiting long-term mining production to an average of 135,000 tons/day for a 5-year rolling average.
- Constructing the Burntlog access road with offsite materials containing "background" levels of arsenic.
- Updating the bulldozing emission factor using the SGP site-specific silt content.

5.2 General Modeling Methods and Parameters

Modeling methods and parameters used in TAP impact analyses presented in the *TAP Addendum* are largely identical to those used in the previously submitted application. These include the air dispersion model used, meteorological data, terrain, building downwash, ambient air boundary, and receptors. TAP modeling was conducted for the 14 operational modeling scenarios, consistent with the NAAQS analyses. Modeling Scenario W5 was eliminated from the arsenic modeling, as discussed in Section 5.8 of this *Modeling Review Attachment*.

The meteorological dataset processed using McCall, Idaho, cloud cover data was used for analyses in the *TAP Addendum*. Impacts were not assessed using the dataset processed using the Bulk Richardson (BULKRN) method for boundary layer parameter calculations. EPA considers both methods to be acceptable. Although modeled impacts tend to be somewhat larger when using meteorological data processed by the BULKRN method, DEQ contends that the impact analyses are still largely conservative compared to actual impacts anticipated. Conservative aspects include: continual operation of the worst-case operational scenario; operation at maximum allowable rates for the averaging period; no reduction in winter-time emissions from fugitive sources, accounting for emission suppression effects of increased moisture.

5.3 TAP Modeling Applicability

Table 1 provides a comparison between applicable facility-wide maximum potential TAP emissions for the highest-emitting scenario (W3) and TAP screening emission levels (ELs) from *Idaho Air Rules* Sections 585 (for non-carcinogens) and 586 (for carcinogens). Note that TAPs also classified as HAPs

emitted from sources "addressed" or "covered" by NSPS or NESHAP were not required to be evaluated for compliance with TAP increments in accordance with *Idaho Air Rules* Section 210.20. Furthermore, PRI has determined that the West End Development Rock Storage Facility will not be constructed. This change eliminated Modeling Scenario W5 (the highest-emitting scenario described in the main body of the DEQ *Modeling Review Memorandum*) as a potential operating scenario. After eliminating Modeling Scenario W5, it was determined that Modeling Scenario W3 is the highest-emitting scenario for all TAPs.

Table 1. TAP MODELING APPLICABILITY DETERMINATION (HIGHEST-EMITTING MODELING SCENARIO: W3).

HAP/TAP	Emissions (lb/hr)			EL (lb/hr)		Determination
	(a)	(b)	Total	(c)	(d)	
1,3-Butadiene	--	--	--	--	2.4E-5	EL not exceeded
3-Methylchloranthrene	--	4.5E-8	4.5E-8	--	2.5E-6	EL not exceeded
Acetaldehyde	--	--	--	--	3.0E-3	EL not exceeded
Acrolein	--	--	--	1.7E-2	--	EL not exceeded
Antimony	1.9E-2	1.6E-6	1.9E-2	3.3E-2	--	EL not exceeded
Arsenic	5.4E-1	8.2E-6	5.4E-1	--	1.5E-6	Carcinogenic EL exceeded
Benzene	--	5.3E-5	5.3E-5	--	8.0E-4	EL not exceeded
Benzo(a)pyrene[e]	--	3.0E-8				
Benz(a)anthracene[e]	--	4.5E-8				
Benzo(b)fluoranthene[e]	--	4.5E-8				
Benzo(k)fluoranthene[e]	--	4.5E-8	2.9E-7	--	2.0E-6	EL not exceeded
Chrysene[e]	--	4.5E-8				
Dibenzo(a,h)anthracene[e]	--	3.0E-8				
Indenol(1,2,3-cd)pyrene[e]	--	4.5E-8				
Beryllium	2.6E-3	3.5E-7	2.6E-3	--	2.8E-5	Carcinogenic EL exceeded
Biphenyl	--	--	--	1.0E-1	--	EL not exceeded
Cadmium	4.1E-4	2.8E-5	4.4E-4	--	3.7E-6	Carcinogenic EL exceeded
Carbon disulfide	1.4E-2	--	1.4E-2	2.0E+0	--	EL not exceeded
Chromium	7.3E-3	4.8E-5	7.4E-3	3.3E-2	--	EL not exceeded
Chromium (VI)	--	3.4E-7	3.4E-7	--	5.6E-7	EL not exceeded
Cobalt	3.3E-3	4.8E-6	3.26E-3	3.3E-3	--	EL not exceeded
Cyanide	4.5E-1	--	4.5E-1	3.3E-1	--	Non-carcinogenic EL exceeded
Dichlorobenzene	--	3.1E-5	3.1E-5	3.0E+1	--	EL not exceeded
Formaldehyde	--	1.9E-3	1.9E-3	--	5.1E-4	Carcinogenic EL exceeded
Hexane	--	4.6E-2	4.6E-2	1.2E+1	--	EL not exceeded
Hydrogen Chloride	--	--	--	5.0E-2	--	EL not exceeded
Manganese	2.4E-1	1.9E-4	2.4E-1	6.7E-2	--	Non-carcinogenic EL exceeded
Naphthalene	--	1.6E-5	1.6E-5	3.3E+0	--	EL not exceeded
Nickel	1.6E-3	5.6E-5	1.7E-3	--	2.7E-5	Carcinogenic EL exceeded
Phenol	--	--	--	1.3E+0	--	EL not exceeded
Phosphorus	5.3E-1	9.3E-5	5.3E-1	7.0E-3	--	Non-carcinogenic EL exceeded
Selenium	3.3E-4	6.2E-7	3.3E-4	1.3E-2	--	EL not exceeded
Toluene	--	8.8E-5	8.8E-5	2.5E+1	--	EL not exceeded
Xylene	--	--	--	2.9E+1	--	EL not exceeded
Aluminum	5.8E+1	6.5E-1	5.9E+1	6.7E-1	--	Non-carcinogenic EL exceeded
Barium	6.5E-1	6.8E-3	6.6E-1	3.3E-2	--	Non-carcinogenic EL exceeded
Calcium Carbonate	1.1E+1	2.2E+0	1.4E+1	6.7E-1	--	Non-carcinogenic EL exceeded
Calcium Oxide	--	7.0E-1	7.0E-1	1.3E-1	--	Non-carcinogenic EL exceeded
Copper	4.1E-3	5.3E-4	4.6E-3	6.7E-2	--	EL not exceeded
Cyclohexane	--	1.0E-3	1.0E-3	7.0E+1	--	EL not exceeded
Hydrogen Sulfide	--	9.0E-1	9.0E-1	9.3E-1	--	EL not exceeded
Iron	1.5E+1	2.1E-1	1.5E+1	6.7E-2	--	Non-carcinogenic EL exceeded
Molybdenum	8.1E-4	4.7E-4	1.3E-3	3.3E-1	--	EL not exceeded
Pentane	--	1.2E-1	1.2E-1	1.2E+2	--	EL not exceeded
Silver	4.1E-4	4.1E-4	8.2E-4	7.0E-3	--	EL not exceeded
Sulfuric Acid	--	2.0E+0	2.0E+0	6.7E-2	--	Non-carcinogenic EL exceeded

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Table 1. TAP MODELING APPLICABILITY DETERMINATION (HIGHEST-EMITTING MODELING SCENARIO: W3).						
HAP/TAP	Emissions (lb/hr)			EL (lb/hr)		Determination
	(a)	(b)	Total	(c)	(d)	
Thallium	8.1E-3	5.2E-4	8.7E-3	7.0E-3	--	Non-carcinogenic EL exceeded
Uranium	8.1E-3	5.2E-4	8.7E-3	1.3E-2	--	EL not exceeded
Vanadium	2.3E-2	8.4E-4	2.4E-2	3.0E-3	--	Non-carcinogenic EL exceeded
Trimethyl Benzene	--	1.1E-2	1.1E-2	8.2E+0	--	EL not exceeded
Tungsten	8.1E-3	5.2E-4	8.7E-3	3.3E-1	--	EL not exceeded
Zinc	2.9E-2	2.2E-3	3.1E-2	6.7E-1	--	EL not exceeded

a. Total HAP/TAP emissions for EL evaluation from mining (i.e., pits, blasting, haul roads, stockpiles and DRSF, tailings storage facility, access road, and underground exploration) and leaching. Emissions from sources covered/addressed by NSPS/NESHAP are not included in the evaluation for modeling applicability.

b. Total HAP/TAP emissions for EL evaluation from processing and production (i.e., ore processing [crushers and transfer, prill silos], ore concentration and refining [autoclave, electrowinning cells and pregnant solution tank, retort, furnace, carbon kiln], process heating [POX boiler, carbon regeneration kiln, propane vaporizer, solution heater], lime production [limestone crushers, screens, mill, transfers, lime kiln, kiln feed, lime mill, pebble lime silo, lime silos, lime mill crushing], aggregate production [portable crushers, screens, transfers], concrete production [central mixer, cement silos, aggregate bin], HVAC [heaters], emergency power [emergency generators, fire pump], fuel storage [gasoline fuel and tanks]). Emissions from sources covered/addressed by NSPS/NESHAP are not included in the evaluation for modeling applicability.

c. Non-carcinogenic EL from *Idaho Air Rules* Section 585.

d. Carcinogenic EL from *Idaho Air Rules* Section 586.

Table 1 shows that the SGP facility-wide potential TAP emissions exceed the respective EL for arsenic, beryllium, cadmium, cyanide, formaldehyde, manganese, nickel, phosphorus, aluminum, barium, calcium carbonate, calcium oxide, iron, sulfuric acid, thallium, and vanadium. Therefore, modeling was required for these 16 TAPs (11 non-carcinogenic and five carcinogenic TAPs) to demonstrate compliance with Acceptable Ambient Concentrations of Non-Carcinogens (AACs) and AACCs.

5.4 TAP Modeled Emission Rates

Table 2 lists the source-specific modeled emission rates for all 11 non-carcinogenic TAPs that required modeling (worst-case modeling scenario for all non-carcinogenic TAPs: W5). Table 3 lists the source-specific modeled emission rates for all five carcinogenic TAPs that required modeling (worst-case impacts for arsenic are associated with modeling scenario W2; worst-case impacts for all other carcinogenic TAPs are associated with modeling scenario W1). Note that all source-specific emission rates listed in Tables 2 and 3 were extracted by DEQ's modeling staff from the submitted modeling input files.

The total modeled emission rates for all non-carcinogenic TAPs are equal to the total facility-wide HAP/TAP emissions as stated in the permitting emissions inventory (excluding sources addressed by NSPS/NESHAP), evaluated at 180,000 T/day (see last two rows of Table 2). However, for carcinogenic TAPs, modeling was performed using an emission inventory that included T-RACT controls, long-term mining production limits, and other emission inventory refinements, as described in Section 4.0 of this *Modeling Review Attachment* (see last three rows of Table 3).

Table 2. MODELED EMISSION RATES FOR NON-CARCINOGENIC TAPS (WORST-CASE MODELING SCENARIOS).												
Type of Source	**Source ID**	**ALUM[a] (lb/hr)[b]**	**BARI[c] (lb/hr)**	**CACA[d] (lb/hr)**	**CAOX[e] (lb/hr)**	**CYAN[f] (lb/hr)**	**IRON[g] (lb/hr)**	**MANG[h] (lb/hr)**	**PHOS[i] (lb/hr)**	**SULF[j] (lb/hr)**	**THAL[k] (lb/hr)**	**VANA[l] (lb/hr)**
Point Sources	LS1L	2.33E-04	1.50E-06	0	7.63E-03	0	1.07E-04	2.44E-06	1.34E-06	0	5.16E-08	1.60E-07
	MILLS2L	2.33E-04	1.50E-06	0	7.63E-03	0	1.07E-04	2.44E-06	1.34E-06	0	5.16E-08	1.60E-07
	AC	2.31E-05	2.31E-05	2.31E-05	0	0	2.31E-05	0	0	2.03E+00	2.31E-05	2.31E-05
	ACB	0	3.06E-06	0	0	0	0	2.64E-07	0	0	0	1.60E-06
	ACS1L	9.32E-04	5.98E-06	0	3.05E-02	0	4.27E-04	9.76E-06	5.36E-06	0	2.06E-07	6.39E-07
	ACS2L	9.32E-04	5.98E-06	0	3.05E-02	0	4.27E-04	9.76E-06	5.36E-06	0	2.06E-07	6.39E-07
	ACS3L	9.32E-04	5.98E-06	0	3.05E-02	0	4.27E-04	9.76E-06	5.36E-06	0	2.06E-07	6.39E-07
	ACS4L	4.66E-04	2.99E-06	0	1.53E-02	0	2.13E-04	4.88E-06	2.68E-06	0	1.03E-07	3.20E-07
	CKD	9.59E-05	9.59E-05	9.59E-05	0	0	9.59E-05	0	0	0	9.59E-05	9.59E-05
	CKB	0	9.73E-06	0	0	0	0	8.40E-07	0	0	0	5.08E-06
	EW	9.59E-05	9.59E-05	9.59E-05	0	0	9.59E-05	0	0	0	9.59E-05	9.59E-05
	MR	9.59E-05	9.59E-05	9.59E-05	0	0	9.59E-05	0	0	0	9.59E-05	9.59E-05
	MF	9.59E-05	9.59E-05	9.59E-05	0	0	9.59E-05	0	0	0	9.59E-05	9.59E-05
	EDG1	0	0	0	0	0	0	0	0	0	0	0
	EDG2	0	0	0	0	0	0	0	0	0	0	0
	EDG3	0	0	0	0	0	0	0	0	0	0	0
	EDFP	0	0	0	0	0	0	0	0	0	0	0
	PV	0	4.31E-07	0	0	0	0	3.73E-08	0	0	0	2.25E-07
	HS	0	2.16E-05	0	0	0	0	1.86E-06	0	0	0	1.13E-05
	H1M	0	1.73E-05	0	0	0	0	1.49E-06	0	0	0	9.02E-06
	H2M	0	1.73E-05	0	0	0	0	1.49E-06	0	0	0	9.02E-06
	HM	0	1.73E-05	0	0	0	0	1.49E-06	0	0	0	9.02E-06
	HAC	0	1.08E-06	0	0	0	0	9.31E-08	0	0	0	5.64E-07
	HR	0	1.08E-06	0	0	0	0	9.31E-08	0	0	0	5.64E-07
	HA	0	1.08E-06	0	0	0	0	9.31E-08	0	0	0	5.64E-07
	HMO	0	2.16E-06	0	0	0	0	1.86E-07	0	0	0	1.13E-06
	HTS	0	8.63E-06	0	0	0	0	7.45E-07	0	0	0	4.51E-06
	HW	0	1.29E-05	0	0	0	0	1.12E-06	0	0	0	6.76E-06
	PSL	0	0	0	0	0	0	0	0	0	0	0
	CS1L	0	0	0	0	0	0	8.01E-07	0	0	0	0
	CS2L	0	0	0	0	0	0	8.01E-07	0	0	0	0
	LS6	3.19E-03	2.05E-05	3.88E-02	0	0	1.46E-03	0	0	0	7.06E-07	2.19E-06
	LSBM	4.30E-02	2.76E-04	5.22E-01	0	0	1.97E-02	0	0	0	9.51E-06	2.95E-05
	LS9	7.54E-04	4.84E-06	9.16E-03	0	0	3.45E-04	0	0	0	1.67E-07	5.17E-07
	LK	2.07E-02	1.33E-04	2.51E-01	0	0	9.47E-03	0	0	0	4.58E-06	1.42E-05
	LKC	0	9.51E-05	0	0	0	0	0	0	0	0	4.97E-05
	LCR	6.43E-03	4.12E-05	0	2.11E-01	0	2.94E-03	0	0	0	1.42E-06	4.41E-06
	LSL	1.40E-04	8.99E-07	0	4.59E-03	0	6.41E-05	0	0	0	3.10E-08	9.60E-08

Table 2. MODELED EMISSION RATES FOR NON-CARCINOGENIC TAPS (WORST-CASE MODELING SCENARIOS).												
Type of Source	**Source ID**	**ALUM[a] (lb/hr)[b]**	**BARI[c] (lb/hr)**	**CACA[d] (lb/hr)**	**CAOX[e] (lb/hr)**	**CYAN[f] (lb/hr)**	**IRON[g] (lb/hr)**	**MANG[h] (lb/hr)**	**PHOS[i] (lb/hr)**	**SULF[j] (lb/hr)**	**THAL[k] (lb/hr)**	**VANA[l] (lb/hr)**
Area Sources	WEP	5.59E+00	6.29E-02	1.10E+00	0	0	1.43E+00	2.35E-02	5.11E-02	0	7.87E-04	2.20E-03
	UGEXP	2.49E-05	2.80E-07	4.91E-06	0	0	6.38E-06	1.05E-07	2.28E-07	0	3.50E-09	9.81E-09
	TSF	0	0	0	0	2.32E-01	0	0	0	0	0	0
Line Sources	AR01	2.02E-02	2.28E-04	3.99E-03	0	0	5.18E-03	8.52E-05	1.85E-04	0	2.85E-06	7.98E-06
	AR02	1.56E-02	1.75E-04	3.07E-03	0	0	3.99E-03	6.55E-05	1.42E-04	0	2.19E-06	6.13E-06
	AR03	3.93E-02	4.43E-04	7.75E-03	0	0	1.01E-02	1.66E-04	3.60E-04	0	5.54E-06	1.55E-05
	AR04	3.77E-02	4.25E-04	7.43E-03	0	0	9.66E-03	1.59E-04	3.45E-04	0	5.31E-06	1.49E-05
Volume Sources	WEPBL	1.90E+00	2.14E-02	3.75E-01	0	0	4.88E-01	8.01E-03	1.74E-02	0	2.68E-04	7.50E-04
	WEDRSF	8.58E-01	9.66E-03	1.69E-01	0	0	2.20E-01	3.61E-03	7.85E-03	0	1.21E-04	3.38E-04
	OC1	1.04E-02	1.17E-04	2.04E-03	0	0	2.65E-03	0	0	0	1.46E-06	4.08E-06
	OC2	1.04E-02	1.17E-04	2.04E-03	0	0	2.65E-03	0	0	0	1.46E-06	4.08E-06
	OC3	1.04E-02	1.17E-04	2.04E-03	0	0	2.65E-03	0	0	0	1.46E-06	4.08E-06
	OC4	1.04E-02	1.17E-04	2.04E-03	0	0	2.65E-03	0	0	0	1.46E-06	4.08E-06
	OC5	1.04E-02	1.17E-04	2.04E-03	0	0	2.65E-03	0	0	0	1.46E-06	4.08E-06
	OC6	1.04E-02	1.17E-04	2.04E-03	0	0	2.65E-03	0	0	0	1.46E-06	4.08E-06
	OC7	8.87E-02	1.00E-03	1.75E-02	0	0	2.28E-02	0	0	0	1.25E-05	3.50E-05
	OC8	1.04E-02	1.17E-04	2.04E-03	0	0	2.65E-03	0	0	0	1.46E-06	4.08E-06
	OC9	4.90E-02	5.52E-04	9.66E-03	0	0	1.26E-02	0	0	0	6.90E-06	1.93E-05
	OC10	4.90E-02	5.52E-04	9.66E-03	0	0	1.26E-02	0	0	0	6.90E-06	1.93E-05
	OC11	4.90E-02	5.52E-04	9.66E-03	0	0	1.26E-02	0	0	0	6.90E-06	1.93E-05
	OC12	9.80E-02	1.10E-03	1.93E-02	0	0	2.51E-02	0	0	0	1.38E-05	3.86E-05
	OC13	1.14E-02	1.29E-04	2.25E-03	0	0	2.93E-03	0	0	0	1.61E-06	4.51E-06
	LS1U	1.13E-03	7.25E-06	0	3.70E-02	0	5.18E-04	1.18E-05	6.50E-06	0	2.50E-07	7.75E-07
	MILLS2U	1.13E-03	7.25E-06	0	3.70E-02	0	5.18E-04	1.18E-05	6.50E-06	0	2.50E-07	7.75E-07
	ACS1U	2.17E-03	1.39E-05	0	7.10E-02	0	9.94E-04	2.27E-05	1.25E-05	0	4.80E-07	1.49E-06
	ACS2U	2.17E-03	1.39E-05	0	7.10E-02	0	9.94E-04	2.27E-05	1.25E-05	0	4.80E-07	1.49E-06
	ACS3U	2.17E-03	1.39E-05	0	7.10E-02	0	9.94E-04	2.27E-05	1.25E-05	0	4.80E-07	1.49E-06
	ACS42U	2.17E-03	1.39E-05	0	7.10E-02	0	9.94E-04	2.27E-05	1.25E-05	0	4.80E-07	1.49E-06
	PSU	0	0	0	0	0	0	0	0	0	0	0
	CS1U	0	0	0	0	0	0	8.01E-07	0	0	0	0
	CS2U	0	0	0	0	0	0	8.01E-07	0	0	0	0
	CAL	1.56E-02	1.00E-04	0	0	0	7.14E-03	0	0	0	3.45E-06	1.07E-05
	CAU	1.56E-02	1.00E-04	0	0	0	7.14E-03	0	0	0	3.45E-06	1.07E-05
	CM	0	0	0	0	0	0	2.59E-05	8.22E-06	0	0	0
	PCSP1	1.41E-02	9.06E-05	1.72E-01	0	0	6.47E-03	0	0	0	3.12E-06	9.69E-06
	PCSP2	1.41E-02	9.06E-05	1.72E-01	0	0	6.47E-03	0	0	0	3.12E-06	9.69E-06
	LS1	3.19E-03	2.05E-05	3.88E-02	0	0	1.46E-03	0	0	0	7.06E-07	2.19E-06
	LS2	5.75E-03	3.69E-05	6.98E-02	0	0	2.63E-03	0	0	0	1.27E-06	3.94E-06
	LS3	2.66E-02	1.71E-04	3.23E-01	0	0	1.22E-02	0	0	0	5.88E-06	1.82E-05

Table 2. MODELED EMISSION RATES FOR NON-CARCINOGENIC TAPS (WORST-CASE MODELING SCENARIOS).												
Type of Source	**Source ID**	**ALUM[a] (lb/hr)[b]**	**BARI[c] (lb/hr)**	**CACA[d] (lb/hr)**	**CAOX[e] (lb/hr)**	**CYAN[f] (lb/hr)**	**IRON[g] (lb/hr)**	**MANG[h] (lb/hr)**	**PHOS[i] (lb/hr)**	**SULF[j] (lb/hr)**	**THAL[k] (lb/hr)**	**VANA[l] (lb/hr)**
	LS4	5.75E-03	3.69E-05	6.98E-02	0	0	2.63E-03	0	0	0	1.27E-06	3.94E-06
	LS5	2.66E-02	1.71E-04	3.23E-01	0	0	1.22E-02	0	0	0	5.88E-06	1.82E-05
	LS7	3.19E-03	2.05E-05	3.88E-02	0	0	1.46E-03	0	0	0	7.06E-07	2.19E-06
	LS8	3.19E-03	2.05E-05	3.88E-02	0	0	1.46E-03	0	0	0	7.06E-07	2.19E-06
	LS10	7.54E-04	4.84E-06	9.16E-03	0	0	3.45E-04	0	0	0	1.67E-07	5.17E-07
	LS11	6.29E-03	4.03E-05	7.63E-02	0	0	2.88E-03	0	0	0	1.39E-06	4.31E-06
	LS12	7.54E-04	4.84E-06	9.16E-03	0	0	3.45E-04	0	0	0	1.67E-07	5.17E-07
	LSU	1.40E-05	8.99E-08	0	4.59E-04	0	6.41E-06	0	0	0	3.10E-09	9.60E-09
	MILLTANKS	0	0	0	0	2.21E-01	0	0	0	0	0	0
	HRT001-HRT072[m]	2.62E-01	2.95E-03	5.16E-02	0	0	6.71E-02	1.10E-03	2.40E-03	0	3.69E-05	1.03E-04
	HRN001-HRN022[m]	2.62E-01	2.95E-03	5.16E-02	0	0	6.71E-02	1.10E-03	2.40E-03	0	3.69E-05	1.03E-04
Total Modeled Rates		***3.37E+01***	***3.79E-01***	***8.76E+00***	***6.96E-01***	***4.53E-01***	***8.69E+00***	***1.39E-01***	***3.03E-01***	***2.03E+00***	***5.17E-03***	***1.39E-02***
Total Emission Rates at 180,000 T/day[n]		***3.37E+01***	***3.79E-01***	***8.76E+00***	***6.96E-01***	***4.53E-01***	***8.69E+00***	***1.39E-01***	***3.03E-01***	***2.03E+00***	***5.17E-03***	***1.39E-02***

a. Aluminum (worst-case modeling scenario: W5).
b. Pounds per hour.
c. Barium (worst-case modeling scenario: W5).
d. Calcium carbonate (worst-case modeling scenario: W5).
e. Calcium oxide (worst-case modeling scenario: W5).
f. Cyanide (worst-case modeling scenario: W5).
g. Iron (worst-case modeling scenario: W5).
h. Manganese (worst-case modeling scenario: W5).
i. Phosphorus (worst-case modeling scenario: W5).
j. Sulfuric acid (worst-case modeling scenario: W5).
k. Thallium (worst-case modeling scenario: W5).
l. Vanadium (worst-case modeling scenario: W5).
m. The Haul Road was represented in the model as a series of volume sources. The emission rates listed in this table represent each individual volume source.
n. Total emission rates at 180,000 tons per day were derived from Worksheet "TblA" in the emission inventory dated October 5, 2021. The total emission rates in this row represent all facility-wide HAP/TAP emission sources from mining, leaching, and processing and production (excluding emissions from sources "addressed" or "covered" by NSPS/NESHAP).

Table 3. MODELED EMISSION RATES FOR CARCINOGENIC TAPS (WORST-CASE MODELING SCENARIOS).						
Type of Source	**Source ID**	**ARSE[a] (lb/hr)[b]**	**BERY[c] (lb/hr)**	**CADM[d] (lb/hr)**	**FORM[e] (lb/hr)**	**NICK[f] (lb/hr)**
Point Sources	LS1L	1.14E-08	3.96E-10	1.24E-10	0	2.47E-09
	MILLS2L	1.14E-08	3.96E-10	1.24E-10	0	2.47E-09
	AC	0	0	0	0	0
	ACB	1.28E-07	7.66E-09	7.02E-07	4.79E-05	1.34E-06
	ACS1L	4.55E-08	1.58E-09	4.94E-10	0	9.89E-09
	ACS2L	4.55E-08	1.58E-09	4.94E-10	0	9.89E-09
	ACS3L	4.55E-08	1.58E-09	4.94E-10	0	9.89E-09
	ACS4L	2.27E-08	7.91E-10	2.47E-10	0	4.94E-09
	CKD	0	0	0	0	0
	CKB	4.07E-07	2.44E-08	2.24E-06	1.52E-04	4.27E-06
	EW	0	0	0	0	0
	MR	0	0	0	0	0
	MF	0	0	0	0	0
	EDG1	0	0	0	0	0
	EDG2	0	0	0	0	0
	EDG3	0	0	0	0	0
	EDFP	0	0	0	0	0
	PV	1.80E-08	1.08E-09	9.91E-08	6.76E-06	1.89E-07
	HS	9.01E-07	5.41E-08	4.96E-06	3.38E-04	9.46E-06
	H1M	7.84E-07	4.71E-08	4.31E-06	2.94E-04	8.24E-06
	H2M	7.84E-07	4.71E-08	4.31E-06	2.94E-04	8.24E-06
	HM	7.84E-07	4.71E-08	4.31E-06	2.94E-04	8.24E-06
	HAC	4.90E-08	2.94E-09	2.70E-07	1.84E-05	5.15E-07
	HR	4.90E-08	2.94E-09	2.70E-07	1.84E-05	5.15E-07
	HA	4.90E-08	2.94E-09	2.70E-07	1.84E-05	5.15E-07
	HMO	9.80E-08	5.88E-09	5.39E-07	3.68E-05	1.03E-06
	HTS	3.92E-07	2.35E-08	2.16E-06	1.47E-04	4.12E-06
	HW	5.88E-07	3.53E-08	3.24E-06	2.21E-04	6.18E-06
	PSL	0	0	0	0	0
	CS1L	2.90E-08	3.33E-09	0	0	2.86E-07
	CS2L	2.90E-08	3.33E-09	0	0	2.86E-07
	LS6	0	0	0	0	0
	LSBM	0	0	0	0	0
	LS9	0	0	0	0	0
	LK	0	0	0	0	0
	LKC	0	0	0	0	0
	LCR	0	0	0	0	0
	LSL	0	0	0	0	0
Area Sources	WEP	9.40E-03	4.51E-05	7.04E-06	0	2.82E-05
	UGEXP	2.34E-07	1.12E-09	1.75E-10	0	7.01E-10
	TSF	0	0	0	0	0
Line Sources	AR01	7.12E-07	9.12E-07	1.42E-07	0	5.70E-07
	AR02	5.48E-07	7.01E-07	1.10E-07	0	4.38E-07
	AR03	1.38E-06	1.77E-06	2.77E-07	0	1.11E-06
	AR04	1.33E-06	1.70E-06	2.65E-07	0	1.06E-06

Table 3. MODELED EMISSION RATES FOR CARCINOGENIC TAPS (WORST-CASE MODELING SCENARIOS).						
Type of Source	**Source ID**	**ARSE[a] (lb/hr)[b]**	**BERY[c] (lb/hr)**	**CADM[d] (lb/hr)**	**FORM[e] (lb/hr)**	**NICK[f] (lb/hr)**
Volume Sources	WEPBL	1.79E-02	8.57E-05	1.34E-05	0	5.36E-05
	FDRSF	4.23E-03				
	STKP		2.72E-05	4.25E-06	0	1.70E-05
	OC1	0	0	0	0	0
	OC2	0	0	0	0	0
	OC3	0	0	0	0	0
	OC4	0	0	0	0	0
	OC5	0	0	0	0	0
	OC6	0	0	0	0	0
	OC7	0	0	0	0	0
	OC8	0	0	0	0	0
	OC9	0	0	0	0	0
	OC10	0	0	0	0	0
	OC11	0	0	0	0	0
	OC12	0	0	0	0	0
	OC13	0	0	0	0	0
	LS1U	5.51E-08	1.92E-09	5.99E-10	0	1.20E-08
	MILLS2U	5.51E-08	1.92E-09	5.99E-10	0	1.20E-08
	ACS1U	2.21E-07	7.67E-09	2.40E-09	0	4.79E-08
	ACS2U	2.21E-07	7.67E-09	2.40E-09	0	4.79E-08
	ACS3U	2.21E-07	7.67E-09	2.40E-09	0	4.79E-08
	ACS42U	1.10E-07	3.84E-09	1.20E-09	0	2.40E-08
	PSU	0	0	0	0	0
	CS1U	2.90E-08	3.33E-09	0	0	2.86E-07
	CS2U	2.90E-08	3.33E-09	0	0	2.86E-07
	CAL	0	0	0	0	0
	CAU	0	0	0	0	0
	CM	2.03E-06	0	4.86E-09	0	1.70E-06
	PCSP1	0	0	0	0	0
	PCSP2	0	0	0	0	0
	LS1	0	0	0	0	0
	LS2	0	0	0	0	0
	LS3	0	0	0	0	0
	LS4	0	0	0	0	0
	LS5	0	0	0	0	0
	LS7	0	0	0	0	0
	LS8	0	0	0	0	0
	LS10	0	0	0	0	0
	LS11	0	0	0	0	0
	LS12	0	0	0	0	0
	LSU	0	0	0	0	0
	MILLTANKS	0	0	0	0	0

Table 3. MODELED EMISSION RATES FOR CARCINOGENIC TAPS (WORST-CASE MODELING SCENARIOS).						
Type of Source	**Source ID**	**ARSE[a] (lb/hr)[b]**	**BERY[c] (lb/hr)**	**CADM[d] (lb/hr)**	**FORM[e] (lb/hr)**	**NICK[f] (lb/hr)**
Volume Sources	HRF001-HRF055[g]	1.03E-03				
	HRQ001-HRQ049[g]	1.03E-03				
	HRR001-HRR006[g]	1.03E-03				
	HRN001-HRN022[g]	1.03E-03	9.27E-06	1.45E-06	0	5.80E-06
	HRB001-HRB003[g]	1.03E-03				
	HRP001-HRP057[g]		9.27E-06	1.45E-06	0	5.80E-06
	HRO001-HRO002[g]	1.03E-03	9.27E-06	1.45E-06	0	5.80E-06
Total Modeled Rates		***1.73E-01***	***9.15E-04***	***1.71E-04***	***1.89E-03***	***6.27E-04***
Total T-RACT Emission Rates[h]		***1.73E-01***	***9.1E-04***	***1.7E-04***	***1.9E-03***	***6.3E-04***
Total Emission Rates at 180,000 T/day[i]		***4.03E-01***	***1.36E-03***	***2.40E-04***	***1.89E-03***	***9.04E-04***

a. Arsenic (worst-case modeling scenario: W2).
b. Pounds per hour.
c. Beryllium (worst-case modeling scenario: W1).
d. Cadmium (worst-case modeling scenario: W1).
e. Formaldehyde (worst-case modeling scenario: W1).
f. Nickel (worst-case modeling scenario: W1).
g. The Haul Road was represented in the model as a series of volume sources. The emission rates listed in this table represent each individual volume source.
h. Total T-RACT emission rates – calculated based on T-RACT controls, long-term mining production limits, and other emission inventory refinements, as described in Section 4.0 of this *Modeling Review Attachment* – are derived from Tables B-W2 (for Arsenic) and B-W1 (for Beryllium, Cadmium, Formaldehyde, and Nickel) in Appendix B of the *TAP Addendum*.
i. Total emission rates at 180,000 tons per day were derived from Worksheet "TblA" in the emission inventory dated October 5, 2021. The total emission rates in this row represent all facility-wide HAP/TAP emission sources from mining, leaching, and processing and production (excluding emissions from sources "addressed" or "covered" by NSPS/NESHAP).

5.5 Cyanide Modeling Emission Source Parameters

Modeling analyses for cyanide introduced two new emission sources that were not previously evaluated by DEQ: tailings storage facility (model ID: TSF) and mill tanks (model ID: MILLTANKS).

1. The tailings storage facility was modeled by Air Sciences as a surface-based (zero release height above ground-level and zero initial vertical dimension) AREA source. The easterly and northerly lengths were calculated as square-root of the TSF area (easterly length = northerly length = $\sqrt{1{,}338{,}158\ square\ meters}$ = 1,157 meters).

2. The mill tanks were grouped and modeled by Air Sciences as a single VOLUME source. The tanks sit on the ground, so the release height was set to the average tank height of 12.2 meters (40 feet). The initial lateral dispersion (σ_y) was calculated as the equivalent diameter of the combined (18) tank area divided by the single VOLUME source coefficient of 4.3:

$$\sigma_{y(MILLTANKS)} = \frac{Equivalent\ diameter}{4.3} = \frac{\sqrt{\Sigma(d)^2}}{4.3} = 42.8\ feet$$

The individual tank diameters (d) are: two tanks at 40 feet, four tanks at 52 feet, six tanks at 54 feet, and six tanks at 20 feet.

DEQ typically requires that tailings storage facilities be modeled as an AREAPOLY source with an outline that follows the contour of the emission source, and that mill tanks be represented in the model as individual volume sources; but, given that the maximum modeled concentration for cyanide is safely below the AAC (0.08%), DEQ's modeling team accepted the modeling analysis submitted by Air Sciences and concluded that it confidently demonstrates that the cyanide AAC will not be exceeded.

5.6 Deposition Modeling

Air Sciences applied particle deposition algorithms in the impact modeling for particulate TAPs. The particulate deposition parameters used in the NAAQS compliance analysis were derived for PM_{10} and $PM_{2.5}$ (see Tables 22 and 23 in the main body of the DEQ *Modeling Review Memorandum*). Dust-related metal TAP emissions include total particulates (all size fractions of particulate matter [PM] up to PM_{30}). Therefore, the deposition parameters for PM were calculated using the same methodology and EPA references used for PM_{10} and $PM_{2.5}$ in the NAAQS compliance demonstration analyses. The PM deposition parameters are provided below in Table 4. The same density values were used as in the previous TAPs modeling analysis. However, an additional deposition characterization bin was added to better handle deposition of 10 µm to 30 µm particulates; mass fractions were adjusted accordingly.

Table 4. PARTICULATE MATTER DEPOSITION PARAMETERS BY SOURCE CATEGORY.

Source Category	Parameter	PM				
		Bin 1	Bin 2	Bin 3	Bin 4	Bin 5
Haul Roads	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.02	0.23	0.75	--	--
	Mass Mean Diameter (µm)	2.50	10.00	30.00	--	--
	Density (g/cm^3) (YPP, HFP, WEP DR average)	2.46	2.46	2.46	--	--
Material Handling (Ore, DR, Limestone)	Bin Upper Diameter (µm)	2.50	5.00	10.00	30.00	--
	Mass Fraction	0.07	0.20	0.20	0.53	--
	Mass Mean Diameter (µm)	2.50	5.00	10.00	30.00	--
	Density (g/cm^3) (Ore)	Pit-specific, see Table 23[a].				
	Density (g/cm^3) (Ore and Waste)	Pit-specific, see Table 23.				
	Density (g/cm^3) (Limestone)	1.09	1.09	1.09	1.09	--
Baghouses	Bin Upper Diameter (µm)	2.50	6.00	10.00	30.00	--
	Mass Fraction	0.25	0.45	0.20	0.10	--
	Mass Mean Diameter (µm)	2.50	6.00	10.00	30.00	--
	Density (g/cm^3) (Ore)	Pit-specific, see Table 23.				
Diesel Engines	Bin Upper Diameter (µm)	1.00	2.50	6.00	10.00	30.00
	Mass Fraction	0.82	0.08	0.03	0.03	0.04
	Mass Mean Diameter (µm)	1.00	2.50	6.00	10.00	30.00
	Density (g/cm^3) (Diesel Combustion)	1.00	1.00	1.00	1.00	1.00
Heaters and Boilers	Bin Upper Diameter (µm)	1.00	2.50	6.00	10.00	30.00
	Mass Fraction	0.23	0.22	0.25	0.09	0.21
	Mass Mean Diameter (µm)	1.00	2.50	6.00	10.00	30.00
	Density (g/cm^3) (Propane Combustion)	1.24	1.24	1.24	1.24	1.24

Table 4. PARTICULATE MATTER DEPOSITION PARAMETERS BY SOURCE CATEGORY.						
Source Category	**Parameter**	**PM**				
		Bin 1	**Bin 2**	**Bin 3**	**Bin 4**	**Bin 5**
Lime Loading and Unloading (Quick, Pebble)	Bin Upper Diameter (μm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.05	0.29	0.66	--	--
	Mass Mean Diameter	2.50	10.00	30.00	--	--
	Density (g/cm^3) (Quick)	0.44	0.44	0.44	--	--
	Density (g/cm^3) (Pebble)	0.96	0.96	0.96	--	--
Lime Unloading (Quick, Pebble)	Bin Upper Diameter (μm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.09	0.49	0.42	--	--
	Mass Mean Diameter (μm)	2.50	10.00	30.00	--	--
	Density (g/cm^3) (Quick)	0.44	0.44	0.44	--	--
	Density (g/cm^3) (Pebble)	0.96	0.96	0.96	--	--
Cement and Aggregate Loading and Unloading	Bin Upper Diameter (μm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.05	0.29	0.66	--	--
	Mass Mean Diameter (μm)	2.50	10.00	30.00	--	--
	Density (g/cm^3) (Cement)	1.44	1.44	1.44	--	--
	Density (g/cm^3) (Aggregate)	1.28	1.28	1.28	--	--
Prill Loading and Unloading	Bin Upper Diameter (μm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.05	0.30	0.65	--	--
	Mass Mean Diameter (μm)	2.50	10.00	30.00	--	--
	Density (g/cm^3) (Prill)	0.84	0.84	0.84	--	--
Refining Processes	Bin Upper Diameter (μm)	1.00	2.50	6.00	10.00	30.00
	Mass Fraction	0.72	0.10	0.07	0.03	0.08
	Mass Mean Diameter (μm)	1.00	2.50	6.00	10.00	30.00
	Density (g/cm^3) (Diesel Combustion)	1.00	1.00	1.00	1.00	1.00
Portable Crushing and Screening Plant	Bin Upper Diameter (μm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.05	0.32	0.63	--	--
	Mass Mean Diameter (μm)	2.50	10.00	30.00	--	--
	Density (g/cm^3) (YPP, HFP, WEP DR average)	2.46	2.46	2.46	--	--
Lime Kiln and Ball Mill	Bin Upper Diameter (μm)	2.50	10.00	30.00	--	--
	Mass Fraction (Kiln)	0.27	0.28	0.45	--	--
	Mass Fraction (Ball Mill)	0.30	0.54	0.16	--	--
	Mass Mean Diameter (μm)	2.50	10.00	30.00	--	--
	Density (g/cm^3)	1.09	1.09	1.09	--	--
Blasting and Drilling	Bin Upper Diameter (μm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.03	0.49	0.48	--	--
	Mass Mean Diameter (μm)	2.50	10.00	30.00	--	--
	Density (g/cm^3) (Ore or DR)	Pit-specific, see Table 23.				
Dozing	Bin Upper Diameter (μm)	2.50	10.00	15.00	30.00	--
	Mass Fraction	0.11	0.08	0.06	0.75	--
	Mass Mean Diameter (μm)	2.50	10.00	15.00	30.00	--
	Density (g/cm^3) (DR)	Pit-specific, see Table 23.				

[a.] See Table 23 in the main body of the DEQ *Modeling Review Memorandum*.

5.7 Carcinogenic TAP Modeling Lifetime Exposure Adjustment

Maximum modeled concentrations for carcinogenic TAPs were adjusted to account for the life-of-mine production limits, which affects the lifetime exposure.

PRI evaluated the highest modeled annual carcinogenic TAP concentration from each of the 14 modeling scenarios for lifetime exposure as follows:

$$Lifetime\ exposure\ \left(\frac{\mu g}{m^3}\right) = \frac{Highest\ annual\ concentration\ \left(\frac{\mu g}{m^3}\right) \times 16\ (mine\ operation\ years)}{70\ (years, lifetime\ exposure)}$$

This equation assumes that the highest annual concentration from the 14 modeling scenarios is repeated for 16 years of mining operation. This was then averaged over 70 years to calculate the 70-year lifetime exposure.

PRI and Air Sciences contend that calculating lifetime exposure based on 16 years of mining operation is conservative. The annual emissions for carcinogenic TAP modeling are based on 135,000 tons/day (see Section 5.1 of this *Modeling Review Attachment*) and 365 days per year. Over 16 years, this equates to a potential mining production of 788.4 million tons:

$$\frac{135{,}000\ \left(\frac{tons}{day}\right) \times 365\ \left(\frac{days}{year}\right) \times 16\ years}{1{,}000{,}000\ \left(\frac{tons}{million\ ton}\right)} = 788.4\ million\ tons$$

The actual life-of-mine total production as described in the SGP *Refined Proposed Action* (*ModPRO2*) mine plan is only 402.86 million tons (Perpetua 2021), which is 51.1% of the potential life-of-mine production represented in the above equation and related emission evaluations.

5.8 Arsenic Compliance Demonstration for Modeling Scenarios W1-W4

To demonstrate compliance with the AACC for arsenic, PRI applied two additional operating limitations:

- The removal of Modeling Scenario W5 as a potential operating scenario
- Limiting the West End Pit's life-of-mine potential mining production to 50% of the total life-of-mine potential mining production of 788.4 million tons: 50% * 788.4 million tons = 394.2 million tons

PRI has determined that the West End Development Rock Storage Facility (DRSF) will not be constructed. This change eliminated Modeling Scenario W5 from the arsenic modeling evaluation. The remaining four West End Pit modeling scenarios (W1–W4) are evaluated using the 70-year lifetime exposure equation from Section 5.7 and adjusting for the proposed West End Pit life-of-mine production limit of 50% of the total production as follows:

$$LifeExpose_{Wi,j,n} = \left[\left(WEPExpose_{Wi,n}\right)(50\%) + \left(nonWEPExpose_{Sj,n}\right)(50\%)\right]\left[\frac{16\ year\ LOM}{70\ year\ exposure}\right]$$

where:

W*i*	=	West End Pit scenario, where *i* = 1 to 4.
S*j*	=	non West End Pit scenario, where *j* = B1, B2, H1, H2, H3, H4, Y1, Y2, and Y3.
n	=	specific receptor.
$LifeExpose_{Wi,j,n}$	=	lifetime exposure in µg/m³ for West End Pit scenario *i*, non West End Pit scenario *j*, at receptor *n*.
$WEPExpose_{Wi,n}$	=	annual maximum impact in µg/m³ for West End Pit scenario *i* at receptor *n*.
$nonWEPExpose_{Sj,n}$	=	annual maximum impact in µg/m³ for non West End Pit scenario *j* at receptor *n*.
16 year LOM	=	maximum life-of-mine.
70 year exposure	=	Lifetime exposure used for development of AACCs in *Idaho Air Rules*.

The above equation was used to calculate the lifetime arsenic exposure from the West End Pit scenarios (W1–W4) on a receptor-by-receptor basis. Combining the concentrations from Modeling Scenarios W1–W4 with the highest concentration from the remaining non-West End Pit scenarios (B1, B2, H1, H2, H3, H4, Y1, Y2, or Y3) conservatively ensures that the maximum potential impacts from applicable sources are evaluated and remain below AACCs.

PRI contends that calculating lifetime arsenic exposure based on the proposed West End Pit life-of-mine production limit of 50% of the total production is conservative. The actual life-of-mine total production from the West End Pit as described in the ModPRO2 mine plan is only 198.26 million tons (Perpetua 2021), which is 50.3% of the proposed West End Pit life-of-mine production limit of 394.2 million tons.

6.0 Impact Results

TAP impact analysis results, as submitted in the *TAP Addendum* and as further assessed by DEQ, are discussed in this section. The effect of various operational refinements also reduced PM_{10} and $PM_{2.5}$ impacts, and this is discussed in Section 6.2.

6.1 TAP Impact Analyses Results

This section describes the revised TAP impact analyses and demonstrates that applicable TAP emissions resulting from operation of the SGP will not result in increased impacts that exceed AACs or AACCs.

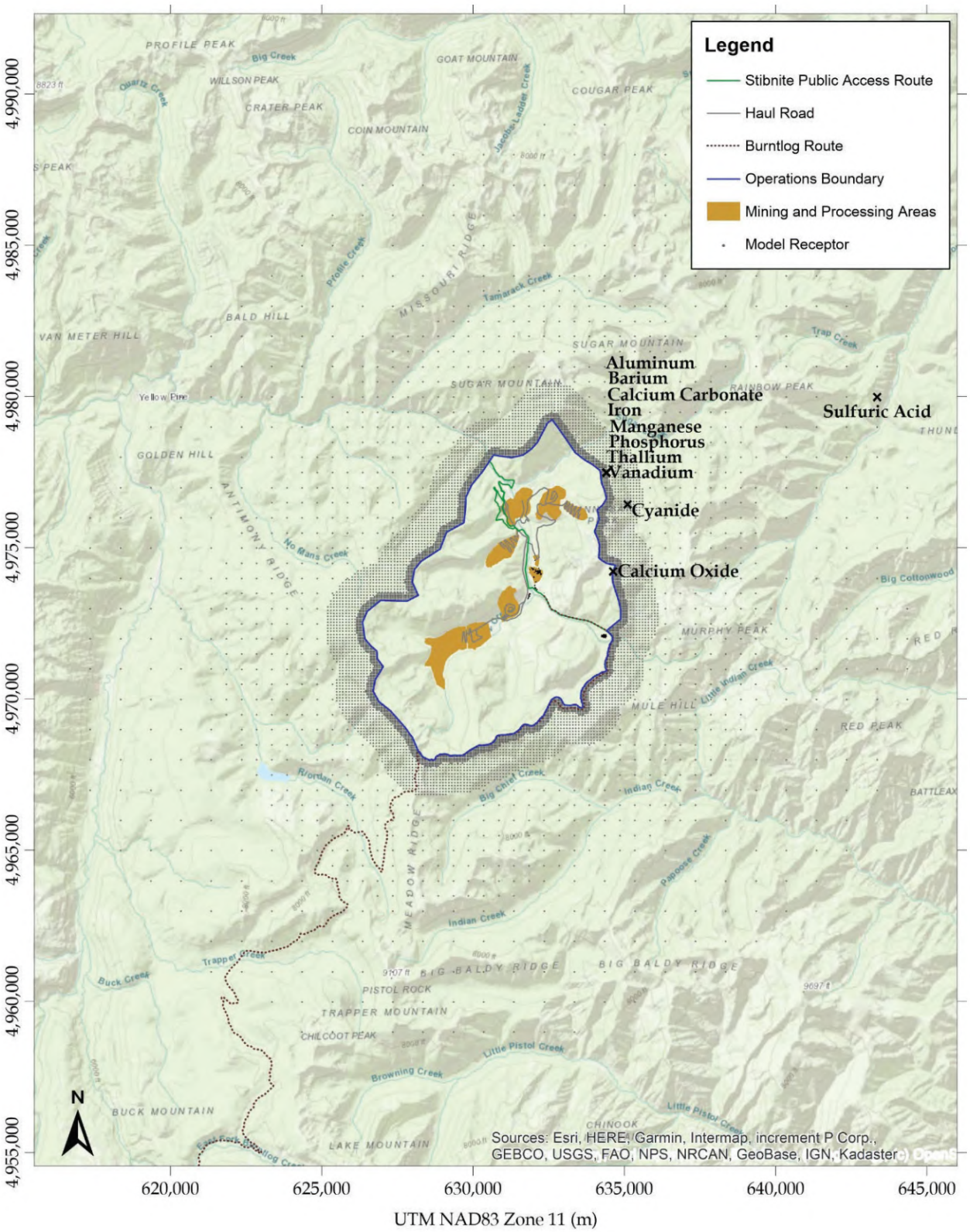
6.1.1 Modeling Non-Carcinogenic TAPs

The non-carcinogenic TAPs subject to impact modeling requirements to demonstrate compliance with AACs of *Idaho Air Rules* Section 585 were modeled at the emission levels shown in Table 1 above. The maximum 24-hour modeled concentration for each of the 14 modeling scenarios demonstrates compliance with the applicable AAC, as summarized below in Table 5. PRI elected to include Scenario W5 in the modeling analysis for non-carcinogenic TAPs. Figure 1 illustrates the locations of the maximum impacts for each non-carcinogenic TAP.

Table 5. RESULTS FOR TAPS IMPACT ANALYSES FOR NON-CARCINOGENIC TAPS.					
Toxic Air Pollutant	**Averaging Time**	**Maximum Modeled Concentration ($\mu g/m^3$)[a]**	**Model Scenario**	**AAC[b] ($\mu g/m^3$)**	**Percent of AAC**
Aluminum	24-hour	6.17	W5	500	1.23%
Barium	24-hour	0.07	W5	25	0.28%
Calcium carbonate	24-hour	1.22	W5	500	0.24%
Calcium oxide	24-hour	0.15	All	100	0.15%
Cyanide	24-hour	0.20	All	250	0.08%
Iron	24-hour	1.58	W5	50	3.16%
Manganese	24-hour	0.03	W5	250	0.01%
Phosphorus	24-hour	0.06	W5	5	1.20%
Sulfuric acid	24-hour	0.41	All	50	0.82%
Thallium	24-hour	0.001	W5	5	0.02%
Vanadium	24-hour	0.002	W5	2.5	0.08%

a. Micrograms per cubic meter.
b. Acceptable Ambient Concentration of a Non-carcinogenic TAP.

Figure 1. SGP NON-CARCINOGENIC MAXIMUM TAP IMPACT LOCATIONS.



6.1.2 Modeling Carcinogenic TAPs

The carcinogenic TAPs subject to impact modeling requirements to demonstrate compliance with AACCs of *Idaho Air Rules* Section 586 were modeled using an emission inventory that includes the T-RACT controls, long-term mining production limits, and other emission inventory refinements, as described in Section 4.0 and 5.0 of this *Modeling Review Attachment*.

The maximum modeled impact for each of the 14 modeling scenarios demonstrated compliance with the T-RACT AACC, as summarized below in Table 6. The SGP maximum concentrations were adjusted to account for the life-of-mine production limits, which affect the lifetime exposure, and to account for the elimination of Modeling Scenario W5. See Sections 5.7 and 5.8 of this *Modeling Review Attachment* for more detail. The locations of the maximum impacts for each carcinogenic TAP are presented in Figure 2. Arsenic concentrations are considerably lower in areas away from the location of maximum impact as shown in Figure 3.

Table 6. RESULTS FOR TAPS IMPACT ANALYSES FOR CARCINOGENIC TAPS.

Toxic Air Pollutant	Averaging Time	Maximum Modeled Lifetime Exposure Concentration ($\mu g/m^3$)[a,b]	Model Scenario	AACC[c] ($\mu g/m^3$)	T-RACT[d] AACC	Percent of T-RACT AACC
Arsenic	Annual	0.00095	W2	0.00023	0.0023	41.30%
Beryllium	Annual	0.00001	W1	0.0042	0.042	0.02%
Cadmium	Annual	0.000002	W1	0.00056	0.0056	0.04%
Formaldehyde	Annual	0.00007	W1	0.077	0.77	0.01%
Nickel	Annual	0.00001	W1	0.042	0.42	<0.01%

a. Micrograms per cubic meter.
b. The lifetime exposure concentrations are based on the proposed restrictions discussed in Sections 5.7 and 5.8 of this *Modeling Review Attachment*.
c. Acceptable Ambient Concentration of a Carcinogenic TAP.
d. Toxic Air Pollutant Reasonably Available Control Technology allows the AACCs to be increased by a factor of ten per *Idaho Air Rules* Section 210.12(b).

Figure 2. SGP CARCINOGENIC MAXIMUM TAP IMPACT LOCATIONS.

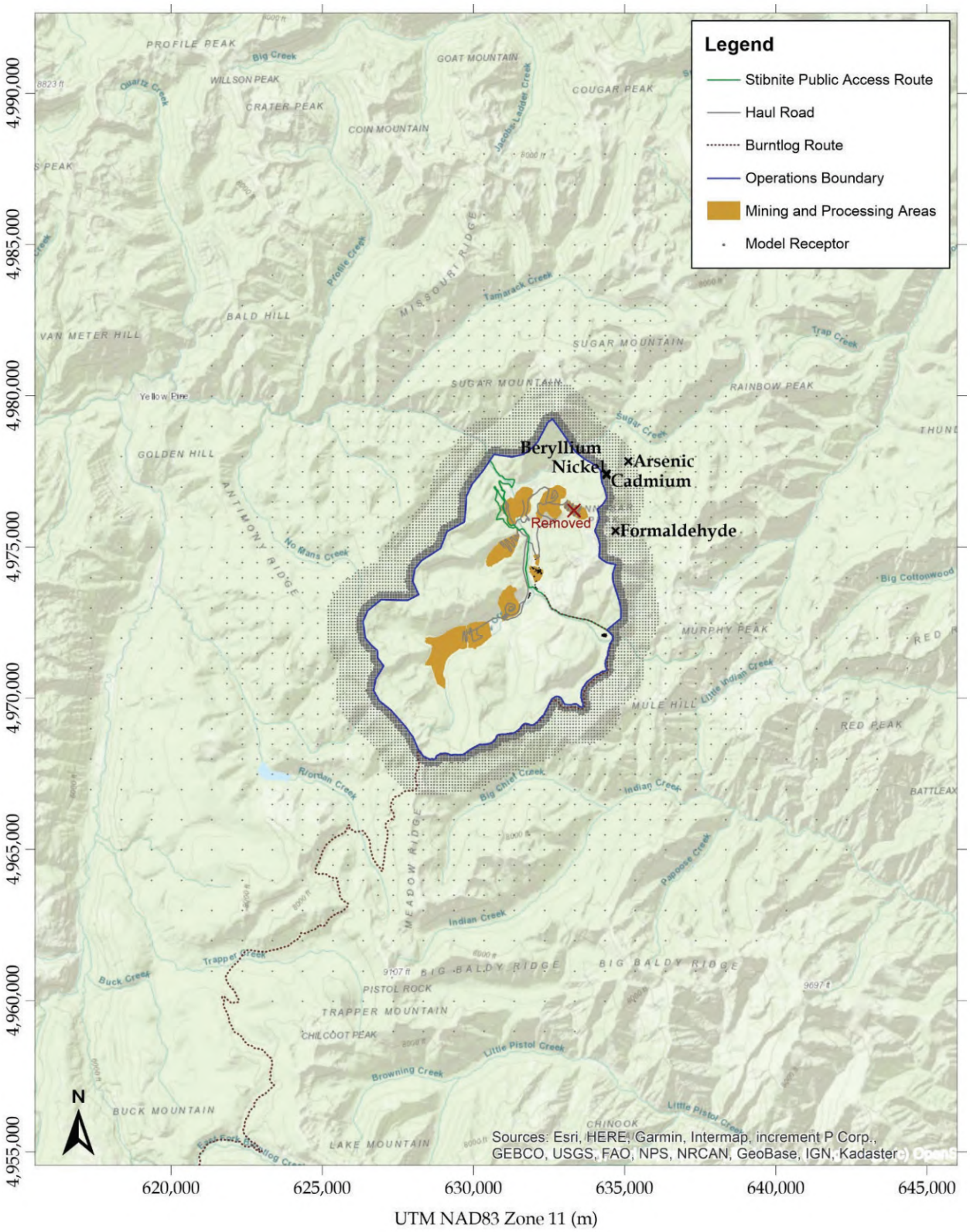
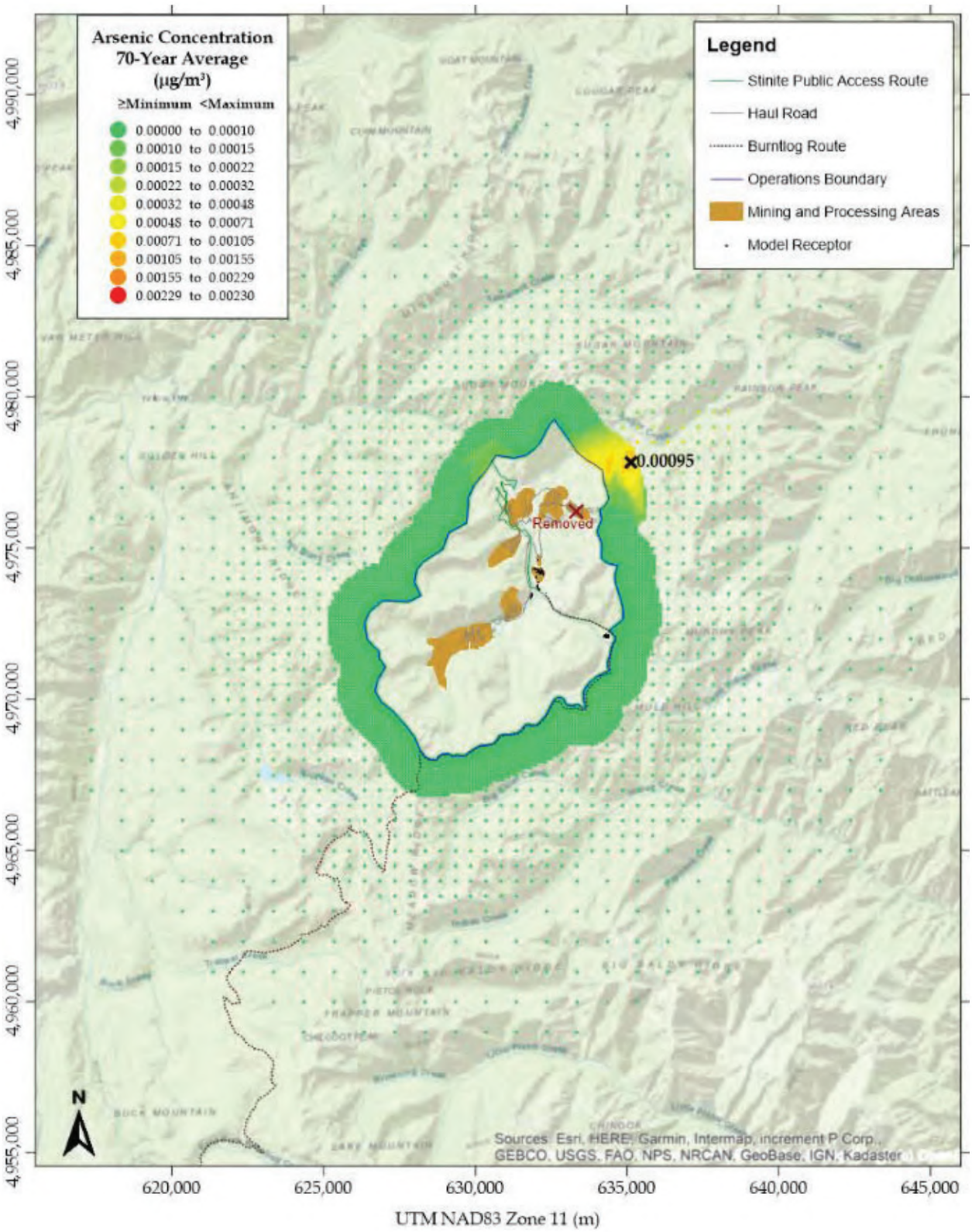


Figure 3. SGP CONTOURS OF LIFETIME ARSENIC IMPACTS.



6.2 *Effect of Changes to Modeled PM_{10} Results*

PRI has determined that the West End Development Rock Storage Facility will not be constructed. This change eliminated Modeling Scenario W5 as a potential operating scenario. In Section 4.1.4 in the main body of the DEQ *Modeling Review Memorandum*, DEQ identified PM_{10} NAAQS exceedances at four hotspot receptors when using the BULKRN meteorological dataset for Modeling Scenario W5 (the highest PM_{10} impact modeling scenario). When Modeling Scenario W5 is removed, the highest modeled impacts are predicted to occur for Modeling Scenario W3, which represents the transport of development rock from the West End Pit to the Hangar Flats Development Rock Storage Facility.

Table 7 presents results for the cumulative NAAQS impact analyses for Scenario W3. Results still exceed the 24-hour PM_{10} NAAQS even when Modeling Scenario W5 is eliminated. However, there is only one hotspot receptor exceeding NAAQS. The modeled violation is also predicted to occur during winter. This is a critical consideration because during winter, not only are fugitive emissions minimized because of the higher moisture content of material handled or driven over, but background concentrations in such remote areas are also generally much lower because of the absence of wildfires and dust-generating sources.

Table 7 also lists the results when using temporally varying backgrounds, instead of a single-value background, in the cumulative NAAQS impact analysis (using the "SEASON" and "MONTH" options in AERMOD). The highest daily average PM_{10} concentrations measured at Stibnite for every season and month in 2014 were used as inputs in the model. Table 7 shows that the SGP facility *safely* demonstrates compliance with the 24-hour PM_{10} NAAQS when temporally varying backgrounds (both seasonal and monthly) are used instead of the single-value background. Summing modeled design values with a single-value background that is on the upper end of the distribution results in a very conservative estimate of total impacts. DEQ strongly believes that using temporally varying backgrounds that respect seasonality is appropriate for the SGP facility, and that using the highest value in the period interval is very conservative.

TABLE 7. RESULTS FOR 24-HOUR PM_{10} CUMULATIVE NAAQS IMPACT ANALYSES FOR MODELING SCENARIO W3.

Backgrounds Scenario	Max. Conc.[a] ($\mu g/m^3$)[b]	Model Scenario	Back. Conc.[c] ($\mu g/m^3$)	Total Conc.[d] ($\mu g/m^3$)	NAAQS ($\mu g/m^3$)	Percent of NAAQS
Single-Value Background	116.9	W3	34.0	150.9[e]	150	100.6%
Seasonally Varying Backgrounds	123.5[f]	W3	*Seasonal*	123.5[f]		82.3%
Monthly Varying Backgrounds	123.5[f]	W3	*Monthly*	123.5[f]		82.3%

a. Max. Conc. = maximum modeled design concentration.
b. Micrograms per cubic meter.
c. Back. Conc. = background concentration.
d. Total Conc. = total (modeled + background) concentration.
e. One hotspot receptor exceeds NAAQS.
f. The maximum modeled design concentration already incorporates the seasonal and monthly background values.

The time series plot in Figure 4 and the box-and-whiskers plot in Figure 5 illustrate the variability in daily average PM_{10} concentrations collected at the Stibnite Site in 2014. Figures 4 and 5 confirm that the highest concentrations from the modeled and monitored datasets do *not* occur simultaneously. Highest modeled impacts are predicted to occur during winter while the highest background concentrations were measured at Stibnite during summer. Therefore, the summation method, where total impacts are

calculated by summing modeled design values with a background concentration that is also consistent in form with the regulatory design value, results in a very conservative estimate of the total impact for comparison to NAAQS. DEQ concludes that use of temporally varying (i.e., seasonal and monthly) backgrounds for SGP is justified. DEQ is highly confident that operation of the SGP will not cause or contribute to a violation of NAAQS.

PM_{10} and $PM_{2.5}$ NAAQS compliance was previously demonstrated prior to refinements and adjustments proposed in the submitted *TAP Addendum*. The main body of the DEQ *Modeling Review Memorandum* discussed and considered results from both modeling with meteorological data processed using the BULKRN method and modeling with data processed using cloud cover data, and DEQ concluded that NAAQS compliance was demonstrated with a high degree of confidence. The adjustments and refinements described in the *TAP Addendum* further increase DEQ's confidence in NAAQS compliance.

Figure 4. TIME SERIES OF DAILY AVERAGE PM_{10} CONCENTRATIONS MEASURED AT STIBNITE IN 2014.

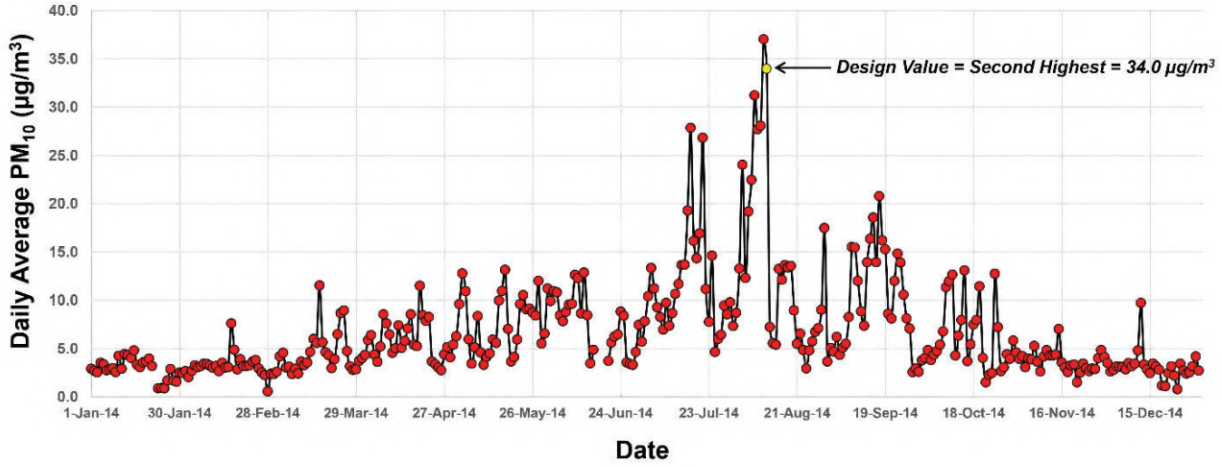
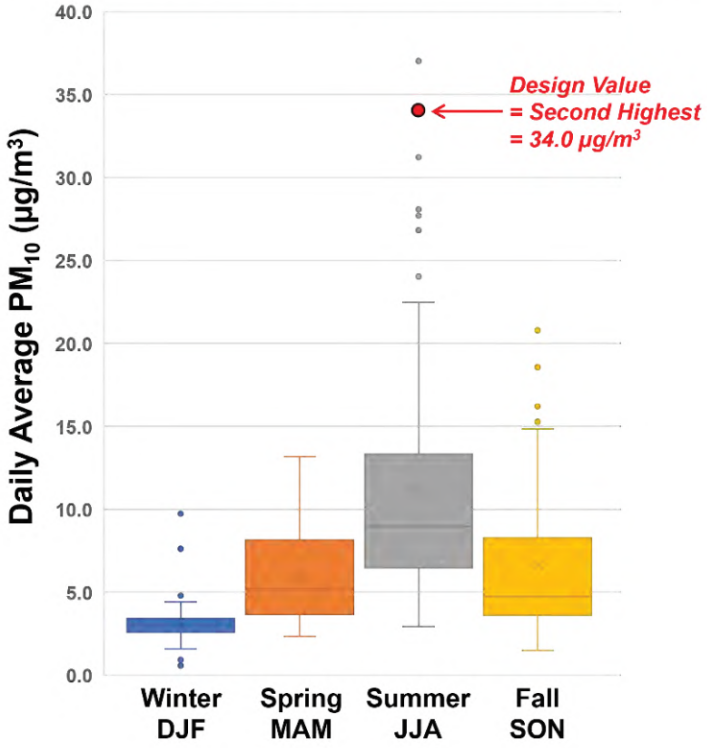


Figure 5. BOX-AND-WHISKERS PLOT FOR SEASONAL PM_{10} BACKGROUND CONCENTRATIONS MEASURED AT STIBNITE IN 2014.



In Figure 5 the middle line of each box represents the median. The "x" in the box represents the mean. The bottom and the top lines of the box represent the 1st quartile (25th percentile) and the 3rd quartile (75th percentile), respectively. The whiskers extend to the minimum and maximum values not considered outliers. Outliers are plotted individually.

7.0 Conclusions

This section provides conclusions of the *TAP Addendum* and DEQ's review of the *TAP Addendum*.

7.1 Conclusions of Revised TAP Analyses

The revised and refined TAP analyses:

- Revised TAP-applicable sources at the SGP facility.
- Proposed additional emission control measure and adjusted operations to reduce TAP emissions.
- Refined the approach used to demonstrate compliance with TAP regulations.

The submitted application, with the adjustments and refinements to analyses as described in the *TAP Addendum*, demonstrated to DEQ's satisfaction that the emissions of applicable TAPs will not result in impacts to ambient air that exceed TAP increments of *Idaho Air Rules* Section 585 and 586.

7.2 Effects of Adjustments/Revisions on NAAQS Compliance Demonstrations

The submitted application, prior to the *TAP Addendum*, demonstrated compliance with NAAQS to DEQ's satisfaction; and the operational measures proposed in the *TAP Addendum* will only further reduce estimated emissions. Eliminating Modeling Scenario W5 impacts, with the elimination of the West End Development Rock Storage Facility, affects the 24-hour PM_{10} impact modeling analysis for SGP. Modeling Scenario W3 is now the scenario producing the highest modeled impacts, and NAAQS compliance is easily demonstrated when using temporally varying background PM_{10} values, which were obtained from onsite monitoring data.

7.3 Conservatism of Permitting Analyses

Emissions and locations from which emissions occur are highly dynamic at mining facilities. This presents unique challenges for permit development because permits must include limits and operational requirements that ensure air quality standards are not violated. Permitting rules require that air impacts be assessed using maximum potential emissions as limited by either the capacity of the unit/operation or as limited by enforceable permit provisions. A permit where actual emissions are nearly representative of maximum allowable emissions, through imposing permit limits, would be exceedingly complex and require overly burdensome monitoring and record-keeping requirements. To avoid this, applicants typically calculate allowable emissions and perform impact analyses based on simplistic operational scenarios that largely overstate emissions estimated to occur from the facility.

PRI and Air Sciences have asserted that the submitted emission estimates, operational scenarios, and air impact analyses associated with the permit application greatly overstate best-estimated values. This point is evident when comparing the permit application materials and analyses with those presented in ModPRO2, PRI's revised mine plan and associated impacts. ModPRO2 is used in support of the Environmental Impact Statement (EIS).

Reference

Perpetua. 2021. "ModPRO2 Mine Plan." *File: Midas Stibnite Mine Plan and Equipment Schedule (10Feb21).xlsx.* Email from R. McCluskey, Perpetua Resources Inc., to E. Memon, Air Sciences Inc., February 11.

EXHIBIT B

State of Idaho
DEPARTMENT OF HEALTH AND WELFARE
Division of Environmental Quality

1410 N. Hilton
Boise, Idaho 83706

CECIL D. ANDRUS
Governor
RICHARD P. DONOVAN
Director

March 7, 1991

M E M O R A N D O M

To: Orvil Green

From: Robert Wilkosz RW
Tim Teater TT

Subject: Request for layman's explanation of URF & TLV

Attached, per your request is a draft explanation of URF and TLV/100 concepts as utilized in TAP NSR. This, of course, represents our tox. based views of what will do the job. We defer this draft to you for final decision as to what a layman might understand.

In developing emissions limits for new permitted facilities, the Idaho Air Quality Bureau (IAQB) uses the terms Unit Risk Factors and Threshold Limit Values. The following is an explanation of these terms and how they are used.

UNIT RISK FACTOR

A unit risk factor (URF) is used to describe the possibility of developing excess cancers over a average 70 year lifetime. This is based on being exposed to concentration of one microgram of a carcinogenic (cancer causing) substance in one cubic meter (1 $ug/m^{3)}$ of air over the 70 years. The term excess cancers means cases of cancers in excess of what would be normal for a given population. For example, if there was normally 5 cases of a given type of cancer in Anytown USA before a given exposure to some substance and 7 after the exposure, there would be 2 excess cancers.

Inhalation URFs are developed by the U.S. Environmental Protection Agency for carcinogenic substances. Each URF represents months of research and often years of policy process. Teams of toxicologists gathered all the toxicological information for each known or suspected carcinogen that could be found around the world. The available data were then rated or point factored per the quality of the research involved. A URF then is a probability statement derived from this process. Each URF was proposed by EPA

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and extensively reviewed and debated in public by scientists, health officials and industry representatives. Every URF represents a consensus of the best science and health opinion of the potency of a given carcinogen.

URFs are usually expressed as a number times 10 to some negative power. For example, benzine, an organic hydrocarbon found in various petroleum products and cigarette smoke has a unit risk factor of 8.3×10^{-6}. This means that there are 8.3 chances in one million of getting cancer if a person is exposed to 1 ug/m^3 24 hours a day for 70 years.

Another example would be asbestos. Asbestos has a URF of 2.3×10^{-1}. That means that if exposed to 1 ug/m^3 concentration for 70 years, the chances of getting cancer would be 2.3 in 10.

Within IAQB New Source Review (NSR) policy, URFs are used to calculate acceptable ambient levels for a given carcinogen. IAQB generally establishes that an ambient concentration which causes no more excess cancers than one in a million (1×10^{-6}) is acceptable. Once an acceptable ambient level is established, IAQB can then back calculate via engineering equations to an acceptable emission rate (in pounds per hour) for a given stack.

THRESHOLD LIMIT VALUE

Threshold Limit Value (TLV) is a time weighted exposure limit developed by the Occupational and Safety Administration and or the American Council of Government Industrial Hygienists. This value is used to limit the exposure of informed workers to a given toxic substance in the work place. The value is based on exposure of adult males working an eight hour shift. The IAQB uses TLV information to screen proposed new source emissions levels. The IAQB divides the TLV first by a value of 10 due to the fact that an ambient air exposure of a carcinogen means people are usually living under that exposure longer than eight hours out of 24. This value is then again divided by 10 to compensate for the fact that not everyone who is potentially exposed is an adult male. Other people may be more sensitive. The TLV thus is divided by a total of 100 for use in setting an acceptable ambient level.

For example, the TLV for cyanide is 5 milligrams per cubic meter (mg/m^3). An acceptable ambient level under IAQB policy would be 5 divided by 100 or 0.05 mg/m^3. For another example, the TLV for Lindane (an insecticide) would be 0.5 mg/m^3 concentration. The acceptable ambient level would be 0.5 divided by 100 or 0.005 mg/m^3.

As with carcinogens, the TLV derived acceptable ambient levels are used by the IAQB engineers to back calculate an acceptable stack emission rate for any proposed new source. A more pointed treatment these concepts can be found in The Toxic Air Pollutant NSR Policy Summary or the more thorough Draft Guidance Manual for Obtaining a Permit to Construct, Modify or Operate an Air Pollution Source.

EXHIBIT C

R. Wilkosz

IDAHO DEPARTMENT
OF HEALTH AND WELFARE

DIVISION OF
ENVIRONMENTAL QUALITY

1410 North Hilton, Statehouse Mail, Boise, ID 83720-9000, (208) 334-0502 Cecil D. Andrus, Governor Richard P. Donovan, Director

July 29, 1992

Dick Rush, Vice President
IACI
P. O. Box 389
Boise, ID 83701

Dear Mr. Rush:

Attached is the DEQ list of ideas for rules to control new sources of toxic air pollutants in Idaho. This submittal should be considered a "straw-man" in that our deputy attorney general has not had adequate time to review this material. Nor has anyone from the State Bureau of Health had opportunity to comment. I will continue to try to get that input prior to our next meeting. But for now, we must consider this specific submittal for discussion purposes only.

The package is formatted so that comparisons can be made to the existing Air Quality Rules. If you have any questions, please call me.

Sincerely,

Robert Wilkosz
Bureau Chief
Technical Services Bureau
Division of Environmental Quality

RW:br/Rush.ltr

Attachment

cc: COF 1.1

TOXIC AIR POLLUTION
-- RULES CHANGE IDEAS FROM DEQ

IDAPA 16.01.01003 -- DEFINITIONS.

Approved Fuels. Natural gas, propane gas, liquified petroleum gas, distillate fuel oils, residual fuel oils, and diesel fuel; except that waste oil, gasoline, or refined gasoline are not approved fuels.

Environmental Remediation Source. An emission source that functions to remediate or recover any release, spill, leak, discharge or disposal of any petroleum product or substance or any hazardous waste as defined by IDAPA 16.01.01003,44, from any soil or ground or surface waters. Any Environmental Remediation Source shall have an operational life of no greater than five (5) years from the inception of actual operations to the cessation of actual operations.

Pilot or Experimental Plant. An emission source that functions to test processing, mechanical, or pollution control equipment to determine full-scale feasibility.

Occupational Exposure Limit. Refers to airborne concentrations of substances and represents conditions under which it is believed that nearly all workers may be repeatedly exposed day after day without adverse effects. Occupational exposure Limits can be found in Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices with Intended Changes for 1991-92 or the current edition, adopted by the American Conference of Governmental Industrial Hygienists, or the National Institute for Occupational Safety and Health (NIOSH) current Relative Exposure Limit (REL), or the Occupational Health and Safety Administration (OSHA) Air Contaminate Standards, current Permissible Exposure Limit (PEL) or current Worker Protection Standards for Agricultural Pesticides promulgated by the Environmental Protection Agency under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA). In the case of conflicting values, the most stringent value shall take precedence.

Unit Risk Factor. *These factors describe the probability of developing excess cancers over a 70 year lifetime exposure to 1 ug/m^3 of a given carcinogen. Unit Risk Factors Can Be Found in the Federal Register Vol. 56 No. 35 / Thursday February 21, 1991 / Rules and Regulations Appendix V. or listed on the Integrated Risk Information System (IRIS) of the U.S. Environmental Protection Agency or listed in the Health Effects Summary Tables promulgated*

by the U.S. Environmental Protection Agency Office of Health Effects Assessment and the Office of Air Quality Planning and Standards. In the absence of U.S. EPA accepted risk factors, risk factors under review by the EPA Carcinogen Risk Assessment Verification Endeavor (CRAVE) shall be used on an interim basis.

IDAPA 16.01.01012, PROCEDURES AND REQUIREMENTS FOR PERMITS TO CONSTRUCT AND OPERATING PERMITS.

IDAPA 16.01.01012,02. *Permit to Construct. No owner or operator may commence construction ..., except that no permit to construct is required for ~~the following classes of equipment which have actual and allowable emissions of less than one hundred (100) tons per year of any air contaminant or and would not significantly increase the emissions of a major facility~~ sources which:*

a. have actual and allowable emissions of less than one hundred (100) tons per year of any air contaminant

and

b. would not significantly increase the emissions of a major facility

and

c. will not have an ambient air concentration of any air contaminant that would, as demonstrated using Department-approved methods:

i. cause or significantly contribute to a violation of an ambient air quality standard,

or

ii. cause an ambient concentration in excess of one percent of the Threshold Limit Value,

or

iii. cause a cancer-risk probability in excess of one in one million:

and

list: including but not limited to.

d. *which belong to one of the following classes of equipment:*

i. *Air conditioning or ventilating equipment not designed to remove air contaminants generated by or released from equipment;*

ii. *Air contaminant detectors or recorders, combustion controllers, or combustion shutoffs;*

iii. *Fuel burning equipment for indirect heating and for heating and reheating furnaces using gas exclusively with a capacity of less than fifty (50) million BTU's per hour input;*

iv. *Other fuel burning equipment for indirect heating with a capacity of less than one million (1,000,000) BTU's per hour input;*

v. *Mobile internal combustion engines, marine installations and locomotives;*

vi. *Stationary internal combustion engines in accordance with the following:*

100 horsepower or less -- unlimited hours of operation
101 to 200 horsepower -- 450 hours per month
201 to 400 horsepower -- 225 hours per month
401 to 600 horsepower -- 150 hours per month

vii. *Stationary internal combustion engines used exclusively for emergency power generation which burn an approved fuel and which operate less than 200 hours per year;*

viii. *Laboratory equipment used exclusively for chemical and physical analyses, including ventilating and exhaust systems for laboratory hoods;*

ix. *Environmental characterization activities including emplacement and operation of field instruments, drilling of sampling and monitoring wells, and any other activities specifically exempted by the Director;*

x. *Pilot or experimental plants located at least 1/4 mile from any recreational area or residence or other structure not occupied or used solely by the owner of the facility or the owner of the property upon which the facility is located; which operate less than one year; and that also meet one of the following conditions:*

1. *use a slip stream from an existing process stream not to exceed ten percent of that existing process stream, or*

2. *have actual uncontrolled emissions which are not significant;*

xi. *Any emission source or sources provided that the actual uncontrolled facility-wide emissions are not significant, and the uncontrolled emissions would not significantly contribute to ambient air quality concentrations;*

xii. *Any other class or size of equipment specifically exempted by the Director. A list of those sources unconditionally exempted by the Director will be maintained by the Department, and made available upon request.*

IDAPA 16.01.01012,13. *Procedure for Issuing Permits*

a. General procedures ...

b. Additional procedures ... attainment or unclassifiable area ...

c. Additional procedures ... federal Class I area ...

d. Procedures for operating permits ...

e. The Department ... fluid model ...

f. Modification of permits ...

g. Additional procedures for demonstrating compliance with the toxic substances provision 01.01011,01.

i. For sources that can demonstrate, using Department-approved methods, that emissions of carcinogens contribute an ambient air cancer risk probability of less than 1:1,000,000 and that emissions of non-carcinogens contribute to an ambient air concentration less than one percent of the Threshold Limit Value, no additional procedures are needed.

ii. For sources not recognized by the Department as environmental remediation sources that cannot demonstrate, using Department-approved methods, that emissions of carcinogens contribute an ambient air cancer risk probability of less than 1:100,000 and that emissions of non-carcinogens contribute to an ambient air concentration of less than one percent of the Threshold Limit Value, a permit cannot be issued unless the source has achieved the greatest degree of emission reduction that has been adequately

demonstrated and declared acceptable by the Department's Division of Health.

iii. *For remediation sources that cannot demonstrate, using Department-approved methods, that emissions of carcinogens contribute an ambient air cancer risk probability of less than 1:10,000 and that emissions of non-carcinogens contribute to an ambient air concentration of less than ten percent of the Threshold Limit Value, a permit cannot be issued unless the source has achieved the greatest degree of emission reduction that has been adequately demonstrated and declared acceptable by the Department's Division of Health.*

iv. *Department-approved methods will consist of the following:*

(a) *Comparison of maximum potential emissions to the screening emission limits for carcinogens and non-carcinogens as documented in Appendix A1 or A2 of the Toxic Air Pollutant list as promulgated but the Division of Environmental Quality. Maximum potential emissions can be determined by actual emissions testing using U.S. Environmental Protection Agency approved methods subject to review and approval by the Division of Environmental Quality or estimates of the maximum potential emissions using standard scientific and engineering principals and practices subject to review and approval by the Division of Environmental Quality*

The State is reviewing and approving EPA policy... this is redundant

We need to open up in that we want to be able to approve more than EPA approved...

(b) *Atmospheric dispersion modeling, using only U.S. Environmental Protection Agency (EPA) currently approved models, applied according to EPA's Guidelines on Air Quality Models, and as approved for the application by the Division of Environmental Quality.*

average in what respect
- emission levels
- met conditions

1. *For carcinogens, multiply the average hourly concentration by a persistence factor of 0.15 to convert the hourly average to an annual average The resulting product is then multiplied by the unit risk factor to obtain a an ambient air cancer risk probability.*

or other long term model procedures allow better factor than 0.15

test

2. *For non-carcinogens, multiply the average hourly concentration by persistence factor of 0.15 to convert the hourly average to an annual average The resulting product is then compared to one one hundredth (1/100 of the appropriate occupational exposure limit.*

(c) *Any other method approved by the Director.*

TOXDEMN2.RUL

This language probably assumes use of T-SCREEN or something. We need to go more general?

We need to get model examples out to rest of group.

RAÚL R. LABRADOR
Attorney General

SCOTT L. CAMPBELL
Deputy Attorney General
Chief, Energy and Natural Resources Division

Hannah M.C. Young, ISB No. 9781
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Telephone: 208.373.0543

Attorneys for Respondent

BEFORE THE BOARD OF ENVIRONMENTAL QUALITY
STATE OF IDAHO

IN THE MATTER OF AIR QUALITY PERMIT TO CONSTRUCT P-2019.0047

NEZ PERCE TRIBE, IDAHO CONSERVATION LEAGUE, and SAVE THE SOUTH FORK SALMON,

Petitioners,

v.

IDAHO DEPARTMENT OF ENVIRONMENTAL QUALITY,

Respondent,

and

PERPETUA RESOURCES IDAHO, INC.,

Intervenor-Respondent.

Case Docket No. 0101-22-01
OAH Case No. 23-245-01

EXPERT DECLARATION OF NORKA E. PADEN, Ph.D.

I, NORKA E. PADEN, Ph.D., hereby declare under penalty of perjury and pursuant to the law of the State of Idaho that the foregoing is true and correct:

Qualifications

1. My name is Norka E. Paden. I am an Environmental Toxicologist with 16 years of experience and have been with the Idaho Department of Environmental Quality's (DEQ's) Toxicologist/Risk Assessor since 2016. I am responsible for toxicological and risk assessment analyses for contaminated sites and toxic exposures statewide. I provide toxicological expertise for contamination issues related to air, water, and soil. I deliver written comments to policy makers and stakeholders during negotiated rulemaking that involves selenium, copper, and arsenic human health water quality criteria. I mentored a professor from Lewis-Clark State College on the risk assessment of air pollutants in the Lewiston Valley and was acknowledged in the paper, "Observations of volatile organic and sulfur compounds in ambient air and health risk assessment near a paper mill in rural Idaho, U.S.A," published in the 2020 *Atmospheric Pollution Journal*. In 2023, I delivered technical comments for the Idaho Department of Health and Welfare's "Letter Health Consultation for the Lewiston Clark Air Quality Study," and DEQ received commendation from the Nez Perce Tribe for the technical support.

2. I received my Master of Science in Human Ecology at the Free University of Brussels, Belgium, and Ph.D. in Environmental Toxicology from Texas Tech University. Prior to joining DEQ, I worked for the Idaho Department of Health and Welfare from 2011 through 2016 and authored six public health consultations and 12 letter health consultations, which are written responses to a specific request for information about health risks related to a hazardous material, chemical release, or specific site, under the Agency for Toxic Substances and Disease Registry (ATSDR) cooperative agreement. While working at GEI Inc., a Colorado environmental consulting firm from 2008 to 2011, I provided technical expertise in preparing risk investigations for Superfund sites, drafted technical reports on toxicity evaluations, and supported clients by writing technical reports and rebuttals during rulemaking meetings. I served as an adjunct faculty member for the Department of Community and Environmental Health at Boise State University from 2012 to 2015. I currently serve on various advisory committees in Idaho including the Cancer/Cluster Analysis Work Group, Fish Consumption Advisory Project, One Health Consortium, Groundwater Monitoring Technical Group, and Federal-State Toxicology Risk Analysis Committee. I am also a member of the Society of Environmental Toxicology and Chemistry (SETAC) and Editorial Board of the Journal of Integrated Environmental Assessment and Management.

Assignment

3. I have been asked by DEQ's Air Quality Division to review and evaluate the issue: "DEQ did not act reasonably and in accordance with law when it applied the 16/70 calculation to the ambient arsenic air concentration analysis" and provide this declaration to assist the Hearing Officer as the trier of fact. This declaration provides evidence in the form of an expert opinion

as a toxicologist, as the Board of Environmental Quality (DEQ Board) suggested in its *Final Order in the Matter of Air Quality Permit to Construct P-2019.0047* (Final Order).[1]

Summary of Opinions

4. Based on the information provided, cancer risk estimates using 16-years, and 70-years of exposure duration are both within the range of public health guidelines of 1 in 1,000,000 to 1 in 10,000 (i.e., one in a million to one in ten thousand) for protection of human health as suggested by the United States Environmental Protection Agency's (EPA's) target cancer risk range. Based on this assessment, the estimated lifetime cancer risk from exposure to arsenic through inhalation using the exposure duration of 16 years (lifetime of the mine) followed EPA's guidelines that are the framework for DEQ's Rules for the Control of Air Pollution in Idaho and falls within EPA's target cancer risk range of 1 in 1,000,000 to 1 in 10,000 (i.e., one in a million to one in ten thousand) and is not expected to increase cancer risk under current permit operating conditions.

Documents reviewed

5. I reviewed the May 1, 2024, DEQ Board meeting minutes transcript and background of the Perpetua-Stibnite Gold Mine Permit to Construct issued in June 2022 and subsequent documents on the case docket No. 0101-55-01 OAH No 23-245-01: May 23 Memorandum in Support of Joint Motion for Reconsideration and/or Clarification of Final Order, June 12 Order on Petitions for Reconsideration and/or Clarification of Final order, and July 8 Scheduling Order.

Background and Discussion

6. Based on my interpretation, the DEQ Board supported DEQ on four of the five matters. The fifth matter related to Section 586 of the "Rules for Control of Air Pollution in Idaho" (IDAPA 58.01.01) and DEQ's approach to arsenic and cancer risk. The DEQ Board found insufficient evidence to support DEQ's ambient arsenic air concentration analysis and determined that further factual development was needed on this issue. The DEQ Board remanded this issue to the Hearing Officer.

7. Dr. McMillan indicates that DEQ misinterpreted the acceptable ambient concentration (AACC) for carcinogens to comply with the air quality rules. He disagrees with the project-specific adjustment factor (16 years of mining operation), contends that DEQ failed to recognize the AACC functions to limit cancer initiation not only after 70 years but every day

[1] *See* REC 3716, *Final Order in the Matter of Air Quality Permit to Construct P-2019.0047*, *Nez Perce Tribe, Idaho Conservation League, and Save the South Fork Salmon v. Idaho Department of Environmental Quality*, Case Docket No. 0101-22-01, OAH Case No. 23-245-01 (Final Order at 22).

of a person's life starting at birth, and posits that DEQ's analysis underestimates the actual cancer risk (MacMillan 2024).[2]

8. Based on the analyses presented below, the cancer risk estimates were accurately calculated; the methodology for the calculations adheres to toxicological guidance and analytical practices to modify exposure duration and did not underestimate risk.

9. After reviewing the permit's cancer risk calculations and the toxic air pollutant rules, I researched cancer risk from arsenic exposures through inhalation. I calculated exposure concentrations and excess cancer risks for a residential inhalation exposure scenario (for a person living at a residence) using the maximum modeled annual concentration (potential worse-case scenario) of 0.00416 µg/m^3, calculated by analyses of the permit application, for the following exposure duration scenarios of 16 years (lifetime of the mine), and 70 years (EPA's lifetime exposure). The following paragraphs summarize my findings.

10. The permit application and DEQ review documentation states that cancer risk calculations used modeling scenarios, applied to develop AACCs outlined in the rules, and evaluated via the 70-year lifetime exposure. The maximum modeled concentrations for carcinogenic toxic air pollutants were modified to account for the life-of-mine production limits that affect the lifetime exposure using the following formula (DEQ 2022)[3]:

$$Lifetime\ exposure\ \left(\frac{\mu g}{m^3}\right) = \frac{Highest\ annual\ concentration\ \left(\frac{\mu g}{m^3}\right) \times 16\ (mine\ operation\ years)}{70\ (years, lifetime\ exposure)}$$

Cancer Risk Calculation in the Idaho Air Rules mirrors EPA's Guidelines

11. Section 586 in IDAPA 58.01.01, "Rules for the Control of Air Pollution in Idaho" (Idaho Air Rules), provides the following values for carcinogen toxic air pollutants: unit risk factors (URF) from EPA, screening emission levels (EL), and acceptable ambient levels for carcinogens (AACCs) (i.e., determined to cause cancer over lifetime exposure). The acceptable ambient levels for carcinogens are based on the cancer unit risk values from EPA and correspond to a one in one million cancer risk (DEQ 2019)[4]. In other words, the AACC for arsenic compounds presented in Idaho Air Rule Section 586 is calculated using EPA's Excess Cancer Risk Probability formula shown below:

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[2] *See* Board of Environmental Quality Special Meeting (May 1, 2024) Transcript ("SM Tr.") 10:19-21 ("I believe DEQ has misinterpreted how the acceptable ambient concentration for carcinogens, the AACC, must be applied if it is to comply with our air quality rules"); *see also* SM Tr. 11:2-11.

[3] REC 710, Idaho Department of Environmental Quality. *TAPs Addendum Modeling Review Attachment* to the *PRI SGP Modeling Review Memorandum* (January 6, 2022) ("DEQ's TAPS Modeling Attachment") at 14. For convenience, a true and correct copy of DEQ's TAPS Modeling Attachment is attached hereto as Exhibit A.

[4] Idaho Department of Environmental Quality. *Idaho Administrative Bulletin*. Boise, ID, September 4, 2019–Vol 19-9, page 388 ("The acceptable ambient levels for carcinogens are based on the cancer unit risk values from the Environmental Protection Agency and correspond to a one in a million cancer risk") (citing EPA 2019). A true and correct copy of page 388 is attached hereto as Exhibit B.

Excess Cancer Risk Probability = IUR x EC

Where Excess Cancer risk = 10^{-6} (1 in 1,000,000 one in a million)

IUR for arsenic is = 4 x 10^{-3} (0.0043)

EC = exposure concentration or acceptable ambient concentration (AACC)

AACC= (10^{-6})/ 4.3 x 10^{-3}

AACC= 2.3 x 10^{-4} = 0.00023 µg/m^3

The arsenic lifetime concentration associated with an excess cancer risk of one in one million is 0.00023 µg/m^3.

12. Under EPA's methodology for human health risk assessments, cancer risk calculations are done using a lifetime exposure set at 70 years. The exposure duration is the amount of time an individual is exposed to the contaminant being evaluated and is typically given in years. The exposure duration can be modified based on the site-specific information using the following formula to calculate screening values (EPA 2009)[5].

EC = (CA x ET x EF x ED)/AT

Where: EC (µg/m^3) = exposure concentration;
CA (µg/m^3) = contaminant concentration in air;
ET (hours/day) = exposure time;
EF (days/year) = exposure frequency;
ED (years) = exposure duration; and
AT (lifetime in years 70 x 365 days/year x 24 hours/day) = averaging time

13. **Step 1: Exposure Concentration Calculations**: I calculated exposure concentrations using the maximum modeled arsenic concentration in air (0.00416 µg/m^3), exposure time (24 hours per day), exposure frequency (365 days per year), and averaging time for 70 years of lifetime (EPA's default value) exposed for 365 days and 24 hours per day for a resident scenario with exposure durations of 16-years (life time of the mine), 70- years (EPA's default lifetime exposure) using EPA's approach and the formulas presented above. Table 1 shows the results for the calculations:

Table 1. Values used for the exposure concentration calculation.

Contaminant Concentration in Air (µg/m^3)	Exposure Time (hours/day)	Exposure Frequency (days/year)	Exposure Duration (years)	Averaging Time	Exposure Concentration µg/m^3
0.00416	24	365	16 (lifetime of the mine)	70x365x24	0.00095
0.00416	24	365	70 (EPA's default lifetime exposure)	70x365x24	0.00416

[5] Environmental Protection Agency (EPA). 2009. Risk Assessment Guidance for Superfund Volume I: Human Health Evaluation Manual (Part F, Supplemental Guidance for Inhalation Risk Assessment). EPA-540-R-070-002. OSWER 9285.7-82. Available at: https://semspub.epa.gov/work/HQ/140530.pdf. Accessed on July 18, 2024.

14. **Step 2: Cancer Risk Calculations:** To calculate cancer risk, I used the Inhalation Unit Risk (IUR) for arsenic from EPA's Integrated Risk Information System (IRIS) and the exposure concentrations calculated in Table 1 using the following formula (EPA 2009).[6] As previously mentioned, this is the same formula used for the AACC calculation in the Idaho Air Rules. Results of these calculations are presented in Table 2. *See* IDAPA 58.01.01.586.

Excess Cancer Risk Probability = IUR x EC

Where: IUR $(\mu g/m^3)^{-1}$ = Inhalation Unit Risk (for arsenic is 0.0043); and
EC $(\mu g/m^3)$ = exposure concentration

EPA defines excess cancer risk as an additional risk of cancer from exposure to a contaminant beyond an individual's risk of cancer from everyday life. Excess cancer risk is the probability that an exposed individual will develop cancer from exposure over a lifetime (70 years)[7]. The methodology EPA uses for the calculation of the excess cancer risk includes the inhalation unit risk (IUR) value, based on toxicological studies, the value selected for the inhalation unit risk represents a continuous exposure (24 hours/day and 7 days/week) and is supported by years of research from scientists at EPA's Integrated Risk Information System (IRIS) and the Superfund Health Risk Technical Support Center[8].

Table 2. Excess cancer risk calculations and interpretation.

Exposure duration (in years)	Inhalation Unit Risk $(\mu g/m^3)^{-1}$	Exposure Concentration $(\mu g/m^3)$	Excess Cancer Risk Probability	Interpretation	Within EPA's Recommended range > 1 in 1 million to < 1 in 10,000
16 (lifetime of the mine)	0.0043	0.00095	4.09E-06	4 in 1 million	Yes
70 (EPA's default lifetime exposure)	0.0043	0.00416	1.79E-05	2 in 100,000	Yes

15. DEQ used EPA's methodology for adjusting exposure duration given the known exposure duration (lifetime of the mine). The modification of the exposure duration is also consistent with DEQ's screening level risk assessment methodology for any contaminated site in Idaho (i.e., EPA's Regional Screening Levels)[9]. Inputs and outputs of the EPA's Regional Screening Levels online calculator using the parameters outlined in Table 1 (i.e., exposure duration, exposure time, lifetime in years) yield the same cancer risk estimates shown in Table 2 and are

[6] *Id.*

[7] Environmental Protection Agency. 2024. Supplementary Materials: Risk Communication. Attachment 6: Useful Terms and Definitions for Explaining Risk. Available at: https://semspub.epa.gov/work/11/176250.pdf. Accessed on July 19, 2024.

[8] *See* fn. 5.

[9] United States Environmental Protection Agency. Regional Screening Levels for Chemical Contaminants at Superfund Sites. Available at: https://www.epa.gov/risk/regional-screening-levels-rsls. Accessed on June 4, 2024.

presented in Exhibit C.[10] Two parameters that were modified in the EPA's Regional Screening Level Calculator were: exposure frequency from 350 days (EPA assumption is that the receptor takes 2 weeks of vacation every year away from the contamination) to 365 days/year, which is more conservative. The other parameter that was modified was the target hazard quotient (THQ) from 0.1 usually used when screening multiple contaminants to THQ=1.0, commonly used when screening only one contaminant, in this case arsenic.

Cancer Risk Estimates and T-RACT within EPA's acceptable range

16. Toxic Air Pollutant Reasonably Available Control Technology (T-RACT) for carcinogens outlined in the Idaho Air Rules: cancer risk probability of less than one in one hundred thousand (1 in 100,000) (IDAPA 58.01.01.210.12.b) falls within the EPA's recommended range of > 1 in 1 million to < 1 in 10,000 presented in Table 2.

17. The cancer risk estimates from exposure to 0.00416 µg/m^3 arsenic (maximum arsenic concentration calculated from modeling using potential worse-case scenario) through inhalation 24 hours a day, 365 days, and for 16 years (lifetime of the mine) is four additional cancers in a population of one million people exposed. The probability for a resident to develop cancer after exposure to 0.00416 µg/m^3 arsenic through inhalation 24 hours a day, 365 days, and for 70 years (EPA's default lifetime exposure) is two additional cancers in 100,000. These excess cancer risk estimates are within the range EPA considers acceptable (<1 in 10,000 to > 1 in 1,000,000) [7]. EPA considers excess cancer risk < 10^{-6} (1 in 1,000,000) to be negligible, 10^{-4} (>1 in 10,000) and 10^{-6} to 10^{-4} (1 in 1,000,000 to 1 in 10,000) to be acceptable (EPA 1989)[11]. This analysis shows at the maximum arsenic levels modeled (0.00416 µg/m^3) for exposures of 16, or 70 years are within the public health guidelines, and DEQ followed EPA's guidelines when using the 16-year exposure scenario (lifetime of the mine).

Cancer Risk Considerations

18. Other factors may play a role in analyzing cancer risk, such as existing cancers in the population, arsenic background concentrations at the site, sensitive populations living near the site, and uncertainty of maximum arsenic concentration derivation. According to the American Cancer Society, cancer affects 1 in 3 people in the United States, meaning that over a lifetime, an American's probability of getting any cancer is 0.333333 (ACS 2024)[12]. Adding the probability of 2 in 100,000 (excess cancer risk calculated for someone exposed for a lifetime of 70) to 0.333333, the probability of an individual getting cancer increases to 0.333353; this difference is very small.

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[10] A true and correct copy of EPA's *Regional Screening Levels Calculator Inputs and Outputs for Exposure Durations 16, and 70 years* is attached hereto as Exhibit C.

[11] Environmental Protection Agency (EPA). 1989. Risk Assessment Guidance for Superfund Volume I Human Health Evaluation Manual (Part A). Available at: https://www.epa.gov/sites/default/files/2015-09/documents/rags_a.pdf. Accessed on June 5, 2024.

[12] American Cancer Society. 2024. Understanding Cancer. Available at: https://www.cancer.org/cancer/understanding-cancer/what-is-cancer.html. Accessed on July 22, 2024.

19. From the toxicological point of view, enough evidence exists on the carcinogenic effects (urinary bladder, lung, and skin) of inorganic arsenic (IARC 2012)[13]. People who accidentally eat arsenic for a long time can develop some diseases. Sources of arsenic for ingestion include food (seafood, fish, algae, cereals), air (coal-fired power and smelting), and water (EFSA 2009)[14]. Evidence indicates that long-term exposure to arsenic mainly through drinking water is of great concern to human health due to daily consumption and occurrence in several regions of the world over the past decades (Martinez et al. 2011)[15]. Some occupational studies have documented lung cancer due to inhalation exposures to arsenic, and EPA has used these studies to derive the Inhalation Unit Risk (IUR) (EPA 2024)[16].

20. Cancer risk depends on a wide variety of factors such as alcohol and tobacco use, sun light and radiation exposures, age, diet, hormones, obesity, infectious agents, cancer-causing agents, family history, immunosuppression, and chronic inflammation (NIH 2015)[17]. The literature indicates that inorganic arsenic causes harmful effects mainly through the initiation of oxidative stress (when there are many molecules called free radicals in the body and not enough antioxidants to eliminate them), alterations to DNA (DNA and RNA are both macromolecules essential for life), protein modification, and RNA expression as Dr. McMillan alluded; however, these effects are mainly documented from exposures to elevated levels of arsenic in drinking water (EPA 2024)[18]. The literature also reveals that further cancer studies are needed to understand the mechanisms of arsenic carcinogenesis (Zhou & Xi 2018; Speer et al. 2022)[19,20].

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[13] International Agency for Research on Cancer (IARC). 2012. Arsenic, Metals and Dusts. Volume 100C. A Review of Human Carcinogens. Lyon, France. Available at: https://publications.iarc.fr/Book-And-Report-Series/Iarc-Monographs-On-The-Identification-Of-Carcinogenic-Hazards-To-Humans/Arsenic-Metals-Fibres-And-Dusts-2012. Accessed on July 22, 2024.

[14] European Food Safety Authority (EFSA). 2009. Scientific opinion on arsenic in food. *EFSA Journal*. 7(10):1351. Available at: https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2009.1351. Accessed on July 21, 2024.

[15] Martinez V.D., Vucic E.A., Becker-Santos D. D., Gil L., Lam W.L. 2011. Arsenic Exposure and the Induction of Human Cancers. *Journal of Toxicology.* Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3235889/. Accessed on July 19, 2024.

[16] Environmental Protection Agency (EPA) & National Center for Environmental Assessment. 2024. Integrated Risk Information System (IRIS). Chemical Summary for Arsenic, inorganic; CASRN 7440-38-2. Available at: https://iris.epa.gov/static/pdfs/0278_summary.pdf. Accessed on July 19, 2024.

[17] National Institutes of Health (NIH). National Cancer Institute. 2015. Risk Factors for Cancer. Available at: https://www.cancer.gov/about-cancer/causes-prevention/risk. Accessed on July 19, 2024.

[18] *See* fn. 14.

[19] Zhou Q., Xi S. 2018. *A review on arsenic carcinogenesis: Epidemiology, metabolism, genotoxicity and epigenetic changes.* Journal of Regulatory Toxicology and Pharmacology 99: 78-88. https://www.sciencedirect.com/science/article/abs/pii/S0273230018302320?via%3Dihub

[20] Speer R. M., Zhou X., Volk L.B., Liu K.J., Hudson L.G. 2022. Arsenic and cancer: evidence and mechanisms. Journal Adv Pharmacol. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10860672/. Accessed on July 18, 2024.

Cancer Risk Calculations were not underestimated

21. Additional information to support DEQ's calculation did not underestimate cancer risk, including the no significant concentration level of 0.067 µg/m^3 (i.e., air concentration at 1 in 100,000 excess lung cancer mortality) from the Texas Commission on Environmental Quality (Erraguntla et al.2012)[21]. The value is used to evaluate ambient air monitoring data to protect the public against adverse health effects from chronic exposure to arsenic. The maximum modeled air concentration 0.00416 µg/m^3 is below this threshold. The maximum modeled air concentration of 0.00416 µg/m^3 is within World Health Organization's recommendations for concentrations of arsenic range from 1–10 ng/m^3 (0.001–0.01 µg/m^3) in rural areas, 3–30 ng/m^3 (0.003–0.03 µg/m^3) in noncontaminated urban areas (WHO 2000)[22].

Conclusion

22. I conclude that DEQ's analysis followed EPA's guidelines and that results from a shorter duration exposure (i.e., 16 years) is within EPA's target risk range of 1 in 1,000,000 to 1 in 10,000 (i.e., one in one million to one in ten thousand) and is not likely to increase cancer risk by the arsenic air emissions calculated by the analyses of the air permit application (maximum arsenic-modeled concentrations).

DATED: August 13, 2024

_/s/ Norka E. Paden, Ph.D._____
NORKA E. PADEN, Ph.D.

[21] Erraguntla N.K., Sielken R.L. Valdez-Flores C., Grant R.L. 2012. An updated inhalation unit risk factor for arsenic and inorganic arsenic compounds based on a combined analysis of epidemiology studies. *Journal Regulatory Toxicology and Pharmacology* 64(2):329-41. Available at: https://www.sciencedirect.com/science/article/abs/pii/S0273230012001304. Accessed on July 23, 2024.

[22] World Health Organization (WHO), 2000, Air Quality Guidelines for Europe: Second Edition (WHO Regional Publications, European Series, No 91) Copenhagen, Denmark, World Health Organization, Regional Office for Europe, Available at https://www.who.int/publications/i/item/9789289013581. Accessed on July 22, 2024

CERTIFICATE OF SERVICE

I hereby certify that on August 13, 2024, a true and correct copy of the foregoing ***EXPERT DECLARATION OF NORKA E. PADEN, Ph.D.*** was served on the following:

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EXHIBIT A

TAPs Addendum Modeling Review Attachment

1.0 Introduction and Summary

Perpetua Resources Idaho, Inc. (PRI) submitted the *Stibnite Gold Project (SGP) Permit to Construct Application TAP Addendum* (*TAP Addendum*), prepared by Air Sciences Inc. (Air Sciences) and submitted to DEQ on October 5, 2021. The TAP Addendum reassessed source applicability to Toxic Air Pollutant (TAP) permitting requirements, refined TAPs regulatory methods to demonstrate compliance with applicable TAP increments, revised and/or refined operations and operational parameters affecting TAP emissions, and refined TAP air impact analyses. The revisions and refinements made for the TAP Addendum also reduced PM_{10} and $PM_{2.5}$ emissions, and this effect is presented in this *TAPs Addendum Modeling Review Attachment* (*Modeling Review Attachment*).

2.0 Scope of TAPs Addendum

DEQ reevaluated TAPs compliance regulatory interpretations and impact assessment methods following the second public comment period of February 18, 2021, through March 19, 2021. Areas of revision in response to issues identified after the public comment period included:

- Revising source-specific TAP impact assessment applicability, primarily identifying what sources can be excluded because they are "covered" or "addressed" by a National Emissions Standard for Hazardous Air Pollutants (NESHAP) or New Source Performance Standard (NSPS).
- Refining regulatory methods used to demonstrate compliance with TAP increments.
- Refining TAP emission calculation methods and dispersion-affecting parameters.
- Reassessing TAP impacts resulting from revised and/or refined methods and data.
- Providing a best-estimate of actual TAP emissions that will occur from operation of the mine, and then comparing this to maximum permit-allowable emissions.

PRI and Air Sciences, PRI's permitting consultant, submitted the *TAP Addendum* on October 5, 2021.

3.0 Revised NESHAP/NSPS TAP Exclusion

DEQ and PRI reevaluated TAP source applicability after the second public comment period in response to expressed concerns regarding sources excluded as per *Idaho Air Rules* Section 210.20 (excluding sources that are "covered" or "addressed" by a NESHAP). TAP applicability is explained in greater detail in the main body of the DEQ Statement of Basis. As a result of the reevaluation, some additional sources were included in the TAP impact modeling analyses that were not previously. TAP sources from gold mining that were modeled in the final TAP analyses included: drilling, blasting, excavating, hauling, prill silos, rock dumps and storage piles, and tailings.

Air Sciences consulted with DEQ to refine TAP compliance demonstration methods from what was originally submitted in the application. The refinement was primarily needed to show compliance with the

arsenic Acceptable Ambient Concentration of a Carcinogen (AACC). The revised methods are described in the submitted *TAP Addendum* and this DEQ *Modeling Review Attachment*.

4.0 TAPs Refined Compliance Demonstration Approach

PRI, in consultation with DEQ, used a highly refined TAPs analysis approach to demonstrate compliance with applicable TAP increments. This approach involved the following:

- AACC Adjustment for Toxic Air Pollutant Reasonably Available Control Technology (T-RACT) Utilization.
- TAP Emission Averaging Period.
- AACC Adjustment for the Operational Life of the Mine.

4.1 AACC Adjustment for T-RACT Utilization

Idaho Air Rules Section 210.12 allows TAP impacts of 10 times the AACC if the application demonstrates that T-RACT is used for the TAP emission sources. This represents a life-time cancer risk of 1-in-100,000. An adjustment cannot be made for non-carcinogenic TAPs listed in *Idaho Air Rules* Section 585.

Review of the T-RACT demonstration is performed by the DEQ permit writer and is described in the main body of the DEQ Statement of Basis.

4.2 TAP Emission Averaging Period

Annual average emissions of carcinogenic TAPs are typically used in the dispersion model to estimate maximum annual impacts. PRI refined the analyses by using source-specific emission rates that are representative of a 5-year averaging period. This approach is appropriate because carcinogenic impacts are of concern from a long-term exposure basis.

4.3 AACC Adjustment for the Operational Life of the Mine

AACCs were established based on a 1-in-1,000,000 cancer risk over a 70-year lifetime, as stated in *Idaho Air Rules* Section 006.125:

> ***Toxic Air Pollutant Carcinogenic Increments**. Those ambient air quality increments based on the probability of developing excess cancers over a seventy (70) year lifetime exposure to one (1) microgram per cubic meter (1 ug/m3) of a given carcinogen and expressed in terms of a screening emission level or an acceptable ambient concentration for a carcinogenic toxic air pollutant. They are listed in Section 586.*

PRI indicated the maximum life-of-mine will be 16 years. Life-time exposures to carcinogenic TAPs were refined by multiplying the maximum modeled annual impact by a ratio of 16/70. Section 5.7 of this *Modeling Review Attachment* provides more details on this adjustment for the project.

5.0 Refined TAP Emission Estimates and Modeling Methods/Parameters

This section describes changes made to TAP emission estimates and to methods/parameters used in the impact modeling analyses.

5.1 Operational Adjustments

PRI and Air Sciences proposed and committed to several operational adjustments to reduce actual and estimated TAP emissions:

- Installing and operating dust collection systems on drilling rigs (determined to be T-RACT).
- Capping the haul roads that are outside of the pits and development rock storage facilities (DRSFs) with clean (lower levels of arsenic) development rock (determined to be T-RACT).
- Eliminating the West End Development Rock Storage Facility, which eliminated the highest-emitting operational scenario W5.
- Limiting long-term mining production to an average of 135,000 tons/day for a 5-year rolling average.
- Constructing the Burntlog access road with offsite materials containing "background" levels of arsenic.
- Updating the bulldozing emission factor using the SGP site-specific silt content.

5.2 General Modeling Methods and Parameters

Modeling methods and parameters used in TAP impact analyses presented in the *TAP Addendum* are largely identical to those used in the previously submitted application. These include the air dispersion model used, meteorological data, terrain, building downwash, ambient air boundary, and receptors. TAP modeling was conducted for the 14 operational modeling scenarios, consistent with the NAAQS analyses. Modeling Scenario W5 was eliminated from the arsenic modeling, as discussed in Section 5.8 of this *Modeling Review Attachment*.

The meteorological dataset processed using McCall, Idaho, cloud cover data was used for analyses in the *TAP Addendum*. Impacts were not assessed using the dataset processed using the Bulk Richardson (BULKRN) method for boundary layer parameter calculations. EPA considers both methods to be acceptable. Although modeled impacts tend to be somewhat larger when using meteorological data processed by the BULKRN method, DEQ contends that the impact analyses are still largely conservative compared to actual impacts anticipated. Conservative aspects include: continual operation of the worst-case operational scenario; operation at maximum allowable rates for the averaging period; no reduction in winter-time emissions from fugitive sources, accounting for emission suppression effects of increased moisture.

5.3 TAP Modeling Applicability

Table 1 provides a comparison between applicable facility-wide maximum potential TAP emissions for the highest-emitting scenario (W3) and TAP screening emission levels (ELs) from *Idaho Air Rules* Sections 585 (for non-carcinogens) and 586 (for carcinogens). Note that TAPs also classified as HAPs

emitted from sources "addressed" or "covered" by NSPS or NESHAP were not required to be evaluated for compliance with TAP increments in accordance with *Idaho Air Rules* Section 210.20. Furthermore, PRI has determined that the West End Development Rock Storage Facility will not be constructed. This change eliminated Modeling Scenario W5 (the highest-emitting scenario described in the main body of the DEQ *Modeling Review Memorandum*) as a potential operating scenario. After eliminating Modeling Scenario W5, it was determined that Modeling Scenario W3 is the highest-emitting scenario for all TAPs.

Table 1. TAP MODELING APPLICABILITY DETERMINATION (HIGHEST-EMITTING MODELING SCENARIO: W3).

HAP/TAP	Emissions (lb/hr)			EL (lb/hr)		Determination
	(a)	(b)	Total	(c)	(d)	
1,3-Butadiene	--	--	--	--	2.4E-5	EL not exceeded
3-Methylchloranthrene	--	4.5E-8	4.5E-8	--	2.5E-6	EL not exceeded
Acetaldehyde	--	--	--	--	3.0E-3	EL not exceeded
Acrolein	--	--	--	1.7E-2	--	EL not exceeded
Antimony	1.9E-2	1.6E-6	1.9E-2	3.3E-2	--	EL not exceeded
Arsenic	5.4E-1	8.2E-6	5.4E-1	--	1.5E-6	Carcinogenic EL exceeded
Benzene	--	5.3E-5	5.3E-5	--	8.0E-4	EL not exceeded
Benzo(a)pyrene[e]	--	3.0E-8				
Benz(a)anthracene[e]	--	4.5E-8				
Benzo(b)fluoranthene[e]	--	4.5E-8				
Benzo(k)fluoranthene[e]	--	4.5E-8	2.9E-7	--	2.0E-6	EL not exceeded
Chrysene[e]	--	4.5E-8				
Dibenzo(a,h)anthracene[e]	--	3.0E-8				
Indenol(1,2,3-cd)pyrene[e]	--	4.5E-8				
Beryllium	2.6E-3	3.5E-7	2.6E-3	--	2.8E-5	Carcinogenic EL exceeded
Biphenyl	--	--	--	1.0E-1	--	EL not exceeded
Cadmium	4.1E-4	2.8E-5	4.4E-4	--	3.7E-6	Carcinogenic EL exceeded
Carbon disulfide	1.4E-2	--	1.4E-2	2.0E+0	--	EL not exceeded
Chromium	7.3E-3	4.8E-5	7.4E-3	3.3E-2	--	EL not exceeded
Chromium (VI)	--	3.4E-7	3.4E-7	--	5.6E-7	EL not exceeded
Cobalt	3.3E-3	4.8E-6	3.26E-3	3.3E-3	--	EL not exceeded
Cyanide	4.5E-1	--	4.5E-1	3.3E-1	--	Non-carcinogenic EL exceeded
Dichlorobenzene	--	3.1E-5	3.1E-5	3.0E+1	--	EL not exceeded
Formaldehyde	--	1.9E-3	1.9E-3	--	5.1E-4	Carcinogenic EL exceeded
Hexane	--	4.6E-2	4.6E-2	1.2E+1	--	EL not exceeded
Hydrogen Chloride	--	--	--	5.0E-2	--	EL not exceeded
Manganese	2.4E-1	1.9E-4	2.4E-1	6.7E-2	--	Non-carcinogenic EL exceeded
Naphthalene	--	1.6E-5	1.6E-5	3.3E+0	--	EL not exceeded
Nickel	1.6E-3	5.6E-5	1.7E-3	--	2.7E-5	Carcinogenic EL exceeded
Phenol	--	--	--	1.3E+0	--	EL not exceeded
Phosphorus	5.3E-1	9.3E-5	5.3E-1	7.0E-3	--	Non-carcinogenic EL exceeded
Selenium	3.3E-4	6.2E-7	3.3E-4	1.3E-2	--	EL not exceeded
Toluene	--	8.8E-5	8.8E-5	2.5E+1	--	EL not exceeded
Xylene	--	--	--	2.9E+1	--	EL not exceeded
Aluminum	5.8E+1	6.5E-1	5.9E+1	6.7E-1	--	Non-carcinogenic EL exceeded
Barium	6.5E-1	6.8E-3	6.6E-1	3.3E-2	--	Non-carcinogenic EL exceeded
Calcium Carbonate	1.1E+1	2.2E+0	1.4E+1	6.7E-1	--	Non-carcinogenic EL exceeded
Calcium Oxide	--	7.0E-1	7.0E-1	1.3E-1	--	Non-carcinogenic EL exceeded
Copper	4.1E-3	5.3E-4	4.6E-3	6.7E-2	--	EL not exceeded
Cyclohexane	--	1.0E-3	1.0E-3	7.0E+1	--	EL not exceeded
Hydrogen Sulfide	--	9.0E-1	9.0E-1	9.3E-1	--	EL not exceeded
Iron	1.5E+1	2.1E-1	1.5E+1	6.7E-2	--	Non-carcinogenic EL exceeded
Molybdenum	8.1E-4	4.7E-4	1.3E-3	3.3E-1	--	EL not exceeded
Pentane	--	1.2E-1	1.2E-1	1.2E+2	--	EL not exceeded
Silver	4.1E-4	4.1E-4	8.2E-4	7.0E-3	--	EL not exceeded
Sulfuric Acid	--	2.0E+0	2.0E+0	6.7E-2	--	Non-carcinogenic EL exceeded

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Table 1. TAP MODELING APPLICABILITY DETERMINATION (HIGHEST-EMITTING MODELING SCENARIO: W3).						
HAP/TAP	Emissions (lb/hr)			EL (lb/hr)		Determination
	(a)	(b)	Total	(c)	(d)	
Thallium	8.1E-3	5.2E-4	8.7E-3	7.0E-3	--	Non-carcinogenic EL exceeded
Uranium	8.1E-3	5.2E-4	8.7E-3	1.3E-2	--	EL not exceeded
Vanadium	2.3E-2	8.4E-4	2.4E-2	3.0E-3	--	Non-carcinogenic EL exceeded
Trimethyl Benzene	--	1.1E-2	1.1E-2	8.2E+0	--	EL not exceeded
Tungsten	8.1E-3	5.2E-4	8.7E-3	3.3E-1	--	EL not exceeded
Zinc	2.9E-2	2.2E-3	3.1E-2	6.7E-1	--	EL not exceeded

a. Total HAP/TAP emissions for EL evaluation from mining (i.e., pits, blasting, haul roads, stockpiles and DRSF, tailings storage facility, access road, and underground exploration) and leaching. Emissions from sources covered/addressed by NSPS/NESHAP are not included in the evaluation for modeling applicability.

b. Total HAP/TAP emissions for EL evaluation from processing and production (i.e., ore processing [crushers and transfer, prill silos], ore concentration and refining [autoclave, electrowinning cells and pregnant solution tank, retort, furnace, carbon kiln], process heating [POX boiler, carbon regeneration kiln, propane vaporizer, solution heater], lime production [limestone crushers, screens, mill, transfers, lime kiln, kiln feed, lime mill, pebble lime silo, lime silos, lime mill crushing], aggregate production [portable crushers, screens, transfers], concrete production [central mixer, cement silos, aggregate bin], HVAC [heaters], emergency power [emergency generators, fire pump], fuel storage [gasoline fuel and tanks]). Emissions from sources covered/addressed by NSPS/NESHAP are not included in the evaluation for modeling applicability.

c. Non-carcinogenic EL from *Idaho Air Rules* Section 585.

d. Carcinogenic EL from *Idaho Air Rules* Section 586.

Table 1 shows that the SGP facility-wide potential TAP emissions exceed the respective EL for arsenic, beryllium, cadmium, cyanide, formaldehyde, manganese, nickel, phosphorus, aluminum, barium, calcium carbonate, calcium oxide, iron, sulfuric acid, thallium, and vanadium. Therefore, modeling was required for these 16 TAPs (11 non-carcinogenic and five carcinogenic TAPs) to demonstrate compliance with Acceptable Ambient Concentrations of Non-Carcinogens (AACs) and AACCs.

5.4 TAP Modeled Emission Rates

Table 2 lists the source-specific modeled emission rates for all 11 non-carcinogenic TAPs that required modeling (worst-case modeling scenario for all non-carcinogenic TAPs: W5). Table 3 lists the source-specific modeled emission rates for all five carcinogenic TAPs that required modeling (worst-case impacts for arsenic are associated with modeling scenario W2; worst-case impacts for all other carcinogenic TAPs are associated with modeling scenario W1). Note that all source-specific emission rates listed in Tables 2 and 3 were extracted by DEQ's modeling staff from the submitted modeling input files.

The total modeled emission rates for all non-carcinogenic TAPs are equal to the total facility-wide HAP/TAP emissions as stated in the permitting emissions inventory (excluding sources addressed by NSPS/NESHAP), evaluated at 180,000 T/day (see last two rows of Table 2). However, for carcinogenic TAPs, modeling was performed using an emission inventory that included T-RACT controls, long-term mining production limits, and other emission inventory refinements, as described in Section 4.0 of this *Modeling Review Attachment* (see last three rows of Table 3).

Table 2. MODELED EMISSION RATES FOR NON-CARCINOGENIC TAPS (WORST-CASE MODELING SCENARIOS).												
Type of Source	**Source ID**	**ALUM[a] (lb/hr)[b]**	**BARI[c] (lb/hr)**	**CACA[d] (lb/hr)**	**CAOX[e] (lb/hr)**	**CYAN[f] (lb/hr)**	**IRON[g] (lb/hr)**	**MANG[h] (lb/hr)**	**PHOS[i] (lb/hr)**	**SULF[j] (lb/hr)**	**THAL[k] (lb/hr)**	**VANA[l] (lb/hr)**
Point Sources	LS1L	2.33E-04	1.50E-06	0	7.63E-03	0	1.07E-04	2.44E-06	1.34E-06	0	5.16E-08	1.60E-07
	MILLS2L	2.33E-04	1.50E-06	0	7.63E-03	0	1.07E-04	2.44E-06	1.34E-06	0	5.16E-08	1.60E-07
	AC	2.31E-05	2.31E-05	2.31E-05	0	0	2.31E-05	0	0	2.03E+00	2.31E-05	2.31E-05
	ACB	0	3.06E-06	0	0	0	0	2.64E-07	0	0	0	1.60E-06
	ACS1L	9.32E-04	5.98E-06	0	3.05E-02	0	4.27E-04	9.76E-06	5.36E-06	0	2.06E-07	6.39E-07
	ACS2L	9.32E-04	5.98E-06	0	3.05E-02	0	4.27E-04	9.76E-06	5.36E-06	0	2.06E-07	6.39E-07
	ACS3L	9.32E-04	5.98E-06	0	3.05E-02	0	4.27E-04	9.76E-06	5.36E-06	0	2.06E-07	6.39E-07
	ACS4L	4.66E-04	2.99E-06	0	1.53E-02	0	2.13E-04	4.88E-06	2.68E-06	0	1.03E-07	3.20E-07
	CKD	9.59E-05	9.59E-05	9.59E-05	0	0	9.59E-05	0	0	0	9.59E-05	9.59E-05
	CKB	0	9.73E-06	0	0	0	0	8.40E-07	0	0	0	5.08E-06
	EW	9.59E-05	9.59E-05	9.59E-05	0	0	9.59E-05	0	0	0	9.59E-05	9.59E-05
	MR	9.59E-05	9.59E-05	9.59E-05	0	0	9.59E-05	0	0	0	9.59E-05	9.59E-05
	MF	9.59E-05	9.59E-05	9.59E-05	0	0	9.59E-05	0	0	0	9.59E-05	9.59E-05
	EDG1	0	0	0	0	0	0	0	0	0	0	0
	EDG2	0	0	0	0	0	0	0	0	0	0	0
	EDG3	0	0	0	0	0	0	0	0	0	0	0
	EDFP	0	0	0	0	0	0	0	0	0	0	0
	PV	0	4.31E-07	0	0	0	0	3.73E-08	0	0	0	2.25E-07
	HS	0	2.16E-05	0	0	0	0	1.86E-06	0	0	0	1.13E-05
	H1M	0	1.73E-05	0	0	0	0	1.49E-06	0	0	0	9.02E-06
	H2M	0	1.73E-05	0	0	0	0	1.49E-06	0	0	0	9.02E-06
	HM	0	1.73E-05	0	0	0	0	1.49E-06	0	0	0	9.02E-06
	HAC	0	1.08E-06	0	0	0	0	9.31E-08	0	0	0	5.64E-07
	HR	0	1.08E-06	0	0	0	0	9.31E-08	0	0	0	5.64E-07
	HA	0	1.08E-06	0	0	0	0	9.31E-08	0	0	0	5.64E-07
	HMO	0	2.16E-06	0	0	0	0	1.86E-07	0	0	0	1.13E-06
	HTS	0	8.63E-06	0	0	0	0	7.45E-07	0	0	0	4.51E-06
	HW	0	1.29E-05	0	0	0	0	1.12E-06	0	0	0	6.76E-06
	PSL	0	0	0	0	0	0	0	0	0	0	0
	CS1L	0	0	0	0	0	0	8.01E-07	0	0	0	0
	CS2L	0	0	0	0	0	0	8.01E-07	0	0	0	0
	LS6	3.19E-03	2.05E-05	3.88E-02	0	0	1.46E-03	0	0	0	7.06E-07	2.19E-06
	LSBM	4.30E-02	2.76E-04	5.22E-01	0	0	1.97E-02	0	0	0	9.51E-06	2.95E-05
	LS9	7.54E-04	4.84E-06	9.16E-03	0	0	3.45E-04	0	0	0	1.67E-07	5.17E-07
	LK	2.07E-02	1.33E-04	2.51E-01	0	0	9.47E-03	0	0	0	4.58E-06	1.42E-05
	LKC	0	9.51E-05	0	0	0	0	0	0	0	0	4.97E-05
	LCR	6.43E-03	4.12E-05	0	2.11E-01	0	2.94E-03	0	0	0	1.42E-06	4.41E-06
	LSL	1.40E-04	8.99E-07	0	4.59E-03	0	6.41E-05	0	0	0	3.10E-08	9.60E-08

Table 2. MODELED EMISSION RATES FOR NON-CARCINOGENIC TAPS (WORST-CASE MODELING SCENARIOS).												
Type of Source	**Source ID**	**ALUM[a] (lb/hr)[b]**	**BARI[c] (lb/hr)**	**CACA[d] (lb/hr)**	**CAOX[e] (lb/hr)**	**CYAN[f] (lb/hr)**	**IRON[g] (lb/hr)**	**MANG[h] (lb/hr)**	**PHOS[i] (lb/hr)**	**SULF[j] (lb/hr)**	**THAL[k] (lb/hr)**	**VANA[l] (lb/hr)**
Area Sources	WEP	5.59E+00	6.29E-02	1.10E+00	0	0	1.43E+00	2.35E-02	5.11E-02	0	7.87E-04	2.20E-03
	UGEXP	2.49E-05	2.80E-07	4.91E-06	0	0	6.38E-06	1.05E-07	2.28E-07	0	3.50E-09	9.81E-09
	TSF	0	0	0	0	2.32E-01	0	0	0	0	0	0
Line Sources	AR01	2.02E-02	2.28E-04	3.99E-03	0	0	5.18E-03	8.52E-05	1.85E-04	0	2.85E-06	7.98E-06
	AR02	1.56E-02	1.75E-04	3.07E-03	0	0	3.99E-03	6.55E-05	1.42E-04	0	2.19E-06	6.13E-06
	AR03	3.93E-02	4.43E-04	7.75E-03	0	0	1.01E-02	1.66E-04	3.60E-04	0	5.54E-06	1.55E-05
	AR04	3.77E-02	4.25E-04	7.43E-03	0	0	9.66E-03	1.59E-04	3.45E-04	0	5.31E-06	1.49E-05
Volume Sources	WEPBL	1.90E+00	2.14E-02	3.75E-01	0	0	4.88E-01	8.01E-03	1.74E-02	0	2.68E-04	7.50E-04
	WEDRSF	8.58E-01	9.66E-03	1.69E-01	0	0	2.20E-01	3.61E-03	7.85E-03	0	1.21E-04	3.38E-04
	OC1	1.04E-02	1.17E-04	2.04E-03	0	0	2.65E-03	0	0	0	1.46E-06	4.08E-06
	OC2	1.04E-02	1.17E-04	2.04E-03	0	0	2.65E-03	0	0	0	1.46E-06	4.08E-06
	OC3	1.04E-02	1.17E-04	2.04E-03	0	0	2.65E-03	0	0	0	1.46E-06	4.08E-06
	OC4	1.04E-02	1.17E-04	2.04E-03	0	0	2.65E-03	0	0	0	1.46E-06	4.08E-06
	OC5	1.04E-02	1.17E-04	2.04E-03	0	0	2.65E-03	0	0	0	1.46E-06	4.08E-06
	OC6	1.04E-02	1.17E-04	2.04E-03	0	0	2.65E-03	0	0	0	1.46E-06	4.08E-06
	OC7	8.87E-02	1.00E-03	1.75E-02	0	0	2.28E-02	0	0	0	1.25E-05	3.50E-05
	OC8	1.04E-02	1.17E-04	2.04E-03	0	0	2.65E-03	0	0	0	1.46E-06	4.08E-06
	OC9	4.90E-02	5.52E-04	9.66E-03	0	0	1.26E-02	0	0	0	6.90E-06	1.93E-05
	OC10	4.90E-02	5.52E-04	9.66E-03	0	0	1.26E-02	0	0	0	6.90E-06	1.93E-05
	OC11	4.90E-02	5.52E-04	9.66E-03	0	0	1.26E-02	0	0	0	6.90E-06	1.93E-05
	OC12	9.80E-02	1.10E-03	1.93E-02	0	0	2.51E-02	0	0	0	1.38E-05	3.86E-05
	OC13	1.14E-02	1.29E-04	2.25E-03	0	0	2.93E-03	0	0	0	1.61E-06	4.51E-06
	LS1U	1.13E-03	7.25E-06	0	3.70E-02	0	5.18E-04	1.18E-05	6.50E-06	0	2.50E-07	7.75E-07
	MILLS2U	1.13E-03	7.25E-06	0	3.70E-02	0	5.18E-04	1.18E-05	6.50E-06	0	2.50E-07	7.75E-07
	ACS1U	2.17E-03	1.39E-05	0	7.10E-02	0	9.94E-04	2.27E-05	1.25E-05	0	4.80E-07	1.49E-06
	ACS2U	2.17E-03	1.39E-05	0	7.10E-02	0	9.94E-04	2.27E-05	1.25E-05	0	4.80E-07	1.49E-06
	ACS3U	2.17E-03	1.39E-05	0	7.10E-02	0	9.94E-04	2.27E-05	1.25E-05	0	4.80E-07	1.49E-06
	ACS42U	2.17E-03	1.39E-05	0	7.10E-02	0	9.94E-04	2.27E-05	1.25E-05	0	4.80E-07	1.49E-06
	PSU	0	0	0	0	0	0	0	0	0	0	0
	CS1U	0	0	0	0	0	0	8.01E-07	0	0	0	0
	CS2U	0	0	0	0	0	0	8.01E-07	0	0	0	0
	CAL	1.56E-02	1.00E-04	0	0	0	7.14E-03	0	0	0	3.45E-06	1.07E-05
	CAU	1.56E-02	1.00E-04	0	0	0	7.14E-03	0	0	0	3.45E-06	1.07E-05
	CM	0	0	0	0	0	0	2.59E-05	8.22E-06	0	0	0
	PCSP1	1.41E-02	9.06E-05	1.72E-01	0	0	6.47E-03	0	0	0	3.12E-06	9.69E-06
	PCSP2	1.41E-02	9.06E-05	1.72E-01	0	0	6.47E-03	0	0	0	3.12E-06	9.69E-06
	LS1	3.19E-03	2.05E-05	3.88E-02	0	0	1.46E-03	0	0	0	7.06E-07	2.19E-06
	LS2	5.75E-03	3.69E-05	6.98E-02	0	0	2.63E-03	0	0	0	1.27E-06	3.94E-06
	LS3	2.66E-02	1.71E-04	3.23E-01	0	0	1.22E-02	0	0	0	5.88E-06	1.82E-05

Table 2. MODELED EMISSION RATES FOR NON-CARCINOGENIC TAPS (WORST-CASE MODELING SCENARIOS).												
Type of Source	**Source ID**	**ALUM[a] (lb/hr)[b]**	**BARI[c] (lb/hr)**	**CACA[d] (lb/hr)**	**CAOX[e] (lb/hr)**	**CYAN[f] (lb/hr)**	**IRON[g] (lb/hr)**	**MANG[h] (lb/hr)**	**PHOS[i] (lb/hr)**	**SULF[j] (lb/hr)**	**THAL[k] (lb/hr)**	**VANA[l] (lb/hr)**
	LS4	5.75E-03	3.69E-05	6.98E-02	0	0	2.63E-03	0	0	0	1.27E-06	3.94E-06
	LS5	2.66E-02	1.71E-04	3.23E-01	0	0	1.22E-02	0	0	0	5.88E-06	1.82E-05
	LS7	3.19E-03	2.05E-05	3.88E-02	0	0	1.46E-03	0	0	0	7.06E-07	2.19E-06
	LS8	3.19E-03	2.05E-05	3.88E-02	0	0	1.46E-03	0	0	0	7.06E-07	2.19E-06
	LS10	7.54E-04	4.84E-06	9.16E-03	0	0	3.45E-04	0	0	0	1.67E-07	5.17E-07
	LS11	6.29E-03	4.03E-05	7.63E-02	0	0	2.88E-03	0	0	0	1.39E-06	4.31E-06
	LS12	7.54E-04	4.84E-06	9.16E-03	0	0	3.45E-04	0	0	0	1.67E-07	5.17E-07
	LSU	1.40E-05	8.99E-08	0	4.59E-04	0	6.41E-06	0	0	0	3.10E-09	9.60E-09
	MILLTANKS	0	0	0	0	2.21E-01	0	0	0	0	0	0
	HRT001-HRT072[m]	2.62E-01	2.95E-03	5.16E-02	0	0	6.71E-02	1.10E-03	2.40E-03	0	3.69E-05	1.03E-04
	HRN001-HRN022[m]	2.62E-01	2.95E-03	5.16E-02	0	0	6.71E-02	1.10E-03	2.40E-03	0	3.69E-05	1.03E-04
Total Modeled Rates		***3.37E+01***	***3.79E-01***	***8.76E+00***	***6.96E-01***	***4.53E-01***	***8.69E+00***	***1.39E-01***	***3.03E-01***	***2.03E+00***	***5.17E-03***	***1.39E-02***
Total Emission Rates at 180,000 T/day[n]		***3.37E+01***	***3.79E-01***	***8.76E+00***	***6.96E-01***	***4.53E-01***	***8.69E+00***	***1.39E-01***	***3.03E-01***	***2.03E+00***	***5.17E-03***	***1.39E-02***

a. Aluminum (worst-case modeling scenario: W5).
b. Pounds per hour.
c. Barium (worst-case modeling scenario: W5).
d. Calcium carbonate (worst-case modeling scenario: W5).
e. Calcium oxide (worst-case modeling scenario: W5).
f. Cyanide (worst-case modeling scenario: W5).
g. Iron (worst-case modeling scenario: W5).
h. Manganese (worst-case modeling scenario: W5).
i. Phosphorus (worst-case modeling scenario: W5).
j. Sulfuric acid (worst-case modeling scenario: W5).
k. Thallium (worst-case modeling scenario: W5).
l. Vanadium (worst-case modeling scenario: W5).
m. The Haul Road was represented in the model as a series of volume sources. The emission rates listed in this table represent each individual volume source.
n. Total emission rates at 180,000 tons per day were derived from Worksheet "TblA" in the emission inventory dated October 5, 2021. The total emission rates in this row represent all facility-wide HAP/TAP emission sources from mining, leaching, and processing and production (excluding emissions from sources "addressed" or "covered" by NSPS/NESHAP).

Table 3. MODELED EMISSION RATES FOR CARCINOGENIC TAPS (WORST-CASE MODELING SCENARIOS).						
Type of Source	**Source ID**	**ARSE[a] (lb/hr)[b]**	**BERY[c] (lb/hr)**	**CADM[d] (lb/hr)**	**FORM[e] (lb/hr)**	**NICK[f] (lb/hr)**
Point Sources	LS1L	1.14E-08	3.96E-10	1.24E-10	0	2.47E-09
	MILLS2L	1.14E-08	3.96E-10	1.24E-10	0	2.47E-09
	AC	0	0	0	0	0
	ACB	1.28E-07	7.66E-09	7.02E-07	4.79E-05	1.34E-06
	ACS1L	4.55E-08	1.58E-09	4.94E-10	0	9.89E-09
	ACS2L	4.55E-08	1.58E-09	4.94E-10	0	9.89E-09
	ACS3L	4.55E-08	1.58E-09	4.94E-10	0	9.89E-09
	ACS4L	2.27E-08	7.91E-10	2.47E-10	0	4.94E-09
	CKD	0	0	0	0	0
	CKB	4.07E-07	2.44E-08	2.24E-06	1.52E-04	4.27E-06
	EW	0	0	0	0	0
	MR	0	0	0	0	0
	MF	0	0	0	0	0
	EDG1	0	0	0	0	0
	EDG2	0	0	0	0	0
	EDG3	0	0	0	0	0
	EDFP	0	0	0	0	0
	PV	1.80E-08	1.08E-09	9.91E-08	6.76E-06	1.89E-07
	HS	9.01E-07	5.41E-08	4.96E-06	3.38E-04	9.46E-06
	H1M	7.84E-07	4.71E-08	4.31E-06	2.94E-04	8.24E-06
	H2M	7.84E-07	4.71E-08	4.31E-06	2.94E-04	8.24E-06
	HM	7.84E-07	4.71E-08	4.31E-06	2.94E-04	8.24E-06
	HAC	4.90E-08	2.94E-09	2.70E-07	1.84E-05	5.15E-07
	HR	4.90E-08	2.94E-09	2.70E-07	1.84E-05	5.15E-07
	HA	4.90E-08	2.94E-09	2.70E-07	1.84E-05	5.15E-07
	HMO	9.80E-08	5.88E-09	5.39E-07	3.68E-05	1.03E-06
	HTS	3.92E-07	2.35E-08	2.16E-06	1.47E-04	4.12E-06
	HW	5.88E-07	3.53E-08	3.24E-06	2.21E-04	6.18E-06
	PSL	0	0	0	0	0
	CS1L	2.90E-08	3.33E-09	0	0	2.86E-07
	CS2L	2.90E-08	3.33E-09	0	0	2.86E-07
	LS6	0	0	0	0	0
	LSBM	0	0	0	0	0
	LS9	0	0	0	0	0
	LK	0	0	0	0	0
	LKC	0	0	0	0	0
	LCR	0	0	0	0	0
	LSL	0	0	0	0	0
Area Sources	WEP	9.40E-03	4.51E-05	7.04E-06	0	2.82E-05
	UGEXP	2.34E-07	1.12E-09	1.75E-10	0	7.01E-10
	TSF	0	0	0	0	0
Line Sources	AR01	7.12E-07	9.12E-07	1.42E-07	0	5.70E-07
	AR02	5.48E-07	7.01E-07	1.10E-07	0	4.38E-07
	AR03	1.38E-06	1.77E-06	2.77E-07	0	1.11E-06
	AR04	1.33E-06	1.70E-06	2.65E-07	0	1.06E-06

Table 3. MODELED EMISSION RATES FOR CARCINOGENIC TAPS (WORST-CASE MODELING SCENARIOS).						
Type of Source	**Source ID**	**ARSE[a] (lb/hr)[b]**	**BERY[c] (lb/hr)**	**CADM[d] (lb/hr)**	**FORM[e] (lb/hr)**	**NICK[f] (lb/hr)**
Volume Sources	WEPBL	1.79E-02	8.57E-05	1.34E-05	0	5.36E-05
	FDRSF	4.23E-03				
	STKP		2.72E-05	4.25E-06	0	1.70E-05
	OC1	0	0	0	0	0
	OC2	0	0	0	0	0
	OC3	0	0	0	0	0
	OC4	0	0	0	0	0
	OC5	0	0	0	0	0
	OC6	0	0	0	0	0
	OC7	0	0	0	0	0
	OC8	0	0	0	0	0
	OC9	0	0	0	0	0
	OC10	0	0	0	0	0
	OC11	0	0	0	0	0
	OC12	0	0	0	0	0
	OC13	0	0	0	0	0
	LS1U	5.51E-08	1.92E-09	5.99E-10	0	1.20E-08
	MILLS2U	5.51E-08	1.92E-09	5.99E-10	0	1.20E-08
	ACS1U	2.21E-07	7.67E-09	2.40E-09	0	4.79E-08
	ACS2U	2.21E-07	7.67E-09	2.40E-09	0	4.79E-08
	ACS3U	2.21E-07	7.67E-09	2.40E-09	0	4.79E-08
	ACS42U	1.10E-07	3.84E-09	1.20E-09	0	2.40E-08
	PSU	0	0	0	0	0
	CS1U	2.90E-08	3.33E-09	0	0	2.86E-07
	CS2U	2.90E-08	3.33E-09	0	0	2.86E-07
	CAL	0	0	0	0	0
	CAU	0	0	0	0	0
	CM	2.03E-06	0	4.86E-09	0	1.70E-06
	PCSP1	0	0	0	0	0
	PCSP2	0	0	0	0	0
	LS1	0	0	0	0	0
	LS2	0	0	0	0	0
	LS3	0	0	0	0	0
	LS4	0	0	0	0	0
	LS5	0	0	0	0	0
	LS7	0	0	0	0	0
	LS8	0	0	0	0	0
	LS10	0	0	0	0	0
	LS11	0	0	0	0	0
	LS12	0	0	0	0	0
	LSU	0	0	0	0	0
	MILLTANKS	0	0	0	0	0

Table 3. MODELED EMISSION RATES FOR CARCINOGENIC TAPS (WORST-CASE MODELING SCENARIOS).						
Type of Source	**Source ID**	**ARSE[a] (lb/hr)[b]**	**BERY[c] (lb/hr)**	**CADM[d] (lb/hr)**	**FORM[e] (lb/hr)**	**NICK[f] (lb/hr)**
Volume Sources	HRF001-HRF055[g]	1.03E-03				
	HRQ001-HRQ049[g]	1.03E-03				
	HRR001-HRR006[g]	1.03E-03				
	HRN001-HRN022[g]	1.03E-03	9.27E-06	1.45E-06	0	5.80E-06
	HRB001-HRB003[g]	1.03E-03				
	HRP001-HRP057[g]		9.27E-06	1.45E-06	0	5.80E-06
	HRO001-HRO002[g]	1.03E-03	9.27E-06	1.45E-06	0	5.80E-06
Total Modeled Rates		***1.73E-01***	***9.15E-04***	***1.71E-04***	***1.89E-03***	***6.27E-04***
Total T-RACT Emission Rates[h]		***1.73E-01***	***9.1E-04***	***1.7E-04***	***1.9E-03***	***6.3E-04***
Total Emission Rates at 180,000 T/day[i]		***4.03E-01***	***1.36E-03***	***2.40E-04***	***1.89E-03***	***9.04E-04***

a. Arsenic (worst-case modeling scenario: W2).
b. Pounds per hour.
c. Beryllium (worst-case modeling scenario: W1).
d. Cadmium (worst-case modeling scenario: W1).
e. Formaldehyde (worst-case modeling scenario: W1).
f. Nickel (worst-case modeling scenario: W1).
g. The Haul Road was represented in the model as a series of volume sources. The emission rates listed in this table represent each individual volume source.
h. Total T-RACT emission rates – calculated based on T-RACT controls, long-term mining production limits, and other emission inventory refinements, as described in Section 4.0 of this *Modeling Review Attachment* – are derived from Tables B-W2 (for Arsenic) and B-W1 (for Beryllium, Cadmium, Formaldehyde, and Nickel) in Appendix B of the *TAP Addendum*.
i. Total emission rates at 180,000 tons per day were derived from Worksheet "TblA" in the emission inventory dated October 5, 2021. The total emission rates in this row represent all facility-wide HAP/TAP emission sources from mining, leaching, and processing and production (excluding emissions from sources "addressed" or "covered" by NSPS/NESHAP).

5.5 Cyanide Modeling Emission Source Parameters

Modeling analyses for cyanide introduced two new emission sources that were not previously evaluated by DEQ: tailings storage facility (model ID: TSF) and mill tanks (model ID: MILLTANKS).

1. The tailings storage facility was modeled by Air Sciences as a surface-based (zero release height above ground-level and zero initial vertical dimension) AREA source. The easterly and northerly lengths were calculated as square-root of the TSF area (easterly length = northerly length = $\sqrt{1{,}338{,}158\ square\ meters}$ = 1,157 meters).

2. The mill tanks were grouped and modeled by Air Sciences as a single VOLUME source. The tanks sit on the ground, so the release height was set to the average tank height of 12.2 meters (40 feet). The initial lateral dispersion (σ_y) was calculated as the equivalent diameter of the combined (18) tank area divided by the single VOLUME source coefficient of 4.3:

$$\sigma_{y(MILLTANKS)} = \frac{Equivalent\ diameter}{4.3} = \frac{\sqrt{\Sigma(d)^2}}{4.3} = 42.8\ feet$$

The individual tank diameters (d) are: two tanks at 40 feet, four tanks at 52 feet, six tanks at 54 feet, and six tanks at 20 feet.

DEQ typically requires that tailings storage facilities be modeled as an AREAPOLY source with an outline that follows the contour of the emission source, and that mill tanks be represented in the model as individual volume sources; but, given that the maximum modeled concentration for cyanide is safely below the AAC (0.08%), DEQ's modeling team accepted the modeling analysis submitted by Air Sciences and concluded that it confidently demonstrates that the cyanide AAC will not be exceeded.

5.6 Deposition Modeling

Air Sciences applied particle deposition algorithms in the impact modeling for particulate TAPs. The particulate deposition parameters used in the NAAQS compliance analysis were derived for PM_{10} and $PM_{2.5}$ (see Tables 22 and 23 in the main body of the DEQ *Modeling Review Memorandum*). Dust-related metal TAP emissions include total particulates (all size fractions of particulate matter [PM] up to PM_{30}). Therefore, the deposition parameters for PM were calculated using the same methodology and EPA references used for PM_{10} and $PM_{2.5}$ in the NAAQS compliance demonstration analyses. The PM deposition parameters are provided below in Table 4. The same density values were used as in the previous TAPs modeling analysis. However, an additional deposition characterization bin was added to better handle deposition of 10 µm to 30 µm particulates; mass fractions were adjusted accordingly.

Table 4. PARTICULATE MATTER DEPOSITION PARAMETERS BY SOURCE CATEGORY.

Source Category	Parameter	PM				
		Bin 1	Bin 2	Bin 3	Bin 4	Bin 5
Haul Roads	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.02	0.23	0.75	--	--
	Mass Mean Diameter (µm)	2.50	10.00	30.00	--	--
	Density (g/cm³) (YPP, HFP, WEP DR average)	2.46	2.46	2.46	--	--
Material Handling (Ore, DR, Limestone)	Bin Upper Diameter (µm)	2.50	5.00	10.00	30.00	--
	Mass Fraction	0.07	0.20	0.20	0.53	--
	Mass Mean Diameter (µm)	2.50	5.00	10.00	30.00	--
	Density (g/cm³) (Ore)	Pit-specific, see Table 23[a].				
	Density (g/cm³) (Ore and Waste)	Pit-specific, see Table 23.				
	Density (g/cm³) (Limestone)	1.09	1.09	1.09	1.09	--
Baghouses	Bin Upper Diameter (µm)	2.50	6.00	10.00	30.00	--
	Mass Fraction	0.25	0.45	0.20	0.10	--
	Mass Mean Diameter (µm)	2.50	6.00	10.00	30.00	--
	Density (g/cm³) (Ore)	Pit-specific, see Table 23.				
Diesel Engines	Bin Upper Diameter (µm)	1.00	2.50	6.00	10.00	30.00
	Mass Fraction	0.82	0.08	0.03	0.03	0.04
	Mass Mean Diameter (µm)	1.00	2.50	6.00	10.00	30.00
	Density (g/cm³) (Diesel Combustion)	1.00	1.00	1.00	1.00	1.00
Heaters and Boilers	Bin Upper Diameter (µm)	1.00	2.50	6.00	10.00	30.00
	Mass Fraction	0.23	0.22	0.25	0.09	0.21
	Mass Mean Diameter (µm)	1.00	2.50	6.00	10.00	30.00
	Density (g/cm³) (Propane Combustion)	1.24	1.24	1.24	1.24	1.24

Table 4. PARTICULATE MATTER DEPOSITION PARAMETERS BY SOURCE CATEGORY.						
Source Category	**Parameter**	**PM**				
		Bin 1	**Bin 2**	**Bin 3**	**Bin 4**	**Bin 5**
Lime Loading and Unloading (Quick, Pebble)	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.05	0.29	0.66	--	--
	Mass Mean Diameter	2.50	10.00	30.00	--	--
	Density (g/cm^3) (Quick)	0.44	0.44	0.44	--	--
	Density (g/cm^3) (Pebble)	0.96	0.96	0.96	--	--
Lime Unloading (Quick, Pebble)	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.09	0.49	0.42	--	--
	Mass Mean Diameter (µm)	2.50	10.00	30.00	--	--
	Density (g/cm^3) (Quick)	0.44	0.44	0.44	--	--
	Density (g/cm^3) (Pebble)	0.96	0.96	0.96	--	--
Cement and Aggregate Loading and Unloading	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.05	0.29	0.66	--	--
	Mass Mean Diameter (µm)	2.50	10.00	30.00	--	--
	Density (g/cm^3) (Cement)	1.44	1.44	1.44	--	--
	Density (g/cm^3) (Aggregate)	1.28	1.28	1.28	--	--
Prill Loading and Unloading	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.05	0.30	0.65	--	--
	Mass Mean Diameter (µm)	2.50	10.00	30.00	--	--
	Density (g/cm^3) (Prill)	0.84	0.84	0.84	--	--
Refining Processes	Bin Upper Diameter (µm)	1.00	2.50	6.00	10.00	30.00
	Mass Fraction	0.72	0.10	0.07	0.03	0.08
	Mass Mean Diameter (µm)	1.00	2.50	6.00	10.00	30.00
	Density (g/cm^3) (Diesel Combustion)	1.00	1.00	1.00	1.00	1.00
Portable Crushing and Screening Plant	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.05	0.32	0.63	--	--
	Mass Mean Diameter (µm)	2.50	10.00	30.00	--	--
	Density (g/cm^3) (YPP, HFP, WEP DR average)	2.46	2.46	2.46	--	--
Lime Kiln and Ball Mill	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--
	Mass Fraction (Kiln)	0.27	0.28	0.45	--	--
	Mass Fraction (Ball Mill)	0.30	0.54	0.16	--	--
	Mass Mean Diameter (µm)	2.50	10.00	30.00	--	--
	Density (g/cm^3)	1.09	1.09	1.09	--	--
Blasting and Drilling	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.03	0.49	0.48	--	--
	Mass Mean Diameter (µm)	2.50	10.00	30.00	--	--
	Density (g/cm^3) (Ore or DR)	Pit-specific, see Table 23.				
Dozing	Bin Upper Diameter (µm)	2.50	10.00	15.00	30.00	--
	Mass Fraction	0.11	0.08	0.06	0.75	--
	Mass Mean Diameter (µm)	2.50	10.00	15.00	30.00	--
	Density (g/cm^3) (DR)	Pit-specific, see Table 23.				

[a.] See Table 23 in the main body of the DEQ *Modeling Review Memorandum*.

5.7 Carcinogenic TAP Modeling Lifetime Exposure Adjustment

Maximum modeled concentrations for carcinogenic TAPs were adjusted to account for the life-of-mine production limits, which affects the lifetime exposure.

PRI evaluated the highest modeled annual carcinogenic TAP concentration from each of the 14 modeling scenarios for lifetime exposure as follows:

$$Lifetime\ exposure\ \left(\frac{\mu g}{m^3}\right) = \frac{Highest\ annual\ concentration\ \left(\frac{\mu g}{m^3}\right) \times 16\ (mine\ operation\ years)}{70\ (years, lifetime\ exposure)}$$

This equation assumes that the highest annual concentration from the 14 modeling scenarios is repeated for 16 years of mining operation. This was then averaged over 70 years to calculate the 70-year lifetime exposure.

PRI and Air Sciences contend that calculating lifetime exposure based on 16 years of mining operation is conservative. The annual emissions for carcinogenic TAP modeling are based on 135,000 tons/day (see Section 5.1 of this *Modeling Review Attachment*) and 365 days per year. Over 16 years, this equates to a potential mining production of 788.4 million tons:

$$\frac{135{,}000\ \left(\frac{tons}{day}\right) \times 365\ \left(\frac{days}{year}\right) \times 16\ years}{1{,}000{,}000\ \left(\frac{tons}{million\ ton}\right)} = 788.4\ million\ tons$$

The actual life-of-mine total production as described in the SGP *Refined Proposed Action* (*ModPRO2*) mine plan is only 402.86 million tons (Perpetua 2021), which is 51.1% of the potential life-of-mine production represented in the above equation and related emission evaluations.

5.8 Arsenic Compliance Demonstration for Modeling Scenarios W1-W4

To demonstrate compliance with the AACC for arsenic, PRI applied two additional operating limitations:

- The removal of Modeling Scenario W5 as a potential operating scenario
- Limiting the West End Pit's life-of-mine potential mining production to 50% of the total life-of-mine potential mining production of 788.4 million tons: 50% * 788.4 million tons = 394.2 million tons

PRI has determined that the West End Development Rock Storage Facility (DRSF) will not be constructed. This change eliminated Modeling Scenario W5 from the arsenic modeling evaluation. The remaining four West End Pit modeling scenarios (W1–W4) are evaluated using the 70-year lifetime exposure equation from Section 5.7 and adjusting for the proposed West End Pit life-of-mine production limit of 50% of the total production as follows:

$$LifeExpose_{Wi,j,n} = \left[\left(WEPExpose_{Wi,n}\right)(50\%) + \left(nonWEPExpose_{Sj,n}\right)(50\%)\right]\left[\frac{16\ year\ LOM}{70\ year\ exposure}\right]$$

where:

W*i*	=	West End Pit scenario, where *i* = 1 to 4.
S*j*	=	non West End Pit scenario, where *j* = B1, B2, H1, H2, H3, H4, Y1, Y2, and Y3.
n	=	specific receptor.
$LifeExpose_{Wi,j,n}$	=	lifetime exposure in µg/m³ for West End Pit scenario *i*, non West End Pit scenario *j*, at receptor *n*.
$WEPExpose_{Wi,n}$	=	annual maximum impact in µg/m³ for West End Pit scenario *i* at receptor *n*.
$nonWEPExpose_{Sj,n}$	=	annual maximum impact in µg/m³ for non West End Pit scenario *j* at receptor *n*.
16 year LOM	=	maximum life-of-mine.
70 year exposure	=	Lifetime exposure used for development of AACCs in *Idaho Air Rules*.

The above equation was used to calculate the lifetime arsenic exposure from the West End Pit scenarios (W1–W4) on a receptor-by-receptor basis. Combining the concentrations from Modeling Scenarios W1–W4 with the highest concentration from the remaining non-West End Pit scenarios (B1, B2, H1, H2, H3, H4, Y1, Y2, or Y3) conservatively ensures that the maximum potential impacts from applicable sources are evaluated and remain below AACCs.

PRI contends that calculating lifetime arsenic exposure based on the proposed West End Pit life-of-mine production limit of 50% of the total production is conservative. The actual life-of-mine total production from the West End Pit as described in the ModPRO2 mine plan is only 198.26 million tons (Perpetua 2021), which is 50.3% of the proposed West End Pit life-of-mine production limit of 394.2 million tons.

6.0 Impact Results

TAP impact analysis results, as submitted in the *TAP Addendum* and as further assessed by DEQ, are discussed in this section. The effect of various operational refinements also reduced PM_{10} and $PM_{2.5}$ impacts, and this is discussed in Section 6.2.

6.1 TAP Impact Analyses Results

This section describes the revised TAP impact analyses and demonstrates that applicable TAP emissions resulting from operation of the SGP will not result in increased impacts that exceed AACs or AACCs.

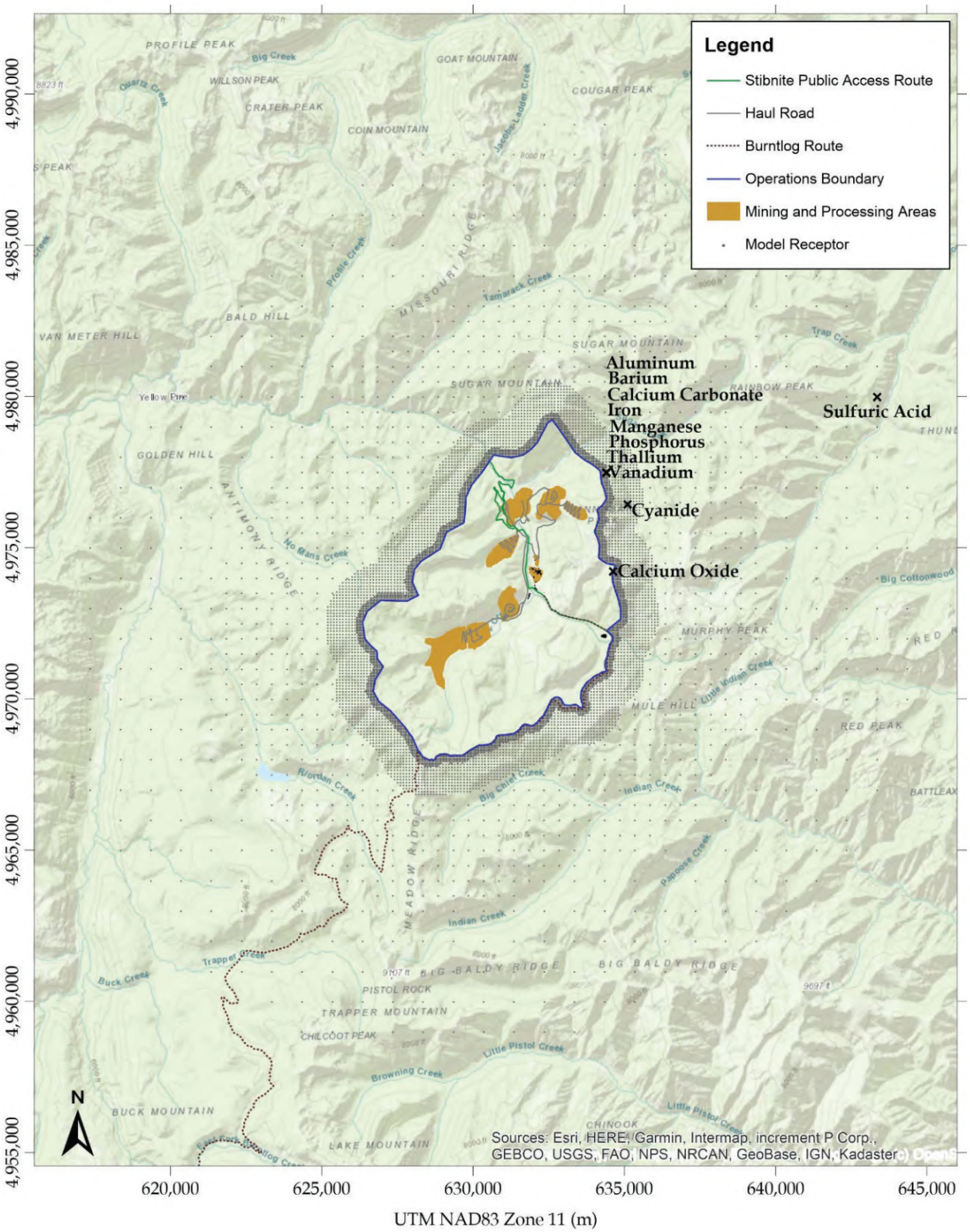
6.1.1 Modeling Non-Carcinogenic TAPs

The non-carcinogenic TAPs subject to impact modeling requirements to demonstrate compliance with AACs of *Idaho Air Rules* Section 585 were modeled at the emission levels shown in Table 1 above. The maximum 24-hour modeled concentration for each of the 14 modeling scenarios demonstrates compliance with the applicable AAC, as summarized below in Table 5. PRI elected to include Scenario W5 in the modeling analysis for non-carcinogenic TAPs. Figure 1 illustrates the locations of the maximum impacts for each non-carcinogenic TAP.

Table 5. RESULTS FOR TAPS IMPACT ANALYSES FOR NON-CARCINOGENIC TAPS.					
Toxic Air Pollutant	**Averaging Time**	**Maximum Modeled Concentration ($\mu g/m^3$)[a]**	**Model Scenario**	**AAC[b] ($\mu g/m^3$)**	**Percent of AAC**
Aluminum	24-hour	6.17	W5	500	1.23%
Barium	24-hour	0.07	W5	25	0.28%
Calcium carbonate	24-hour	1.22	W5	500	0.24%
Calcium oxide	24-hour	0.15	All	100	0.15%
Cyanide	24-hour	0.20	All	250	0.08%
Iron	24-hour	1.58	W5	50	3.16%
Manganese	24-hour	0.03	W5	250	0.01%
Phosphorus	24-hour	0.06	W5	5	1.20%
Sulfuric acid	24-hour	0.41	All	50	0.82%
Thallium	24-hour	0.001	W5	5	0.02%
Vanadium	24-hour	0.002	W5	2.5	0.08%

a. Micrograms per cubic meter.
b. Acceptable Ambient Concentration of a Non-carcinogenic TAP.

Figure 1. SGP NON-CARCINOGENIC MAXIMUM TAP IMPACT LOCATIONS.



6.1.2 Modeling Carcinogenic TAPs

The carcinogenic TAPs subject to impact modeling requirements to demonstrate compliance with AACCs of *Idaho Air Rules* Section 586 were modeled using an emission inventory that includes the T-RACT controls, long-term mining production limits, and other emission inventory refinements, as described in Section 4.0 and 5.0 of this *Modeling Review Attachment*.

The maximum modeled impact for each of the 14 modeling scenarios demonstrated compliance with the T-RACT AACC, as summarized below in Table 6. The SGP maximum concentrations were adjusted to account for the life-of-mine production limits, which affect the lifetime exposure, and to account for the elimination of Modeling Scenario W5. See Sections 5.7 and 5.8 of this *Modeling Review Attachment* for more detail. The locations of the maximum impacts for each carcinogenic TAP are presented in Figure 2. Arsenic concentrations are considerably lower in areas away from the location of maximum impact as shown in Figure 3.

Table 6. RESULTS FOR TAPS IMPACT ANALYSES FOR CARCINOGENIC TAPS.

Toxic Air Pollutant	Averaging Time	Maximum Modeled Lifetime Exposure Concentration ($\mu g/m^3$)[a,b]	Model Scenario	AACC[c] ($\mu g/m^3$)	T-RACT[d] AACC	Percent of T-RACT AACC
Arsenic	Annual	0.00095	W2	0.00023	0.0023	41.30%
Beryllium	Annual	0.00001	W1	0.0042	0.042	0.02%
Cadmium	Annual	0.000002	W1	0.00056	0.0056	0.04%
Formaldehyde	Annual	0.00007	W1	0.077	0.77	0.01%
Nickel	Annual	0.00001	W1	0.042	0.42	<0.01%

a. Micrograms per cubic meter.
b. The lifetime exposure concentrations are based on the proposed restrictions discussed in Sections 5.7 and 5.8 of this *Modeling Review Attachment*.
c. Acceptable Ambient Concentration of a Carcinogenic TAP.
d. Toxic Air Pollutant Reasonably Available Control Technology allows the AACCs to be increased by a factor of ten per *Idaho Air Rules* Section 210.12(b).

Figure 2. SGP CARCINOGENIC MAXIMUM TAP IMPACT LOCATIONS.

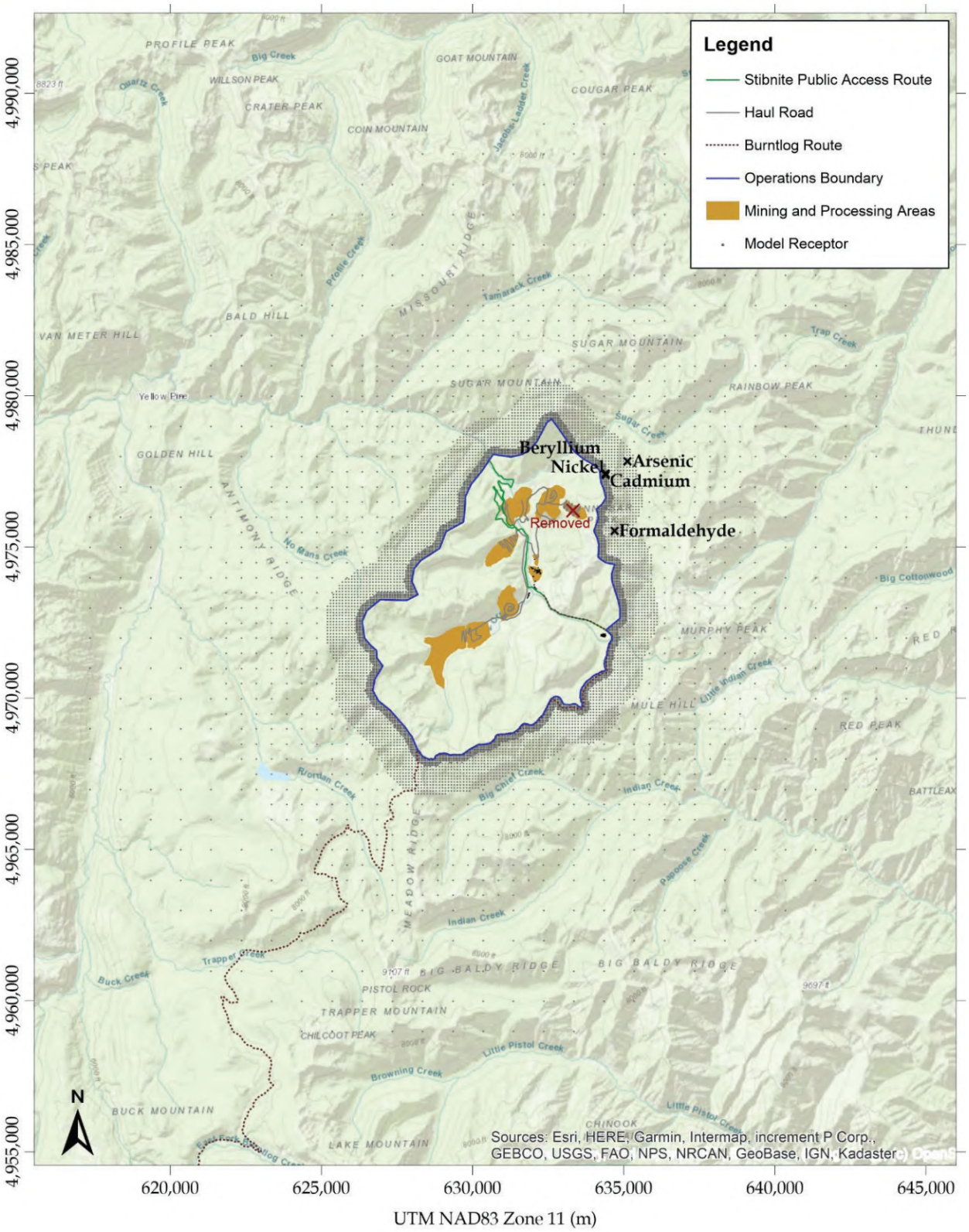
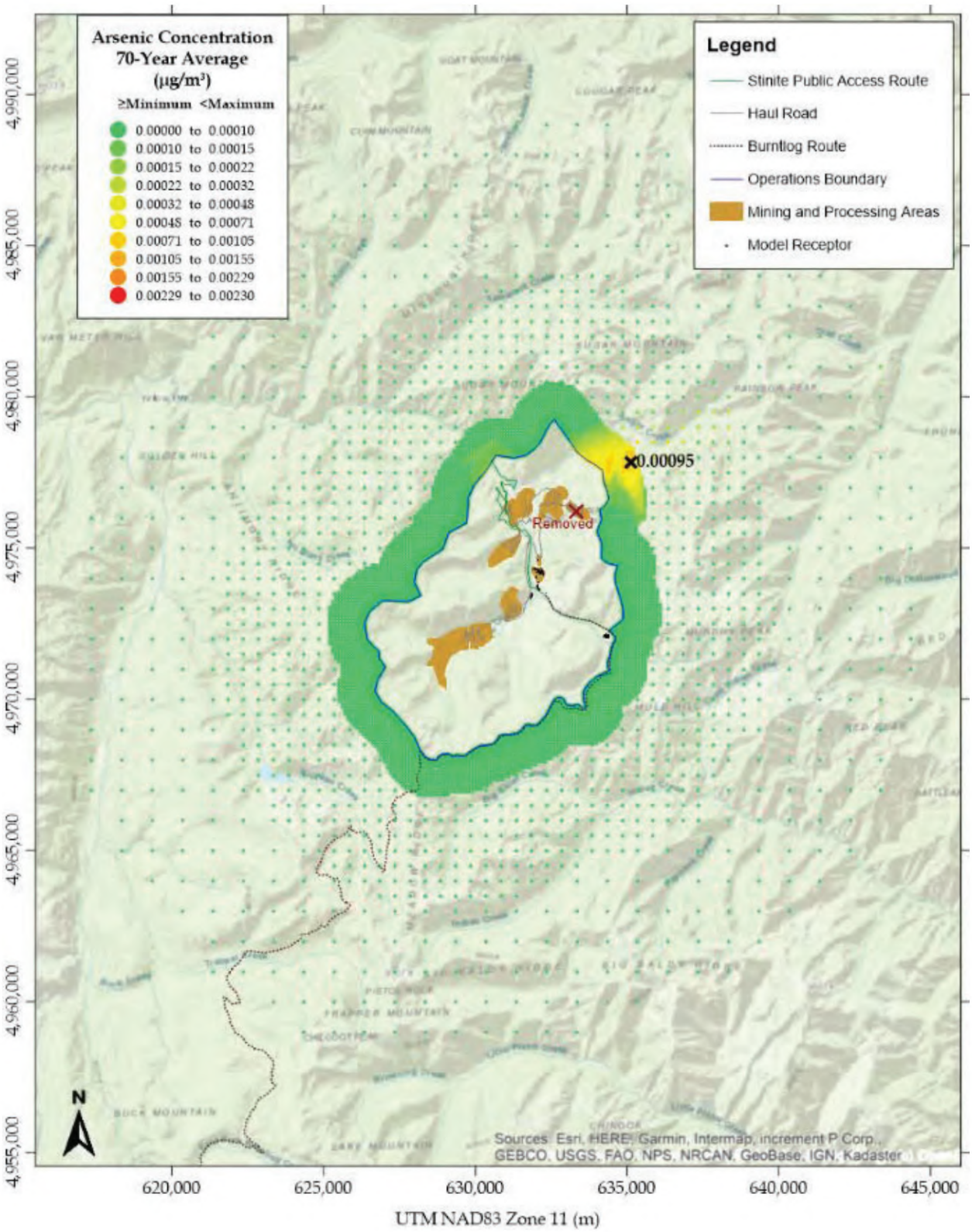


Figure 3. SGP CONTOURS OF LIFETIME ARSENIC IMPACTS.



6.2 *Effect of Changes to Modeled PM_{10} Results*

PRI has determined that the West End Development Rock Storage Facility will not be constructed. This change eliminated Modeling Scenario W5 as a potential operating scenario. In Section 4.1.4 in the main body of the DEQ *Modeling Review Memorandum*, DEQ identified PM_{10} NAAQS exceedances at four hotspot receptors when using the BULKRN meteorological dataset for Modeling Scenario W5 (the highest PM_{10} impact modeling scenario). When Modeling Scenario W5 is removed, the highest modeled impacts are predicted to occur for Modeling Scenario W3, which represents the transport of development rock from the West End Pit to the Hangar Flats Development Rock Storage Facility.

Table 7 presents results for the cumulative NAAQS impact analyses for Scenario W3. Results still exceed the 24-hour PM_{10} NAAQS even when Modeling Scenario W5 is eliminated. However, there is only one hotspot receptor exceeding NAAQS. The modeled violation is also predicted to occur during winter. This is a critical consideration because during winter, not only are fugitive emissions minimized because of the higher moisture content of material handled or driven over, but background concentrations in such remote areas are also generally much lower because of the absence of wildfires and dust-generating sources.

Table 7 also lists the results when using temporally varying backgrounds, instead of a single-value background, in the cumulative NAAQS impact analysis (using the "SEASON" and "MONTH" options in AERMOD). The highest daily average PM_{10} concentrations measured at Stibnite for every season and month in 2014 were used as inputs in the model. Table 7 shows that the SGP facility *safely* demonstrates compliance with the 24-hour PM_{10} NAAQS when temporally varying backgrounds (both seasonal and monthly) are used instead of the single-value background. Summing modeled design values with a single-value background that is on the upper end of the distribution results in a very conservative estimate of total impacts. DEQ strongly believes that using temporally varying backgrounds that respect seasonality is appropriate for the SGP facility, and that using the highest value in the period interval is very conservative.

TABLE 7. RESULTS FOR 24-HOUR PM_{10} CUMULATIVE NAAQS IMPACT ANALYSES FOR MODELING SCENARIO W3.

Backgrounds Scenario	Max. Conc.[a] ($\mu g/m^3$)[b]	Model Scenario	Back. Conc.[c] ($\mu g/m^3$)	Total Conc.[d] ($\mu g/m^3$)	NAAQS ($\mu g/m^3$)	Percent of NAAQS
Single-Value Background	116.9	W3	34.0	150.9[e]	150	100.6%
Seasonally Varying Backgrounds	123.5[f]	W3	*Seasonal*	123.5[f]		82.3%
Monthly Varying Backgrounds	123.5[f]	W3	*Monthly*	123.5[f]		82.3%

a. Max. Conc. = maximum modeled design concentration.
b. Micrograms per cubic meter.
c. Back. Conc. = background concentration.
d. Total Conc. = total (modeled + background) concentration.
e. One hotspot receptor exceeds NAAQS.
f. The maximum modeled design concentration already incorporates the seasonal and monthly background values.

The time series plot in Figure 4 and the box-and-whiskers plot in Figure 5 illustrate the variability in daily average PM_{10} concentrations collected at the Stibnite Site in 2014. Figures 4 and 5 confirm that the highest concentrations from the modeled and monitored datasets do *not* occur simultaneously. Highest modeled impacts are predicted to occur during winter while the highest background concentrations were measured at Stibnite during summer. Therefore, the summation method, where total impacts are

calculated by summing modeled design values with a background concentration that is also consistent in form with the regulatory design value, results in a very conservative estimate of the total impact for comparison to NAAQS. DEQ concludes that use of temporally varying (i.e., seasonal and monthly) backgrounds for SGP is justified. DEQ is highly confident that operation of the SGP will not cause or contribute to a violation of NAAQS.

PM_{10} and $PM_{2.5}$ NAAQS compliance was previously demonstrated prior to refinements and adjustments proposed in the submitted *TAP Addendum*. The main body of the DEQ *Modeling Review Memorandum* discussed and considered results from both modeling with meteorological data processed using the BULKRN method and modeling with data processed using cloud cover data, and DEQ concluded that NAAQS compliance was demonstrated with a high degree of confidence. The adjustments and refinements described in the *TAP Addendum* further increase DEQ's confidence in NAAQS compliance.

Figure 4. TIME SERIES OF DAILY AVERAGE PM_{10} CONCENTRATIONS MEASURED AT STIBNITE IN 2014.

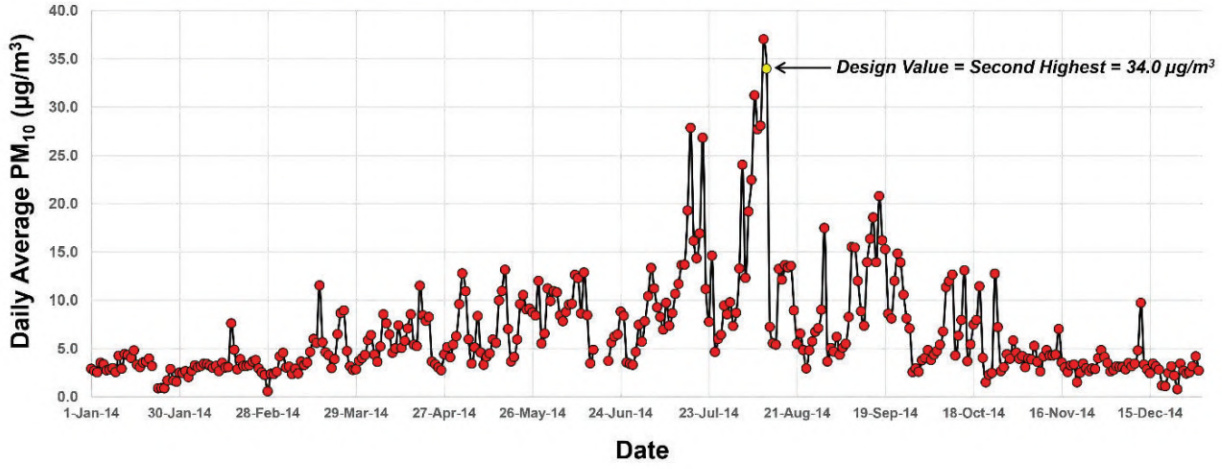
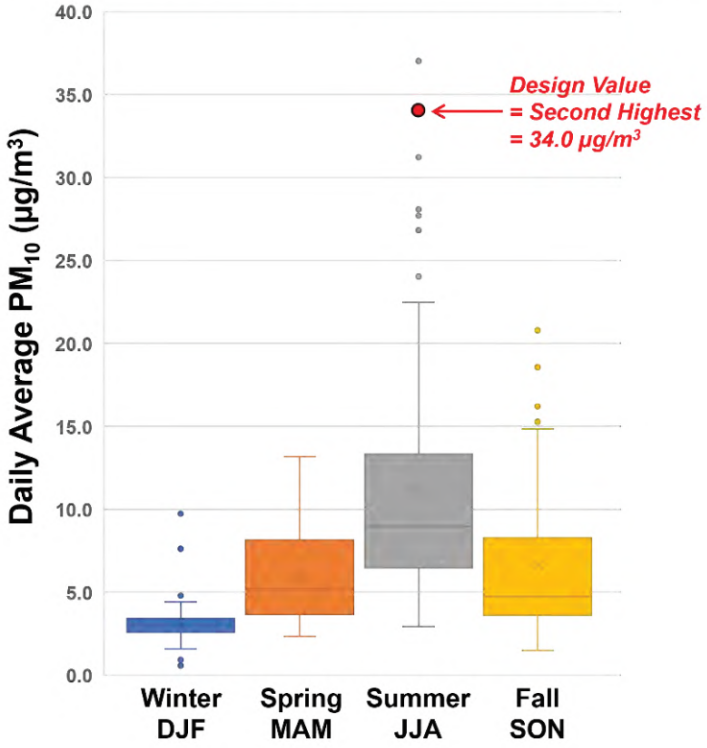


Figure 5. BOX-AND-WHISKERS PLOT FOR SEASONAL PM_{10} BACKGROUND CONCENTRATIONS MEASURED AT STIBNITE IN 2014.



In Figure 5 the middle line of each box represents the median. The "x" in the box represents the mean. The bottom and the top lines of the box represent the 1st quartile (25th percentile) and the 3rd quartile (75th percentile), respectively. The whiskers extend to the minimum and maximum values not considered outliers. Outliers are plotted individually.

7.0 Conclusions

This section provides conclusions of the *TAP Addendum* and DEQ's review of the *TAP Addendum*.

7.1 Conclusions of Revised TAP Analyses

The revised and refined TAP analyses:

- Revised TAP-applicable sources at the SGP facility.
- Proposed additional emission control measure and adjusted operations to reduce TAP emissions.
- Refined the approach used to demonstrate compliance with TAP regulations.

The submitted application, with the adjustments and refinements to analyses as described in the *TAP Addendum*, demonstrated to DEQ's satisfaction that the emissions of applicable TAPs will not result in impacts to ambient air that exceed TAP increments of *Idaho Air Rules* Section 585 and 586.

7.2 Effects of Adjustments/Revisions on NAAQS Compliance Demonstrations

The submitted application, prior to the *TAP Addendum*, demonstrated compliance with NAAQS to DEQ's satisfaction; and the operational measures proposed in the *TAP Addendum* will only further reduce estimated emissions. Eliminating Modeling Scenario W5 impacts, with the elimination of the West End Development Rock Storage Facility, affects the 24-hour PM_{10} impact modeling analysis for SGP. Modeling Scenario W3 is now the scenario producing the highest modeled impacts, and NAAQS compliance is easily demonstrated when using temporally varying background PM_{10} values, which were obtained from onsite monitoring data.

7.3 Conservatism of Permitting Analyses

Emissions and locations from which emissions occur are highly dynamic at mining facilities. This presents unique challenges for permit development because permits must include limits and operational requirements that ensure air quality standards are not violated. Permitting rules require that air impacts be assessed using maximum potential emissions as limited by either the capacity of the unit/operation or as limited by enforceable permit provisions. A permit where actual emissions are nearly representative of maximum allowable emissions, through imposing permit limits, would be exceedingly complex and require overly burdensome monitoring and record-keeping requirements. To avoid this, applicants typically calculate allowable emissions and perform impact analyses based on simplistic operational scenarios that largely overstate emissions estimated to occur from the facility.

PRI and Air Sciences have asserted that the submitted emission estimates, operational scenarios, and air impact analyses associated with the permit application greatly overstate best-estimated values. This point is evident when comparing the permit application materials and analyses with those presented in ModPRO2, PRI's revised mine plan and associated impacts. ModPRO2 is used in support of the Environmental Impact Statement (EIS).

Reference

Perpetua. 2021. "ModPRO2 Mine Plan." *File: Midas Stibnite Mine Plan and Equipment Schedule (10Feb21).xlsx.* Email from R. McCluskey, Perpetua Resources Inc., to E. Memon, Air Sciences Inc., February 11.

EXHIBIT B

order to effectively implement 161, the department developed a policy that set emission limits for certain toxic air pollutants. Idaho industry requested that the policy be implemented in rule (instead of a policy) to provide greater certainty and transparency for industry. Through many discussions with industry and the public, a rule was developed that was responsibly protective of environmental quality while being reasonably permissive of industrial activity. As noted in Section 203.03, by complying with the TAPs rules developed in sections 210, 585 and 586, a facility adequately demonstrated compliance with 161.

Because TAPs are generally known to be hazardous to human health (EPA 1991), the federal government also implemented rules to control emissions of TAPs through National Emission Standards for Hazardous Air Pollutants (NESHAPs). EPA first tried to implement risk based standards according to the Clean Air Act (CAA) amendments of 1970. Between 1970 and 1990, EPA was only able to implement standards for 8 pollutants (asbestos, benzene, beryllium, coke oven emissions, inorganic arsenic, mercury, radionuclides, and vinyl chloride). Because of EPA's inability to address air toxics in a timely and efficient manner, Congress revised the CAA in 1990 to develop a program to control a list of hazardous air pollutants (HAPs) through technology standards for specific industries. Congress itself developed the list of 188 HAPs. They also prescribed maximum achievable control (MACT) standards for large (major) sources of HAPs and generally achievable control technology (GACT) standards for smaller (area) sources. The area source NESHAPs also only focused on a subset of 30 HAPs that were identified as being the most problematic in urban areas. Congress's intent was to address the major risks associated with TAPs by focusing on the most toxic pollutants and most significant source categories. The original list of 188 HAPs was based on the list of pollutants subject to the Emergency Planning and Community Right-to-Know Act (EPCRA). After the HAPs list was created in the early 1990's, the list of pollutants subject to EPCRA has doubled, while the list of HAPs has remained essentially unchanged.

The Idaho TAPs rules were developed to complement the federal NESHAPs, thus the rules are not more stringent than federal law. IDAPA 58.01.01.210.20 specifically states that if a facility is subject to a federal NESHAP, they have met the requirements of our state air toxics rules. These rules do regulate an activity not regulated by the federal government. They are a uniquely Idaho solution of addressing air toxics emissions. An argument could be made that the rules are broader in scope than federal law, as they do regulate an activity not regulated by federal law.

(2) To the degree that a department action is based on science, in proposing any rule or portions of any rule subject to this section, the department shall utilize:

(a) The best available peer reviewed science and supporting studies conducted in accordance with sound and objective scientific practices; and

The Idaho TAPs rules were developed to protect public health by developing risk based standards that would apply to new or modified industrial sources only. There are two lists of pollutants that facilities need to consider, but only if the facility is not subject to a federal air toxics standard.

The first list of pollutants are non-carcinogens (do not cause cancer) in IDAPA 58.01.01.585. They may cause adverse health effects based on short term (24-hour) exposures. Examples include methyl isocyanate, chlorine, cyanide and xylene. The acceptable ambient levels for non-carcinogens are based on occupational exposure levels from the American Conference of Government Industrial Hygienists (ACGIH) threshold limit values (TLV). (ACGIH 2019). The TLV is typically an 8 hour time weighted average concentration and it is the concentration to which workers may be repeatedly exposed during a 40 hour work week without adverse effect. Two safety factors were applied to the TLV value: 1) to extrapolate the 8 hour exposure level to a 24 hour public exposure, and 2) to extrapolate from the relatively healthy mostly male working population to a general population that included women, children and the elderly. Thus the TAP increment values are 1/20th the TLV values.

Because ambient monitoring values can sometimes be difficult to determine, the department also developed stack emission screening levels (ELs) for easier analysis (in pounds/hour). These were based on a conservative stack modeling analysis.

The second list of pollutants are carcinogens (i.e., have been determined to cause cancer over a lifetime of exposure) in IDAPA 58.01.01.586. Examples include formaldehyde, benzene, and polycyclic aromatic hydrocarbons. The acceptable ambient levels for carcinogens are based on the cancer unit risk values from the Environmental Protection Agency and correspond to a one in a million cancer risk. (EPA 2019). An EL was also determined for

Exhibit C:

EPA's Regional Screening Levels Calculator Inputs and Outputs for Exposure Durations: 16, and 70 years

Site-specific
Resident Air Inputs

Variable	Resident Air Default Value	Site-Specific Value
ED_{res} (exposure duration) years	26	16
ED_{0-2} (mutagenic exposure duration first phase) years	2	2
ED_{2-6} (mutagenic exposure duration second phase) years	4	4
ED_{6-16} (mutagenic exposure duration third phase) years	10	10
ED_{16-26} (mutagenic exposure duration fourth phase) years	10	10
EF_{res} (exposure frequency) days/year	350	365
EF_{0-2} (mutagenic exposure frequency first phase) days/year	350	350
EF_{2-6} (mutagenic exposure frequency second phase) days/year	350	350
EF_{6-16} (mutagenic exposure frequency third phase) days/year	350	350
EF_{16-26} (mutagenic exposure frequency fourth phase) days/year	350	350
ET_{res} (exposure time) hours/day	24	24
ET_{0-2} (mutagenic exposure time first phase) hours/day	24	24
ET_{2-6} (mutagenic exposure time second phase) hours/day	24	24
ET_{6-16} (mutagenic exposure time third phase) hours/day	24	24
ET_{16-26} (mutagenic exposure time fourth phase) hours/day	24	24
THQ (target hazard quotient) unitless	0.1	1
LT (lifetime) years	70	70
TR (target risk) unitless	1.0E-06	1.0E-06

Site-specific

Resident Risk-Based Regional Screening Levels (RSL) for Air

Key: I = IRIS; P = PPRTV; O = OPP; A = ATSDR; T = ATSDR DRAFT; C = Cal EPA; X = PPRTV Screening Level; H = HEAST; D = OW; R = ORD; N = WI; W = TEF applied; E = RPF applied; G = see user guide; U = user provided; ca = cancer; nc = noncancer; * = where: nc SL < 100X ca SL; ** = where nc SL < 10X ca SL; SSL values are based on DAF=1; max = ceiling limit exceeded; sat = Csat exceeded.

Chemical	CAS Number	Mutagen?	Volatile?	Chemical Type	IUR (ug/m^3)$^{-1}$	IUR Ref	RfC (mg/m^3)	RfC Ref	Carcinogenic SL TR=1E-06 (ug/m^3)	Noncarcinogenic SL THI=1 (ug or fibers/m^3)	Screening Level (ug or fibers/m^3)
Arsenic, Inorganic	7440-38-2	No	No	Inorganics	4.30E-03	I	1.50E-05	C	1.02E-03	1.50E-02	1.02E-03 ca*

Site-specific
Resident Risk for Air

Chemical	IUR $(ug/m^3)^{-1}$	IUR Ref	RfC (mg/m^3)	RfC Ref	Concentration (ug or fibers/m^3)	Carcinogenic Risk	Noncarcinogenic HI
Arsenic, Inorganic	4.30E-03	I	1.50E-05	C	4.16E-03	4.09E-06	2.77E-01
**Total Risk/HI*	-		-		-	*4.09E-06*	*2.77E-01*

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Site-specific
Resident Air Inputs

Variable	Resident Air Default Value	Site-Specific Value
ED_{res} (exposure duration) years	26	70
ED_{0-2} (mutagenic exposure duration first phase) years	2	2
ED_{2-6} (mutagenic exposure duration second phase) years	4	4
ED_{6-16} (mutagenic exposure duration third phase) years	10	10
ED_{16-26} (mutagenic exposure duration fourth phase) years	10	10
EF_{res} (exposure frequency) days/year	350	365
EF_{0-2} (mutagenic exposure frequency first phase) days/year	350	350
EF_{2-6} (mutagenic exposure frequency second phase) days/year	350	350
EF_{6-16} (mutagenic exposure frequency third phase) days/year	350	350
EF_{16-26} (mutagenic exposure frequency fourth phase) days/year	350	350
ET_{res} (exposure time) hours/day	24	24
ET_{0-2} (mutagenic exposure time first phase) hours/day	24	24
ET_{2-6} (mutagenic exposure time second phase) hours/day	24	24
ET_{6-16} (mutagenic exposure time third phase) hours/day	24	24
ET_{16-26} (mutagenic exposure time fourth phase) hours/day	24	24
THQ (target hazard quotient) unitless	0.1	1
LT (lifetime) years	70	70
TR (target risk) unitless	1.0E-06	1.0E-06

Site-specific

Resident Risk-Based Regional Screening Levels (RSL) for Air

Key: I = IRIS; P = PPRTV; O = OPP; A = ATSDR; T = ATSDR DRAFT; C = Cal EPA; X = PPRTV Screening Level; H = HEAST; D = OW; R = ORD; N = WI; W = TEF applied; E = RPF applied; G = see user guide; U = user provided; ca = cancer; nc = noncancer; * = where: nc SL < 100X ca SL; ** = where nc SL < 10X ca SL; SSL values are based on DAF=1; max = ceiling limit exceeded; sat = Csat exceeded.

Chemical	CAS Number	Mutagen?	Volatile?	Chemical Type	IUR (ug/m^3)$^{-1}$	IUR Ref	RfC (mg/m^3)	RfC Ref	Carcinogenic SL TR=1E-06 (ug/m^3)	Noncarcinogenic SL THI=1 (ug or $fibers/m^3$)	Screening Level (ug or $fibers/m^3$)
Arsenic, Inorganic	7440-38-2	No	No	Inorganics	4.30E-03	I	1.50E-05	C	2.33E-04	1.50E-02	2.33E-04 ca*

Site-specific
Resident Risk for Air

Chemical	IUR $(ug/m^3)^{-1}$	IUR Ref	RfC (mg/m^3)	RfC Ref	Concentration (ug or fibers/m^3)	Carcinogenic Risk	Noncarcinogenic HI
Arsenic, Inorganic	4.30E-03	I	1.50E-05	C	4.16E-03	1.79E-05	2.77E-01
**Total Risk/HI*	-		-		-	*1.79E-05*	*2.77E-01*

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Attorneys for Perpetua Resources Idaho, Inc.

BEFORE THE BOARD OF ENVIRONMENTAL QUALITY
STATE OF IDAHO

IN THE MATTER OF AIR QUALITY PERMIT TO CONSTRUCT P-2019.0047

NEZ PERCE TRIBE, IDAHO CONSERVATION LEAGUE, and SAVE THE SOUTH FORK SALMON,

Petitioner,

v.

IDAHO DEPARTMENT OF ENVIRONMENTAL QUALITY,

Respondent,

and

PERPETUA RESOURCES IDAHO, INC.

Intervenor-Respondent.

Case Docket No. 0101-22-01
OAH Case No. 23-245-01

EXPERT DECLARATION OF KEVIN LEWIS

PERPETUA RESOURCES EXHIBIT
200

I, Kevin Lewis, hereby declare and affirm as follows:

1. I am currently a Principal Air Quality Engineer at Air Sciences Inc. (Air Sciences). I have prepared this declaration in support of the Permit to Construct (PTC) issued for the Stibnite Gold Project (SGP) on June 17, 2022. Perpetua Resources Idaho, Inc. (Perpetua) received the PTC that was challenged in this proceeding, Case Docket No. 0101-22-01; OAH Case No. 23-245-01.

A. Qualifications and Experience

2. I earned a Bachelor of Science (BS) degree in Chemical Engineering from the University of Wisconsin, Madison, in 1990.

3. From 1990 to 1992, I worked at the Wisconsin Department of Natural Resources, where I wrote air quality permits for toxic pollutants and conducted compliance inspections.

4. In 1993, I joined Air Sciences, became an owner in 1996, and served as President from 2011 to 2021. Air Sciences is a consulting firm specializing in ambient air quality analyses, permitting, and compliance.

5. With over 33 years of experience in air quality, I have conducted air quality analyses for permits across more than 25 states and internationally. At Air Sciences, I focus primarily on air permitting for the gold mining industry. In collaboration with the Nevada Mining Association and the U.S. Environmental Protection Agency (EPA), I compiled, analyzed, and summarized technical data to help develop the National Emissions Standard for Hazardous Air Pollutants (NESHAP): Gold Mine Ore Processing and Production Area Source Category rules under 40 CFR Part 63, Subpart EEEEEEE, which applies to the SGP.

6. During my time at Air Sciences, I developed air quality analyses for hundreds of air permits, renewals, and modifications. I also provided technical support to state agencies throughout the technical review, permit drafting, and public comment phases.

7. I led the modeling and permit development for Perpetua, ensuring compliance with ambient air quality standards while achieving project objectives. This included using reliable emissions data and appropriate modeling techniques to reflect permit conditions.

8. I began working with Perpetua as an air quality consultant in 2017, and I continue to provide consultancy services to this day.

B. Scope of Review

9. I reviewed the in the *Final Order* issued by the Board of Environmental Quality (Board) on May 9, 2024 in the Matter of Air Quality Permit to Construct P-2019.0047 (Final Order), which remanded "this matter back for the development of further evidence regarding ambient air concentrations of arsenic that will be produced by the SGP and whether those levels comply with the Air Rules." Final Order at 23. Based on my review of the Final Order the Board found the following issues to be addressed on remand:

a. DEQ did not act reasonably in using a five-year rolling average for T-RACT that was not properly supported by permit conditions.

b. There was insufficient evidence to support the T-RACT analysis limiting the non-West End pit production limit.

c. DEQ did not act reasonably and in accordance with law when it applied the 16/70 calculation to the ambient arsenic air concentration analysis.

10. I will address items (a), (b) and (c) in this declaration.

C. Documents Reviewed

11. I have reviewed the permitting record in this case, the expert declarations of Theresa Lopez, Norka Paden, and Kevin Schilling, and documents referenced below and attached as an exhibit to this declaration.

D. Summary of Opinions

12. Based on my expertise and multi-state permitting experiences:

a. DEQ properly established a five-year rolling average compliance demonstration in the PTC for ambient arsenic concentrations from the SGP.

b. DEQ sufficiently supported the permitting for the non-West End Pit activities.

c. DEQ correctly applied the provisions of IDAPA[1] 586 to perform an "apples to apples" toxic air pollutant (TAP) risk evaluation using an adjusted arsenic concentration and exposure duration to compare to the T-RACT Acceptable Ambient Concentration for Carcinogens (AACC).

Following rigorous analyses of Perpetua's application, as well as addressing repeated comments from stakeholders, DEQ prepared a thorough and conservative record in support of the PTC.

E. General Permitting and Modeling Context

13. With over thirty years of experience as an air permit consultant, including the development and review of hundreds of permits, I have identified two key objectives in the permitting process:

a. The permittee must submit a thorough and complete permit application.

[1] The Rules for the Control of Air Pollution in Idaho (Air Rules), IDAPA 58.01.01, provide for the control of air pollution in Idaho and govern issuance of air quality permits, including permits to construct. For brevity, citations to the Air Rules are abbreviated "IDAPA," followed by the specific section of IDAPA 58.01.01.

b. The permitting agency must issue a permit that includes operating restrictions and monitoring requirements to ensure compliance with air quality regulations.

14. Integral to these objectives is the creation of accurate emissions data and modeling to support compliance with ambient air quality standards.

15. To obtain a permit in Idaho, an applicant must satisfy for DEQ that the proposal will comply with all applicable state or federal emission standards, will not cause or contribute to a violation of the National Ambient Air Quality Standards, and using the methods provided in IDAPA 210, the emissions of toxic air pollutants will not injure or unreasonably affect human or animal life or vegetation as required by IDAPA 161. IDAPA 202.01, 202.02, 202.03.

16. Compliance with all applicable toxic air pollutant carcinogenic increments demonstrates preconstruction compliance with IDAPA 161 with regards to the pollutants listed in IDAPA 586: the Ambient Air Concentrations for Carcinogenic increments. IDAPA 202.03.

17. Modeling is necessary to meet the requirements of IDAPA 202.02 and 202.03. Specifically, the project proponent must determine the ambient concentrations of relevant toxic air pollutants from the project and compare these concentrations to the AACC.

18. Perpetua and DEQ took a conservative approach throughout the process of demonstrating compliance with IDAPA 202. Specifically, the analyses included arsenic emissions from fugitive dust related to mining activities. This is significant because fugitive dust is the primary source of arsenic emissions from the project. Furthermore, fugitive dust emissions of arsenic are "addressed" by NESHAP Subpart EEEEEEE and therefore would normally be

excluded from the analysis per IDAPA 210.20. *See* Statement of Basis, Permit to Construct No. P-2019.0047 at 28 (Feb. 18, 2021) (Proposed for Public Comment).[2]

19. Modeling of arsenic emissions from the SGP to comply with the Air Rules included fugitive dust from mining activities and involved the following steps: (1) quantifying annual arsenic emissions from all sources while accounting for process scenarios and emission control measures, (2) inputting the emissions data, emission locations, and initial dispersion parameters into the model, and (3) running the model with one year of onsite meteorological data to determine the annual average concentration at specific receptors located at and beyond the ambient air boundary.

20. The results of the modeling performed by Air Sciences and DEQ contain multiple layers of conservatism.

21. First, the model itself is conservative. EPA's evaluation studies for the type of modeling conducted for the SGP showed that the model, specifically AERMOD, over predicts pollutant concentrations by 1.41 to 3.21 times. REC 1834

22. Second, the quantification of arsenic emissions from the SGP was conservative. For haul road dust, the largest source of arsenic emissions, we used the higher of the two published emission factors in the emissions calculations. The emission factor used is five times greater than the lower factor. REC 1834

23. Third, the control and reduction in arsenic emissions from haul road dust was calculated conservatively. We used a control efficiency of 90% for chemical suppressants; the actual range is 90-99%. We also used a control efficiency of 33% for watering dust; the actual range is 75-95%. REC 1834

[2] The 2021 Statement of Basis, along with selected appendices, is attached hereto as Attachment 1.

24. Finally, we conducted fourteen modeling scenarios, each using conservative process and operating assumptions. Each scenario assumed mining activity in a single deposit and hauling to a single location year-round at the maximum permitted production level to maximize predicted arsenic impacts. Actual operation will be more varied in location and rates resulting in significantly lower arsenic impacts.

25. These analyses led to predicted arsenic impacts that are one to two orders of magnitude higher than the actual impacts will be.

26. In my experience, applying multiple layers of conservatism in the permitting review process is standard practice across all air quality permitting agencies, and DEQ's process is no exception. The goal is always to ensure compliance with air quality regulations under all circumstances.

27. DEQ also provided extra opportunities for public involvement. DEQ provided the most robust opportunity for public participation in the SGP permitting process that I've encountered in my 33 years of permitting experience. DEQ afforded commenters unprecedented accommodations that responded to public input. All comments, suggestions, and challenges were thoroughly reviewed. DEQ addressed each comment and, in some instances, conducted additional, more conservative analyses in response to the comments submitted.

F. Opinions

The IDAPA 586 AACC Annual Averaging Period is Not the Compliance Period.

28. As an expert on the relationship between air quality regulations and air quality modeling, I have a comprehensive understanding of the meaning and purpose of IDAPA 586 that reads "The AACC in this section are annual averages."

29. This text led the Board to infer that "the rule specifies compliance on an annual basis." Final Order at 19. This inference incorrectly conflates the AACC *averaging period* specified in IDAPA 586 with the *compliance period* described in IDAPA 006.125.[3]

30. Regulations often differentiate between the averaging period and the compliance period for health-based air contaminant concentration standards, especially when assessing long-term health risks.[4]

31. Treatment of the AACC as requiring compliance on an annual basis introduces an improper compliance period into IDAPA 586 and overlooks the adopted rules defining the methods and EPA scientific principles for determining cancer risk probability.

32. Within the full context of IDAPA 586, "The AACC in this section are annual averages" describes the annual average concentration that will result in a 1-in-1,000,000 excess cancer risk probability assuming constant lifetime exposure (70 years) to that concentration of ambient air emissions.

33. The AACC values listed in IDAPA 586 encompass three components:

a. The ***annual average*** concentration (0.00023 µg/m³ for arsenic) that correlates to

b. The ***1-in-1,000,000*** cancer risk probability as defined by the URF in IDAPA 586 over

c. A ***70-year*** exposure duration or compliance period per IDAPA 006.125.

---

[3] Definition from Air Rules in effect during the PTC application review: "**Toxic Air Pollutant Carcinogenic Increments**. Those ambient air quality increments based on the probability of developing excess cancers over a seventy (70) year lifetime exposure to one (1) microgram per cubic meter (1 ug/m3) of a given carcinogen and expressed in terms of a screening emission level or an acceptable ambient concentration for a carcinogenic toxic air pollutant. They are listed in Section 586."

[4] For example, the new $PM_{2.5}$ National Ambient Air Quality Standard of 9.0 µg/m³ specifies an averaging period as the "annual arithmetic mean" (or annual average) per 40 CFR 50.20(a), while the compliance period is defined as a three-year average according to 40 CFR Part 50, Appendix N. *See* 89 Fed. Reg. 16202, 16203 (Mar. 6, 2024).

34. Neglecting any of these components when assessing the cancer risk probability, such as the 70-year exposure duration, not only conflicts with the rule, but fundamentally alters the rule itself and ignores the EPA scientific principles underlying the rule.

35. When comparing modeling results to the AACC values listed in IDAPA 586, all three components must align for a correct comparison:

a. The model output must be expressed as an ***annual average*** in $\mu g/m^3$;

b. The target cancer risk probability must be ***1-in-1,000,000;*** and

c. The exposure duration must occur or be permitted to occur over a ***70-year*** period.

36. The Final Order's statement that "the rule specifies compliance on an annual basis," Final Order at 19, rewrites one of the three essential components of the AACC, namely the exposure duration. Under the Board's interpretation, a project with a 5-year operational permit limit would pose the same risk as a project without a limit. Limiting the exposure duration reduces the cancer risk, as demonstrated by the EPA's risk calculation methods. Declaration of Norka Paden (Paden Decl.) ¶¶ 4, 13.

37. If the project proposal includes a different actual exposure duration that is less than the 70-year lifetime default or the project proposal includes a different target risk (like the 1-in-100,000 T-RACT), then either the model output concentration, the AACC itself, or both must be adjusted according to EPA's methods to ensure all components align.

38. Adjustment for actual project facts is necessary for a correct assessment of cancer risk. Failing to adjust components of the AACC is inconsistent with the rule and contrary to the EPA scientific principles upon which the rule is based.

DEQ Properly Established a Five-Year Rolling Average Compliance Demonstration Period.

39. The IDAPA 586 "annual average" does not represent the compliance period for project emissions; it represents the annual average concentration of emissions that presents a 1-in-1,000,000 (or 1-in-100,000 T-RACT) cancer risk probability assuming constant exposure over a 70-year lifetime.

40. The Final Order stated that "there was no evidence in the record explaining how the five-year rolling average comports with the annual AACC limits." This conclusion conflated the averaging period specified in IDAPA 586 with the notion of a compliance period.

41. The AACC value is defined as a lifetime of exposure, specifically 70 years. This means that cumulative exposure over this 70-year period must not exceed levels that would result in a cancer risk probability of 1-in-1,000,000, or 1-in-100,000 for T-RACT sources.

42. DEQ imposed a daily production limit of 135,000 tons per day (T/day) because production generates arsenic emissions (primarily from fugitive dust emissions). Limiting production proportionally reduces arsenic emissions, concentrations and exposure.

43. DEQ correctly established a compliance demonstration period of 5 years for the 135,000-T/day limit using a 5-year rolling average. The 5-year rolling average represents a more conservative (shorter) timeframe than the exposure duration of 70 years inherent in the AACC. The 5-year rolling average is also a more conservative (shorter) timeframe than the T-RACT AACC exposure duration for the SGP of 16 years.

44. A five-year rolling average production limit in Permit Condition 3.5 is appropriate because "any permit limits must only assure that concentrations in ambient air over the total duration of the project do not cause a potential exposure concentration associated with a 1-in

1,000,000 [AACC] or a 1-in-100,000 [T-RACT] cancer risk." Declaration of Kevin Schilling (Schilling Decl.) ¶ 25.

45. The Board asserted that a "five-year rolling average allows considerable daily and annual increases in exposures which are contrary to limits set forth in the Air Rules." As explained by Theresa Lopez in her Declaration, the T-RACT AACC represents the lifetime probability of cancer risk from a ***cumulative*** dose of arsenic over a specific period of exposure. During the 16-year SGP project life, the ***cumulative*** dose is unaffected by variability in exposures (daily or annual) that may occur over the 5-year averaging period. In addition, Kevin Schilling states, "any daily and annual variability is inconsequential to the exposure concentration and resulting risk." Schilling Decl. ¶ 26.

46. The notion that the Air Rules prohibit daily variability in exposure, and therefore, a daily production limit with a daily compliance demonstration is needed to protect public health, is inaccurate. Limiting daily production activity does not eliminate exposure variability. The modeled output emissions concentration is inherently variable due to a multitude of factors unrelated to production and emissions. For example, for a given day when the wind blows from northeast to southwest, the predicted concentration (and exposure) at the northeast side of the ambient air boundary will be zero, regardless of the production and emissions.

DEQ Sufficiently Justified the Permitting for the Non-West End Pit Activities.

47. The permit imposes a total mining production limit of 788.4 million tons for the life of the project (Permit Condition 3.6). This limit applies to the aggregate amount of mining from all deposits, whether from a single deposit or a combination of deposits, ensuring that the total does not exceed 788.4 million tons over the life of the mine.

48. During permit development, Air Sciences performed 14 different model runs reflecting 14 different operating scenarios to assess arsenic concentrations based on production activity from each of the deposits individually

49. The modeling analysis for arsenic emissions from the Non-West End Pit (non-WEP) deposit scenarios demonstrated that mining activities at the non-WEP deposits result in ambient arsenic concentrations at or below the T-RACT adjusted AACC, even when the full 788.4 million tons of production comes from any one of those deposits. Schilling Decl. ¶¶ 28, 30.

50. The modeling analyses for arsenic emissions from the West End Pit (WEP) deposit scenarios resulted in proportionally higher impacts. This is attributed to the WEP's proximity to the northeastern ambient air boundary and prevailing wind patterns, as illustrated in Figure 1, attached as Exhibit A.

51. To address these elevated arsenic impacts associated with mining at the WEP, DEQ imposed an additional specific production limit for WEP activity. The limit is set at 394.2 million tons over the life of the project (Permit Condition 3.6), which represents 50% of the total mining production limit of 788.4 million tons.

52. Two life-of-mine production limits effectively constrain operations as follows:

a. Total mining from WEP and non-WEP locations cannot exceed 788.4 million tons.

b. Mining at the WEP cannot exceed 394.2 million tons.

c. Mining at non-WEP locations cannot exceed 788.4 million tons minus any mining at the WEP.

53. These restrictions work together as follows: A + B = C, where A represents WEP mining, B represents non-WEP mining, and C represents total mining. There is no need to

establish another limit for non-WEP mining because B can only be the difference between the total (788.4 million) and the volume from the WEP (limited to 394.2 million) as set forth in Permit Condition 3.6. Imposing an additional production limit for non-WEP activity would not offer any further protection of public health or the environment.

DEQ Correctly Applied the Permit Conditions Limiting the Project Life to 16 Years to the Analysis of Compliance with the T-RACT AACC

54. Based on my extensive multi-state permitting experience, DEQ's interpretation and analyses of the cancer risk associated with arsenic from the SGP followed sound permitting practices and scientific methods for TAPs evaluations.

55. In specific, DEQ correctly interpreted that "annual average" referred to in IDAPA 586 is simply the output of the air dispersion model that will result in a **1-in-1,000,000** excess cancer risk probability assuming the emissions impact will occur ***each year for 70 years***. Schilling Decl. ¶ 20.

56. The air dispersion model, specifically EPA's AERMOD, predicts ambient air concentrations as annual averages. For assessing long-term health impacts, such cancer risk probability (the AACC), the annual average output from the model serves as the default long-term averaging period. Defining the AACC as "annual averages" is consistent with the model's output and informs the compliance demonstration. It does not negate the other components of the AACC essential to properly assessing the cancer risk from the project's arsenic emissions.

57. Again, the AACC values in IDAPA 586 encompass three components: (1) the annual average concentration (0.00023 $\mu g/m^3$ for arsenic), (2) a cancer risk probability of 1-in-1,000,000, and (3) a 70-year exposure duration. For a proper comparison of modeling results all three components must align.

58. The annual average output concentration from the model can only be compared directly to AACC values in IDAPA 586 under the following conditions: 1) a target risk of ***1-in-1,000,000*** and 2) an emissions impact duration (or exposure duration) of ***70 years***. If one or both conditions are adjusted, then an adjustment to either the AACC and/or the annual average model output concentration must also be made for an "apple-to-apples" comparison.

59. For example, the annual average concentration for a 5-year project cannot be compared to the listed AACC because the exposure durations differ: five (5) years for the actual project and 70 years for the listed AACC. This example is found in IDAPA 210.15. To adjust for exposure duration, the example found in IDAPA 210.15 prompts the AACC to be multiplied by 10 to adjust for the shorter duration of the project. See Schilling Decl. ¶ 19.

60. DEQ properly applied these principles in the arsenic analysis for the SGP. The listed AACC was adjusted in accordance with IDAPA 210.12 to reflect the permit conditions establishing T-RACT. Per IDAPA 210.12 the AACC was multiplied by 10 to represent a risk of ***1-in-100,000*** for an emissions impact duration of ***70 years***; this is the T-RACT AACC. Then the annual average output concentration from the model was adjusted for the life-of-mine permit condition to reflect a 16-year exposure duration. This is shown mathematically by multiplying the modeled concentration by 16/70. This adjustment represents the equivalent modeled concentration over a 70-year period, known as the Exposure Concentration (EC). Detailed explanations are provided in the declarations of Norka Paden (¶¶ 4, 13) and Kevin Schilling (¶¶ 6.c, 18, 20).

61. With the AACC adjusted to the T-RACT AACC and the modeled annual average concentration adjusted to the EC, DEQ established a scientifically appropriate comparison to

determine acceptable risk. If the EC is less than the T-RACT AACC, as in the case of the SGP, then the risk of the project is less than ***1-in-100,000***.

62. As described in the declarations of Kevin Schilling and Norka Paden, DEQ applied these adjustments properly in their analyses of the SGP arsenic emissions impacts. Not applying these adjustments would be contrary to DEQ's toxic air pollutant rule and contrary to EPA's scientific approach and risk factors used for calculating excess risk probability adopted by the rule.

I declare under penalty of perjury under the laws of the United States that the foregoing is true and correct to the best of my knowledge, information, and belief.

DATED: August 30, 2024.

Kevin Lewis, Air Sciences Inc.

CERTIFICATE OF SERVICE

I hereby certify that on August 30, 2024, a true and correct copy of the **EXPERT DECLARATION OF KEVIN LEWIS** was served on the following:

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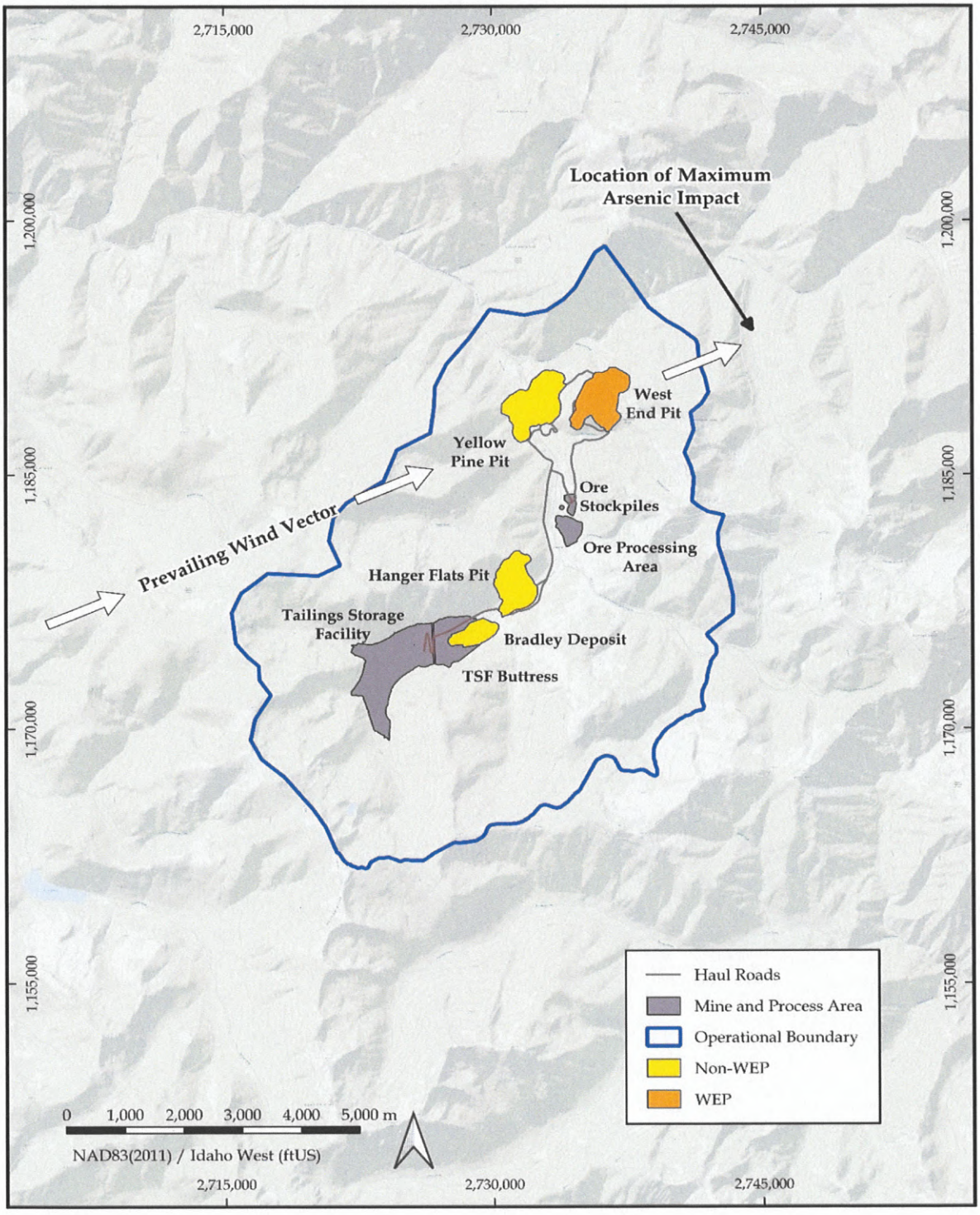
EXHIBIT A
Figure 1. Location of Maximum Arsenic Impacts



Attachment 1

Attachment 1

Statement of Basis

Permit to Construct No. P-2019.0047
Project ID 62288

Midas Gold Idaho, Inc.
Stibnite, Idaho

Facility ID 085-00011

Proposed for Public Comment

February 18, 2021
Morrie Lewis
Permit Writer

The purpose of this Statement of Basis is to satisfy the requirements of IDAPA 58.01.01.et seq, Rules for the Control of Air Pollution in Idaho, for issuing air permits.

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ACRONYMS, UNITS, AND CHEMICAL NOMENCLATURE

AAC	acceptable ambient concentrations
AACC	acceptable ambient concentrations for carcinogens
acfm	actual cubic feet per minute
ANFO	ammonium nitrate/fuel oil
As	arsenic
ASTM	American Society for Testing and Materials
bkW	brake kilowatt
BT	Bradley Tailings
Btu	British thermal units
CAA	Clean Air Act
CAM	Compliance Assurance Monitoring
CAS No.	Chemical Abstracts Service registry number
Cd	cadmium
CEMS	continuous emission monitoring systems
cfm	cubic feet per minute
CFR	Code of Federal Regulations
CI	compression ignition
CIP	Carbon-in-Pulp
CIL	Carbon-in-Leach
CMS	continuous monitoring systems
CO	carbon monoxide
CO_2	carbon dioxide
CO_2e	CO_2 equivalent emissions
COC	contaminants of concern
COMS	continuous opacity monitoring systems
DEQ	Department of Environmental Quality
DR	development rock
DRSF	development rock storage facilities
dscf	dry standard cubic feet
EF	emission factors
EIS	Environmental Impact Statement required by the National Environmental Policy Act
EL	screening emission levels
EPA	United States Environmental Protection Agency
FDCP	Fugitive Dust Control Plan
FDRSF	Fiddle Development Rock Storage Facility
Forest Service	United States Forest Service
GACT	Generally Available Control Technology
gpm	gallons per minute
gr	grains (1 lb = 7,000 grains)
H_2SO_4	Sulfuric Acid
HAP	hazardous air pollutants
HFDRSF	Hangar Flats Development Rock Storage Facility
HFP	Hangar Flats Pit
Hg	mercury
hp	horsepower
hr/yr	hours per consecutive 12-calendar-month period
HVAC	heating, ventilation, and air conditioning
ICE	internal combustion engines
IDAPA	a numbering designation for all administrative rules in Idaho promulgated in accordance with the Idaho Administrative Procedures Act
km	kilometers

lb/hr	pounds per hour
lb/qtr	pound per quarter
LMP	lime manufacturing plant
MACT	Maximum Achievable Control Technology
Midas Gold	Midas Gold Idaho, Inc.
MMBtu	million British thermal units
MMscf	million standard cubic feet
NAAQS	National Ambient Air Quality Standard
NESHAP	National Emission Standards for Hazardous Air Pollutants
Ni	nickel
NF	National Forest System road
NMMP	nonmetallic mineral processing
NO_2	nitrogen dioxide
NO_x	oxides of nitrogen
NSPS	New Source Performance Standards
NSR	New Source Review
O&M	operation and maintenance
O_2	oxygen
PAH	polycyclic aromatic hydrocarbons
Pb	lead
PM	particulate matter
$PM_{2.5}$	particulate matter with an aerodynamic diameter less than or equal to a nominal 2.5 micrometers
PM_{10}	particulate matter with an aerodynamic diameter less than or equal to a nominal 10 micrometers
POM	polycyclic organic matter
POX	pressure oxidation
ppm	parts per million
PSD	Prevention of Significant Deterioration
PTC	permit to construct
PTE	potential to emit
PW	process weight rate
RICE	reciprocating internal combustion engines
Rules	*Rules for the Control of Air Pollution in Idaho*
SAG	semi-autogenous grinding
Sb	antimony
scf	standard cubic feet
SCL	significant contribution limits
Se	selenium
SGP	Stibnite Gold Project
SIP	State Implementation Plan
SM	synthetic minor
SM80	synthetic minor facility with emissions greater than or equal to 80% of a major source threshold
SO_2	sulfur dioxide
STKP	crusher stockpile
Subsection 210.20	HAP TAP exemption for NSPS and NESHAP sources in IDAPA 58.01.01.210.20
T/day	tons per calendar day
T/hr	tons per hour
T/yr	tons per consecutive 12-calendar-month period
TAP	toxic air pollutants
ULSD	ultra-low sulfur diesel
U.S.C.	United States Code
VOC	volatile organic compounds

WEDRSF	West End Development Rock Storage Facility
WEP	West End pit
YPDRSF	Yellow Pine Development Rock Storage Facility
YPP	Yellow Pine Pit
$\mu g/m^3$	micrograms per cubic meter

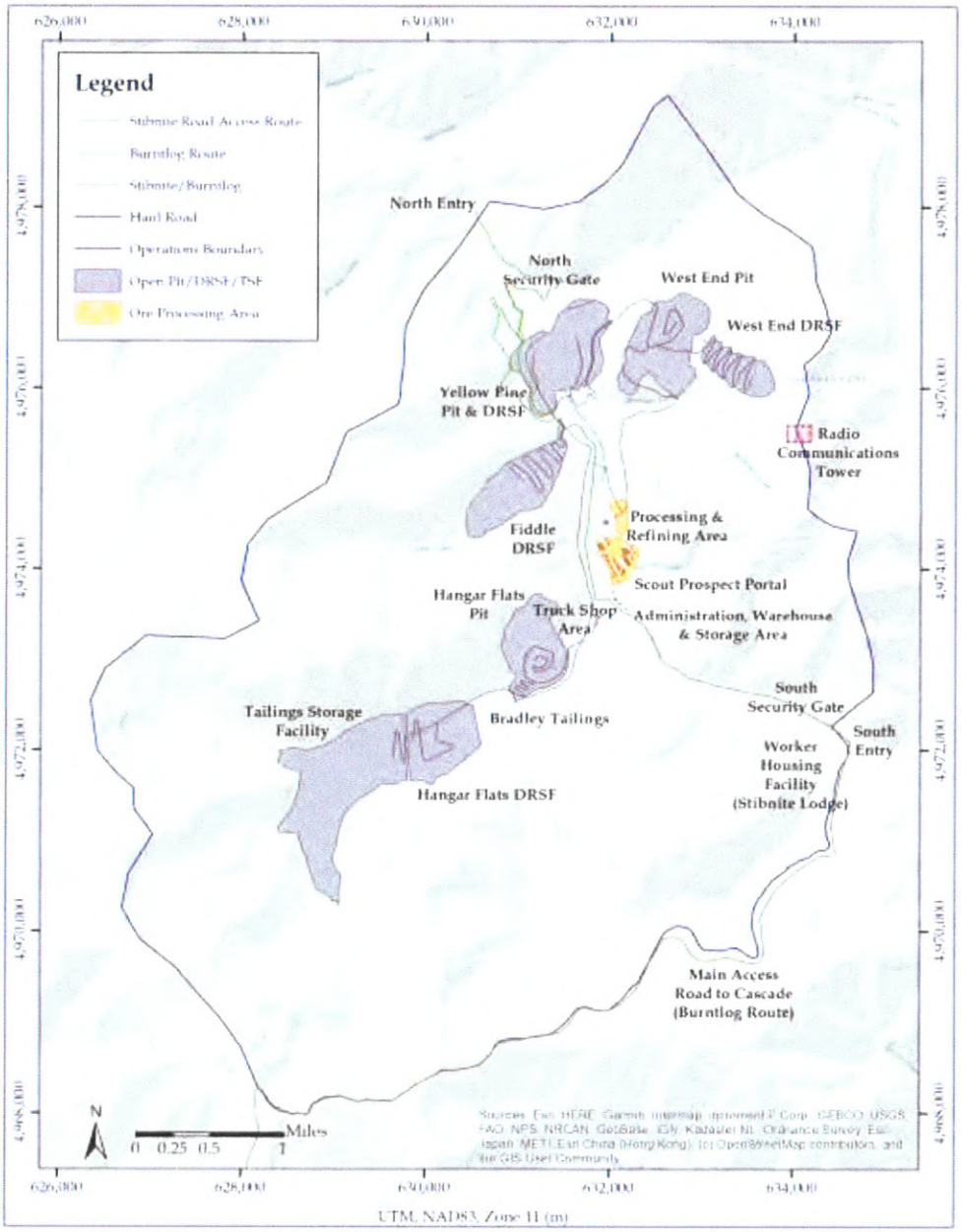
FACILITY INFORMATION

Description

Midas Gold Idaho, Inc. (Midas Gold) proposes to construct and operate the Stibnite Gold Project (SGP), consisting of conventional open-pit mining, ore preparation, and gold extraction operations.

SGP is to be located in Valley County at the intersection Forest Service roads NF-374 and NF-412 (Stibnite Road), approximately 10 miles east of Yellow Pine. The proposed Burntlog Route access road will provide year-round access to the site. The project comprises a combination of public national forest and private lands. The mining operations boundary within which public access will be excluded is defined in Figure 1. This operations boundary also defines the ambient air boundary used in all ambient air quality impact analyses.

Figure 1 PROJECT AREA OF OPERATIONS

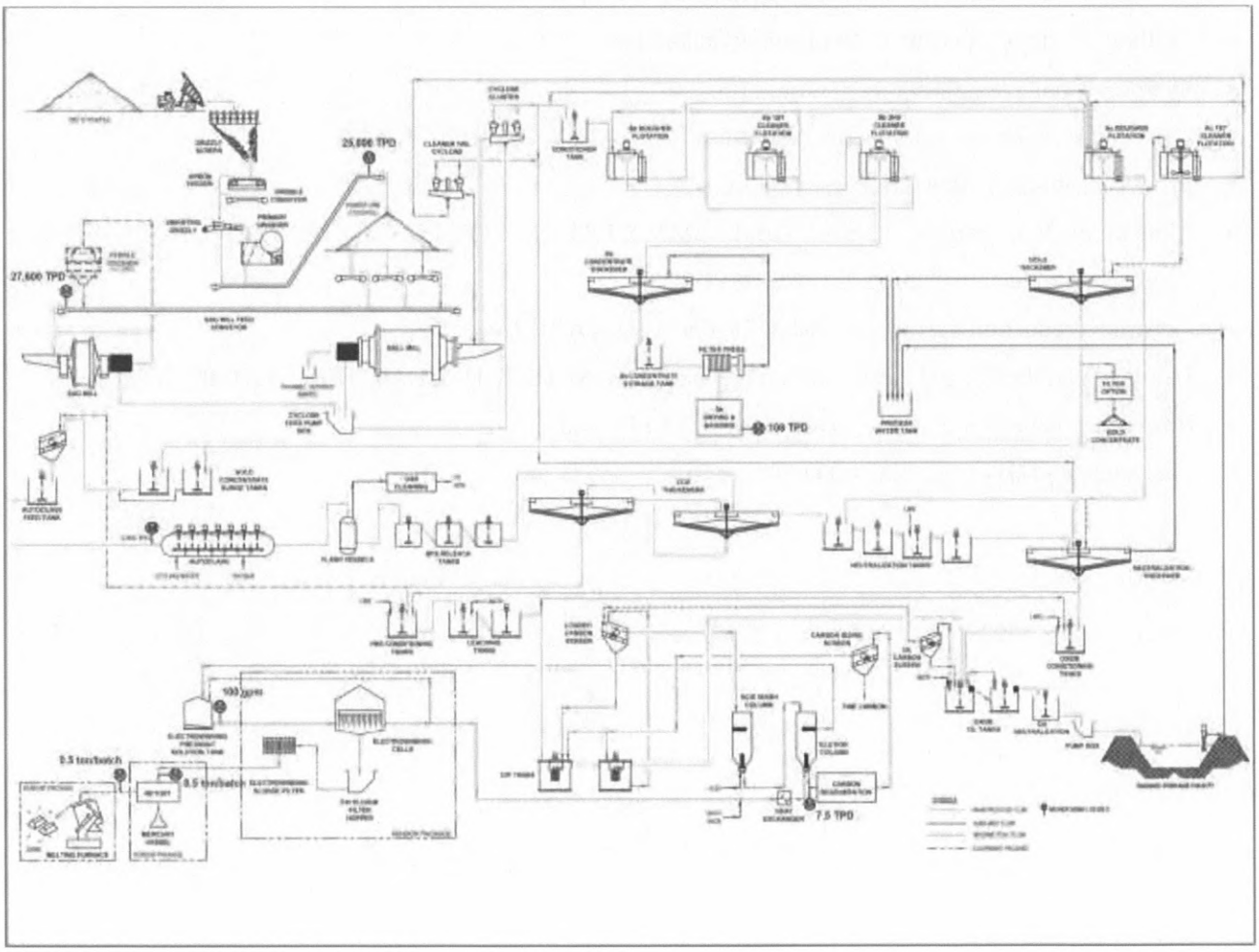


SGP will require the construction of significant infrastructure, including a power transmission line, a primary mine site access road, onsite haul roads, an ore processing facility, onsite workspaces, employee housing and recreation, water storage and distribution facilities, and sewage disposal facilities.

Conventional open-pit mining methods including drilling, blasting, excavating, and hauling will be used to extract ore and waste rock, termed development rock (DR). Hydraulic shovels and front-end loaders will be used to load ore and DR into haul trucks. DR will be used for construction, restoration, and backfilling, or hauled to the dedicated development rock storage facilities (DRSF). Approximately 340 million tons of DR will be handled over the life of the mine.

The SGP will include three years of pre-mining development and construction activities, followed by an operating mine life of approximately 12 years. Mining will occur in three open pits: Yellow Pine Pit (YPP), Hangar Flats pit (HFP), and West End pit (WEP). Although there will be overlap in mine development construction and operations, the general sequence of mining will be the YPP deposit, followed by the HFP and WEP deposits. Legacy tailings from the Meadow Creek valley (Bradley Tailings [BT]) will also be reclaimed and reprocessed during the initial project schedule. Surface exploration drilling will occur within the pits and within the Scout Prospect decline (underground exploration) throughout the mine operation period. Restoration and reclamation of other legacy mining features will occur prior to mining, throughout the life of the mine, and as part of the mine closure.

Figure 2 DIAGRAM OF PROCESS FLOWS



Ore will be hauled to the primary crusher area, where it will be fed directly into the crusher dump pocket or stockpiled. The ore crushing plant will be designed to operate at a maximum rate of 25,000 tons per calendar day (T/day). Approximately 100 million tons of ore will be mined from the three pits over the life of the project. The metal-recovery process from ore will include conventional crushing and grinding, followed by froth-flotation circuits that will generate separate gold-silver and antimony-silver concentrates. The antimony-silver concentrate will be shipped offsite for refining, whereas additional onsite processing of the gold-silver concentrate will include pressure oxidation, carbon-in-leach circuits, and refining processes to recover gold and minor amounts of silver. The finely ground leftover ore material from the mineral-recovery process, termed tailings, will be neutralized, thickened, and transported via a pipeline to the tailings storage facility. A diagram of ore processing and ore concentration and refining process flows is provided in Figure 2.

Permitting History

This is the initial PTC for a new facility, thus there is no permitting history.

Application Scope

This permit is the initial PTC for this facility.

The applicant has proposed to conduct mining operations and to install and operate ore processing, ore concentration and refining, and ancillary equipment:

- Drilling, blasting, excavating, and hauling operations;
- Ore processing operations (OC1–OC13, PS);
- Ore concentration and refining operations (AC, EW, MR, MF, CKD);
- Process heating (ACB, CKB, PV, HS, LKC);
- Lime production operations (LS1–LS12, LSBM, LS-L/U, LK, LCR, LS1-L/U, MillS2-L/U, ACS1–ACS4);
- Aggregate production operations (PCSP1, PCSP2);
- Concrete production operations (CM; CS1–CS2-L/U, CA-L/U);
- Heating, Ventilation, and Air Conditioning heaters (H1M–H2M, HM, HAC, HR, HA, HMO, HTS, HW);
- Emergency generator engines (EDG1–EDG3, EDFP); and
- Fuel storage (TG1–TG2, TD3—TD10).

Application Chronology

August 20, 2019	DEQ received an application and an application fee.
August 29 – September 13, 2019	DEQ provided an opportunity to request a public comment period on the application and proposed permitting action.
September 19, 2019	DEQ determined that the application was incomplete.
October 4, 2019	DEQ received a preliminary response and supplemental information from the applicant, including a request to delegate authority of responsible official.
October 9, 2019	DEQ approved the request to delegate authority of responsible official.
October 15, 2019	DEQ met with the applicant to review and discuss the preliminary response.
October 22, 2019	DEQ determined that the application remained incomplete while the applicant prepared a response to the remaining items previously identified (9/19/19), and included a summary of recommendations provided at the meeting (10/15/19).
November 8, 2019	DEQ requested additional information from the applicant via email, relating to items previously identified (9/19/19).
November 21, 2019	DEQ received a request from the applicant for extension until November 27, 2019 to respond.
November 27, 2019	DEQ received supplemental information from the applicant, including a revised application with updated emissions inventories and modeling analyses.
December 24, 2019	DEQ determined that the application was incomplete.
January 8, 2020	DEQ received a request from the applicant for extension until February 7, 2020 to respond.
January 31, 2020	DEQ requested additional information from the applicant via email, relating to items previously identified (12/24/19).
February 5, 2020	DEQ received supplemental information from the applicant, including a revised application with updated emissions inventories and modeling analyses.
March 6, 2020	DEQ determined that the application was incomplete.
April 2, 2020	DEQ received a request from the applicant for extension until April 15, 2020 to respond.
April 15, 2020	DEQ received supplemental information from the applicant, including updated modeling analyses.
May 15, 2020	DEQ determined that the application was complete.
June 24, 2020	DEQ received the final application including all updates.
July 6, 2020	DEQ made available the draft permit and statement of basis for peer and regional office review.
July 14, 2020	DEQ made available the draft permit and statement of basis for applicant review.
July 31, 2020	DEQ made available an updated draft statement of basis Appendix B for applicant review.

August 3 and 13, 2020	DEQ received comments from the applicant on the draft permit and statement of basis.
August 20, 2020	DEQ received the permit processing fee.
September 10 – October 12, 2020	DEQ provided a public comment period on the proposed action.
October 12, 2020	DEQ received a request to extend the public comment period.
October 13 – November 11, 2020	DEQ extended the public comment period on the proposed action.
October 27, 2020	DEQ provided an information meeting during the extended public comment period.
November 20, 2020	DEQ requested additional information from the applicant to address substantive public comments received, including missing TAP and HAP emission estimates.
November 25 and December 11, 2020	DEQ extended the response to public comment period until February 22, 2021 to allow additional time for the applicant and DEQ to respond to substantive public comments.
December 17, 2020	DEQ received a response to the request for additional information from the applicant.[1]
December 18 and 21, 2020	DEQ received supplemental information from the applicant, including a response and HAP/TAP addendum to the application,[2] updated HAP and TAP emissions estimates,[3] updated TAP modeling analyses,[4] and supporting references.[5]
January 28, 2021	DEQ received updated modeling files with corrections for formaldehyde and sulfuric acid, and an updated figure showing TAP modeled impacts.
February XX – March XX, 2021	DEQ provided a public comment period on the proposed action as updated to address the HAP and TAP addendum and updates.
February XX, 2020	DEQ provided an information meeting during the public comment period.
DRAFT February 18, 2021	DEQ issued the final permit, statement of basis, and response to public comments.

[1] "Response to DEQ's Request for Information," Midas Gold, December 17, 2020 (2020AAG2130).

[2] "HAP/TAP Addendum," Midas Gold, December 18, 2020. (2020AAG2150)

[3] "20200623-Midas Gold SGP PTC EI - Final-TAPr2.2.xls," Midas Gold, December 21, 2020. (2020AAG2152)

[4] "Modeling Files 2020-12.zip," Midas Gold, December 21, 2020. (2020AAG2154)

[5] "References-20201222T020853Z-001.zip," Midas Gold, December 21, 2020. (2020AAG2153)

TECHNICAL ANALYSIS

Emissions Units and Control Equipment

Table 1 lists all sources of regulated emissions for informational purposes.

Table 1 EMISSIONS UNIT AND CONTROL EQUIPMENT INFORMATION

Source ID No.	Source	Control Equipment	Maximum Process Rate
Mining			
	Drilling activities	Reasonable control and Fugitive Dust Control Plan (FDCP)	1,200 holes/day
	Blasting activities	Reasonable control & FDCP	2 blasts/day
	Excavating and hauling activities	Reasonable control & FDCP – Chemical suppression and water sprays Control efficiency: 93.3% for PM/PM_{10} (haul roads)	180,000 T/day
	Rock dumps and storage piles	Reasonable control & FDCP	n/a
PS1–2-L/U	(2) Prill Silos #1-2 Maximum capacity: 100 T (each)	Loading – None Unloading – None	200 T/day and 9,000 T/yr (combined)
Ore Processing			
OC1	Loader Transfer of Ore to Grizzly	Reasonable control & FDCP – Water sprays and moisture carryover	25,000 T/day
OC2	Grizzly to Apron Feeder		
OC3	Conveyor – Apron Feeder to Dribble		
OC4	Conveyor – Apron Feeder to Grizzly		
OC5	Conveyor – Dribble to Grizzly		
OC6	Grizzly to Primary Crusher or Coarse Ore Stockpile Feed		
OC7	Primary Crusher	Reasonable control & FDCP – Water sprays and moisture carryover	
OC8	Conveyor – Coarse Ore Stockpile Feed Transfer to Stockpile		
OC9	Stockpile Transfer to Reclaim Conveyors	Reasonable control & FDCP – Below-grade of storage piles Control efficiency: 80% for PM/PM_{10}	27,600 T/day
OC10	Conveyor – Reclaim Conveyors to SAG Mill Feed Conveyor		
OC11	Conveyor – SAG Mill Feed Transfer to SAG Mill	Reasonable control & FDCP – Enclosure Control efficiency: 80% for PM/PM_{10}	
OC12	Pebble Crusher	Reasonable control & FDCP – Water sprays and moisture carryover	
OC13	Pebble Discharge to SAG Mill Feed		
Ore Concentration and Refining			
CIP Leach 1–4	Carbon-in-Pulp Leach Tanks	Chemical treatment (lime, caustic soda, hydrogen peroxide, copper sulfate, etc.)	125 g/m^3 CN, 10.25 pH, and 1,700 T/yr PAX
CIL 1–6	Carbon-in-Leach Tanks	Chemical treatment	
CIP 1–6	Carbon-in-Pulp Tanks	Chemical treatment	
CN Detox 1–2	Cyanide Detox Tanks	Chemical treatment	25 g/m^3 CN, and 8.5 pH

Table 1 EMISSIONS UNIT AND CONTROL EQUIPMENT INFORMATION

Source ID No.	Source	Control Equipment	Maximum Process Rate
AC	Autoclave (AC)	Venturi Scrubber (VS1) Vent Gas Cleaning Tower (ST1) Vent Gas Steam Condensation Tower (CT1) Carbon Filter (CA5) Type: sulfur-impregnated activated carbon Form: granulated	6,960 T/day
EW	Electrowinning Cells and Pregnant Solution Tank	Shared Carbon Filter (CA2) Type: sulfur-impregnated activated carbon Form: granulated	100 gpm
MR	Mercury Retort	Condenser Carbon Filter (CA3) Type: sulfur-impregnated activated carbon Form: granulated	1,000 lb/batch and 21 T/yr
MF	Induction Melting Furnace	Baghouse (BH2) Carbon Filter (CA4) Type: sulfur-impregnated activated carbon Form: granulated	
CKD	Carbon Regeneration Kiln (Drum)	Wet Scrubber (WS2) Carbon Filter (CA1) Type: sulfur-impregnated activated carbon Form: granulated	7.2 T/day
	Tailings and Maintenance Pond activities	Chemical treatment, reasonable control & FDCP	1 g/m^3 CN
Process Heating			
ACB	POX Boiler (for AC) Maximum capacity: 17 MMBtu/hr Fuel: propane	None	operation is limited to AC startup only
HS	Strip Circuit Solution Heater Maximum capacity: 5 MMBtu/hr Fuel: propane	None	n/a
CKB	Carbon Regeneration Kiln Burners Maximum capacity: 2.255 MMBtu/hr Fuel: propane	None	(n/a)
PV	Propane Vaporizer Maximum capacity: 0.1 MMBtu/hr Fuel: propane	None	n/a
LKC	PFR Shaft Lime Kiln Combustion Maximum capacity: 22.0 MMBtu/hr Fuel: propane	None	n/a

Table 1 EMISSIONS UNIT AND CONTROL EQUIPMENT INFORMATION

Source ID No.	Source	Control Equipment	Maximum Process Rate
Lime Production			
LS1	Limestone transfer to Primary Crusher Hopper	None	1,130 T/day
LS2	Primary Crusher Maximum capacity: 1,130 T/day	None	
LS3	Primary Screen	None	
LS4	Secondary Crusher	None	
LS5	Secondary Screen	None	
LS6	Conveyor – Limestone to Ball Mill Feed Bin	None	
LS7	Conveyor – Limestone to Ball Mill Feed	None	
LS8	Conveyor – Ball Mill Feed to Ball Mill	None	
LSBM	Limestone Ball Mill	Baghouse (BH3)	
LS9	Conveyor – Limestone to Kiln Feed Bin	None	267 T/day
LS10	Conveyor – Limestone to Lime Kiln Feed	None	
LS11	Fines Screen	None	
LS12	Conveyor – Kiln Feed to PFR Shaft Lime Kiln	None	
LK	Parallel Flow Regenerative (PFR) Shaft Kiln	Baghouse (BH4)	169 T/day and 52,377 T/yr
LCR	Lime Mill Crusher	Baghouse (BH5)	
LS-L/U	Bucket Elevator – Pebble Lime Silo Loading	Loading – Bin Vent Filter	
	Pebble Lime Silo discharge to Lime Slaker	Unloading – Wet Scrubber (WS3)	
LS1-L/U	SAG Mill Lime Silo #1 Maximum capacity: 250 T/day	Loading – Bin Vent Filter Unloading – None	4,000 T/day and 70,000 T/yr (combined)
MillS2-L/U	SAG Mill Lime Silo #2 Maximum capacity: 250 T/day	Loading – Bin Vent Filter Unloading – None	
ACS1	AC Lime Silo #1 Maximum capacity: 1,000 T/day	Loading – Bin Vent Filter Unloading – None	
ACS2	AC Lime Silo #2 Maximum capacity: 1,000 T/day	Loading – Bin Vent Filter Unloading – None	
ACS3	AC Lime Silo #3 Maximum capacity: 1,000 T/day	Loading – Bin Vent Filter Unloading – None	
ACS4	AC Lime Silo #4 Maximum capacity: 500 T/day	Loading – Bin Vent Filter Unloading – None	
Aggregate Production			
PCSP1	Portable Crushing and Screening Plant 1 Crushers, screens, and conveyors	Reasonable control & FDCP – water sprays and moisture carryover	2,000 T/day (aggregate)
PCSP2	Portable Crushing and Screening Plant 2 Crushers, screens, and conveyors	Reasonable control & FDCP – water sprays and moisture carryover	2,000 T/day (aggregate)
Concrete Production			
CM	Central Mixer Loading Maximum capacity: 120 T/hr	Reasonable control & FDCP – Controls may include water sprays, enclosures, hoods, curtains, shrouds, movable and telescoping chutes, and central duct collection systems.	2,480 T/day and 560,000 T/yr (cement + aggregate)
CS1-L/U	Cement/Shotcrete Silo #1 Maximum capacity: 80 T	Loading – Bin Vent Filter Unloading – None	
CS2-L/U	Cement/Shotcrete Silo #2 Maximum capacity: 80 T	Loading – Bin Vent Filter Unloading – None	
CA-L/U	Aggregate Bin Maximum capacity: 2,400 T	Loading – None Unloading – None	

Table 1 EMISSIONS UNIT AND CONTROL EQUIPMENT INFORMATION

Source ID No.	Source	Control Equipment	Maximum Process Rate
Heating, Ventilation, and Air Conditioning (HVAC)			
H1M	Mine Air Heater #1 Maximum capacity: 4 MMBtu/hr Fuel: propane	None	n/a
H2M	Mine Air Heater #2 Maximum capacity: 4 MMBtu/hr Fuel: propane	None	n/a
HM	(4) Mill HVAC Heaters #1-4 Maximum capacity: 1.0 MMBtu/hr (each) Fuel: propane	None	n/a
HAC	Autoclave HVAC Heater Maximum capacity: 0.25 MMBtu/hr Fuel: propane	None	n/a
HR	Refinery HVAC Heater Maximum capacity: 0.25 MMBtu/hr Fuel: propane	None	n/a
HA	Admin HVAC Heater Maximum capacity: 0.25 MMBtu/hr Fuel: propane	None	n/a
HMO	(2) Mine Ops. HVAC Heaters Maximum capacity: 0.25 MMBtu/hr (each) Fuel: propane	None	n/a
HTS	(2) Truck Shop HVAC Heaters Maximum capacity: 1.0 MMBtu/hr (each) Fuel: propane	None	n/a
HW	(3) Warehouse HVAC Heaters Maximum capacity: 1.0 MMBtu/hr (each) Fuel: propane	None	n/a

Table 1 EMISSIONS UNIT AND CONTROL EQUIPMENT INFORMATION

Source ID No.	Source	Control Equipment	Maximum Process Rate
Emergency Power Generation and Fire Suppression			
EDG1	Camp Emergency Generator Date of construction: 2007 or later Maximum capacity: 1,000 bkW Maximum operation: 100 hr/yr (non-emergency) Fuel: ultra-low sulfur diesel (ULSD) Displacement: <10 L/cyl	EPA Tier 2 technologies	1 hr/day and 100 hr/yr
EDG2	Plant Emergency Generator #1 Date of construction: 2007 or later Maximum capacity: 1,000 bkW Maximum operation: 100 hr/yr (non-emergency) Fuel: ULSD Displacement: <10 L/cyl	EPA Tier 2 technologies	1 hr/day and 100 hr/yr
EDG3	Plant Emergency Generator #2 Date of construction: 2007 or later Maximum capacity: 1,000 bkW Maximum operation: 100 hr/yr (non-emergency) Fuel: ULSD Displacement: <10 L/cyl	EPA Tier 2 technologies	1 hr/day and 100 hr/yr
EDFP	Mill Fire Pump Date of construction: 2009 or later Maximum capacity: 200 bkW Maximum operation: 100 hr/yr (non-emergency) Fuel: ULSD Displacement: <10 L/cyl	None	1 hr/day and 100 hr/yr
Fuel Storage			
TG1–TG2	Mine Site Gasoline Tanks (#1 through #2) Maximum capacity: 5,000 gal each	Lids or other appropriate closure with gasketed seal and submerged filling	<100,000 gal/mo
TD3–TD10	Mine Site Diesel Tanks (#3 through #10)	Lids or other appropriate closure	n/a

Emissions Inventories

Potential to Emit

IDAPA 58.01.01 defines Potential to Emit (PTE) as the maximum capacity of a facility or stationary source to emit an air pollutant under its physical and operational design. Any physical or operational limitation on the capacity of the facility or source to emit an air pollutant, including air pollution control equipment and restrictions on hours of operation or on the type or amount of material combusted, stored or processed, shall be treated as part of its design if the limitation or the effect it would have on emissions is state or federally enforceable. Secondary emissions did not count in determining the PTE of a facility or stationary source.

Using this definition of PTE, an emissions inventory was developed for the SGP (see Appendix A). Emissions estimates of criteria pollutant and hazardous air pollutant (HAP) PTE were based on project-specific activity rates (e.g., continuous operation with the exception of the POX Boiler and emergency generator engines, design production rates, material haul rates, blasting agent usage rates, reagent usage rates, etc.), process design (e.g., open-pit mining, process concentration and pH, parallel flow regenerative lime production, central mix concrete production, haul fleet, etc.), emission abatement techniques (e.g., dust suppressant, chemical treatment, carbon filter, baghouse, bin vent filtration, wet scrubber, venturi scrubber, vent gas cleaning tower, and vent gas steam condensation tower control equipment), material characteristics (e.g., moisture content, road silt content, haul route distances, etc.), site conditions (onsite meteorological data, precipitation, etc.), and emission factors based on AP-42,[6] representative source test emissions data, and representative emission limits. Estimated emissions from the autoclave and the carbon regeneration kiln relied on emissions data from representative source test emissions data, scaled to the proposed equipment capacity. Estimated emissions from fuel storage tanks relied on TANKS[7] emission estimation software and projected annual gasoline and ULSD usage rates. Estimated emissions from the emergency generator engines relied on the use of certified engine emission factors.

Uncontrolled PTE

Using the definition of PTE, uncontrolled PTE is then defined as the maximum capacity of a facility or stationary source to emit an air pollutant under its physical and operational design. Any physical or operational limitation on the capacity of the facility or source to emit an air pollutant, including air pollution control equipment and restrictions on hours of operation or on the type or amount of material combusted, stored or processed, shall **not** be treated as part of its design **since** the limitation or the effect it would have on emissions **is not** state or federally enforceable.

The uncontrolled PTE is used to determine if a facility is a "synthetic minor" source of emissions. Synthetic minor sources are facilities that have an uncontrolled PTE for regulated air pollutants or HAP above an applicable major source threshold without permit limits.

For Midas Gold, uncontrolled PTE was based upon a worst-case for operation of the facility of continuous operation at proposed maximum material throughput and fuel input rates (Table 1), without consideration of control equipment. For batch operations, the number of operations necessary to achieve the proposed daily throughput rates was assumed in estimating emissions (MR, MF). Silo loading and unloading operations were assumed to occur at most once per day (LS1-L/U, MillS2-L/U, LS-L/U, PS-L/U, ACS1–ACS4-L/U, CS1–CS2-L/U, CA-L/U). Fuel storage was based on estimated facility-wide fuel usage rates (TG1, TG2 and TD3—TD10). For the purposes of maintenance and testing, emergency power generation operations were assumed to occur 1 hour per day and 100 hours per year (EDG1–EDG3, EDFP). With the exception of the POX Boiler in which operation is limited to AC startup only, continuous operation at maximum fuel input rates was assumed for all process heating and HVAC equipment.

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[6] Compilation of Air Pollutant Emission Factors, AP-42, Volume I, Fifth Edition (AP-42), Section 1.3 –Fuel Oil Combustion, 1.4 –Natural Gas Combustion, 1.5 – LPG Combustion, 3.2 – Natural Gas-Fired Reciprocating Engines, 3.3 – Gasoline and Diesel Industrial Engines, 3.4 – Large Stationary Diesel and All Stationary Dual-Fuel Engines, 8.3 – Ammonium Nitrate, 11.9 – Western Surface Coal Mining, 11.12 – Concrete Batching, 11.17 – Lime Manufacturing, 11.19 – Construction and Aggregate Processing, 13.2 – Fugitive Dust Sources, and 13.3 – Explosives Detonation, Office of Air Quality Planning and Standards Office of Air and Radiation (OAQPS), EPA, updated as of August 2011.

[7] TANKS Storage Tank Emissions Calculation Software Version 4.09D, OAQPS, EPA, released October 5, 2006.

The following table presents the uncontrolled PTE for regulated air pollutants as submitted by the applicant and verified by DEQ staff. Refer to Appendix A for a summary of the calculations and the assumptions used to determine emissions for each source, and the Facility Classification section for a review of facility classification based on uncontrolled and controlled PTE.

Table 2 UNCONTROLLED POTENTIAL TO EMIT FOR CRITERIA AIR POLLUTANTS

Source	PM	PM_{10}	$PM_{2.5}$	CO	NO_x	VOC	SO_2
	T/yr	T/yr	T/yr	T/yr	T/yr	T/yr	T/yr
OC1	13.69	5.02	0.78				
OC2	13.69	5.02	0.78				
OC3	13.69	5.02	0.78				
OC4	13.69	5.02	0.78				
OC5	13.69	5.02	0.78				
OC6	13.69	5.02	0.78				
OC7	24.64	10.95	1.64				
OC8	13.69	5.02	0.78				
OC9	15.11	5.54	0.86				
OC10	15.11	5.54	0.86				
OC11	15.11	5.54	0.86				
OC12	27.20	12.09	1.81				
OC13	15.11	5.54	0.86				
PS-L	0.07	0.03	0.004				
PS-U	0.07	0.03	0.004				
AC	74.10	74.10	74.10				2.86
MF	1.77	1.77	1.77				
CKD (EW, MR)	6.13	6.13	6.13	0.53	0.05	0.48	
LS1	0.48	0.17	0.03				
LS2	0.86	0.38	0.06				
LS3	3.97	1.38	0.21				
LS4	0.86	0.38	0.06				
LS5	3.97	1.38	0.21				
LS6	0.48	0.17	0.03				
LSBM	64.22	53.89	19.23				
LS7	0.48	0.17	0.03				
LS8	0.48	0.17	0.03				
LS9	0.12	0.05	0.007				
LS10	0.12	0.05	0.007				
LS11	1.03	0.36	0.05				
LS12	0.12	0.05	0.007				
LS-L	0.23	0.23	0.23				
LS-U	0.02	0.02	0.02				
LK	34.05	34.05	34.05	11.78	6.29		0.03
LCR	10.58	8.88	3.17				
LS1-L	1.60	1.03	0.16				
LS1-U	0.01	0.006	0.001				
MillS2-L	1.60	1.03	0.16				
MillS2-U	0.01	0.006	0.001				
ACS1-L	6.39	4.11	0.62				
ACS1-U	0.04	0.02	0.004				
ACS2-L	6.39	4.11	0.62				
ACS2-U	0.04	0.02	0.004				
ACS3-L	6.39	4.11	0.62				
ACS3-U	0.04	0.02	0.004				
ACS4-L	3.19	2.06	0.31				
ACS4-U	0.02	0.01	0.002				
PCSP1	27.67	10.11	1.54				
PCSP2	27.67	10.11	1.54				
CM	17.16	4.68	0.71				
CS1-L	21.90	14.10	2.14				
CS1-U	0.14	0.08	0.01				
CS2-L	21.90	14.10	2.14				

Table 2 UNCONTROLLED POTENTIAL TO EMIT FOR CRITERIA AIR POLLUTANTS

Source	PM	PM_{10}	$PM_{2.5}$	CO	NO_x	VOC	SO_2
	T/yr	T/yr	T/yr	T/yr	T/yr	T/yr	T/yr
CS2-U	0.14	0.08	0.01				
CA-L	1.73	0.83	0.13				
CA-U	1.73	0.83	0.13				
ACB	0.002	0.002	0.002	0.02	0.04	0.002	0.004
CKB	0.08	0.08	0.08	0.81	1.40	0.09	0.17
PV	0.003	0.003	0.003	0.04	0.06	0.004	0.008
HS	0.17	0.17	0.17	1.80	3.11	0.19	0.38
LKC	0.63	0.63	0.63	6.72	11.65	0.72	1.42
H1M	0.13	0.13	0.13	1.44	2.49	0.15	0.30
H2M	0.13	0.13	0.13	1.44	2.49	0.15	0.30
HM	0.13	0.13	0.13	1.44	2.49	0.15	0.30
HAC	0.008	0.008	0.008	0.09	0.16	0.01	0.02
HR	0.008	0.008	0.008	0.09	0.16	0.01	0.02
HA	0.008	0.008	0.008	0.09	0.16	0.01	0.02
HMO	0.02	0.02	0.02	0.18	0.31	0.02	0.04
HTS	0.07	0.07	0.07	0.72	1.24	0.08	0.15
HW	0.10	0.10	0.10	1.08	1.87	0.11	0.23
EDG1	0.02	0.02	0.02	0.39	0.71	0.14	0.001
EDG2	0.02	0.02	0.02	0.39	0.71	0.14	0.001
EDG3	0.02	0.02	0.02	0.39	0.71	0.14	0.001
EDFP	0.004	0.004	0.004	0.08	0.09	0.09	0.0001
TG1–TG2						1.91	
TD3—TD10						0.06	
Total	**560**	**337**	**164**	**29.47**	**36.16**	**4.68**	**6.27**

Although not explicitly calculated, it was confirmed by Midas Gold in the response to a request for additional information[1] that the uncontrolled HAP PTE for SGP is estimated to exceed 25 tons per year (T/yr) without application of the specified control equipment (Table 1). Arsenic HAP PTE from haul roads at a controlled emission rate of 0.464 pounds per hour (lb/hr) and accounting for 93.3% control efficiency exceeds 20 T/yr, supporting that uncontrolled HAP PTE exceeds 10 T/yr of single HAP and 25 T/yr of total HAP.

Pre-Project PTE

Pre-project PTE is used to establish the change in emissions at a facility as a result of this project. Because this is a new facility, pre-project emissions are set to zero for all criteria pollutants.

Post-Project PTE

Post-project PTE is used in determining the change in emissions at a facility and in determining the facility's classification as a result of this project. Post-project PTE includes all permit limits resulting from this project.

In addition to assuming continuous operation of the facility at the proposed material throughput and fuel input rates, post-project emissions estimates account for the use of dust suppressant, chemical treatment, carbon filter, baghouse, bin vent filtration, wet scrubber, venturi scrubber, vent gas cleaning tower, and vent gas steam condensation tower control equipment.

A variety of factors impact emissions from unpaved roadways, and it was recognized that accurate determination of site-specific parameters characterizing road conditions and vehicle traffic was critical to estimating particulate matter emissions and ambient air impacts. Midas Gold provided site-specific information to support parameters such as silt content, mean vehicle weight, and dust suppressant control efficiencies, and provided an analysis evaluating the conservatism of the resulting emission factor (AP-42).[8] To ensure operation consistent with these parameters and to reasonably control fugitive emissions, compliance with requirements identified in the FDCP is

[8] Appendix A – Model Parameter / Assumption / Data Level of Conservatism IDEQ Forms to the Stibnite Gold Project Permit to Construct Application, Midas Gold, revised June 23, 2020 (2020AAG1078).

required by the permit. Further discussion of the sensitivity of predicted air quality impacts is provided in the Ambient Air Quality Impact Analyses section.

The following table presents the post-project PTE for criteria pollutants from all emissions units at the facility as determined by DEQ staff. Because this is a new facility, the post-project PTE is equivalent to the facility-wide PTE. Refer to Appendix A for a summary of the calculations and the assumptions used to determine emissions from each source, and the Facility Classification section for a review of facility classifications based on uncontrolled and controlled PTE.

Table 3 POST-PROJECT POTENTIAL TO EMIT FOR CRITERIA AIR POLLUTANTS

Source	PM	PM_{10}	$PM_{2.5}$	CO	NO_x	VOC	SO_2
	T/yr [(a)a)]	T/yr [(a)]	T/yr [(a)]	T/yr [(a)]	T/yr [(a)]	T/yr [(a)]	T/yr [(a)]
POINT SOURCE EMISSIONS							
OC1	0.64	0.21	0.06				
OC2	0.64	0.21	0.06				
OC3	0.64	0.21	0.06				
OC4	0.64	0.21	0.06				
OC5	0.64	0.21	0.06				
OC6	0.64	0.21	0.06				
OC7	5.48	2.46	0.46				
OC8	0.64	0.21	0.06				
OC9	3.02	1.11	0.17				
OC10	3.02	1.11	0.17				
OC11	3.02	1.11	0.17				
OC12	6.04	2.72	0.50				
OC13	0.71	0.23	0.07				
PS-L	0.07	0.03	0.004				
PS-U	0.07	0.03	0.004				
AC	22.23	22.23	22.23				2.86
EW	0.31	0.31	0.31				
MR	0.006	0.006	0.006				
MF	0.89	0.89	0.89				
CKD	1.84	1.84	1.84	0.53	0.05	0.48	
LS1	0.48	0.18	0.03				
LS2	0.86	0.38	0.06				
LS3	3.97	1.38	0.21				
LS4	0.86	0.38	0.06				
LS5	3.97	1.38	0.21				
LS6	0.48	0.18	0.03				
LSBM	6.42	5.39	1.92				
LS7	0.48	0.18	0.03				
LS8	0.48	0.18	0.03				
LS9	0.12	0.05	0.01				
LS10	0.12	0.05	0.01				
LS11	1.03	0.36	0.06				
LS12	0.12	0.05	0.01				
LS-L	0.02	0.02	0.02				
LS-U	0.002	0.002	0.002				
LK	3.40	3.40	3.40	11.79	6.29		0.03
LCR	1.06	0.89	0.32				
LS1-L	0.002	0.001	0.0001				
LS1-U	0.01	0.006	0.001				
MillS2-L	0.002	0.001	0.0001				
MillS2-U	0.01	0.006	0.001				
ACS1-L	0.009	0.003	0.0004				
ACS1-U	0.04	0.02	0.004				
ACS2-L	0.009	0.003	0.0004				
ACS2-U	0.04	0.02	0.004				
ACS3-L	0.009	0.003	0.0004				
ACS3-U	0.04	0.02	0.004				
ACS4-L	0.004	0.001	0.0002				

Table 3 POST-PROJECT POTENTIAL TO EMIT FOR CRITERIA AIR POLLUTANTS

Source	PM	PM_{10}	$PM_{2.5}$	CO	NO_x	VOC	SO_2
	T/yr [(a)a)]	T/yr [(a)]	T/yr [(a)]	T/yr [(a)]	T/yr [(a)]	T/yr [(a)]	T/yr [(a)]
ACS4-U	0.02	0.01	0.002				
PCSP1	2.74	1.02	0.13				
PCSP2	2.74	1.02	0.13				
CM	0.55	0.17	0.02				
CS1-L	0.03	0.01	0.002				
CS1-U	0.14	0.08	0.01				
CS2-L	0.03	0.01	0.002				
CS2-U	0.14	0.08	0.01				
CA-L	1.73	0.83	0.13				
CA-U	1.73	0.83	0.13				
ACB	0.002	0.002	0.002	0.02	0.04	0.002	0.004
CKB	0.08	0.08	0.08	0.81	1.40	0.09	0.17
PV	0.003	0.003	0.003	0.04	0.06	0.004	0.008
HS	0.17	0.17	0.17	1.80	3.11	0.19	0.38
LKC	0.63	0.63	0.63	6.72	11.65	0.72	1.42
H1M	0.13	0.13	0.13	1.44	2.49	0.15	0.30
H2M	0.13	0.13	0.13	1.44	2.49	0.15	0.30
HM	0.13	0.13	0.13	1.44	2.49	0.15	0.30
HAC	0.008	0.008	0.008	0.09	0.16	0.01	0.02
HR	0.008	0.008	0.008	0.09	0.16	0.01	0.02
HA	0.008	0.008	0.008	0.09	0.16	0.01	0.02
HMO	0.02	0.02	0.02	0.18	0.31	0.02	0.04
HTS	0.07	0.07	0.07	0.72	1.24	0.08	0.15
HW	0.10	0.10	0.10	1.08	1.87	0.12	0.23
EDG1	0.02	0.02	0.02	0.39	0.71	0.14	0.001
EDG2	0.02	0.02	0.02	0.39	0.71	0.14	0.001
EDG3	0.02	0.02	0.02	0.39	0.71	0.14	0.001
EDFP	0.004	0.004	0.004	0.08	0.09	0.09	0.0001
TG1–TG2						1.91	
TD3—TD10						0.06	
Post-Project PTE [(c)]	**86.6**	**55.7**	**35.8**	**29.5**	**36.2**	**4.7**	**6.3**
FUGITIVE EMISSIONS							
Blasting activities	117.35	61.02	3.52	635.83	17.08		0.03
Drilling activities	284.70	148.04	8.54				
Hauling	2901.27	712.95	71.29				
Material load / unload (L/UL) [(b)]	15.00	7.10	1.07				
Dozing	103.56	19.78	10.87				
Grading	36.80	11.04	1.14				
Water Truck Travel	109.27	26.85	2.69				
Access Roads	6.95	1.72	0.17				
Wind Erosion [(b)]	5.72	2.86	0.43				
Surface Exploration	1.12	0.39	0.06				
Underground Exploration	0.002	0.001	0.0001				
Fugitive Total [(b)]	**3,569**	**986**	**100**	**636**	**17.1**		**0.03**

a) Controlled average emission rate in tons per year is an annual average, based on the proposed annual operating scenarios and annual limits.

b) Estimated emissions from the "W3" scenario resulted in the most emissions across most activities, with the exception of material load/unload and wind erosion activities, which occurred in the Y1, H1, W1, and B1 scenarios. Totals reported are for the "W3" scenario.

c) In the response to a request for additional information, Midas Gold confirmed that antimony process dryer and bagging operation emission sources (Sb1 and Sb2) initially proposed would be replaced by a dewatering/packaging circuit. As a result, these emission sources have been removed from the permit and post-project PTE.

Fourteen operational scenarios were evaluated by the applicant and verified by DEQ in order to estimate maximum hourly, daily, and annual potential emissions from sources. These scenarios encompassed all feasible origin and destination location combinations for locating ore and development rock. A summary of these scenarios is provided in Table 4. Although drilling, blasting, excavating, and hauling activities are not expected to be confined to a single scenario in practice, emissions in each scenario were conservatively estimated at the maximum daily proposed processing rate (180,000 of ore and rock) to allow for maximum operational flexibility, and to evaluate potential air quality impacts. Scenarios having the greatest potential emissions (i.e., the top seven) were those with the longest origin-to-destination distances, which resulted in increased emissions evident in onsite hauling and material loading and unloading activities. Consequently, the W3 scenario having the maximum origin-to-destination distance (16,415 daily vehicle miles traveled) is representative of maximum potential emissions.

Table 4 OPERATING SCENARIOS

Scenario	Origin [a]	Destination [a]
Y1	YPP	STKP
Y2	YPP	FDRSF
Y3	YPP	HFDRSF
H1	HFP	STKP
H2	HFP	FDRSF
H3	HFP	HFDRSF
H4	HFP	YPDRSF
W1	WEP	STKP
W2	WEP	FDRSF
W3	WEP	HFDRSF
W4	WEP	YPDRSF
W5	WEP	WEDRSF
B1	BT	STKP
B2	BT	HFDRSF

a) Where ore and rock origin and destination locations as depicted in Figure 1 are abbreviated as follows:
YPP = Yellow Pine Pit, HFP = Hangar Flats pit, WEP = West End pit,
BT = Bradley Tailings, STKP = Primary Crusher Stockpile,
FDRSF = Fiddle DRSF, HFDRSF = Hangar Flats DRSF,
YPDRSF = Yellow Pine DRSF, WEDRSF = West End DRSF, and
DRSF = development rock storage facilities.

There are numerous sources of fugitive dust emissions at the facility, including drilling and blasting activities, crushing and ore handling equipment, ore and rock storage piles, and unpaved roadways. Calculated at maximum daily processing rates, emissions from these sources would tend to be conservatively estimated. But it is also recognized that uncertainties exist in some of the emission factors used, and that predicted modeled impacts may be sensitive to emissions from such sources. In particular, it may prove challenging to consistently and continuously achieve the targeted level of fugitive dust control for emissions from traffic on unpaved roadways, with over 55 miles of haul truck routes within the mining operations boundary, a fleet of 32 haul trucks weighing between 37 and 357 tons, and a targeted dust control efficiency of 93.3% accomplished by application of both dust suppressant and water controls. Based on this, and the scale of operations, a detailed Fugitive Dust Control Plan (FDCP) was required (Permit Conditions 2.6). It is noted that Midas Gold projected actual annual production at approximately 42.7 million T/yr, or 65% of the permitted annual production limit of 65.7 million T/yr (Permit Condition 3.5), and that as a result actual emissions are expected to be lower than presented.

Change in PTE

The change in facility-wide PTE is used to determine if a public comment period may be required and to determine the processing fee per IDAPA 58.01.01.225. The following table presents the facility-wide change in the potential to emit for criteria pollutants, which for a new source is equivalent to the facility-wide and post-project PTE.

Table 5 CHANGES IN PTE FOR REGULATED AIR POLLUTANTS

Source	PM	PM_{10}	$PM_{2.5}$	CO	NO_x	VOC	SO_2
	T/yr [a]	T/yr [a]	T/yr [a]	T/yr [a]	T/yr [a]	T/yr [a]	T/yr [a]
Pre-Project PTE	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Post-Project PTE	86.6	55.7	35.8	29.5	36.2	4.7	6.3
Changes in Potential to Emit	**86.6**	**55.7**	**35.8**	**29.5**	**36.2**	**4.70**	**6.30**

a) Controlled average emission rate in tons per year is an annual average, based on the proposed annual operating scenarios and annual limits.

Controlled Hazardous and Toxic Air Pollutant Emissions

A summary of the estimated PTE for hazardous air pollutants (HAP) and emissions increases (PTE) for non-carcinogenic and carcinogenic toxic air pollutants (TAP) and for potential is provided in the following table (Table 6). This table and the Ambient Air Quality Impact Analyses were updated to include new and updated TAP emission estimates from additional emission sources identified in public comments and in a response and HAP/TAP addendum to the application provided by Midas Gold.[2,3]

All permitted fugitive and point emission sources were evaluated in the new HAP and TAP emission estimates. In Table 6 below, HAP and TAP PTE emissions estimates are for the highest emissions year Scenario "W3" referenced from Table B1-W3 of Appendix B to the HAP/TAP addendum and 'TblB1' worksheet in the supporting spreadsheet. Process and production activities include ore processing; ore concentration and refining; process heating; aggregate production; concrete production; heating, ventilation, and air conditioning (HVAC); emergency power generation and fire suppression; and fuel storage. Mining and leaching activities include drilling, blasting, excavating, hauling, prill silos, rock dumps and storage piles, and tailings. Metal HAP and TAP emissions from process materials were based on metal concentration profiles from onsite core samples of ore and limestone materials, including 98 samples of SGP limestone[9] and over 55,000 samples of SGP ore.[10,11] As a conservative assumption, the limestone profile was also used for emissions from aggregate materials. Mercury emissions from the LK were estimated by assuming all mercury in the limestone feed is volatilized and emitted. For each non-mercury metal HAP and TAP, emissions from the LK were calculated as PM emissions multiplied by the median metal concentration measured. Elemental analysis of core samples was complemented with an evaluation of whether each result represented a regulated HAP and/or TAP substance (element or compound) in Table 2 of the HAP/TAP addendum.[2]

TAP also classified as HAP emitted from sources addressed by New Source Performance Standards (NSPS) or National Emission Standards for Hazardous Air Pollutants (NESHAP) were not required to be evaluated for compliance with TAP increments in accordance with IDAPA 58.01.01.210.20 (Subsection 210.20). Guidance and clarification of Subsection 210.20 source exemptions were included in the Subsection 210.20 (IDAPA 58.01.01.210.20) section and in the response to public comments document that is part of the final permit package for this permitting action. Some of the screening levels for non-carcinogenic and carcinogenic TAP were exceeded as a result of this project and required modeling. Modeling was required for aluminum, barium, calcium carbonate, calcium oxide, iron, sulfuric acid, thallium, and vanadium because the 24-hour average non-carcinogenic screening emission levels (EL) in IDAPA 58.01.01.585 were exceeded. Modeling was required for arsenic, cadmium, formaldehyde, and nickel because the annual average carcinogenic EL in IDAPA 58.01.01.586 were exceeded. Refer to the Ambient Air Quality Impact Analyses section and Appendix B for additional discussion.

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[9] "M3-PN170045 Stibnite Gold Feasibility Study RE: M3-MGI-029E Lime Kiln Analysis Memo" and MGI-17-431-FullGeochem - MB.xlsx, M3 Engineering & Technology, June 14, 2018. (ref. M3 2018; 2020AAG2153)

[10] "Geochemistry Statistics" email R. McCluskey to E. Memon, Stibnite Gold Project, Air Sciences, September 26, 2017. (ref. Midas Gold 2017c; 2020AAG205)

[11] "Re: Te-2" and 2020-12-09_Fe and Se data.xlsx, Stibnite Gold Project, December 9, 2020. 1,500 of these samples were tested for selenium. (ref. Midas Gold 2020; 2020AAG2153)

Table 6 POTENTIAL TO EMIT FOR HAZARDOUS & TOXIC AIR POLLUTANTS (HAP/TAP) [a]

HAP/TAP	Mining and Leaching Emissions		Processing and Production Emissions		Facility-Wide Total Emissions		Adjusted TAP Emissions	Screening Emission Level
	lb/hr [b]	T/yr [c]	lb/hr [b]	T/yr [c]	lb/hr [b]	T/yr [c]	lb/hr [b,d]	lb/hr [d]
1,3-Butadiene [e]	0	0	8.4E-07	3.7E-06	8.4E-07	3.7E-06	0	2.4E-05
2-Methylnaphthalene [e,f]	0	0	1.1E-06	4.6E-06	1.1E-06	4.6E-06	0	9.1E-05
3-Methylcholanthrene [e]	0	0	7.8E-08	3.4E-07	7.8E-08	3.4E-07	3.2E-08	2.5E-06
7,12-Dimethylbenz(a)anthracene [e,f]	0	0	7.6E-07	3.0E-06	7.6E-07	3.0E-06	0	9.1E-05
Acenaphthene [e,f]	0	0	5.7E-06	7.1E-06	5.7E-06	7.1E-06	0	9.1E-05
Acenaphthylene [e,f]	0	0	1.1E-05	1.4E-05	1.1E-05	1.4E-05	0	9.1E-05
Acetaldehyde [e]	0	0	2.5E-05	1.1E-04	2.5E-05	1.1E-04	0	3.0E-03
Acrolein	0	0	1.6E-05	2.0E-05	1.6E-05	2.0E-05	0	0.017
Anthracene [e,f]	0	0	1.7E-06	2.4E-06	1.7E-06	2.4E-06	0	9.1E-05
Antimony	0.019	0.082	5.7E-04	2.5E-03	0.019	0.085	0	0.033
Arsenic [e]	0.544	2.381	4.5E-03	0.020	0.548	2.400	**5.7E-06**	1.5E-06
Benzene [e]	0	0	7.4E-03	0.032	7.4E-03	0.032	3.8E-05	8.0E-04
Benzo(a)pyrene [e,f]	0	0	1.4E-07	6.1E-07				
Benz(a)anthracene [e,f]	0	0	3.1E-07	1.4E-06				
Benzo(b)fluoranthene [e,f]	0	0	4.4E-07	1.9E-06				
Benzo(k)fluoranthene [e,f]	0	0	1.5E-07	6.6E-07	2.0E-06	8.8E-06	2.0E-07	2.0E-06
Chrysene [e,f]	0	0	5.8E-07	2.5E-06				
Dibenz(a,h)anthracene [e,f]	0	0	1.8E-07	7.7E-07				
Indeno(1,2,3-cd)pyrene [e,f]	0	0	2.2E-07	9.6E-07				
Benzo(g,h,i)perylene [e,f]	0	0	7.5E-07	1.1E-06	7.5E-07	1.1E-06	0	9.1E-05
Beryllium [e]	2.6E-03	0.011	4.3E-04	1.9E-03	3.0E-03	0.013	2.3E-07	2.8E-05
Biphenyl	0	0	4.4E-05	1.9E-04	4.4E-05	1.9E-04	0	0.1
Cadmium [e]	4.1E-04	1.8E-03	4.6E-04	2.0E-03	8.7E-04	3.8E-03	**2.0E-05**	3.7E-06
Carbon disulfide	0.014	0.063	0	0	0.014	0.063	0	2
Chromium	7.3E-03	0.032	6.8E-04	2.8E-03	8.0E-03	0.035	2.7E-05	0.033
Chromium (VI) [e]	0	0	3.4E-07	1.5E-06	3.4E-07	1.5E-06	3.4E-07	5.6E-07
Cobalt	3.3E-03	0.014	4.7E-04	2.0E-03	3.7E-03	0.016	1.5E-06	3.3E-03
Cyanide	0.453	1.983	1.2E-03	5.3E-03	0.454	1.988	0	0.333
Dichlorobenzene	0	0	5.7E-05	2.3E-04	5.7E-05	2.3E-04	2.1E-05	20 [j]
Fluoranthene [e,f]	0	0	5.5E-06	7.0E-06	5.5E-06	7.0E-06	0	9.1E-05
Fluorene [e,f]	0	0	1.7E-05	2.1E-05	1.7E-05	2.1E-05	0	9.1E-05
Formaldehyde [e]	0	0	3.3E-03	0.015	3.3E-03	0.015	**1.3E-03**	5.1E-04
Hexane	0	0	0.117	0.480	0.117	0.48	0.032	12
Hydrogen Chloride	0	0	0.986	3.666	0.986	**3.666**	0	0.05
Lead	6.5E-03	0.029	4.8E-04	2.1E-03	7.0E-03	0.031	0	
Manganese	0.244	1.067	4.6E-03	0.017	0.248	1.085	3.6E-05	0.067
Mercury [g]	1.3E-03	5.7E-03	7.1E-04	2.9E-03	*< 0.028*	*< 0.122*	*0.041 lb/yr*	*25 lb/yr*
Naphthalene	0	0	2.1E-03	8.8E-03	2.1E-03	8.8E-03	1.1E-05	3.33
Nickel [e]	1.6E-03	7.1E-03	5.5E-04	2.4E-03	2.2E-03	9.5E-03	**4.0E-05**	2.7E-05
Phenanthrene [e,f]	0	0	5.1E-05	6.3E-05	5.1E-05	6.3E-05	0	9.1E-05
Phenol	0	0	2.4E-04	1.1E-03	2.4E-04	1.1E-03	0	1.27
Phosphorus	0.53	2.32	5.6E-03	0.023	0.535	2.343	8.2E-06	7.0E-03
Pyrene [e,f]	0	0	5.0E-06	6.6E-06	5.0E-06	6.6E-06	0	9.1E-05
Selenium	3.3E-04	1.4E-03	4.1E-04	1.8E-03	7.4E-04	3.2E-03	4.3E-07	0.013
Toluene	0	0	0.032	0.139	0.032	0.139	6.1E-05	25
Xylene	0	0	0.032	0.138	0.032	0.138	0	29
Total HAP [h]	1.83	8.00	1.20	4.57	3.05	12.68	0.03	

Table 6 POTENTIAL TO EMIT FOR HAZARDOUS & TOXIC AIR POLLUTANTS (HAP/TAP) [a]

HAP/TAP	Mining and Leaching Emissions		Processing and Production Emissions		Facility-Wide Total Emissions		Adjusted TAP Emissions	Screening Emission Level
	lb/hr [b]	T/yr [c]	lb/hr [b]	T/yr [c]	lb/hr [b]	T/yr [c]	lb/hr [b,d]	lb/hr [d]
Aluminum [i]	57.855	253	0.648	2.577	58.504	256	**58.504**	0.667
Barium [i]	0.652	2.855	6.8E-03	0.028	0.659	2.883	**0.659**	0.033
Calcium Carbonate [i]	11.408	49.967	2.244	8.125	13.652	58.092	**13.652**	0.667
Calcium Oxide [i]	0	0	0.696	0.952	0.696	0.952	**0.696**	0.133
Copper [i]	4.1E-03	0.018	5.3E-04	2.2E-03	4.6E-03	0.020	0.0046	0.067
Cyclohexane [i]	0	0	1.0E-03	4.6E-03	1.0E-03	4.6E-03	0.0010	70
Hydrogen Sulfide [i]	0	0	0.900	3.942	0.900	3.942	0.900	0.933
Iron [i]	14.831	64.958	0.213	0.812	15.043	65.770	**15.043**	0.067
Molybdenum [i]	8.1E-04	3.6E-03	4.7E-04	2.0E-03	1.3E-03	5.6E-03	0.0013	0.333
Pentane [i]	0	0	0.123	0.495	0.123	0.495	0.123	118
Silver [i]	4.1E-04	1.8E-03	4.1E-04	1.8E-03	8.2E-4	3.6E-03	0.00082	7.0E-03
Sulfuric Acid [i]	0	0	2.030	8.891	2.030	8.891	**2.030**	0.067
Thallium [i]	8.1E-03	0.036	5.2E-04	2.2E-03	8.7E-03	0.038	**0.0087**	0.007
Uranium [i]	8.1E-03	0.036	5.2E-04	2.2E-03	8.7E-03	0.038	0.0087	0.013
Vanadium [i]	0.023	0.100	8.4E-04	3.5E-03	0.024	0.103	**0.024**	0.003
Trimethyl Benzene [i]	0	0	0.011	0.048	0.011	0.048	0.011	8.2
Tungsten [i]	8.1E-03	0.036	5.2E-04	2.2E-03	8.7E-03	0.038	0.0087	0.333
Zinc [i]	0.029	0.125	2.2E-03	8.8E-03	0.031	0.134	0.031	0.667

a) HAP and TAP PTE emissions estimates are for the highest emissions year Scenario W3, referenced from Table B1-W3 of Appendix B to the HAP/TAP addendum and 'TblB1' worksheet in the supporting spreadsheet. Process and production activities include ore processing; ore concentration and refining; process heating; aggregate production; concrete production; heating, ventilation, and air conditioning (HVAC); emergency power generation and fire suppression; and fuel storage. Mining and leaching activities include drilling, blasting, excavating, hauling, prill silos, rock dumps and storage piles, and tailings.

b) Controlled average emissions rates in pounds per hour (lb/hr). Emissions rates for non-carcinogens are daily averages, based on the proposed daily operating scenarios and limits. Emissions rates for carcinogens are annual averages, based on the proposed annual operating scenarios and limits.

c) Controlled average emissions rates in tons per year (T/yr) are annual averages, based on the proposed annual operating scenarios and annual limits.

d) Adjusted TAP emissions and screening emission levels (EL) as specified in IDAPA 58.01.01.585-586 for purposes of TAP preconstruction compliance demonstrations. For TAP, adjusted emissions do not include sources addressed by NSPS and NESHAP in accordance with IDAPA 58.01.01.210.20Table 8.

e) Carcinogenic TAP as identified in IDAPA 58.01.01.586.

f) Polycyclic aromatic hydrocarbon (PAH). The group of seven PAH with a single EL are regulated as polycyclic organic matter (POM) equivalent in potency to benzo(a)pyrene as specified in IDAPA 58.01.01.586.

g) Adjusted mercury emissions (which are not TAP) are reported in pounds per year (lb/yr) and do not include fugitive sources and sources addressed by NESHAP 40 CFR 63 for comparison to the Mercury Emission Standard threshold of 25 lb/yr. Facility-wide mercury PTE emission rates were calculated as annual average based on federally-enforceable NESHAP Subpart EEEEEEE limits, and exceed values referenced from Table B1-W3 of Appendix B to the HAP/TAP addendum and 'TblB1' worksheet in the supporting spreadsheet (which account for the proposed mercury control devices for refinery process sources AC, EW, MR, MF, CKD).

h) Total hazardous air pollutant (HAP) emissions from all permitted sources and activities (combined). The maximum potential emissions of any single HAP is hydrogen chloride.

i) Toxic air pollutant that is not also a hazardous air pollutant (i.e., non-HAP TAP) and is not included in HAP totals.

j) Dichlorobenzene is regulated as both the ortho- and para- isomers (o-dichlorobenzene and 1,4-dichlorobenzene). For the purposes of TAP compliance, the lowest EL (and therefore most conservative) is listed.

HAP and TAP particulate metals are indirectly regulated via facility-wide fugitive dust requirements for particulate matter (PM) (Permit Conditions 2.1–2.8, 3.9, 5.9), material throughput and operational limits (Permit Conditions 3.3–3.8, 4.7–4.12, 5.4–5.8, 6.2), PM emission limits (Permit Conditions 4.3, 5.3), control device requirements (Permit Conditions 3.10, 4.13–4.17, 5.9–5.15), and associated testing, monitoring, recordkeeping, and reporting requirements. Because usage of process reagents were not correlated to material throughput rates and not otherwise inherently limited, HAP emissions limits and usage limits were established for potassium amyl xanthate (PAX) and sodium cyanide (Permit Conditions 4.4–4.6). Cyanide emissions were sensitive to leachant concentration and basicity, and monitoring of these parameters was established (Permit Condition 4.5) to ensure compliance with the emission limit. Monitoring of these limits and process parameters also ensure compliance with the major threshold for each individual HAP of 10 tons per year (T/yr).

Ambient Air Quality Impact Analyses

The applicant has demonstrated preconstruction compliance to DEQ's satisfaction that emissions from this facility will not cause nor significantly contribute to a violation of any ambient air quality standard. The applicant has also demonstrated preconstruction compliance to DEQ's satisfaction that the emissions increase due to this permitting action will not exceed any acceptable ambient concentration (AAC) or acceptable ambient concentration for carcinogens (AACC) for toxic air pollutants (TAP). A summary of the Ambient Air Impact Analysis for TAP is provided in Appendix B.

As presented in the modeling memorandum in Appendix B, the estimated emission rates of PM_{10}, $PM_{2.5}$, SO_2, CO, NO_x, and certain TAP from this project exceeded applicable screening emission levels (EL) and published DEQ modeling thresholds established in IDAPA 58.01.01.585-586 and in the State of Idaho Air Quality Modeling Guideline.[12] The facility-wide emission rate of lead (Pb) was determined to be below the "below regulatory concern" (BRC) threshold level of less than 10% of the "significant" emission rate defined in IDAPA 58.01.01.006 (i.e., less than 0.06 T/yr) and therefore modeling was not required.[12] Refer to the Emissions Inventories section for additional information concerning the emissions inventories.

New and updated TAP increment compliance demonstrations[4] were provided after evaluation of fugitive particulate TAP emissions from emission sources (Table 6) as identified in public comments and in a response and HAP/TAP addendum to the application provided by Midas Gold.[2] For non-HAP TAP, all sources were evaluated for TAP compliance by comparison of facility-wide emissions to applicable screening emission levels (EL). After exclusion of sources addressed by NSPS and NESHAP (Table 8), applicable concrete production and HVAC emission sources were evaluated for HAP TAP compliance by comparison of adjusted emissions to applicable EL. Refer to the Emissions Inventories section for estimates of HAP and TAP emissions (as summarized in Table 6) and to the Subsection 210.20 (IDAPA 58.01.01.210.20) section for relevant guidance and discussion of sources addressed by NSPS and NESHAP. With the exception of 12 TAP, estimated emission increases of non-carcinogenic and carcinogenic TAP demonstrated preconstruction compliance with TAP standards in accordance with IDAPA 58.01.01.210.07 using controlled average emission rates. Modeling analyses conducted in the development of TAP rules supports that if controlled average emission rates do not exceed applicable screening emission levels (EL) in IDAPA 58.01.01.585–586, controlled ambient concentrations are expected to be below the applicable acceptable ambient concentration (AAC/AACC).

Estimated emission increases of aluminum, arsenic, barium, cadmium, calcium carbonate, calcium oxide, formaldehyde, iron, nickel, sulfuric acid, thallium, and vanadium (12 TAP) demonstrated preconstruction compliance with TAP standards in accordance with IDAPA 58.01.01.210.08 for controlled ambient concentrations. Modeling analyses demonstrated preconstruction compliance with the acceptable ambient concentrations for these TAP (AAC/AACC) in IDAPA 58.01.01.585–586. Emission limits (Permit Condition 4.3), operational and material throughput limits (Permit Conditions 3.3–3.8, 4.5–4.12, and 5.4–5.8), fugitive dust control requirements (Permit Conditions 2.1–2.8), and control equipment requirements (Permit Conditions 2.6, 3.9–3.11, 4.13–4.17, and 5.9–5.15) limit these TAP emissions in accordance with IDAPA 58.01.01.210.08.c, limit Pb to BRC, and limit PM, PM_{10} ,and $PM_{2.5}$ to below the emission rates relied upon in the NAAQS evaluation of ambient air impacts in the modeling analyses.

Arsenic represented the single greatest HAP TAP emission; adjusted arsenic HAP TAP emissions at 5.7E-06 pounds per hour (lb/hr) did not exceed 2% of the applicable EL. Iron (Fe) represented the greatest single non-HAP TAP emission at over 15 lb/hr, which did not exceed 15% of the applicable EL. Any uncertainties in metal TAP emission estimates are not expected to affect compliance with TAP provisions.

It was recognized that accurately defining the mining operations boundary and controlling public access within that boundary was critical to estimating ambient air impacts. To ensure operation consistent with the defined mining operations boundary, site-specific access control measures will be employed. Midas Gold has committed

[12] Criteria pollutant thresholds in Table 2, State of Idaho Guideline for Performing Air Quality Impact Analyses, Doc ID AQ-011, September 2013, criteria pollutant BRC thresholds as provided in IDAPA 58.01.01.221.01, and DEQ guidance pertaining to BRC (2014ACF3).

to identifying and complying with these site-specific access control measures in an Access Management Plan (AMP, as required by Permit Condition 2.7).[13] Refer to Appendix E for a description and discussion of the mining operations boundary and control measures that may be included in this plan.

An ambient air quality impact analyses document has been crafted by DEQ based on a review of the modeling analysis submitted in the application. That document is part of the final permit package for this permitting action (refer to Appendix B). Refer to the Emissions Inventories section and Appendix A for additional information concerning development of the emissions inventories.

REGULATORY ANALYSIS

Attainment Designation (40 CFR 81.313)

The facility is located in Valley County, which is designated as attainment or unclassifiable for $PM_{2.5}$, PM_{10}, SO_2, NO_2, CO, and Ozone. Refer to 40 CFR 81.313 for additional information.

Facility Classification

The AIRS/AFS facility classification codes are as follows:

For HAP (hazardous air pollutants) only:

A = Use when any one HAP has permitted emissions > 10 T/yr or if the aggregate of all HAP (Total HAP) has permitted emissions > 25 T/yr.

SM80 = Use if a synthetic minor (uncontrolled HAP emissions are > 10 T/yr or if the aggregate of all uncontrolled HAP (Total HAP) emissions are > 25 T/yr and permitted emissions fall below applicable major source thresholds) and the permit sets limits > 8 T/yr of a single HAP or ≥ 20 T/yr of Total HAP.

SM = Use if a synthetic minor (uncontrolled HAP emissions are > 10 T/yr or if the aggregate of all uncontrolled HAP (Total HAP) emissions are > 25 T/yr and permitted emissions fall below applicable major source thresholds) and the permit sets limits < 8 T/yr of a single HAP and/or < 20 T/yr of Total HAP.

B = Use when the potential to emit (i.e. uncontrolled emissions and permitted emissions) are below the 10 and 25 T/yr HAP major source thresholds.

UNK = Class is unknown.

For All Other Pollutants:

A = Use when permitted emissions of a pollutant are > 100 T/yr.

SM80 = Use if a synthetic minor for the applicable pollutant (uncontrolled emissions are > 100 T/yr and permitted emissions fall below 100 T/yr) and permitted emissions of the pollutant are ≥ 80 T/yr.

SM = Use if a synthetic minor for the applicable pollutant (uncontrolled emissions are > 100 T/yr and permitted emissions fall below 100 T/yr) and permitted emissions of the pollutant are < 80 T/yr.

B = Use when the potential to emit (i.e. uncontrolled emissions and permitted emissions) are below the 100 T/yr major source threshold.

UNK = Class is unknown.

[13] Attachment 2 – Stibnite Road Access Management Plan to the Stibnite Gold Project Permit to Construct Application, Midas Gold, revised June 23, 2020 (2020AAG1078).

Table 7 REGULATED AIR POLLUTANT FACILITY CLASSIFICATION

Pollutant	Uncontrolled PTE (T/yr)	Permitted PTE (T/yr)	Major Source Thresholds (T/yr)	AIRS/AFS Classification
PM	560	86.6	100	SM80
PM_{10}	337	55.7	100	SM
$PM_{2.5}$	164	35.8	100	SM
SO_2	6.27	6.3	100	B
NO_x	36.16	36.2	100	B
CO	29.47	29.5	100	B
VOC	4.68	4.7	100	B
HAP (single)	>20	3.666	10	SM
Total HAP	>25	12.68	25	SM

Based on the uncontrolled PTE summarized in Table 2 and controlled PTE summarized above and in Table 3, Table 6, and Appendix A, the permittee will be a "synthetic minor" source of PM, PM_{10}, $PM_{2.5}$, and HAP emissions for new source review and Title V (Tier I) permitting purposes. The uncontrolled PTE for the remaining criteria pollutants (SO_2, NO_x, CO, VOC) confirm Midas Gold will be a natural minor source for these emissions.

Permit to Construct (IDAPA 58.01.01.201)

The permittee has requested that a PTC be issued to the facility for the proposed new emission sources. Therefore, a permit to construct is required in accordance with IDAPA 58.01.01.201. This permitting action was processed in accordance with the procedures of IDAPA 58.01.01.200-228.

Tier II Operating Permit (IDAPA 58.01.01.401)

IDAPA 58.01.01.401 ..... Tier II Operating Permit

The application was submitted for a permit to construct (refer to the Permit to Construct (IDAPA 58.01.01.201) section), and an optional Tier II operating permit has not been requested. Therefore, the procedures of IDAPA 58.01.01.400–410 were not applicable to this permitting action.

Subsection 210.20 (IDAPA 58.01.01.210.20)

IDAPA 58.01.01.210.20..... NSPS and NESHAP Sources

No demonstration of compliance with the TAP provisions is required to obtain a PTC or to demonstrate PTC exemption criteria for a new source or for modification of an existing source if the TAP is also a listed HAP from:

- *The equipment or activity covered by a NSPS or NESHAP; or*
- *The source category of equipment or activity addressed by a NSPS or NESHAP even if the equipment or activity is not subject to compliance requirements under the federal rule.*

Emission sources covered or addressed by NSPS or NESHAP are identified in the following table, and guidance on interpretation of "addressed" is provided in Appendix F. Each emission source and activity listed in the table is addressed by the corresponding NSPS and NESHAP. For the sources identified, emissions of TAP that are also HAP (HAP TAP) were excluded from TAP compliance demonstrations (i.e., excluded from comparison to TAP EL and from modeling to demonstrate compliance with TAP AAC/AACC, as discussed in the Ambient Air Quality Impact Analyses).

Table 8 NSPS and NESHAP Sources

NESHAP / NSPS	Source Category Subject & Addressed	Sources
NESHAP Subpart ZZZZ [a] NSPS Subpart IIII	Any industry using a stationary internal combustion engine	*Emergency Power Generation* EDG1, EDG2, EDG3, EDFP
NESHAP Subpart AAAAA [a] NSPS Subpart HH	Any lime manufacturing plant	*Lime Production* LK, LKC, LS1–LS12, LSBM, LS-L/U, LCR, LS1-L/U, MillS2-L/U, and ACS1-4-L/U
NESHAP Subpart DDDDD [a] NESHAP Subpart JJJJJJ [a] NSPS Subpart Dc etc.	Any facility using a boiler or process heater (indirect fire)	*Process Heating* ACB, CKB, PV, HS [b]
NESHAP Subpart CCCCCC [a]	Any gasoline dispensing facility Includes any operation that transfers and stores gasoline	*Gasoline Fuel Storage and Dispensing* TG1–TG2
NESHAP Subpart EEEEEEE [a]	Gold ore mining Includes an establishment engaged in developing the mine site, mining, and/or beneficiating ores valued chiefly for their gold content, or in transformation of gold into bullion or doré bar in combination with mining activities	*Mining* drilling, blasting, excavating, hauling, prill silos, rock dumps and storage piles, tailings *Ore Processing* OC1–OC13 [b] *Ore Concentration and Refining* CIP Leach 1–4, CIL 1–6, CIP 1–6, CN Detox 1–2, AC, EW, MR, MF, CKD *Process Heating* ACB, CKB, PV, HS [b]
NSPS Subpart LL	Any metallic mineral plant Includes any combination of equipment that extracts aluminum, copper, gold, iron, lead, molybdenum, silver, titanium, tungsten, uranium, zinc, and zirconium	*Ore Processing* OC1–OC13 [b]
NSPS Subpart OOO	Any nonmetallic mineral plant Includes plants processing crushed and broken stone, crushed and broken limestone, lime plants, sand and gravel, clay, etc.	*Aggregate Production* PCSP1, PCSP2 *Concrete Production* CA-L/U *Lime Production* LK, LKC, LS1–LS12, LSBM, LS-L/U, LCR, LS1-L/U, MillS2-L/U, and ACS1-4-L/U [b]
Source category that may not be subject to and may not be addressed by NSPS or NESHAP		*Concrete Production* CM, CS1-L/U, CS2-L/U *Heating, Ventilation, and Air Conditioning* H1M–H2M, HM, HAC, HR, HA, HMO, HTS, HW

a) NESHAP in 40 CFR 63
b) Ore Processing emission sources are addressed by both the gold ore mining and metallic mineral plant source categories, Process Heating emission sources are addressed by both the gold ore mining and boiler/process heater source categories, and Lime Production emission sources are addressed by both the lime production and nonmetallic mineral processing plant source categories.

After exclusion of sources addressed by NSPS and/or NESHAP, concrete production (central mixer, cement/shotcrete silos, aggregate bin) and heating, ventilation, and air conditioning (HVAC) units comprise the remaining sources that are applicable to compliance with TAP provisions. Emissions of each TAP from these sources (non-NESHAP-addressed) were estimated and compared to the applicable screening emission level (as summarized in Table 6).

Mercury Emission Standard (IDAPA 58.01.01.215)

IDAPA 58.01.01.215..... Mercury Emission Standard for New or Modified Sources

No owner or operator may commence construction or modification of a stationary source or facility that results in an increase in annual potential emissions of mercury of 25 pounds or more unless the owner or operator has obtained a PTC under Sections 200–228 of the Rules. The PTC application shall include an MBACT analysis for the new or modified source or sources for review and approval by DEQ. A determination of applicability under Section 215 shall be based upon the best available information.

Fugitive emissions shall not be included in a determination of applicability under Section 215.

New or modified stationary sources within a source category subject to 40 CFR 63 are exempt from the requirements of Section 215.

IDAPA 58.01.01.215 sets requirements for mercury emissions. For this standard, fugitive emissions and sources in a source category subject to 40 CFR 63 are exempt. As identified in Table 8, emission sources within a source category subject to NESHAP 40 CFR 63, including Subpart ZZZZ, Subpart AAAAA, Subpart CCCCCC, and Subpart EEEEEEE were therefore exempt from this standard. Although non-applicable to area sources of HAP such as Midas Gold, as a source category lime manufacturing plants are subject to NESHAP 40 CFR 63, Subpart AAAAA and associated sources (identified in Table 8) therefore exempt from this standard. Fugitive emissions from drilling, blasting, excavating, roadways (hauling), dozing, grading, storage piles, tailings and other fugitive and mobile emission sources were also exempt from this standard. Refer to the MACT/GACT Applicability (40 CFR 63) section for regulatory applicability analysis. No mercury emissions are expected from fuel storage, emergency power generation, and fire suppression sources.

After exclusion of sources within a source category subject to an area source NESHAP (40 CFR 63), aggregate production (crushers, screens, and conveyors), concrete production (aggregate bin), and heating, ventilation, and air conditioning (HVAC) units comprise the remaining sources that are applicable to the Mercury Emission Standard. Mercury emissions from these sources (non-fugitive and non-NESHAP-addressed) were estimated at less than 0.041 pounds per year (lb/yr), below the level at which MBACT review is required. Mercury emissions from propane combustion in HVAC sources are uncontrolled. Mercury emissions from materials processed in aggregate production and concrete production are controlled via water sprays and moisture carryover. As such controls are required for the portable crushing and screening plant, central mixer, and cement/shotcrete silos (Permit Conditions 2.1–2.8, 5.9, 5.10, and 5.15).

For the autoclave, electrowinning cells and pregnant solution tank, mercury retort, and induction melting furnace refinery sources (AC, EW, MR, MF) with enforceable NESHAP Subpart EEEEEEE mercury emission limits, potential emissions estimates (PTE) calculated consistent with these limits were included in the facility-wide mercury emission totals in Table 6. These values were substituted in lieu of the controlled emission estimates referenced from Table B1-W3 of Appendix B to the HAP/TAP addendum and 'TblB1' worksheet in the supporting spreadsheet. Although the mercury emissions from these sources are ultimately not included in the adjusted mercury emission totals for the purposes of the Mercury Emission Standard, these were used for the purposes of estimating HAP PTE consistent with enforceable limits.

Particulate Matter – New Equipment Process Weight Limitations (IDAPA 58.01.01.701)

IDAPA 58.01.01.701 ..... Particulate Matter – New Equipment Process Weight Limitations

IDAPA 58.01.01.700 through 703 set PM emission limits for process equipment based on when the piece of equipment commenced operation and the piece of equipment's process weight (PW) in pounds per hour (lb/hr). IDAPA 58.01.01.701 establishes PM emission limits for equipment that commenced operation on or after October 1, 1979.

For equipment commencing operation on or after October 1, 1979, the PM allowable emission rate (E) is based on one of the following equations:

IDAPA 58.01.01.701.01.a: If PW is $< 9{,}250$ lb/hr; $E = 0.045\ (PW)^{0.60}$

IDAPA 58.01.01.701.01.b: If PW is $\geq 9{,}250$ lb/hr; $E = 1.10\ (PW)^{0.25}$

For the new ore processing, ore concentration and refining, lime production, aggregate production, and concrete production equipment sources (Table 1) emissions (E) were calculated at the proposed maximum throughput rates (Table 1), and estimated emissions from all sources demonstrated compliance with this requirement. Compliance with operational and material throughput limits (Permit Conditions 3.3–3.8, 4.5–4.12, and 5.4–5.8) and control equipment requirements (Permit Conditions 2.6, 3.9–3.11, 4.13–4.17, and 5.9–5.15) assure compliance with this standard, resulting in much lower emission rates.

Title V Classification (IDAPA 58.01.01.300, 40 CFR Part 70)

IDAPA 58.01.01.301 ..... Requirement to Obtain Tier I Operating Permit

Any source subject to 40 CFR 63, Subpart EEEEEEE is a Tier I source as defined in IDAPA 58.01.01.006.122.c. In accordance with IDAPA 58.01.01.313.01.b., the permittee must submit a complete application to DEQ for an initial Tier I operating permit within 12 months of becoming a Tier I source.

Midas Gold has committed to applying for a Tier I permit. Detailed federal regulatory applicability were provided in the PTC application, and specific federally-applicable requirements will be incorporated into the Tier I. Refer to the NSPS Applicability (40 CFR 60), NESHAP Applicability (40 CFR 61), and MACT/GACT Applicability (40 CFR 63) sections below for additional information regarding applicable requirements.

Post-project facility-wide emissions from this facility do not have a PTE greater than 100 tons per year for criteria pollutants or 10 tons per year for any one HAP or 25 tons per year for all HAP combined as demonstrated previously in the Emissions Inventories section of this analysis. Although not a major facility as defined in IDAPA 58.01.01.008.10, any source subject to 40 CFR 63, Subpart EEEEEEE is a Tier I source as defined in IDAPA 58.01.01.006.122.c. In accordance with IDAPA 58.01.01.313.01.b., the permittee must submit a complete application to DEQ for an initial Tier I operating permit within 12 months of becoming a Tier I source. Refer to the NESHAP Applicability (40 CFR 61) section for additional discussion of Subpart EEEEEEE applicability.

Permit Condition 2.24 incorporates the requirement to obtain a Tier I permit in accordance with IDAPA 58.01.01.313.01.b.

PSD Classification (40 CFR 52.21)

40 CFR 52.21 ..... Prevention of Significant Deterioration of Air Quality

The facility is not a major stationary source as defined in 40 CFR 52.21(b)(1), nor is it undergoing any physical change at a stationary source not otherwise qualifying under paragraph 40 CFR 52.21(b)(1) as a major stationary source which would constitute a major stationary source by itself as defined in 40 CFR 52. PSD requirements were therefore not applicable to this permitting action in accordance with 40 CFR 52.21(a)(2).

The facility includes a lime manufacturing plant (LMP) that uses a Parallel Flow Regenerative Shaft Kiln (LK, LKC) to produce lime product from limestone by calcination, which is a designated facility as defined in 40 CFR 52.21(b)(1)(i)(a). For each criteria pollutant, LMP emissions do not exceed 100 T/yr and facility-wide emissions do not exceed 250 T/yr.

NSPS Applicability (40 CFR 60)

The permittee has affected facilities subject to New Source Performance Standards (NSPS). The POX Boiler (ACB) meets the definition of process heater rather than steam generating unit, and the use of a rotary lime kiln has not been proposed in the production of lime; therefore Subpart Dc and Subpart HH are not applicable. Initial regulatory applicability analyses and determinations are provided below; detailed analyses and explicit incorporation of applicable requirements is left to the required Tier I permit action as discussed in the Title V Classification (IDAPA 58.01.01.300, 40 CFR Part 70) section.

- Standards of Performance for New Stationary Sources (NSPS) 40 CFR 60, Subpart A – General Provisions. DEQ is delegated this Subpart.

- NSPS 40 CFR 60, Subpart LL – Standards of Performance for Metallic Mineral Processing Plants. DEQ is delegated this Subpart. Each crusher, conveyor belt transfer point, and truck unloading station is an affected facility.
- NSPS 40 CFR 60, Subpart OOO – Standards of Performance for Nonmetallic Mineral Processing Plants. DEQ is delegated this Subpart. Each crusher, grinding mill, screening operation, belt conveyor, and storage bin is an affected facility.
- NSPS 40 CFR 60, Subpart IIII – Standards of Performance for Stationary Compression Ignition Internal Combustion Engines. DEQ is delegated this Subpart. Each emergency generator engine and fire pump is an affected facility.

Emission sources regulated by Subpart LL, Subpart OOO, and Subpart IIII are identified in the incorporation of federal requirements condition (Permit Condition 2.22)

40 CFR 60, Subpart A ..... General Provisions

§60.1 ..... Applicability

(a) Except as provided in subparts B and C, the provisions of this part apply to the owner or operator of any stationary source which contains an affected facility, the construction or modification of which is commenced after the date of publication in this part of any standard (or, if earlier, the date of publication of any proposed standard) applicable to that facility.

(b) Any new or revised standard of performance promulgated pursuant to section 111(b) of the Act shall apply to the owner or operator of any stationary source which contains an affected facility, the construction or modification of which is commenced after the date of publication in this part of such new or revised standard (or, if earlier, the date of publication of any proposed standard) applicable to that facility.

Because the permittee will own or operate NSPS affected facilities, which have been proposed to commence construction after the date of publication of the relevant applicable NSPS standards (as listed above), general provisions in Subpart A are applicable.

40 CFR 60, Subpart A is incorporated by reference into Permit Condition 2.22, and specific applicable requirements will be incorporated into the Tier I operating permit.

40 CFR 60, Subpart Dc ..... Standards of Performance for Small Industrial-Commercial-Institutional Steam Generating Units

§60.40c ..... Applicability and delegation of authority.

(a) Except as provided in paragraphs (d), (e), (f), and (g) of this section, the affected facility to which this subpart applies is each steam generating unit for which construction, modification, or reconstruction is commenced after June 9, 1989 and that has a maximum design heat input capacity of 29 megawatts (MW) (100 million British thermal units per hour (MMBtu/h)) or less, but greater than or equal to 2.9 MW (10 MMBtu/h).

§60.41c ..... Definitions.

As used in this subpart, all terms not defined herein shall have the meaning given them in the Clean Air Act and in subpart A of this part.

...

Heat input *means heat derived from combustion of fuel in a steam generating unit and does not include the heat derived from preheated combustion air, recirculated flue gases, or exhaust gases from other sources (such as stationary gas turbines, internal combustion engines, and kilns).*

Heat transfer medium *means any material that is used to transfer heat from one point to another point.*

...

Process heater *means a device that is primarily used to heat a material to initiate or promote a chemical reaction in which the material participates as a reactant or catalyst.*

...

Steam generating unit *means a device that combusts any fuel and produces steam or heats water or heats any heat transfer medium. This term includes any duct burner that combusts fuel and is part of a combined cycle system. This term does not include process heaters as defined in this subpart.*

Although the Pressure Oxidation Boiler (POX Boiler) is between 10 and 100 MMBtu/hr in design heat input capacity (17 MMBtu/hr) and is proposed for construction after June 9, 1989, it meets the definition of process heater rather than steam generating unit, and therefore is not applicable to this subpart. The POX Boiler (ACB) is a device used to directly heat ore material via steam injection into the autoclave, to promote chemical oxidation reactions in which the heated ore participates as a reactant. DEQ is delegated this Subpart.

40 CFR 60, Subpart HH ..... Standards of Performance for Lime Manufacturing Plants

§60.340 ..... Applicability and designation of affected facility.

(a) The provisions of this subpart are applicable to each rotary lime kiln used in the manufacture of lime.

(b) The provisions of this subpart are not applicable to facilities used in the manufacture of lime at kraft pulp mills.

(c) Any facility under paragraph (a) of this section that commences construction or modification after May 3, 1977, is subject to the requirements of this subpart.

§60.341 ..... Definitions.

As used in this subpart, all terms not defined herein shall have the same meaning given them in the Act and in the General Provisions.

(a) Lime manufacturing plant *means any plant which uses a rotary lime kiln to produce lime product from limestone by calcination.*

(b) Lime product *means the product of the calcination process including, but not limited to, calcitic lime, dolomitic lime, and dead-burned dolomite.*

(c) Positive-pressure fabric filter *means a fabric filter with the fans on the upstream side of the filter bags.*

(d) Rotary lime kiln *means a unit with an inclined rotating drum that is used to produce a lime product from limestone by calcination.*

(e) Stone feed *means limestone feedstock and mill scale or other iron oxide additives that become part of the product.*

The use of a rotary lime kiln has not been proposed in the production of lime, and therefore the requirements of Subpart HH are not applicable. DEQ is delegated this Subpart.

40 CFR 60, Subpart LL ..... Standards of Performance for Metallic Mineral Processing Plants

§60.380 ..... Applicability and designation of affected facility.

(a) The provisions of this subpart are applicable to the following affected facilities in metallic mineral processing plants: Each crusher and screen in open-pit mines; each crusher, screen, bucket elevator, conveyor belt transfer point, thermal dryer, product packaging station, storage bin, enclosed storage area, truck loading station, truck unloading station, railcar loading station, and railcar unloading station at the mill or concentrator with the following exceptions. All facilities located in underground mines are exempted from the provisions of this subpart. At uranium ore processing plants, all facilities subsequent to and including the beneficiation of uranium ore are exempted from the provisions of this subpart.

(b) An affected facility under paragraph (a) of this section that commences construction or modification after August 24, 1982, is subject to the requirements of this part.

Because the permittee will own or operate a metallic mineral processing plant with a crusher at an open-pit mine; with crushers, conveyor belt transfer points, and truck unloading stations at the mill or concentrator; and because these are proposed to commence construction after August 24, 1982, requirements in Subpart LL are applicable.

40 CFR 60, Subpart LL is incorporated by reference into Permit Condition 2.22, and specific applicable requirements will be incorporated into the Tier I operating permit.

40 CFR 60, Subpart OOO ..... Standards of Performance for Nonmetallic Mineral Processing Plants

§60.670 ..... Applicability and designation of affected facility.

(a)(1) Except as provided in paragraphs (a)(2), (b), (c), and (d) of this section, the provisions of this subpart are applicable to the following affected facilities in fixed or portable nonmetallic mineral processing plants: each crusher, grinding mill, screening operation, bucket elevator, belt conveyor, bagging operation, storage bin, enclosed truck or railcar loading station. Also, crushers and grinding mills at hot mix asphalt facilities that reduce the size of nonmetallic minerals embedded in recycled asphalt pavement and subsequent affected facilities up to, but not including, the first storage silo or bin are subject to the provisions of this subpart.

(2) The provisions of this subpart do not apply to the following operations: All facilities located in underground mines; plants without crushers or grinding mills above ground; and wet material processing operations (as defined in §60.671).

(b) An affected facility that is subject to the provisions of subparts F or I of this part or that follows in the plant process any facility subject to the provisions of subparts F or I of this part is not subject to the provisions of this subpart.

(c) Facilities at the following plants are not subject to the provisions of this subpart:

(1) Fixed sand and gravel plants and crushed stone plants with capacities, as defined in §60.671, of 23 megagrams per hour (25 tons per hour) or less;

(2) Portable sand and gravel plants and crushed stone plants with capacities, as defined in §60.671, of 136 megagrams per hour (150 tons per hour) or less; and

(3) Common clay plants and pumice plants with capacities, as defined in §60.671, of 9 megagrams per hour (10 tons per hour) or less.

(d)(1) When an existing facility is replaced by a piece of equipment of equal or smaller size, as defined in §60.671, having the same function as the existing facility, and there is no increase in the amount of emissions, the new facility is exempt from the provisions of §§60.672, 60.674, and 60.675 except as provided for in paragraph (d)(3) of this section.

(2) An owner or operator complying with paragraph (d)(1) of this section shall submit the information required in §60.676(a).

(3) An owner or operator replacing all existing facilities in a production line with new facilities does not qualify for the exemption described in paragraph (d)(1) of this section and must comply with the provisions of §§60.672, 60.674 and 60.675.

(e) An affected facility under paragraph (a) of this section that commences construction, modification, or reconstruction after August 31, 1983, is subject to the requirements of this part.

(f) Table 1 of this subpart specifies the provisions of subpart A of this part 60 that do not apply to owners and operators of affected facilities subject to this subpart or that apply with certain exceptions.

Because the project contains crushers, grinding mills, screening operations, belt conveyors, and storage bins in a fixed or portable nonmetallic mineral processing plant, which are proposed to commence construction after August 31, 1983, requirements in Subpart OOO are applicable. The portable crushing and screening plants (PCSP1, PCSP2) will be rated at below 150 tons per hour (T/hr), and are therefore not subject to the provisions of Subpart OOO.

40 CFR 60, Subpart OOO is incorporated by reference into Permit Condition 2.22, and specific applicable requirements will be incorporated into the Tier I operating permit.

40 CFR 60, Subpart IIII..... Standards of Performance for Stationary Compression Ignition Internal Combustion Engines

§60.4200..... Am I subject to this subpart?

(a) The provisions of this subpart are applicable to manufacturers, owners, and operators of stationary compression ignition (CI) internal combustion engines (ICE) and other persons as specified in paragraphs (a)(1) through (4) of this section. For the purposes of this subpart, the date that construction commences is the date the engine is ordered by the owner or operator.

(1) Manufacturers of stationary CI ICE with a displacement of less than 30 liters per cylinder where the model year is:

(i) 2007 or later, for engines that are not fire pump engines;

(ii) The model year listed in Table 3 to this subpart or later model year, for fire pump engines.

(2) Owners and operators of stationary CI ICE that commence construction after July 11, 2005, where the stationary CI ICE are:

(i) Manufactured after April 1, 2006, and are not fire pump engines, or

(ii) Manufactured as a certified National Fire Protection Association (NFPA) fire pump engine after July 1, 2006.

(3) Owners and operators of any stationary CI ICE that are modified or reconstructed after July 11, 2005 and any person that modifies or reconstructs any stationary CI ICE after July 11, 2005.

(4) The provisions of §60.4208 of this subpart are applicable to all owners and operators of stationary CI ICE that commence construction after July 11, 2005.

(b) The provisions of this subpart are not applicable to stationary CI ICE being tested at a stationary CI ICE test cell/stand.

(c) If you are an owner or operator of an area source subject to this subpart, you are exempt from the obligation to obtain a permit under 40 CFR part 70 or 40 CFR part 71, provided you are not required to obtain a permit under 40 CFR 70.3(a) or 40 CFR 71.3(a) for a reason other than your status as an area source under this subpart. Notwithstanding the previous sentence, you must continue to comply with the provisions of this subpart applicable to area sources.

(d) Stationary CI ICE may be eligible for exemption from the requirements of this subpart as described in 40 CFR part 1068, subpart C (or the exemptions described in 40 CFR part 89, subpart J and 40 CFR part 94, subpart J, for engines that would need to be certified to standards in those parts), except that owners and operators, as well as manufacturers, may be eligible to request an exemption for national security.

(e) Owners and operators of facilities with CI ICE that are acting as temporary replacement units and that are located at a stationary source for less than 1 year and that have been properly certified as meeting the standards that would be applicable to such engine under the appropriate nonroad engine provisions, are not required to meet any other provisions under this subpart with regard to such engines.

Because the permittee will own or operate compression ignition (CI) internal combustion engines (ICE) which are proposed to commence construction after July 11, 2005 and which will be ordered after April 1, 2006 for the emergency generator engines, and which will be ordered after July 1, 2006 for the fire pump engine, requirements in Subpart IIII are applicable. The permittee has not requested or qualified for exemption pursuant to §60.4200(b), (d), or (e).

40 CFR 60, Subpart IIII is incorporated by reference into Permit Condition 2.22, and specific applicable requirements will be incorporated into the Tier I operating permit.

NESHAP Applicability (40 CFR 61)

The facility is not subject to any NESHAP requirements in 40 CFR 61.

MACT/GACT Applicability (40 CFR 63)

The permittee has proposed to operate as a minor source of hazardous air pollutant (HAP) emissions, and has affected facilities subject to the following National Emission Standards for Hazardous Air Pollutants (NESHAP). The lime manufacturing plant is proposed at an area source of HAP, and therefore is not applicable to Subpart AAAAA. The process boiler is at an area source of Applicability determinations and regulatory analyses are provided below.

- National Emission Standards for Hazardous Air Pollutants for Source Categories (NESHAP) 40 CFR 63, Subpart A – General Provisions. DEQ is delegated this Subpart for Tier I sources.
- NESHAP 40 CFR 63, Subpart ZZZZ – National Emission Standards for Hazardous Air Pollutants for Stationary Reciprocating Internal Combustion Engines (RICE). DEQ is delegated this Subpart. The emergency generator and fire pump engines (EDG1, EDG2, EDG3, and EDFP) are affected sources.
- NESHAP 40 CFR 63, Subpart CCCCCC – National Emission Standards for Hazardous Air Pollutants for Source Category: Gasoline Dispensing Facilities. DEQ is delegated this Subpart for Tier I sources. The gasoline fuel storage tanks (TG1, TG2) are affected sources.
- NESHAP 40 CFR 63, Subpart EEEEEEE – National Emission Standards for Hazardous Air Pollutants: Gold Mine Ore Processing and Production Area Source Category. DEQ is delegated this Subpart for Tier I sources. The collection of ore pretreatment processes and the carbon process with mercury retort are affected sources. Ore pretreatment processes include the autoclave (AC). Carbon processes with mercury retort include the electrowinning cells and pregnant solution tank (EW), the mercury retort (MR), induction melting furnace (MF), and the carbon regeneration kiln (CKD).

Emission sources regulated by Subpart EEEEEEE, Subpart CCCCCC, and Subpart ZZZZ are identified in the incorporation of federal requirements condition (Permit Condition 2.22)

40 CFR 63, Subpart A ..... General Provisions

§63.1 ..... Applicability.

(a) General. *(1) Terms used throughout this part are defined in §63.2 or in the Clean Air Act (Act) as amended in 1990, except that individual subparts of this part may include specific definitions in addition to or that supersede definitions in §63.2.*

(2) This part contains national emission standards for hazardous air pollutants (NESHAP) established pursuant to section 112 of the Act as amended November 15, 1990. These standards regulate specific categories of stationary sources that emit (or have the potential to emit) one or more hazardous air pollutants listed in this part pursuant to section 112(b) of the Act. This section explains the applicability of such standards to sources affected by them. The standards in this part are independent of NESHAP contained in 40 CFR part 61. The NESHAP in part 61 promulgated by signature of the Administrator before November 15, 1990 (i.e., the date of enactment of the Clean Air Act Amendments of 1990) remain in effect until they are amended, if appropriate, and added to this part.

(3) No emission standard or other requirement established under this part shall be interpreted, construed, or applied to diminish or replace the requirements of a more stringent emission limitation or other applicable requirement established by the Administrator pursuant to other authority of the Act (section 111, part C or D or any other authority of this Act), or a standard issued under State authority. The Administrator may specify in a specific standard under this part that facilities subject to other provisions under the Act need only comply with the provisions of that standard.

(4)(i) Each relevant standard in this part 63 must identify explicitly whether each provision in this subpart A is or is not included in such relevant standard.

(ii) If a relevant part 63 standard incorporates the requirements of 40 CFR part 60, part 61 or other part 63 standards, the relevant part 63 standard must identify explicitly the applicability of each corresponding part 60, part 61, or other part 63 subpart A (General) provision.

(iii) The General Provisions in this subpart A do not apply to regulations developed pursuant to section 112(r) of the amended Act, unless otherwise specified in those regulations.

...

(b) Initial applicability determination for this part. *(1) The provisions of this part apply to the owner or operator of any stationary source that—*

(i) Emits or has the potential to emit any hazardous air pollutant listed in or pursuant to section 112(b) of the Act; and

(ii) Is subject to any standard, limitation, prohibition, or other federally enforceable requirement established pursuant to this part.

(2) [Reserved]

(3) An owner or operator of a stationary source who is in the relevant source category and who determines that the source is not subject to a relevant standard or other requirement established under this part must keep a record as specified in §63.10(b)(3).

Because the permittee will own or operate stationary sources that emit HAP which are subject to standards, limitations, prohibitions, or other federally-enforceable requirements established pursuant to NESHAP, provisions in Subpart A are applicable.

40 CFR 63, Subpart A is incorporated by reference into Permit Condition 2.22, and specific applicable requirements will be incorporated into the Tier I operating permit.

40 CFR 63, Subpart ZZZZ..... National Emissions Standards for Hazardous Air Pollutants for Stationary Reciprocating Internal Combustion Engines

§63.6580..... What is the purpose of subpart ZZZZ?

Subpart ZZZZ establishes national emission limitations and operating limitations for hazardous air pollutants (HAP) emitted from stationary reciprocating internal combustion engines (RICE) located at major and area sources of HAP emissions. This subpart also establishes requirements to demonstrate initial and continuous compliance with the emission limitations and operating limitations.

§63.6585..... Am I subject to this subpart?

You are subject to this subpart if you own or operate a stationary RICE at a major or area source of HAP emissions, except if the stationary RICE is being tested at a stationary RICE test cell/stand.

(a) A stationary RICE is any internal combustion engine which uses reciprocating motion to convert heat energy into mechanical work and which is not mobile. Stationary RICE differ from mobile RICE in that a stationary RICE is not a non-road engine as defined at 40 CFR 1068.30, and is not used to propel a motor vehicle or a vehicle used solely for competition.

(b) A major source of HAP emissions is a plant site that emits or has the potential to emit any single HAP at a rate of 10 tons (9.07 megagrams) or more per year or any combination of HAP at a rate of 25 tons (22.68 megagrams) or more per year, except that for oil and gas production facilities, a major source of HAP emissions is determined for each surface site.

(c) An area source of HAP emissions is a source that is not a major source.

(d) If you are an owner or operator of an area source subject to this subpart, your status as an entity subject to a standard or other requirements under this subpart does not subject you to the obligation to obtain a permit under 40 CFR part 70 or 71, provided you are not required to obtain a permit under 40 CFR 70.3(a) or 40 CFR 71.3(a) for a reason other than your status as an area source under this subpart. Notwithstanding the previous sentence, you must continue to comply with the provisions of this subpart as applicable.

(e) If you are an owner or operator of a stationary RICE used for national security purposes, you may be eligible to request an exemption from the requirements of this subpart as described in 40 CFR part 1068, subpart C.

(f) The emergency stationary RICE listed in paragraphs (f)(1) through (3) of this section are not subject to this subpart. The stationary RICE must meet the definition of an emergency stationary RICE in §63.6675, which includes operating according to the provisions specified in §63.6640(f).

(1) Existing residential emergency stationary RICE located at an area source of HAP emissions that do not operate or are not contractually obligated to be available for more than 15 hours per calendar year for the purposes specified in §63.6640(f)(2)(ii) and (iii) and that do not operate for the purpose specified in §63.6640(f)(4)(ii).

(2) Existing commercial emergency stationary RICE located at an area source of HAP emissions that do not operate or are not contractually obligated to be available for more than 15 hours per calendar year for the purposes specified in §63.6640(f)(2)(ii) and (iii) and that do not operate for the purpose specified in §63.6640(f)(4)(ii).

(3) Existing institutional emergency stationary RICE located at an area source of HAP emissions that do not operate or are not contractually obligated to be available for more than 15 hours per calendar year for the purposes specified in §63.6640(f)(2)(ii) and (iii) and that do not operate for the purpose specified in §63.6640(f)(4)(ii).

Because the permittee will own or operate stationary RICE at an area source of HAP which are subject to standards, limitations, prohibitions, or other federally-enforceable requirements established pursuant to NESHAP, requirements in Subpart ZZZZ are applicable.

40 CFR 63, Subpart ZZZZ is incorporated by reference into Permit Condition 2.22, and specific applicable requirements will be incorporated into the Tier I operating permit.

40 CFR 63, Subpart AAAAA..... National Emission Standards for Hazardous Air Pollutants for Lime Manufacturing Plants

§63.7080..... What is the purpose of this subpart?

This subpart establishes national emission standards for hazardous air pollutants (NESHAP) for lime manufacturing plants. This subpart also establishes requirements to demonstrate initial and continuous compliance with the emission limitations.

§63.7081..... Am I subject to this subpart?

(a) You are subject to this subpart if you own or operate a lime manufacturing plant (LMP) that is a major source, or that is located at, or is part of, a major source of hazardous air pollutant (HAP) emissions, unless the LMP is located at a kraft pulp mill, soda pulp mill, sulfite pulp mill, beet sugar manufacturing plant, or only processes sludge containing calcium carbonate from water softening processes.

(1) An LMP is an establishment engaged in the manufacture of lime product (calcium oxide, calcium oxide with magnesium oxide, or dead burned dolomite) by calcination of limestone, dolomite, shells or other calcareous substances.

(2) A major source of HAP is a plant site that emits or has the potential to emit any single HAP at a rate of 9.07 megagrams (10 tons) or more per year or any combination of HAP at a rate of 22.68 megagrams (25 tons) or more per year from all emission sources at the plant site.

(b) [Reserved]

§63.7143..... What definitions apply to this subpart?

Terms used in this subpart are defined in the Clean Air Act, in §63.2, and in this section as follows:

...

Lime manufacturing plant (LMP) *means any plant which uses a lime kiln to produce lime product from limestone or other calcareous material by calcination.*

Lime product *means the product of the lime kiln calcination process including, calcitic lime, dolomitic lime, and dead-burned dolomite.*

Limestone *means the material comprised primarily of calcium carbonate (referred to sometimes as calcitic or high calcium limestone), magnesium carbonate, and/or the double carbonate of both calcium and magnesium (referred to sometimes as dolomitic limestone or dolomite).*

...

The lime manufacturing plant is proposed at an area source of HAP, and therefore is not subject to this Subpart.

40 CFR 60, Subpart CCCCCC..... National Emission Standards for Hazardous Air Pollutants for Source Category: Gasoline Dispensing Facilities

§63.11110..... What is the purpose of this subpart?

This subpart establishes national emission limitations and management practices for hazardous air pollutants (HAP) emitted from the loading of gasoline storage tanks at gasoline dispensing facilities (GDF). This subpart also establishes requirements to demonstrate compliance with the emission limitations and management practices.

§63.11111..... Am I subject to the requirements in this subpart?

(a) The affected source to which this subpart applies is each GDF that is located at an area source. The affected source includes each gasoline cargo tank during the delivery of product to a GDF and also includes each storage tank.

(b) If your GDF has a monthly throughput of less than 10,000 gallons of gasoline, you must comply with the requirements in §63.11116.

(c) If your GDF has a monthly throughput of 10,000 gallons of gasoline or more, you must comply with the requirements in §63.11117.

(d) If your GDF has a monthly throughput of 100,000 gallons of gasoline or more, you must comply with the requirements in §63.11118.

(e) An affected source shall, upon request by the Administrator, demonstrate that their monthly throughput is less than the 10,000-gallon or the 100,000-gallon threshold level, as applicable. For new or reconstructed affected sources, as specified in §63.11112(b) and (c), recordkeeping to document monthly throughput must begin upon startup of the affected source. For existing sources, as specified in §63.11112(d), recordkeeping to document monthly throughput must begin on January 10, 2008. For existing sources that are subject to this subpart only because they load gasoline into fuel tanks other than those in motor vehicles, as defined in §63.11132, recordkeeping to document monthly throughput must begin on January 24, 2011. Records required under this paragraph shall be kept for a period of 5 years.

(f) If you are an owner or operator of affected sources, as defined in paragraph (a) of this section, you are not required to obtain a permit under 40 CFR part 70 or 40 CFR part 71 as a result of being subject to this subpart. However, you must still apply for and obtain a permit under 40 CFR part 70 or 40 CFR part 71 if you meet one or more of the applicability criteria found in 40 CFR 70.3(a) and (b) or 40 CFR 71.3(a) and (b).

(g) The loading of aviation gasoline into storage tanks at airports, and the subsequent transfer of aviation gasoline within the airport, is not subject to this subpart.

(h) Monthly throughput is the total volume of gasoline loaded into, or dispensed from, all the gasoline storage tanks located at a single affected GDF. If an area source has two or more GDF at separate locations within the area source, each GDF is treated as a separate affected source.

(i) If your affected source's throughput ever exceeds an applicable throughput threshold, the affected source will remain subject to the requirements for sources above the threshold, even if the affected source throughput later falls below the applicable throughput threshold.

(j) The dispensing of gasoline from a fixed gasoline storage tank at a GDF into a portable gasoline tank for the on-site delivery and subsequent dispensing of the gasoline into the fuel tank of a motor vehicle or other gasoline-fueled engine or equipment used within the area source is only subject to §63.11116 of this subpart.

(k) For any affected source subject to the provisions of this subpart and another Federal rule, you may elect to comply only with the more stringent provisions of the applicable subparts. You must consider all provisions of the rules, including monitoring, recordkeeping, and reporting. You must identify the affected source and provisions with which you will comply in your Notification of Compliance Status required under §63.11124. You also must demonstrate in your Notification of Compliance Status that each provision with which you will comply is at least as stringent as the otherwise applicable requirements in this subpart. You are responsible for making accurate determinations concerning the more stringent provisions, and noncompliance with this rule is not excused if it is later determined that your determination was in error, and, as a result, you are violating this subpart. Compliance with this rule is your responsibility and the Notification of Compliance Status does not alter or affect that responsibility.

§63.11132..... What definitions apply to this subpart?

As used in this subpart, all terms not defined herein shall have the meaning given them in the Clean Air Act (CAA), or in subparts A and BBBBBB of this part. For purposes of this subpart, definitions in this section supersede definitions in other parts or subparts.

Dual-point vapor balance system *means a type of vapor balance system in which the storage tank is equipped with an entry port for a gasoline fill pipe and a separate exit port for a vapor connection.*

Gasoline *means any petroleum distillate or petroleum distillate/alcohol blend having a Reid vapor pressure of 27.6 kilopascals or greater, which is used as a fuel for internal combustion engines.*

Gasoline cargo tank *means a delivery tank truck or railcar which is loading or unloading gasoline, or which has loaded or unloaded gasoline on the immediately previous load.*

Gasoline dispensing facility (GDF) *means any stationary facility which dispenses gasoline into the fuel tank of a motor vehicle, motor vehicle engine, nonroad vehicle, or nonroad engine, including a nonroad vehicle or nonroad engine used solely for competition. These facilities include, but are not limited to, facilities that dispense gasoline into on- and off-road, street, or highway motor vehicles, lawn equipment, boats, test engines, landscaping equipment, generators, pumps, and other gasoline-fueled engines and equipment.*

Monthly throughput *means the total volume of gasoline that is loaded into, or dispensed from, all gasoline storage tanks at each GDF during a month. Monthly throughput is calculated by summing the volume of gasoline loaded into, or dispensed from, all gasoline storage tanks at each GDF during the current day, plus the total volume of gasoline loaded into, or dispensed from, all gasoline storage tanks at each GDF during the previous 364 days, and then dividing that sum by 12.*

Motor vehicle *means any self-propelled vehicle designed for transporting persons or property on a street or highway.*

Nonroad engine *means an internal combustion engine (including the fuel system) that is not used in a motor vehicle or a vehicle used solely for competition, or that is not subject to standards promulgated under section 7411 of this title or section 7521 of this title.*

Nonroad vehicle *means a vehicle that is powered by a nonroad engine, and that is not a motor vehicle or a vehicle used solely for competition.*

Submerged filling *means, for the purposes of this subpart, the filling of a gasoline storage tank through a submerged fill pipe whose discharge is no more than the applicable distance specified in §63.11117(b) from the bottom of the tank. Bottom filling of gasoline storage tanks is included in this definition.*

Vapor balance system *means a combination of pipes and hoses that create a closed system between the vapor spaces of an unloading gasoline cargo tank and a receiving storage tank such that vapors displaced from the storage tank are transferred to the gasoline cargo tank being unloaded.*

Vapor-tight *means equipment that allows no loss of vapors. Compliance with vapor-tight requirements can be determined by checking to ensure that the concentration at a potential leak source is not equal to or greater than 100 percent of the Lower Explosive Limit when measured with a combustible gas detector, calibrated with propane, at a distance of 1 inch from the source.*

Vapor-tight gasoline cargo tank *means a gasoline cargo tank which has demonstrated within the 12 preceding months that it meets the annual certification test requirements in §63.11092(f) of this part.*

Because the permittee will own or operate a gasoline dispensing facility (GDF) at an area source of HAP, requirements in Subpart CCCCCC are applicable. Because the permittee has committed to loading and dispensing of less than 100,000 gallons of gasoline per month (gal/mo), the requirements of 40 CFR 63.11117 will become applicable in accordance with 40 CFR 63.11111(b) and (c). Gasoline loading and dispensing is limited by Permit Condition 2.18 to avoid requirements applicable to GDF exceeding 100,000 gal/mo, and requires recordkeeping in accordance with 40 CFR 63.11111(e).

40 CFR 63, Subpart CCCCCC is incorporated by reference into Permit Condition 2.22, and specific applicable requirements will be incorporated into the Tier I operating permit.

40 CFR 63, Subpart EEEEEEE..... National Emission Standards for Hazardous Air Pollutants: Gold Mine Ore Processing and Production Area Source Category

§40 CFR 63.11640..... Am I subject to this subpart?

(a) You are subject to this subpart if you own or operate a gold mine ore processing and production facility as defined in §63.11651, that is an area source.

(b) This subpart applies to each new or existing affected source. The affected sources are each collection of "ore pretreatment processes" at a gold mine ore processing and production facility, each collection of "carbon processes with mercury retorts" at a gold mine ore processing and production facility, each collection of "carbon processes without mercury retorts" at a gold mine ore processing and production facility, and each collection of "non-carbon concentrate processes" at a gold mine ore processing and production facility, as defined in §63.11651.

(1) An affected source is existing if you commenced construction or reconstruction of the affected source on or before April 28, 2010.

(2) An affected source is new if you commenced construction or reconstruction of the affected source after April 28, 2010.

(c) This subpart does not apply to research and development facilities, as defined in section 112(c)(7) of the Clean Air Act (CAA).

(d) If you own or operate a source subject to this subpart, you must have or you must obtain a permit under 40 CFR part 70 or 40 CFR part 71.

§40 CFR 63.11651..... What definitions apply to this subpart?

Terms used in this subpart are defined in the Clean Air Act, in §63.2, and in this section as follows:

Autoclave *means a pressure oxidation vessel that is used to treat gold ores (primarily sulfide refractory ore) and involves pumping a slurry of milled ore into the vessel which is highly pressurized with oxygen and heated to temperatures of approximately 350° to 430 °F.*

Calomel-based mercury control system *means a mercury emissions control system that uses scrubbers to remove mercury from the gas stream of a roaster or combination of roasters by complexing the mercury from the gas stream with mercuric chloride to form mercurous chloride (calomel). These scrubbers are also referred to as "mercury scrubbers."*

Carbon adsorber *means a control device consisting of a single fixed carbon bed, multiple carbon beds or columns, carbon filter packs or modules, and other variations that uses activated carbon to remove pollutants from a gas stream.*

Carbon kiln *means a kiln or furnace where carbon is regenerated by heating, usually in the presence of steam, after the gold has been stripped from the carbon.*

Carbon processes with mercury retorts *means the affected source that includes carbon kilns, preg tanks, electrowinning cells, mercury retorts, and melt furnaces at gold mine ore processing and production facilities that use activated carbon, or resins that can be used as a substitute for activated carbon, to recover (adsorb) gold from the pregnant cyanide solution.*

Carbon processes without mercury retorts *means the affected source that includes carbon kilns, preg tanks, electrowinning cells, and melt furnaces, but has no retorts, at gold mine ore processing and production facilities that use activated carbon, or resins that can be used as a substitute for activated carbon, to recover (adsorb) gold from the pregnant cyanide solution.*

Concentrate *means the sludge-like material that is loaded with gold along with various other metals (such as silver, copper, and mercury) and various other substances, that is produced by electrowinning, the Merrill-Crowe process, flotation and gravity separation processes. Concentrate is measured as the input to mercury retorts, or for facilities without mercury retorts, as the input to melt furnaces before any drying takes place. For facilities without mercury retorts or melt furnaces, concentrate is measured as the quantity shipped.*

Deviation *means any instance where an affected source subject to this subpart, or an owner or operator of such a source:*

(1) Fails to meet any requirement or obligation established by this subpart, including but not limited to any emissions limitation or work practice standard;

(2) Fails to meet any term or condition that is adopted to implement an applicable requirement in this subpart and that is included in the operating permit for any affected source required to obtain such a permit; or

(3) Exceeds any operating limit established under this subpart.

Electrowinning *means a process that uses induced voltage on anode and cathode plates to remove metals from the continuous flow of solution, where the gold in solution is plated onto the cathode. Steel wool is typically used as the plating surface.*

Electrowinning Cells *means a tank in which the electrowinning takes place.*

Gold mine ore processing and production facility *means any industrial facility engaged in the processing of gold mine ore that uses any of the following processes: Roasting operations, autoclaves, carbon kilns, preg tanks, electrowinning, mercury retorts, or melt furnaces. Laboratories (see CAA section 112(c)(7)), individual prospectors, and very small pilot scale mining operations that processes or produces less than 100 pounds of concentrate per year are not a gold mine ore processing and production facility. A facility that produces primarily metals other than gold, such as copper, lead, zinc, or nickel (where these metals other than gold comprise 95 percent or more of the total metal production) that may also recover some gold as a byproduct is not a gold mine ore processing and production facility. Those facilities whereby 95 percent or more of total mass of metals produced are metals other than gold, whether final metal production is onsite or offsite, are not part of the gold mine ore processing and production source category.*

Melt furnace *means a furnace (typically a crucible furnace) that is used for smelting the gold-bearing material recovered from mercury retorting, or the gold-bearing material from electrowinning, the Merrill-Crowe process, or other processes for facilities without mercury retorts.*

Mercury retort *means a vessel that is operated under a partial vacuum at approximately 1,100° to 1,300 °F to remove mercury and moisture from the gold bearing sludge material that is recovered from electrowinning, the Merrill-Crowe process, or other processes. Mercury retorts are usually equipped with condensers that recover liquid mercury during the processing.*

Merrill-Crowe process *means a precipitation technique using zinc oxide for removing gold from a cyanide solution. Zinc dust is added to the solution, and gold is precipitated to produce a concentrate.*

Non-carbon concentrate processes *means the affected source that includes mercury retorts and melt furnaces at gold mine ore processing and production facilities that use the Merrill-Crowe process or other processes and do not use carbon (or resins that substitute for carbon) to recover (adsorb) gold from the pregnant cyanide solution.*

Ore dry grinding *means a process in which the gold ore is ground and heated (dried) prior to additional preheating or prior to entering the roaster.*

Ore preheating *means a process in which ground gold ore is preheated prior to entering the roaster.*

Ore pretreatment processes *means the affected source that includes roasting operations and autoclaves that are used to pre-treat gold mine ore at gold mine ore processing and production facilities prior to the cyanide leaching process.*

Pregnant solution tank (or preg tank) *means a storage tank for pregnant solution, which is the cyanide solution that contains gold-cyanide complexes that is generated from leaching gold ore with cyanide solution.*

Pregnant cyanide solution *means the cyanide solution that contains gold-cyanide complexes that are generated from leaching gold ore with a dilute cyanide solution.*

Quenching *means a process in which the hot calcined ore is cooled and quenched with water after it leaves the roaster.*

Roasting operation *means a process that uses an industrial furnace in which milled ore is combusted across a fluidized bed to oxidize and remove organic carbon and sulfide mineral grains in refractory gold ore. The emissions points of the roasting operation subject to this subpart include ore dry grinding, ore preheating, the roaster stack, and quenching.*

Because the permittee will own or operate a gold mine ore processing and production facility at an area source of HAP, requirements in Subpart EEEEEEE are applicable. The collection of ore pretreatment processes and the carbon process with mercury retort are affected sources. Ore pretreatment processes include the autoclave (AC). Carbon processes with mercury retort include the electrowinning cells and pregnant solution tank (EW), the mercury retort (MR), induction melting furnace (MF), and the carbon regeneration kiln (CKD).

Any source subject to 40 CFR 63, Subpart EEEEEEE is a Tier I source as defined in IDAPA 58.01.01.006.122.c. In accordance with IDAPA 58.01.01.313.01.b., the permittee must submit a complete application to DEQ for an initial Tier I operating permit within 12 months of becoming a Tier I source.

This subpart includes mercury emissions limits for the collection of new ore pretreatment processes and for the new carbon processes with mercury retort. This subpart also requires weight measurement devices for measuring ore throughput for the autoclave (AC) and mineral-bearing solution throughput for the electrowinning cells and pregnant solution tank (EW). Requires monitoring of mercury emissions, and monitoring of either inlet gas temperature for each process unit with a carbon filter (EW, MR, MF, CKD) or both water flow and pressure drop for each process unit with a wet scrubber not followed by a carbon filter (AC).

40 CFR 63, Subpart EEEEEEE is incorporated by reference into Permit Condition 2.22, and specific applicable requirements will be incorporated into the Tier I operating permit.

Permit Conditions Review

This section describes the permit conditions for this initial permit.

Permit Conditions 1.1–1.2 describe the purpose of this permitting action and the emission sources and the control equipment regulated by this permit. This reflects information presented in the application and relied upon in the development of emissions inventories, and in the evaluation of ambient air impacts in the modeling analyses. Refer to the Emissions Inventories and the Ambient Air Quality Impact Analyses sections for additional information concerning these analyses.

Because specific vendor and manufacturer information was unavailable at the time of permitting, documentation and testing requirements were included (Permit Condition 2.20) to verify consistency with the information specified in the application. Production values and limits were based on process flow diagrams and engineering design information provided.

Permit Conditions 2.1–2.8 incorporate fugitive dust emission limits and control requirements as required by IDAPA 58.01.01.650-651. Compliance is ensured by implementing reasonable control precautions and corrective actions when appropriate, excluding public access to operations, and complying with inspection, monitoring, recordkeeping, and notification requirements. Specific precautions are identified and required in the fugitive dust control plan (FDCP), and specific measures to control public access within the operations boundary are identified in and required by the Access Management Plan (AMP; Permit Conditions 2.6 and 2.7, respectively). A trigger level for haul roads was also established requiring employment of control measures (Permit Condition 2.5).

Reduction of PM emissions from each of the identified conveyors by 80% was supported by assuming location of these material transfers at below grade (OC9, OC10) or enclosure on all sides (OC11). Reduction of PM emissions from haul roads by a combined 93.3% was supported by assuming appropriate application of water and magnesium chloride dust suppression; DEQ is cognizant that to consistently achieve this level of control requires conscientious efforts, vigilant inspection and monitoring, and a comprehensive FDCP. Because continuous operation was proposed, suppression measures will need to account for and accommodate all weather conditions including diurnal and seasonal variability, and all traffic loads including mining and public traffic along publicly accessible roads. Conditions outside of what may normally be anticipated may require additional measures such as a reduction in vehicle speeds or selection of a more effective chemical dust suppressant. Although the FDCP specifies a minimum of efforts required, additional operational limits and monitoring are to be considered moving forward and evaluated for incorporation into the FDCP. Certification of employees for visible emissions inspection, training and orientation of relevant employees, and periodic evaluation of FDCP requirements are also required.

Access control measures are described in the Ambient Air Boundary section of the application (Section 5.6), and address primary access points, secondary access points, and surveillance.

Permit Conditions 2.9–2.12 incorporate visible emission limits and control requirements (Permit Condition 2.9) in accordance with IDAPA 58.01.01.625. Compliance is ensured by implementing corrective actions when appropriate and complying with inspection, monitoring, and recordkeeping requirements. Certification of employees for visible emissions inspection is also required.

Permit Condition 2.13 incorporates PM emission limits for process equipment as defined in IDAPA 58.01.01.006, in accordance with IDAPA 58.01.01.700-703, which includes all ore processing, ore concentration and refining, lime production, aggregate production, and concrete production equipment (Table 1). Compliance with operational and material throughput limits (Permit Conditions 3.3–3.8, 4.5–4.12, and 5.4–5.8) and control equipment requirements (Permit Conditions 2.6, 3.9–3.11, 4.13–4.17, and 5.9–5.15) and associated monitoring were considered adequate to ensure compliance with process weight-based PM emission limitations.

Permit Conditions 2.14–2.15 incorporate odorous emission limits in accordance with IDAPA 58.01.01.776.01. Compliance is ensured by complying with monitoring and recordkeeping requirements, including corrective action when appropriate.

Permit Conditions 2.16–2.17 incorporate sulfur content limits for distillate fuel oil, in accordance with IDAPA 58.01.01.725. Compliance is ensured by complying with monitoring and recordkeeping requirements.

Permit Conditions 2.18–2.19 limit facility-wide gasoline fuel throughput. Limiting gasoline throughput limits PTE, ensures avoidance of Subpart CCCCCC requirements applicable to GDF exceeding 100,000 gal/mo, and requires recordkeeping in accordance with 40 CFR 63.11111(e). Compliance is ensured by complying with monitoring and recordkeeping requirements.

Permit Conditions 2.20–2.21 require developing and complying with the requirements of an O&M manual to ensure compliance with control equipment maintenance and operation general provisions (Permit Condition 7.2). Documentation of as-built process equipment specifications and control equipment performance guarantees and establishing control equipment operating parameters and procedures were required, since these were relied upon in the development of emissions inventories, and in the evaluation of ambient air impacts in the modeling analyses. Compliance is ensured by complying with monitoring and recordkeeping requirements.

Permit Condition 2.22 incorporates applicable general compliance, notification, recordkeeping, reporting, general provisions, and other federal requirements by reference in accordance with IDAPA 58.01.01.107.03 and 590-591. Compliance is ensured by complying with applicable federal testing, monitoring, recordkeeping, and reporting requirements. In the event there is a conflict between the subparts and/or emission sources listed (Permit Condition 2.22), the federal requirements shall apply.

With regard to permit conditions referenced in accordance with federal requirements (i.e., NSPS and NESHAP requirements), should there be a conflict between the language of the permit condition and the language of the requirement, the language of the requirement shall govern. Refer to NSPS Applicability (40 CFR 60) and MACT/GACT Applicability (40 CFR 63) sections for additional information concerning applicable requirements.

Permit Conditions 2.23–2.24 require notification upon becoming a Tier I source and require the permittee to obtain a Tier I operation permit within 12 months of commencement of operation of any ore concentration and refining equipment (i.e., NESHAP Subpart EEEEEEE-affected sources) in accordance with IDAPA 58.01.01.313.01.b.

Permit Condition 2.25 specifies recommended test methods to be used when performance testing is required, unless otherwise specified in the permit, in accordance with IDAPA 58.01.01.157. The permittee is required to comply with notification and reporting requirements and is encouraged to submit performance test protocol to DEQ for approval prior to any performance testing in accordance with the performance testing general provisions (Permit Condition 7.7–7.9).

Permit Condition 2.26 provides DEQ agency contact information.

Permit Conditions 3.1–3.2 describe mining and ore processing equipment and controls. This reflects information presented in the application and relied upon in the development of emissions inventories, and in the evaluation of ambient air impacts in the modeling analyses.

Permit Conditions 3.3–3.8 and 3.11–3.16 establish limits on material throughput and production. These limits were relied upon in the development of emissions inventories and in the evaluation of ambient air impacts in the modeling analyses. Overall mine throughput is limited by hauling and excavating limits (Permit Condition 3.5). Compliance is ensured by complying with monitoring and recordkeeping requirements (Permit Conditions 3.11–3.16).

Permit Conditions 3.9–3.10 require measures to include in the FDCP to control fugitive emissions. Use of reasonable controls were relied upon in the development of emissions inventories and in the evaluation of ambient air impacts in the modeling analyses. Compliance is ensured by complying with fugitive dust monitoring and recordkeeping requirements (Permit Conditions 2.1–2.8).

Permit Conditions 4.1–4.2 describe ore concentration and refining equipment and controls. This reflects information presented in the application and relied upon in the development of emissions inventories, and in the evaluation of ambient air impacts in the modeling analyses.

Permit Condition 4.3, and 4.33–4.34 establish emissions limits for ore concentration and refining equipment, consistent with estimates relied upon in the development of emissions inventories and in the evaluation of ambient air impacts in the modeling analyses for these sources. A sulfuric acid emission limit consistent with the modeled TAP emission rate from the autoclave was established in accordance with IDAPA 58.01.01.210.08. Compliance is ensured by complying with equipment operating and testing requirements (Permit Conditions 4.5–4.17, and 4.33–4.34).

Permit Conditions 4.4, 4.5–4.6, 4.7–4.12 and 4.18–4.25 limit operations of ore concentration and refining process equipment, consistent with the hours of operation, reagent usage, and material throughput assumptions relied upon in the development of emissions inventories and in the evaluation of ambient air impacts in the modeling analyses for these sources. Compliance is ensured by complying with monitoring and recordkeeping requirements (Permit Conditions 4.18–4.25). Cyanide is consumed, recycled, and destroyed in the process, and cyanide HAP emissions (and emission factors) dependent upon leachant concentration and basicity. Monitoring of these parameters was established to ensure that emissions do not exceed 10 T/yr of cyanide HAP to avoid classification as a HAP major source. Re-classification as a major source would affect NSPS and NESHAP applicability determinations, such as Subpart AAAAA as discussed in the NESHAP Applicability (40 CFR 61) section.

Permit Conditions 4.13–4.17 and 4.26–4.32 require control equipment for ore concentration and refining processes, consistent with controls relied upon in the development of emissions inventories and in the evaluation of ambient air impacts in the modeling analyses. Compliance is ensured by complying with monitoring and recordkeeping requirements (Permit Conditions 4.26–4.32).

Permit Condition 4.33 and 4.34 require testing of ore concentration and refining emission sources to demonstrate compliance with emissions limits (Permit Condition 4.3).

Permit Conditions 5.1–5.2 describe lime, aggregate, and concrete production equipment and controls. This reflects information presented in the application and relied upon in the development of emissions inventories, and in the evaluation of ambient air impacts in the modeling analyses.

Permit Condition 5.3 establishes emissions limits for lime, aggregate, and concrete production equipment, consistent with estimates relied upon in the development of emissions inventories and in the evaluation of ambient air impacts in the modeling analyses for these sources. Compliance is ensured by complying with equipment operating requirements (Permit Conditions 5.4–5.15).

Permit Conditions 5.4–5.8 and 5.16–5.20 limit operations of each lime, aggregate, and concrete production process equipment, consistent with material throughput assumptions relied upon in the development of emissions inventories and in the evaluation of ambient air impacts in the modeling analyses for these sources. Compliance is ensured by complying with monitoring and recordkeeping requirements (Permit Conditions 5.15–5.20).

Permit Conditions 5.9–5.10 require measures to include in the FDCP to control fugitive emissions. Use of water sprays, building enclosures, and reasonable controls were relied upon in the development of emissions inventories and in the evaluation of ambient air impacts in the modeling analyses. Compliance is ensured by complying with fugitive dust monitoring and recordkeeping requirements (Permit Conditions 2.1–2.8).

Permit Conditions 5.11–5.15 and 5.21–5.24 require control equipment for lime, aggregate, and concrete production processes, consistent with controls relied upon in the development of emissions inventories and in the evaluation of ambient air impacts in the modeling analyses. Compliance is ensured by complying with monitoring and recordkeeping requirements (Permit Conditions 5.21–5.24).

Permit Condition 6.1 describes the emergency power generation equipment. This reflects information presented in the application and relied upon in the development of emissions inventories, and in the evaluation of ambient air impacts in the modeling analyses.

Permit Conditions 6.2 and 6.3–6.4 limit operations of each emergency power generation engine, consistent with the purpose and hours of operation assumptions relied upon in the development of emissions inventories, in the determination of federal regulatory applicability, and in the evaluation of ambient air impacts in the modeling analyses for these sources. Compliance is ensured by complying with monitoring, recordkeeping, and notification requirements (Permit Conditions 6.3–6.4).

Permit Condition 7.1, the duty to comply general compliance provision, requires that the permittee comply with all of the permit terms and conditions pursuant to Idaho Code §39-101.

Permit Condition 7.2, the maintenance and operation general compliance provision, requires that the permittee maintain and operate all treatment and control facilities at the facility in accordance with IDAPA 58.01.01.211.

Permit Condition 7.3, the obligation to comply general compliance provision, specifies that no permit condition is intended to relieve or exempt the permittee from compliance with applicable state and federal requirements, in accordance with IDAPA 58.01.01.212.01.

Permit Condition 7.4, the inspection and entry provision, requires that the permittee allow DEQ inspection and entry pursuant to Idaho Code §39-108.

Permit Condition 7.5, the permit expiration construction and operation provision, specifies that the permit expires if construction has not begun within two years of permit issuance or if construction has been suspended for a year in accordance with IDAPA 58.01.01.211.02.

Permit Condition 7.6, the notification of construction and operation provision, requires that the permittee notify DEQ of the dates of construction and operation, in accordance with IDAPA 58.01.01.211.01 and 211.03.

Permit Condition 7.7, the performance testing notification of intent provision, requires that the permittee notify DEQ at least 15 days prior to any performance test to provide DEQ the option to have an observer present, in accordance with IDAPA 58.01.01.157.03.

Permit Condition 7.8, the performance test protocol provision, requires that any performance testing be conducted in accordance with the procedures of IDAPA 58.01.01.157 and encourages the permittee to submit a protocol to DEQ for approval prior to testing.

Permit Condition 7.9, the performance test report provision, requires that the permittee report any performance test results to DEQ within 60 days of completion, in accordance with IDAPA 58.01.01.157.04-05.

Permit Condition 7.10, the monitoring and recordkeeping provision, requires that the permittee maintain sufficient records to ensure compliance with permit conditions, in accordance with IDAPA 58.01.01.211.

Permit Condition 7.11, the excess emissions provision, requires that the permittee follow the procedures required for excess emissions events, in accordance with IDAPA 58.01.01.130-136.

Permit Condition 7.12, the certification provision, requires that a responsible official certify all documents submitted to DEQ, in accordance with IDAPA 58.01.01.123.

Permit Condition 7.13, the false statement provision, requires that no person make false statements, representations, or certifications, in accordance with IDAPA 58.01.01.125.

Permit Condition 7.14, the tampering provision, requires that no person render inaccurate any required monitoring device or method, in accordance with IDAPA 58.01.01.126.

Permit Condition 7.15, the transferability provision, specifies that this permit to construct is transferable, in accordance with the procedures of IDAPA 58.01.01.209.06.

Permit Condition 7.16, the severability provision, specifies that permit conditions are severable, in accordance with IDAPA 58.01.01.211.

PUBLIC REVIEW

Public Comment Opportunity

An opportunity for public comment period on the application was provided in accordance with IDAPA 58.01.01.209.01.c. During this time, there was a request for a public comment period on DEQ's proposed action. Refer to the Application Chronology for public comment opportunity dates.

Public Comment Period

Comment periods were made available to the public in accordance with IDAPA 58.01.01.209.01.c. An initial comment period and extension were provided to address the initial application and proposed action (i.e., permit and technical statement of basis), and a final comment period was provided to address updates to the proposed action resulting from a HAP/TAP application addendum[2] submitted by Midas Gold that included new HAP and TAP emission estimates, additional information and discussion supporting HAP and TAP emission estimates, new and updated TAP increment compliance demonstrations which included particulate TAP emissions from fugitive sources, and a source-by-source inventory of HAP and TAP emissions. During this time, comments were submitted in response to DEQ's proposed action. Refer to the Application Chronology for the dates of each public comment period.

A response to public comments document has been crafted by DEQ based on comments submitted during each public comment period. That document is part of the final permit package for this permitting action.

APPENDIX B – AMBIENT AIR QUALITY IMPACT ANALYSES REVIEW MEMORANDUM

MEMORANDUM

DATE: February 8, 2021

TO: Morrie Lewis, Permit Writer, Air Program

FROM: Pao Baylon, Modeling Review Analyst, Air Program
Through Kevin Schilling, Modeling Supervisor, Air Program

PROJECT: P-2019.0047 PROJ 62288, Permit for an Open-pit Gold Mine and On-site Ore Preparation and Gold Extraction Operation located in Valley County, Idaho.

SUBJECT: Demonstration of Compliance with IDAPA 58.01.01.203.02 (NAAQS) and 203.03 (TAPs) as it relates to air quality impact analyses.

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Acronyms, Units, and Chemical Nomenclature

AAC	Acceptable Ambient Concentration of a non-carcinogenic TAP
AACC	Acceptable Ambient Concentration of a Carcinogenic TAP
acfm	Actual cubic feet per minute
ADJ_U*	AERMOD Adjusted Friction Velocity Model Option
AERMAP	The terrain data preprocessor for AERMOD
AERMET	The meteorological data preprocessor for AERMOD
AERMOD	American Meteorological Society/Environmental Protection Agency Regulatory Model
Air Sciences	Air Sciences, Inc. (permittee's permitting and modeling consultant)
amsl	Above mean sea level
ANFO	Ammonium Nitrate Fuel Oil
Appendix W	40 CFR 51, Appendix W – Guideline on Air Quality Models
ASOS	Automated Surface Observing System
B_o	Bowen Ratio
BNF	Boise National Forest
BPIP	Building Profile Input Program
BRC	Below Regulatory Concern
BT	Bradley Tailings
BULKRN	Meteorological data processed using Bulk Richardson Method
CAPCOA	California Air Pollution Control Officers Association
CFR	Code of Federal Regulations
CMAQ	Community Multi-Scale Air Quality Modeling System
CO	Carbon Monoxide
CSIRO	Commonwealth Scientific and Industrial Research Organization
DEQ	Idaho Department of Environmental Quality
DR	Development Rock
DRSF	Development Rock Storage Facility
DV	Design Values
EF	Emission Factors
EFSFSR	East Fork of the South Fork of the Salmon River
EIS	Environmental Impact Statement
EL	Emissions Screening Level of a TAP
EPA	United States Environmental Protection Agency
FDRSF	Fiddle Development Rock Storage Facility
g/cm^3	Grams per Cubic Centimeter
GEP	Good Engineering Practice
H_2SO_4	Sulfuric Acid Gas
HAP	Hazardous Air Pollutant
HFDRSF	Hangar Flats Development Rock Storage Facility
HFP	Hangar Flats Pit
Hg	Mercury
hr	Hours
Idaho Air Rules	Rules for the Control of Air Pollution in Idaho, located in the Idaho Administrative Procedures Act 58.01.01

REC 4196

TR 0881

in	Inches
ISCST3	Industrial Source Complex Short Term 3 dispersion model
K	Kelvin
km	Kilometers
lb/hr	Pounds per hour
lb/yr	Pounds per year
LOM	Life of Mine
m	Meters
m/sec	Meters per second
MBACT	Mercury Best Available Control Technology
MERPs	Modeled Emission Rates for Precursors
mg/m^3	Milligrams per Cubic Meter
Midas Gold	Midas Gold Idaho, Inc. (permittee)
MM	Million
MMBtu	Million British Thermal Units
mph	Miles per hour
NAAQS	National Ambient Air Quality Standards
NAD83	North American Datum of 1983
NED	National Elevation Dataset
NESHAP	National Emission Standards for Hazardous Air Pollutants
NO	Nitrogen Oxide
NO_2	Nitrogen Dioxide
NON-BULKRN	Meteorological data processed without Bulk Richardson Method
NOx	Oxides of Nitrogen
NSPS	New Source Performance Standards
NSR	New Source Review
NW AIRQUEST	Northwest International Air Quality Environmental Science and Technology Consortium
NWS	National Weather Service
O_3	Ozone
OLM	Ozone Limiting Method
Pb	Lead
PM_{10}	Particulate matter with an aerodynamic particle diameter less than or equal to a nominal 10 micrometers
$PM_{2.5}$	Particulate matter with an aerodynamic particle diameter less than or equal to a nominal 2.5 micrometers
PNF	Payette National Forest
ppb	parts per billion
ppm	parts per million
PRIME	Plume Rise Model Enhancement
PRO	Midas Gold Plan of Restoration and Operations
PSD	Prevention of Significant Deterioration
PTC	Permit to Construct
PTE	Potential to Emit
PVMRM	Plume Volume Molar Ratio Method
r	Albedo

scfm	Standard cubic feet per minute
SED	Segment Emission Denominator
SGP	Stibnite Gold Project
SIL	Significant Impact Level
SO_2	Sulfur Dioxide
STKP	Crusher Stockpile
TAP	Toxic Air Pollutant
ton/day	Tons per Day
ton/year	Tons per Year
TSF	Tailings Storage Facility
TSP	Total Suspended Particulate
USGS	United States Geological Survey
UTM	Universal Transverse Mercator
VOC	Volatile Organic Compounds
WBAN	Weather-Bureau-Army-Navy
WEDRSF	West End Development Rock Storage Facility
WEP	West End Pit
YPDRSF	Yellow Pine Development Rock Storage Facility
YPP	Yellow Pine Pit
z_o	Surface Roughness Length
°F	Degrees Fahrenheit
$\mu g/m^3$	Micrograms per cubic meter of air
µm	Microns

1.0 Summary

Midas Gold Idaho, Inc. (Midas Gold) submitted a Permit to Construct (PTC) application to construct and operate the Stibnite Gold Project (SGP) in Valley County, Idaho. The SGP will consist of conventional open-pit mining operations and onsite ore preparation and gold extraction processes. The potential air emissions from the SGP are less than the applicable major source thresholds for both criteria and hazardous air pollutants (HAP), and therefore, the facility is designated as a minor source for Title V and New Source Review (NSR) requirements, and an area source for National Emission Standards for Hazardous Air Pollutants (NESHAP) applicability. Project-specific air quality analyses involving atmospheric dispersion modeling of estimated emissions associated with the facility were submitted to DEQ to demonstrate that applicable emissions do not result in violation of a National Ambient Air Quality Standard (NAAQS) or Toxic Air Pollutant (TAP) increment as required by the Idaho Administrative Procedures Act 58.01.01.203.02 and 203.03 (Idaho Air Rules Section 203.02 and 203.03). This memorandum provides a summary of the applicability assessment for analyses and air impact analyses used to demonstrate compliance with applicable NAAQS and TAP increments, as required by Idaho Air Rules Section 203.02 and 203.03.

Air Sciences, Inc. (Air Sciences), on behalf of Midas Gold, prepared the PTC application and performed ambient air impact analyses for this project. DEQ review of submitted data and DEQ analyses summarized by this memorandum addressed only the rules, policies, methods, and data pertaining to the air impact analyses used to demonstrate that estimated emissions associated with operation of the facility will not cause or significantly contribute to a violation of any applicable air quality standard. This review did not address/evaluate compliance with other rules or analyses not pertaining to the air impact analyses. Evaluation of emission estimates was the responsibility of the DEQ permit writer and is addressed in the main body of the DEQ Statement of Basis, and emission calculation methods were not evaluated in this modeling review memorandum.

Table 1 presents key assumptions and results to be considered in the development of the permit. Idaho Air Rules require air impact analyses be conducted in accordance with methods outlined in 40 Code of Federal Regulations (CFR) 51, Appendix W *Guideline on Air Quality Models* (Appendix W). Appendix W requires that air quality impacts be assessed using atmospheric dispersion models with emissions and operations representative of design capacity or as limited by a federally enforceable permit condition.

The submitted information and analyses: 1) utilized appropriate methods and models; 2) was conducted using reasonably accurate or conservative model parameters and input data (review of emission estimates was addressed by the DEQ permit writer); 3) adhered to established DEQ guidelines for new source review dispersion modeling; 4) showed either a) that estimated potential/allowable emissions are at a level defined as below regulatory concern (BRC) and do not require a NAAQS compliance demonstration; b) that predicted pollutant concentrations from emissions associated with the project as modeled were below Significant Impact Levels (SILs) or other applicable regulatory thresholds; or c) that predicted pollutant concentrations from emissions associated with the project, when appropriately combined with co-contributing sources and background concentrations, were below applicable NAAQS at ambient air locations where and when the project has a significant impact; 5) showed that TAP emission increases associated with the project will not result in increased ambient air impacts exceeding allowable TAP increments. This conclusion assumes that conditions in Table 1 are representative of facility design capacity or operations as limited by a federally enforceable permit condition. The DEQ permit writer should use Table 1 and other information presented in this memorandum to generate appropriate permit provisions/restrictions to assure emissions do not exceed applicable regulatory thresholds requiring further analyses and to assure the requirements of Appendix W are met regarding emissions representative of design capacity or permit allowable rates.

Table 1. KEY ASSUMPTIONS USED IN MODELING ANALYSES.	
Criteria/Assumption/Result	**Explanation/Consideration**
General Emission Rates. Emission rates used in the air impact analyses must represent maximum potential emissions as given by design capacity, inherently limited by the nature of the process or configuration of the facility, or as limited by the issued permit for the specific pollutant and averaging period.	Compliance has not been demonstrated for emission rates greater than those used in the air impact analyses.
Air Impact Analyses for Criteria Pollutant Emissions. Stibnite Gold Project (SGP) facility-wide maximum potential to emit are greater than the respective Level I thresholds for all criteria pollutants and averaging periods except for Lead. Therefore, modeling is triggered for applicable averaging periods for $PM_{2.5}$[a], PM_{10}[b], CO[c], NOx[d], and SO_2[e]. Modeling was not required for Lead.	Project-specific air impact analyses demonstrating compliance with NAAQS, as required by Idaho Air Rules Section 203.02, are required for pollutant increases above Below Regulatory Concern (BRC) thresholds, or for pollutants having an emissions increase that is greater than Level I modeling applicability thresholds (where the BRC exclusion cannot be used).
Air Impact Analyses for TAP Emissions. SGP facility-wide potential Toxic Air Pollutant (TAP) emissions exceed the respective screening emission levels (ELs) for arsenic, cadmium, formaldehyde, nickel, aluminum, barium, calcium carbonate, calcium oxide, iron, sulfuric acid, thallium, and vanadium. Therefore, air dispersion modeling was required for these 12 TAPs. TAPs also classified as Hazardous Air Pollutants (HAPs) emitted from sources addressed by New Source Performance Standards (NSPS) or National Emission Standards for Hazardous Air Pollutants (NESHAP) were not required to be evaluated for compliance with TAP increments in accordance with IDAPA 58.01.01.210.20.	A TAP increment compliance demonstration would be required for any TAPs with emissions above ELs. IDAPA 58.01.01.210.20 states that if TAP emissions from a specific source are addressed by NSPS or NESHAP, then a TAP impact analysis is not required for that TAP from that specific source.
Significant Impact Level Analysis Not Conducted. A Significant Impact Level (SIL) analysis was not conducted for the SGP facility.	Based on the magnitude of the facility-wide emissions and preliminary modeling analyses, it was determined that the impacts from the SGP emissions exceeded the SIL for most criteria pollutants. Therefore, SIL analyses were considered redundant and not performed for the project.
Multiple Modeling Scenarios. To evaluate the worst-case air impacts from the SGP facility, a total of 14 scenarios were modeled. These scenarios represent the hauling of material, which can be either ore or development rock (DR), from four possible origins (three pits and a tailings facility) to five possible destinations (ore will be hauled to the crushing area while DR will be hauled to one of four development rock storage facilities [DRSF]). Modeled design values listed in this modeling memo represent the worst-case modeling scenario for every modeled pollutant and averaging period.	Conventional open-pit methods will be used to extract ore and DR from four possible origins (Yellow Pine Pit [YPP], Hangar Flats Pit [HFP], West End Pit [WEP], and Bradley Tailings [BT]). Ore and DR will be hauled to five possible destinations (Stockpile [STKP], Yellow Pine DRSF [YPDRSF], Hangar Flats DRSF [HFDRSF], West End DRSF [WEDRSF], and Fiddle DRSF [FDRSF]). Only 14 of the 20 possible scenarios were modeled. Six scenarios were not feasible because the timing of the activity within the sequence of mine operations makes the scenarios logistically impossible. Modeled results listed in this memo represent worst-case modeling scenarios.
Modeling of Material Origin and Destination. Each material origin location (YPP, HFP, WEP, and BT) was modeled as an AREA source. Ore destination (STKP) was modeled as a VOLUME source. Each DR destination (YPDRSF, HFDRSF, WEDRSF, and FDRSF) was modeled as a VOLUME source.	Each material origin location comprised appropriate emissions from drilling, material loading, dozing, and surface exploration. Ore destination comprised ore unloading emissions. Each DR destination comprised appropriate emissions from DR unloading, dozing, and wind erosion. For the four AREA and five VOLUME sources, the dimensions were developed by reasonably fitting an equal-area rectangle within the actual footprint of each fugitive source. For the pit and DRSF fugitive activity locations, the release height was based on the haul truck height. The applicable initial lateral dispersion for each VOLUME source was calculated from the respective shorter dimension and EPA-specified methods. The applicable initial vertical dispersion for each AREA and VOLUME source was

Table 1. KEY ASSUMPTIONS USED IN MODELING ANALYSES.	
Criteria/Assumption/Result	**Explanation/Consideration**
	calculated from the respective vertical dimension and EPA-specified methods.
Modeling of Haul Roads. A representative haul road network for hauling material from inside the pit to various destinations was developed for each of the 14 modeling scenarios.	The haul road network was divided into 22 sections. Each section was further divided into multiple segments with a length equal to twice the adjusted haul road width. Each of the segments was characterized as an individual VOLUME source in the model. Material hauling emissions associated with each origin-destination route were assigned to each segment along the route based on estimated total emissions along the route and traffic distribution along each section.
Modeling of Blasting Emissions. Blasting emissions were represented by a VOLUME source inside a pit (YPPBL, HFPBL, and WEPBL). Blasting is not expected to occur in BT but was modeled (BTBL) in order to streamline the permitting process.	The blasting physical parameters were developed from dimensions based on blast area used in the emission calculation. The blasting release height was the midpoint of the blasting height. The initial lateral and vertical dispersion dimensions for blasting were calculated per methods specified in the AERMOD User's Guide.
Modeling of Burntlog Route Access Road. The access road portion within the operations boundary was characterized by a series of LINE sources laid along the actual route.	Emissions associated with the portion of the Burntlog Route mine access road that is within project boundary (from the south gate to the process area) are included in the SGP analyses. These include dust emissions generated from travel of maintenance equipment, light-duty pickup trucks and buses used for employee, visitor, and contractor transportation, and heavy-duty trucks used for cargo (including fuel, consumables, machine parts, ore processing supplies, ore concentrate, etc.) and services (including food supplies, trash, recyclables, etc.) transportation. Release parameters for the LINE sources were based on an estimated average vehicle height. The access road emissions were evenly distributed along the road by dividing the total access road emissions by its total area.
Control of Fugitive Dust from Roadways. Fugitive particulate emissions from roadways were assumed to be controlled above 93%, which is an aggressive level of control.	The high level of emission control was needed to demonstrate compliance with NAAQS. Compliance is not demonstrated for emissions greater than those associated with above 93% control.
NOx Chemistry and NO_2/NOx In-Stack Ratios. Ozone Limiting Method (OLM), a Tier 3 NO_2 screening method, was used to estimate the 1-hour and annual NO_2 impacts. The following NO_2/NOx In-Stack Ratios (ISR) were used in the modeling analyses: Blasting: 0.036 Diesel engines: 0.11 Propane heaters: 0.10	The OLM method requires an input of NO_2/NOx ISRs for each modeled source. The NO_2/NOx ratio for blasting was based on blasting plume measurements provided in published literature. The NO_2/NOx ratio for stationary diesel combustion sources was based on heavy-duty diesel trucks in the California Air Pollution Control Officers Association (CAPCOA) Guidance Document. This NO_2/NOx ratio (11 percent) is conservatively higher than the diesel combustion NO_2/NOx ratio provided in the EPA ISR database: 6 percent average, 9.8 percent maximum. The CAPCOA document and the EPA ISR database do not provide an NO_2/NOx ratio for propane boilers. The CAPCOA-recommended NO_2/NOx ratio for natural gas boilers was selected for the propane boilers. The natural gas boilers NO_2/NOx ratio is considered appropriate for the propane boilers because both are gaseous fuels with relatively similar combustion characteristics and are expected to have similar NO_2/NOx ratios. DEQ performed a sensitivity analysis using Tier 2 (Ambient Ratio Method 2), a more conservative NO_2 screening method, and found that the facility is safely below the 1-hour and annual NO_2 NAAQS.

Table 1. KEY ASSUMPTIONS USED IN MODELING ANALYSES.	
Criteria/Assumption/Result	**Explanation/Consideration**
Alternate Meteorological Data Processed Using Cloud Cover. An alternative meteorological dataset was processed without using the Bulk Richardson (BULKRN) method. This alternate processing (NON-BULKRN) used upper air data from Boise airport, supplemented with the cloud-cover data collected at the National Weather Service station in McCall, Idaho.	Meteorological data processing with and without BULKRN are considered acceptable regulatory options by EPA. The NON-BULKRN meteorological data yielded lower modeled design values than the meteorological data processed using the BULKRN method.
Ambient Air Boundary. Midas Gold will legally control the SGP, an active industrial site where mining activities will occur, such as heavy equipment operation. Most areas of the mine will require strict safety protocols and controlled access. Midas Gold has established an operations boundary to identify the area where public access will be excluded. Public access inside the operations boundary will be restricted for the life of the mine by physical barriers at points of potential access, including the current Stibnite Road point of entry and proposed site access via the Burntlog Route, as well as natural features of the landscape that prevent access.	Ambient air is defined in Section 006 of the Idaho Air Rules as "that portion of the atmosphere, external to buildings, to which the general public has access." Receptors must be placed at any portion of the atmosphere that is considered ambient air.
Onsite Background $PM_{2.5}$ and PM_{10} Concentrations. The following background $PM_{2.5}$ and PM_{10} concentrations were measured at SGP in 2014 and used in the cumulative NAAQS impact analysis: Annual $PM_{2.5}$: 3.5 $\mu g/m^3$ (weighted average of quarterly means) 24-hour $PM_{2.5}$: 15.0 $\mu g/m^3$ (98th percentile/8th high) 24-hour PM_{10}: 37.0 $\mu g/m^3$ (highest 1st high)	Midas Gold developed an onsite monitoring program to collect site-specific meteorological parameters and determine ambient particulate matter ($PM_{2.5}$ and PM_{10}) concentrations at its Stibnite monitoring station. $PM_{2.5}$ and PM_{10} background concentrations were based on calendar year 2014 instead of the complete dataset (November 2013 through June 2015). For 24-hour PM_{10}, the design value is the *second-highest* 24-hour average concentration in a given year. However, the background value that was used in the modeling analyses represents the *first-highest* 24-hour average concentration measured in 2014. Therefore, using a larger background concentration adds a layer of conservatism to the calculated total impact for 24-hour PM_{10}.
NW AIRQUEST Background CO, NO_2, and SO_2 Concentrations. The following background concentrations for CO, NO_2, and SO_2 were used in the cumulative NAAQS impact analysis: 1-hour CO: 1,740 $\mu g/m^3$ 8-hour CO: 1,110 $\mu g/m^3$ 1-hour NO_2: 4.3 $\mu g/m^3$ Annual NO_2: 0.9 $\mu g/m^3$ 1-hour SO_2: 12.3 $\mu g/m^3$ 3-hour SO_2: 16.8 $\mu g/m^3$	Gaseous pollutant background concentrations were determined using the Northwest International Air Quality Environmental Science and Technology Consortium (NW AIRQUEST) online tool. The NW AIRQUEST tool uses regional scale modeling of pollutants in Washington, Oregon, and Idaho, with model results adjusted according to available monitoring data.
Medium-Traffic Background Concentrations. To provide additional information regarding the relative contribution of traffic emissions, background concentrations were obtained from NW AIRQUEST for the road section between mile markers 143 and 144 on Highway 55 passing through the town of McCall.	The McCall location is approximately 38 miles west of the SGP. The annual average daily traffic count for this road section is over 10,000 vehicles per day. Although the background concentrations at McCall are not representative of the rural SGP area, they provide additional information regarding the relative contribution of traffic emissions.
Weight-of-Evidence Analyses for 24-hour PM_{10}. PM_{10} modeling with meteorological dataset processed using the site-specific BULKRN method shows up to five hotspot receptors for Scenario W5 (the highest PM_{10} modeling scenario) that exceed NAAQS. All modeled violations occur during winter when the average snow depth and average precipitation at the project site are 21-68 inches and 6.0 inches, respectively. Therefore, fugitive road dust emissions during high-modeled impact hours could be overestimated. PM_{10} modeling simulation was based on a mining production rate of 180,000 ton/day of development rock (65,700,000 ton/year, which is more conservative than the	Meteorological data processing with and without BULKRN are considered acceptable by EPA, with the BULKRN method utilizing more of the onsite collected meteorological parameters. However, the BULKRN-processed meteorological data yielded higher modeled design value impacts for the SGP facility than the meteorological data processed without the BULKRN method. DEQ's supplemental analyses suggest that when emissions are more-closely representative of typical daily mining production rates for a high-production period (everything else held constant), the SGP facility is able to demonstrate

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Table 1. KEY ASSUMPTIONS USED IN MODELING ANALYSES.	
Criteria/Assumption/Result	**Explanation/Consideration**
expected peak production rate of 42,692,000 ton/year). To investigate the effect of a lower modeled mining production rate on design value concentrations, DEQ performed a modeling simulation where mining production rate was assumed to be 120,000 ton/day instead of 180,000 ton/day, but everything else was held constant. Maximum modeled concentration, when summed with the background concentration, is lower than the 24-hour PM_{10} NAAQS thereby demonstrating NAAQS compliance. DEQ's weight-of-evidence analyses conclude that, considering all the collective conservative layers of the modeling analyses, including the use of meteorological data processed by two different methods, there is a satisfactory level of confidence that operation of the project as described in the application will not cause or contribute to a violation of NAAQS.	compliance with 24-hour PM_{10} NAAQS at those few receptors showing a potential violation when using meteorological data processed with the BULKRN method.

[a] Particulate matter with an aerodynamic diameter less than or equal to a nominal 2.5 micrometers.
[b] Particulate matter with an aerodynamic diameter less than or equal to a nominal 10 micrometers.
[c] Carbon monoxide.
[d] Nitrogen oxides.
[e] Sulfur dioxide.

Summary of Submittals and Actions

May 30, 2019	Modeling protocol was submitted to DEQ by Brown and Caldwell on behalf of the applicant.
June 27, 2019	Conditional modeling protocol approval was provided to Brown and Caldwell by DEQ.
August 21, 2019	Regulatory start date. PTC application and modeling report were prepared by Air Sciences on behalf of the applicant.
September 19, 2019	Application deemed incomplete by DEQ.
October 4, 2019	DEQ received a preliminary response and supplemental information from the applicant.
October 15, 2019	DEQ met with the applicant to review and discuss the preliminary response.
October 22, 2019	DEQ determined that the application remained incomplete while the applicant prepared a response to remaining items previously identified, and included a summary of recommendations provided at the meeting.
November 8, 2019	DEQ requested additional information from the applicant via e-mail, relating to items previously identified.
November 21, 2019	Applicant requested extension until November 27, 2019 to respond to incompleteness.
November 27, 2019	DEQ received supplemental information from the applicant, including a revised application with updated emission inventories and modeling analyses.

December 24, 2019	DEQ determined that the application was incomplete.
January 8, 2020	Applicant requested extension until February 7, 2020 to respond to incompleteness.
February 5, 2020	DEQ received supplemental information from the applicant, including a revised application with updated emission inventories and modeling analyses.
March 6, 2020	DEQ determined that the application was incomplete.
April 2, 2020	Applicant requested extension until April 15, 2020 to respond to incompleteness.
April 15, 2020	DEQ received supplemental information from the applicant, including updated modeling analyses.
May 15, 2020	DEQ determined that the application was complete.
June 24, 2020	DEQ received the final updated application.
July 14, 2020	DEQ made available the draft permit and statement of basis for applicant review.
July 31, 2020	DEQ made available an updated draft statement of basis for applicant review.
August 3 and 13, 2020	DEQ received comments from the applicant on the draft permit and statement of basis.
September 10 – October 12, 2020	DEQ provided a public comment period on the proposed action.
October 12, 2020	DEQ received a request to extend the public comment period.
October 13 – November 11, 2020	DEQ extended the public comment period.
November 20, 2020	DEQ requested additional information from the applicant to address substantive public comments received, including missing HAP and TAP emission estimates.
December 18, 2020	DEQ received supplemental information from the applicant, including a HAP/TAP addendum, updated HAP and TAP emission estimates, and updated TAP modeling analyses.
January 28, 2021	DEQ received updated modeling files with corrections for formaldehyde and sulfuric acid, and an updated figure showing TAP modeled impacts.

2.0 Background Information

This section provides background information applicable to the project and the site proposed for the facility. It also provides a brief description of the applicable air impact analyses requirements for the project.

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2.1 Project Description

The SGP will require the construction of significant infrastructure, including a power transmission line, a primary mine site access road, onsite haul roads, an ore processing facility, onsite workspaces, employee housing and recreation, water storage and distribution facilities, and sewage disposal facilities.

The SGP will include three years of pre-mining development and construction activities, followed by an operating mine life of approximately 12 years. Mining will occur in three open pits: Yellow Pine Pit (YPP), Hangar Flats Pit (HFP), and West End Pit (WEP). The general sequence of mining will be the YPP deposit, followed by the HFP and WEP deposits. Legacy tailings from the Meadow Creek valley (Bradley Tailings [BT]) also will be reclaimed and reprocessed during the initial project schedule. Surface exploration drilling will continue within the pits and the Scout Prospect decline (underground exploration) throughout the mine operation period. Restoration and reclamation of other legacy mining features will occur prior to mining, throughout the life of the mine, and as part of the mine closure.

Conventional open-pit methods including drilling, blasting, excavating, and hauling will be used to extract ore and waste rock, termed development rock (DR). Hydraulic shovels and front-end loaders will be used to load ore and DR into haul trucks. DR will be used for construction, restoration, and backfilling, or hauled to the dedicated development rock storage facilities (DRSF). Approximately 340 million tons of DR will be handled over the life of the mine. Ore will be hauled to the primary crusher area, where it will be fed directly into the crusher dump pocket or stockpiled. The ore crushing plant will be designed to operate at a maximum rate of 25,000 tons per day (ton/day). Approximately 100 million tons of ore will be mined from the three pits over the life of the project.

The metal-recovery process from ore will include conventional crushing and grinding, followed by froth-flotation circuits that will generate separate gold-silver and antimony-silver concentrates. The antimony-silver concentrate will be shipped offsite for refining, whereas additional onsite processing of the gold-silver concentrate will include pressure oxidation, carbon-in-leach circuits, and refining processes to recover gold and minor amounts of silver. The finely ground leftover ore material from the mineral-recovery process, termed tailings, will be neutralized, thickened, and transported via a pipeline to the tailings storage facility (TSF).

Lime used in the ore processing will either be purchased or manufactured onsite from limestone available at the site. In addition, certain construction and maintenance activities during operations may require sized aggregate. To allow for the operational flexibility to produce construction aggregate onsite, the application included two portable crushing and screening plants.

The following air pollutants are expected from operations at the SGP facility:

- Criteria air pollutants: carbon monoxide (CO), oxides of nitrogen (NOx), particulate matter less than 2.5 microns (μm) and 10 μm ($PM_{2.5}$ and PM_{10}), sulfur dioxide (SO_2), lead (Pb), and ozone (O_3) precursor volatile organic compounds (VOC)
- Hazardous air pollutants (HAP), including mercury (Hg)
- Other non-HAP toxic air pollutants (TAP)
- Greenhouse gases

Based on the uncontrolled potential to emit (PTE) and controlled PTE, the SGP facility will be a "synthetic minor" source of PM, PM_{10}, $PM_{2.5}$, and HAP emissions for new source review (NSR) and Title V (Tier I) permitting purposes. The uncontrolled PTE for the remaining criteria pollutants (SO_2, NOx,

CO, VOC) confirm that the SGP facility will be a natural minor source for these emissions. Facility classification is reviewed by the permit writer. Detailed calculations and explanations are provided in the DEQ Statement of Basis.

The PTC addresses all air pollutant-emitting activities associated with the facility.

2.2 Facility Location and Area Classification

The SGP is located in the Stibnite-Yellow Pine Mining District in Valley County, central Idaho (Northing: 4,973,751 meters [m]; Easting: 632,038 m; UTM Zone 11), approximately 100 miles northeast of Boise, 38 miles east of McCall, and approximately 10 miles east of Yellow Pine. A facility location map for the SGP is presented in Figure 1. This figure also shows the proposed Burntlog Route (access road) that will provide a year-round safe access to the site. The SGP site layout is presented in Figure 2.

The Stibnite-Yellow Pine Mining District is characterized by historic mining activities and unpatented (federal land) and patented (private land) mining claims that include deposits of gold, silver, tungsten, and antimony. The district lies in both Boise National Forest (BNF) and Payette National Forest (PNF), but is administered by the PNF's Krassel Ranger District (Midas Gold 2017a). The project area terrain is characterized by narrow valleys 6,000 to 6,600 feet above mean sea level (amsl), surrounded by steep mountains ranging over 8,500 feet amsl. The main drainage basin in the project area is the East Fork of the South Fork of the Salmon River (EFSFSR).

The EFSFSR joins Johnson Creek 16 miles downstream, near the village of Yellow Pine. The project area is encompassed by the watersheds of EFSFSR tributaries, including Sugar Creek, Meadow Creek, Johnson Creek, Riordan Creek, Burntlog Creek, Midnight Creek, and Trout Creek. Primary commercial activity in the area comprises mineral exploration, mining, logging, and dispersed recreation.

This area is designated as an attainment or unclassifiable area for SO_2, NO_2, CO, Lead, O_3, PM_{10}, and $PM_{2.5}$. The area is not classified as non-attainment for any criteria pollutants.

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Figure 1. SGP FACILITY LOCATION MAP.

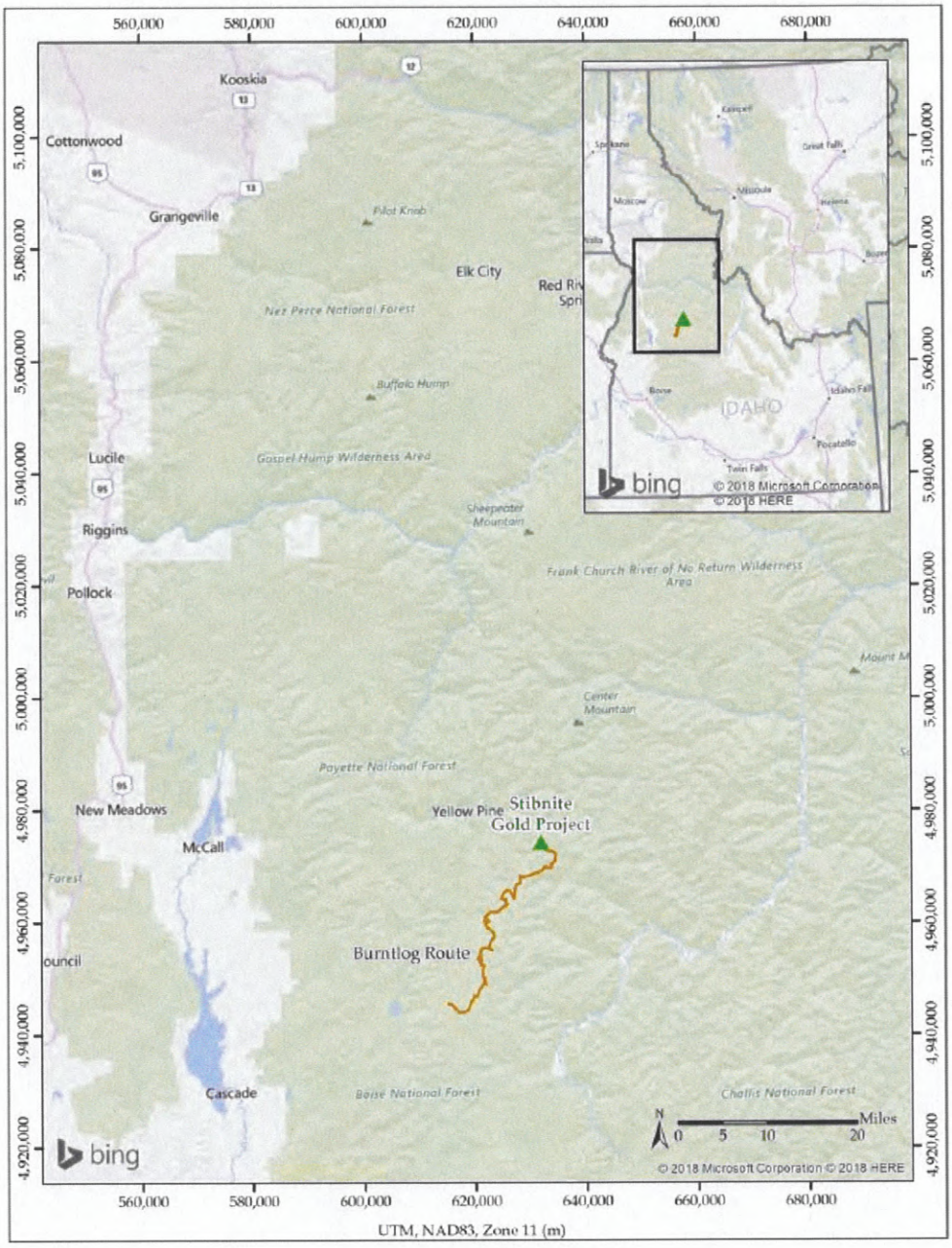
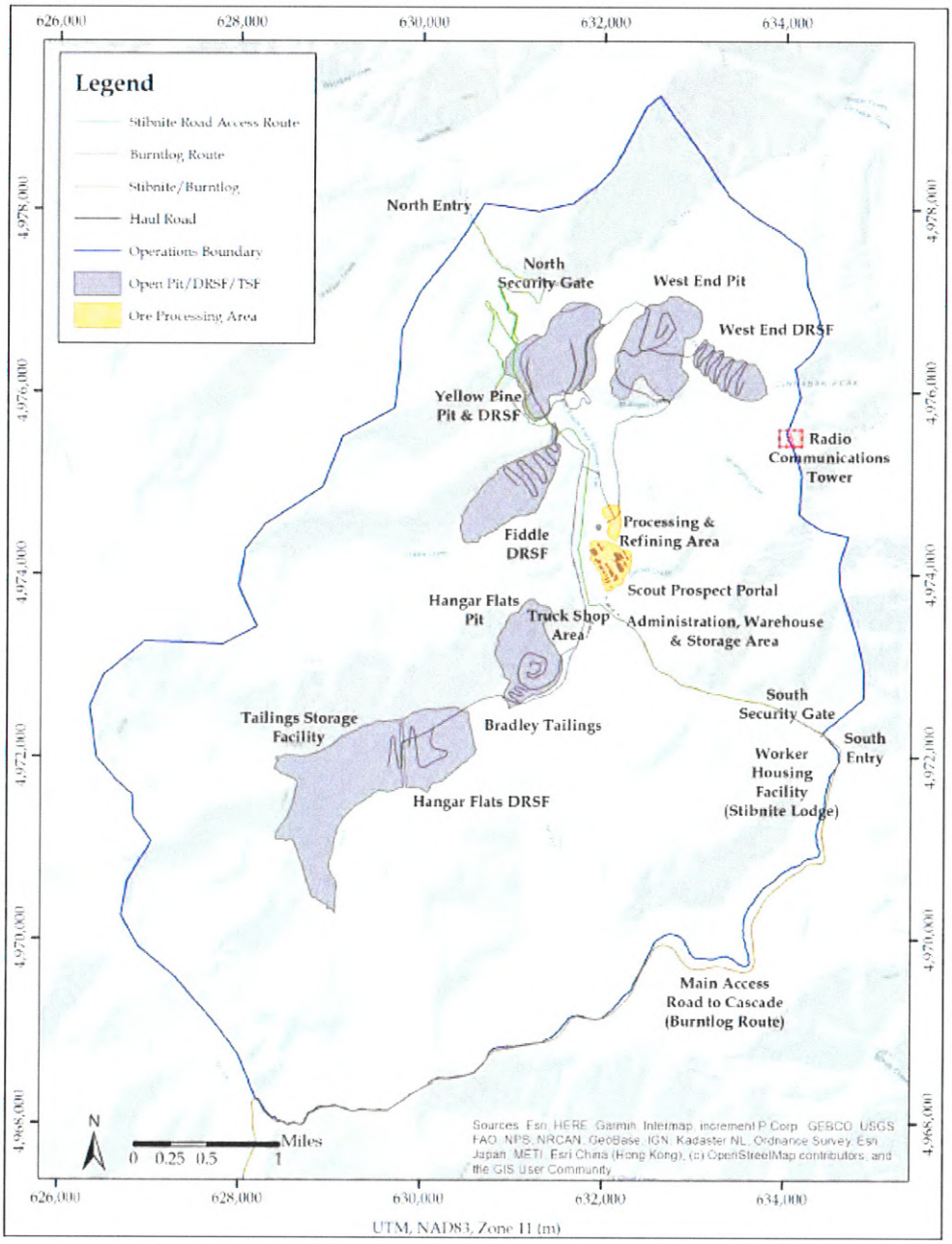


Figure 2. SGP SITE LAYOUT AND STIBNITE ROAD ACCESS ROUTE.



2.3 *Air Impact Analyses Required for All Permits to Construct*

Idaho Air Rules Sections 203.02 and 203.03:

> *No permit to construct shall be granted for a new or modified stationary source unless the applicant shows to the satisfaction of the Department all of the following:*

***02. NAAQS**. The stationary source or modification would not cause or significantly contribute to a violation of any ambient air quality standard.*

***03. Toxic Air Pollutants.** Using the methods provided in Section 210, the emissions of toxic air pollutants from the stationary source or modification would not injure or unreasonably affect human or animal life or vegetation as required by Section 161. Compliance with all applicable toxic air pollutant carcinogenic increments and toxic air pollutant non-carcinogenic increments will also demonstrate preconstruction compliance with Section 161 with regards to the pollutants listed in Sections 585 and 586.*

Atmospheric dispersion modeling, using computerized simulations, is used to demonstrate compliance with both NAAQS and TAPs. Idaho Air Rules Section 202.02 states:

***02. Estimates of Ambient Concentrations**. All estimates of ambient concentrations shall be based on the applicable air quality models, data bases, and other requirements specified in 40 CFR 51 Appendix W (Guideline on Air Quality Models).*

2.4 Significant Impact Level and Cumulative NAAQS Impact Analyses

If specific criteria pollutant emission increases associated with the proposed permitting project cannot qualify for a BRC exemption as per Idaho Air Rules Section 221, then the permit cannot be issued unless the application demonstrates that applicable emission increases will not cause or significantly contribute to a violation of NAAQS, as required by Idaho Air Rules Section 203.02.

The first phase of a NAAQS compliance demonstration is to evaluate whether the proposed facility/project could have a significant impact to ambient air. Section 3.1.1 of this memorandum describes the applicability evaluation of Idaho Air Rules Section 203.02. The Significant Impact Level (SIL) analysis for a new facility or proposed modification to a facility involves modeling estimated criteria air pollutant emissions from the facility or modification to determine the potential impacts to ambient air. Air impact analyses are required by Idaho Air Rules to be conducted in accordance with methods outlined in Appendix W. Appendix W requires that facilities be modeled using emissions and operations representative of design capacity or as limited by a federally enforceable permit condition.

A facility or modification is considered to have a significant impact on air quality if maximum modeled impacts to ambient air exceed the established SIL listed in Idaho Air Rules Section 006 (referred to as a "significant contribution" in Idaho Air Rules) or as incorporated by reference as per Idaho Air Rules Section 107.03.b. Table 2 lists the applicable SILs.

Table 2. APPLICABLE REGULATORY LIMITS.

Pollutant	Averaging Period	Significant Impact Levels[a] ($\mu g/m^3$)[b]	Regulatory Limit[c] ($\mu g/m^3$)	Modeled Design Value Used[d]
PM_{10}[e]	24-hour	5.0	150[f]	Maximum 6th highest[g]
$PM_{2.5}$[h]	24-hour	1.2	35[i]	Mean of maximum 8th highest[j]
	Annual	0.2	12[k]	Mean of maximum 1st highest[l]
Carbon monoxide (CO)	1-hour	2,000	40,000[m]	Maximum 2nd highest[n]
	8-hour	500	10,000[m]	Maximum 2nd highest[n]
Sulfur Dioxide (SO_2)	1-hour	3 ppb[o] (7.8 $\mu g/m^3$)	75 ppb[p] (196 $\mu g/m^3$)	Mean of maximum 4th highest[q]
	3-hour	25	1,300[m]	Maximum 2nd highest[n]
Nitrogen Dioxide (NO_2)	1-hour	4 ppb (7.5 $\mu g/m^3$)	100 ppb[s] (188 $\mu g/m^3$)	Mean of maximum 8th highest[t]
	Annual	1.0	100[r]	Maximum 1st highest[n]
Lead (Pb)	3-month[u]	NA	0.15[r]	Maximum 1st highest[n]

	Quarterly	NA	1.5[r]	Maximum 1st highest[n]
Ozone (O_3)	8-hour	40 TPY VOC[v]	70 ppb[w]	Not typically modeled

a. Idaho Air Rules Section 006 (definition for significant contribution) or as incorporated by reference as per Idaho Air Rules Section 107.03.b.
b. Micrograms per cubic meter.
c. Incorporated into Idaho Air Rules by reference, as per Idaho Air Rules Section 107.
d. The maximum 1st highest modeled value is always used for the significant impact analysis unless indicated otherwise. Modeled design values are calculated for each ambient air receptor.
e. Particulate matter with an aerodynamic diameter less than or equal to a nominal 10 micrometers.
f. Not to be exceeded more than once per year on average over 3 years.
g. Concentration at any modeled receptor when using five years of meteorological data.
h. Particulate matter with an aerodynamic diameter less than or equal to a nominal 2.5 micrometers.
i. 3-year mean of the upper 98th percentile of the annual distribution of 24-hour concentrations.
j. 5-year mean of the 8th highest modeled 24-hour concentrations at the modeled receptor for each year of meteorological data modeled. For the SIL analysis, the 5-year mean of the 1st highest modeled 24-hour impacts at the modeled receptor for each year.
k. 3-year mean of annual concentration.
l. 5-year mean of annual averages at the modeled receptor.
m. Not to be exceeded more than once per year.
n. Concentration at any modeled receptor.
o. Interim SIL established by EPA policy memorandum.
p. 3-year mean of the upper 99th percentile of the annual distribution of maximum daily 1-hour concentrations.
q. 5-year mean of the 4th highest daily 1-hour maximum modeled concentrations for each year of meteorological data modeled. For the significant impact analysis, the 5-year mean of 1st highest modeled 1-hour impacts for each year is used.
r. Not to be exceeded in any calendar year.
s. 3-year mean of the upper 98th percentile of the annual distribution of maximum daily 1-hour concentrations.
t. 5-year mean of the 8th highest daily 1-hour maximum modeled concentrations for each year of meteorological data modeled. For the significant impact analysis, the 5-year mean of maximum modeled 1-hour impacts for each year is used.
u. 3-month rolling average.
v. An annual emissions rate of 40 ton/year of VOCs is considered significant for O_3.
w. Annual 4th highest daily maximum 8-hour concentration averaged over three years.

If modeled maximum pollutant impacts to ambient air from the emission sources associated with a new facility or modification exceed the SILs, then a cumulative NAAQS impact analysis is necessary to demonstrate compliance with NAAQS and Idaho Air Rules Section 203.02.

A cumulative NAAQS impact analysis for attainment area pollutants involves assessing ambient impacts (typically the design values consistent with the form of the standard) from potential/allowable emissions resulting from the project and emissions from any nearby co-contributing sources (including existing emissions from the facility that are unrelated to the project), and then adding a DEQ-approved background concentration value to the modeled result that is appropriate for the criteria pollutant/averaging-period at the facility location and the area of significant impact. The resulting pollutant concentrations in ambient air are then compared to the NAAQS listed in Table 2. Table 2 also specifies the modeled design value that must be used for comparison to the NAAQS. NAAQS compliance is evaluated on a receptor-by-receptor basis for the modeling domain.

If the cumulative NAAQS impact analysis indicates an exceedance of NAAQS, a culpability analysis can determine if this exceedance is due to emissions from the proposed project. The permit may not be issued if the proposed project has a significant contribution (exceeding the SIL) to the modeled violation. If project-specific impacts are below the SIL, then the project does not have a significant contribution to the specific violations.

Compliance with Idaho Air Rules Section 203.02 is generally demonstrated if: a) applicable specific criteria pollutant emission increases are at a level defined as BRC, using the criteria established by DEQ regulatory interpretation (DEQ 2014); or b) all modeled impacts of the SIL analysis are below the

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applicable SIL or other level determined to be inconsequential to NAAQS compliance; or c) modeled design values of the cumulative NAAQS impact analysis (modeling all emissions from the facility and co-contributing sources, and adding a background concentration) are less than applicable NAAQS at receptors where impacts from the proposed facility/modification exceeded the SIL or other identified level of consequence; or d) if the cumulative NAAQS analysis showed NAAQS violations, the impact of proposed facility/modification to any modeled violation was inconsequential (typically assumed to be less than the established SIL) for that specific receptor and for the specific modeled time when the violation occurred.

2.5 Toxic Air Pollutant Analyses

Emissions of toxic substances are generally addressed by Idaho Air Rules Section 161:

> *Any contaminant which is by its nature toxic to human or animal life or vegetation shall not be emitted in such quantities or concentrations as to alone, or in combination with other contaminants, injure or unreasonably affect human or animal life or vegetation.*

Permitting requirements for toxic air pollutants (TAPs) from new or modified sources are specifically addressed by Idaho Air Rules Section 203.03 and require the applicant to demonstrate to the satisfaction of DEQ the following:

> *Using the methods provided in Section 210, the emissions of toxic air pollutants from the stationary source or modification would not injure or unreasonably affect human or animal life or vegetation as required by Section 161. Compliance with all applicable toxic air pollutant carcinogenic increments and toxic air pollutant non-carcinogenic increments will also demonstrate preconstruction compliance with Section 161 with regards to the pollutants listed in Sections 585 and 586.*

Per Section 210, if the total project-wide emission increase of any TAP associated with a new source or modification exceeds screening emission levels (ELs) of Idaho Air Rules Section 585 or 586, then the ambient impact of the emission increase must be estimated. If ambient impacts are less than applicable Acceptable Ambient Concentrations (AACs) for non-carcinogens of Idaho Air Rules Section 585 and Acceptable Ambient Concentrations for Carcinogens (AACCs) of Idaho Air Rules Section 586, then compliance with TAP requirements has been demonstrated.

TAPs also classified as HAPs emitted from sources addressed by New Source Performance Standards (NSPS) or National Emission Standards for Hazardous Air Pollutants (NESHAP) were not required to be evaluated for compliance with TAP increments in accordance with IDAPA 58.01.01.210.20 (Subsection 210.20). The DEQ permit writer evaluates the applicability of specific TAPs to the Subsection 210.20 exclusion. Guidance and clarification of Subsection 210.20 source exemptions are included in the DEQ Statement of Basis.

IDAPA 58.01.01.215 sets requirements for mercury emissions. For this standard, fugitive emissions and sources in a source category subject to 40 CFR 63 are exempt. The DEQ permit writer evaluates the applicability of mercury emissions to the exemption criteria. Details are provided in the DEQ Statement of Basis. Adjusted mercury emissions from non-fugitive and non-NESHAP-addressed sources were below the level (25 pounds per year) at which Mercury Best Available Control Technology (MBACT) review is required.

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3.0 Analytical Methods and Data

This section describes the methods and data used in the analyses to demonstrate compliance with applicable air quality impact requirements. The DEQ Statement of Basis provides a discussion of the methods and data used to estimate criteria and TAP emission rates.

3.1 Emission Source Data

Emissions of criteria pollutants and TAPs resulting from operation of the SGP facility were estimated by Air Sciences for various applicable averaging periods. The calculation of potential emissions is the responsibility of the DEQ permit writer, and the representativeness and accuracy of emission estimates is not addressed in this modeling memorandum. DEQ air impact analysts are responsible for assuring that potential emission rates provided in the emission inventory are properly used in the model. The rates listed must represent the maximum allowable rate as averaged over the specified period.

Emission rates used in the impact modeling applicability analyses and any modeling analyses, as listed in this memorandum, should be reviewed by the DEQ permit writer and compared with those in the final emission inventory. All modeled criteria air pollutant and TAP emission rates must be equal to or greater than the facility's potential emissions calculated in the PTC emission inventory or proposed permit allowable emission rates.

Emissions from unpaved roads were calculated based on a control efficiency of 90% from chemical application and 33% from watering (combined control efficiency above 93%). Emission controls and emission calculations are not reviewed in this modeling memorandum. However, it is critical for NAAQS compliance that this high level of control be achieved.

Activity-specific (e.g., drilling, blasting, material crushing and conveying, refining, and other ancillary sources) emissions were estimated based on maximum activity rates, coupled with applicable emission estimation techniques. Maximum emissions were calculated on a short-term (hourly and daily) and long-term (annual) basis for ore processing and mining operations, as discussed below.

The ore-processing rate will range from 20,000 ton/day to 25,000 ton/day at full production. Therefore, maximum potential daily ore processing emissions were based on the maximum design rate of 25,000 ton/day. Maximum potential annual emissions were based on potential daily emissions multiplied by 365 days per year.

Emissions from mining operations (drilling, blasting, material extraction and movement, mobile mine machinery use, and other ancillary sources) vary for each year of the life of the mine (LOM). However, for the modeling analyses, the mining operation potential emissions were estimated using conservatively high maximum activity rates provided in Table 3.

Table 3. MINING ACTIVITY RATES FOR POTENTIAL EMISSION CALCULATIONS.

Activity	Maximum Rate		Comments
Drilling	600	holes per blast	--
Blasting	2	blasts per day	--
	1	blast per hour	--
Material extraction and hauling	180,000	tons per day	Ore or DR
Onsite dozing	144	hours per day	6 dozers operating continuously
Onsite grading	72	hours per day	3 graders operating continuously
Onsite water trucking	48	hours per day	2 trucks operating continuously

The potential hourly emission rates for ore processing and mining operation activities were calculated by dividing the daily rate by the 24 hour-per-day operation schedule, and annual rates were calculated by multiplying maximum daily emissions with 365 days per year. This is conservative because the mine is expected to operate for only 355 days per year.

The maximum mine production rate is approximately 42.7 million (MM) tons per year (ton/yr); however, a maximum daily production rate of 180,000 ton/day used for potential emission calculations results in a conservatively higher production rate of approximately 65.7 MMton/yr, approximately 50 percent higher than the projected production rate.

Midas Gold will employ newer model year mining and maintenance machines (excavators, shovels, haul trucks, dozers, graders, portable light plants, etc.) that are expected to meet or exceed applicable regulatory emission standards. Non-road mobile equipment engines are exempt from permitting requirements; therefore, the tailpipe emissions resulting from fuel combustion in the non-road mobile equipment are not quantified for the SGP facility. Background concentrations from McCall, 38 miles west of the SGP, were used in the cumulative NAAQS impact analyses (Section 4.1.2) to conservatively account for the impact contribution of traffic emissions.

The approximately 38-mile long Burntlog Route mine access road will be outside the project ambient air boundary and open to the public. Traffic emissions on public roads generally are considered to be part of background concentrations. Therefore, emissions on the Burntlog Route mine access road that are outside of the project boundary are not included in the SGP analyses. However, the emissions associated with the portion of the Burntlog Route mine access road that is within project boundary (from the south gate to the process area) are included in the SGP analyses. These include dust emissions generated from travel of maintenance equipment, light-duty pickup trucks and buses used for employee, visitor, and contractor transportation, and heavy-duty trucks used for cargo (including fuel, consumables, machine parts, ore processing supplies, ore concentrate, etc.) and services (including food supplies, trash, recyclables, etc.) transportation.

3.1.1 Criteria Pollutant Modeling Applicability and Modeled Emission Rates

If project-specific emission increases for criteria pollutants would qualify for a BRC permit exemption as per Idaho Air Rules Section 221 if it were not for potential emissions of one or more pollutants exceeding the BRC threshold of 10 percent of emissions defined by Idaho Air Rules as significant, then a NAAQS compliance demonstration may not be required for those pollutants with emissions below BRC levels. DEQ's regulatory interpretation policy of exemption provisions of Idaho Air Rules is that: "*A DEQ NAAQS compliance assertion will not be made by the DEQ modeling group for specific criteria pollutants having a project emissions increase below BRC levels, provided the proposed project would have qualified for a Category I Exemption for BRC emissions quantities except for the emissions of another criteria pollutant*" (DEQ 2014). The interpretation policy also states that the exemption criteria of uncontrolled potential to emit (PTE) not to exceed 100 ton/year (Idaho Air Rules Section 220.01.a.i) is not applicable when evaluating whether a NAAQS impact analyses is required. A permit will be issued limiting PTE below 100 ton/year, thereby negating the need to maintain calculated uncontrolled PTE under 100 ton/year. The BRC exemption cannot be used to exempt a project from a pollutant-specific NAAQS compliance demonstration in most cases where a PTC is required for the action regardless of emission quantities, such as the modification of an existing emission or throughput limit.

A NAAQS compliance demonstration must be performed for pollutant increases that would not qualify for the BRC exemption from the requirement to demonstrate compliance with NAAQS.

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Site-specific air impact modeling analyses may not be necessary for some pollutants, even where such emissions do not qualify for the BRC exemption. DEQ has developed modeling applicability thresholds, below which a site-specific modeling analysis is not required. DEQ generic air impact modeling analyses that were used to develop the modeling thresholds provide a conservative SIL analysis for projects with emissions below identified threshold levels. Project-specific modeling applicability thresholds are provided in the *Idaho Air Modeling Guideline* (DEQ 2013). These thresholds were based on assuring an ambient impact of less than the established SIL for specific pollutants and averaging periods.

If total project-specific emission rate increases of a pollutant are below Level I Modeling Applicability Thresholds, then project-specific air impact analyses are not necessary for permitting. Use of Level II Modeling Applicability Thresholds is conditional, requiring DEQ approval. DEQ approval is based on dispersion-affecting characteristics of the emission sources such as stack height, stack gas exit velocity, stack gas temperature, distance from sources to ambient air, presence of elevated terrain, and potential exposure to sensitive public receptors.

For the SGP analyses, several modeling scenarios were considered to evaluate the worst-case air impacts from the SGP facility. The different modeling scenarios are discussed in Section 3.1.3. Table 4 provides a comparison between facility-wide maximum PTE for the highest-emitting scenario (W3) and modeling applicability thresholds. The short-term and long-term PTE emissions are equal to the sum of process and ancillary emissions and mining fugitive emissions. It is important to note that the process and ancillary source emissions remain the same for each modeling scenario discussed in Section 3.1.3.

Table 4. SITE-SPECIFIC CRITERIA POLLUTANT MODELING APPLICABILITY.

Source Category	Carbon Monoxide (CO)	Nitrogen Oxides (NOx)		$PM_{2.5}$[a]		PM_{10}[b]	Sulfur Dioxide (SO_2)		Lead (Pb)
	lb/hr[c]	ton/yr[d]	lb/hr	ton/yr	lb/hr	lb/hr	ton/yr	lb/hr	lb/month[e]
Process and ancillary	33.5	37.9	55.4	36.4	13.4	21.7	6.5	1.88	0.0437
Mining fugitive	1,742.0	17.1	46.8	98.9	22.5	224.7	0.03	0.09	--
Total	1,775.5	55.0	102.2	135.3	35.9	246.4	6.5	1.97	0.0437
Level I threshold	15.0	1.2	0.2	0.35	0.054	0.22	1.2	0.21	14.0
Modeling required	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No

[a] Particulate matter with an aerodynamic diameter less than or equal to a nominal 2.5 micrometers.
[b] Particulate matter with an aerodynamic diameter less than or equal to a nominal 10 micrometer.
[c] Pounds per hour.
[d] Tons per year.
[e] Pounds per month.

As indicated in Table 4, the SGP facility-wide maximum PTE are greater than the respective Level I thresholds for all criteria pollutants and averaging periods except for Pb. Therefore, modeling is triggered for applicable averaging periods for CO, NOx, $PM_{2.5}$, PM_{10}, and SO_2. Modeling is not required for Pb. The use of Level II modeling thresholds was not approved by DEQ for this project.

Tables 5-7 list criteria pollutant emission rates used in the cumulative NAAQS impact analyses for the worst-case modeling scenarios. Significant Impact Level (SIL) analyses were not performed. Based on the magnitude of the facility-wide emissions and preliminary modeling analyses, it was determined that the impacts from the SGP emissions exceeded the SIL for most criteria pollutants. Therefore, SIL

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analyses were considered redundant and not performed for this report. Table 5 lists the source-specific modeled emission rates for 24-hour and annual $PM_{2.5}$ and 24-hour PM_{10} (worst-case modeling scenario: W5). Table 6 lists the source-specific modeled emission rates for 1-hour and 8-hour CO and annual NO_2 (worst-case modeling scenario: W1). Table 7 lists the source-specific modeled emission rates for 1-hour NO_2 and 1-hour and 3-hour SO_2 (worst-case modeling scenario: B1). Modeling scenarios are discussed in Section 3.1.3. For 1-, 3-, and 8-hour averaging times, hourly emission rates provided in pounds per hour were used. For 24-hour averaging time, daily emission rates provided in pounds per day were used. For the annual averaging time, annual emission rates provided in tons per year were used. All modeled emission rates in Tables 5-7 are listed in units of pounds per hour (lb/hr). The total modeled input emission rates (highest emission scenario) are listed in Table 8.

Table 5. MODELED 24-HOUR PM_{10}, 24-HOUR $PM_{2.5}$, AND ANNUAL $PM_{2.5}$ EMISSION RATES FOR CUMULATIVE NAAQS IMPACT ANALYSES (WORST-CASE MODELING SCENARIO, W5).

Type of Source	Source ID	Description	24-hour PM_{10} (lb/hr)[a]	24-hour $PM_{2.5}$ (lb/hr)	Annual $PM_{2.5}$ (lb/hr)
Point Sources	LS1L	Mill Lime Silo #1 Loading	3.54E-03	5.21E-04	2.50E-05
	MILLS2L	Mill Lime Silo #2 Loading	3.54E-03	5.21E-04	2.50E-05
	SB1	Sb Dryer (2.72 MMBtu/hr Propane-Fired)	2.08E-02	2.08E-02	2.08E-02
	SB2	Sb Bagging	1.18E-01	1.18E-01	1.18E-01
	AC	Autoclave	5.08E+00	5.08E+00	5.08E+00
	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	5.42E-03	5.42E-03	4.45E-04
	ACS1L	AC Lime Silo #1 Loading	1.42E-02	2.08E-03	9.99E-05
	ACS2L	AC Lime Silo #2 Loading	1.42E-02	2.08E-03	9.99E-05
	ACS3L	AC Lime Silo #3 Loading	1.42E-02	2.08E-03	9.99E-05
	ACS4L	AC Lime Silo #4 Loading	7.08E-03	1.04E-03	4.99E-05
	CKD	Carbon Regeneration (Drum)	4.20E-01	4.20E-01	4.20E-01
	CKB	Carbon Regeneration (Kiln)	1.73E-02	1.73E-02	1.73E-02
	EW	Electrowinning Cells and Pregnant Solution Tank	7.00E-02	7.00E-02	7.00E-02
	MR	Mercury Retort	1.00E-02	1.00E-02	1.42E-03
	MF	Induction Melting Furnace	1.42E+00	1.42E+00	2.02E-01
	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	1.84E-02	1.84E-02	5.03E-03
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	1.84E-02	1.84E-02	5.03E-03
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	1.84E-02	1.84E-02	5.03E-03
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	3.67E-03	3.67E-03	1.01E-03
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	7.65E-04	7.65E-04	7.65E-04
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	3.83E-02	3.83E-02	3.83E-02
	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	3.06E-02	3.06E-02	3.06E-02
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	3.06E-02	3.06E-02	3.06E-02
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	3.06E-02	3.06E-02	3.06E-02
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	1.91E-03	1.91E-03	1.91E-03
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	1.91E-03	1.91E-03	1.91E-03
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	1.91E-03	1.91E-03	1.91E-03

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Table 5. MODELED 24-HOUR PM_{10}, 24-HOUR $PM_{2.5}$, AND ANNUAL $PM_{2.5}$ EMISSION RATES FOR CUMULATIVE NAAQS IMPACT ANALYSES (WORST-CASE MODELING SCENARIO, W5).					
Type of Source	**Source ID**	**Description**	**24-hour PM_{10} (lb/hr)[a]**	**24-hour $PM_{2.5}$ (lb/hr)**	**Annual $PM_{2.5}$ (lb/hr)**
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	3.83E-03	3.83E-03	3.83E-03
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	1.53E-02	1.53E-02	1.53E-02
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	2.30E-02	2.30E-02	2.30E-02
	PSL	Prill Silos Loading (2 x 100 ton)	5.83E-02	8.83E-03	8.83E-04
	CS1L	Cement/Shotcrete Silo #1 Loading	1.13E-03	1.67E-04	3.42E-04
	CS2L	Cement/Shotcrete Silo #2 Loading	1.13E-03	1.67E-04	3.42E-04
	LS6	Limestone transfer to Ball Mill Feed Bin	5.18E-02	8.00E-03	6.17E-03
	LSBM	Limestone Ball Mill	1.60E+00	5.70E-01	4.39E-01
	LS9	Limestone transfer to Kiln Feed Bin	1.22E-02	1.89E-03	1.60E-03
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	9.15E-01	9.15E-01	7.77E-01
	LKC	PFR Shaft Lime Kiln Combustion	1.69E-01	1.69E-01	1.43E-01
	LCR	Lime Mill Crushing and associated transfers In and Out	2.39E-01	8.52E-02	7.23E-02
	LSL	Pebble Lime Silo Loading via Bucket Elevator	6.20E-03	6.20E-03	5.26E-03
Area Sources	WEP	West End Pit	3.69E+01	3.32E+00	3.32E+00
	UGEXP	Underground Exploration	1.66E-04	2.51E-05	2.51E-05
Line Sources	AR01	Access Road within Operations Boundary	7.02E-02	7.02E-03	7.03E-03
	AR02	Access Road within Operations Boundary	5.39E-02	5.40E-03	5.41E-03
	AR03	Access Road within Operations Boundary	1.36E-01	1.36E-02	1.37E-02
	AR04	Access Road within Operations Boundary	1.31E-01	1.31E-02	1.31E-02
Volume Sources	WEPBL	West End Pit Blasting	1.39E+01	8.04E-01	8.04E-01
	WEDRSF	West End Pit Development Rock Storage Facility	2.38E+00	1.26E+00	1.26E+00
	OC1	Loader Transfer of Ore to Grizzly	4.79E-02	1.35E-02	1.35E-02
	OC2	Grizzly to Apron Feeder	4.79E-02	1.35E-02	1.35E-02
	OC3	Apron Feeder to Dribble Conveyor	4.79E-02	1.35E-02	1.35E-02
	OC4	Apron Feeder to Vibrating Grizzly	4.79E-02	1.35E-02	1.35E-02
	OC5	Dribble Conveyor to Vibrating Grizzly	4.79E-02	1.35E-02	1.35E-02
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	4.79E-02	1.35E-02	1.35E-02
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	5.63E-01	1.04E-01	1.04E-01
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	4.79E-02	1.35E-02	1.35E-02
	OC9	Stockpile Transfers to Reclaim Conveyors	2.53E-01	3.91E-02	3.91E-02
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	2.53E-01	3.91E-02	3.91E-02
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	2.53E-01	3.91E-02	3.91E-02
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	6.21E-01	1.15E-01	1.15E-01
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	5.29E-02	1.50E-02	1.50E-02
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	2.92E-02	4.37E-03	2.10E-04
	MILLS2U	Mill Lime Silo #2 Unloading to SAG Mill	2.92E-02	4.37E-03	2.10E-04

Table 5. MODELED 24-HOUR PM_{10}, 24-HOUR $PM_{2.5}$, AND ANNUAL $PM_{2.5}$ EMISSION RATES FOR CUMULATIVE NAAQS IMPACT ANALYSES (WORST-CASE MODELING SCENARIO, W5).					
Type of Source	**Source ID**	**Description**	**24-hour PM_{10} (lb/hr)[a]**	**24-hour $PM_{2.5}$ (lb/hr)**	**Annual $PM_{2.5}$ (lb/hr)**
		Conveyor			
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	5.60E-02	8.00E-03	7.99E-04
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	5.60E-02	8.00E-03	7.99E-04
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	5.60E-02	8.00E-03	7.99E-04
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	5.60E-02	8.00E-03	4.00E-04
	PSU	Prill Silos Unloading (2 x 100 ton)	5.83E-02	8.83E-03	8.83E-04
	CS1U	Cement/Shotcrete Silo #1 Unloading	9.33E-03	1.33E-03	2.74E-03
	CS2U	Cement/Shotcrete Silo #2 Unloading	9.33E-03	1.33E-03	2.74E-03
	CAL	Aggregate Bin Loading	3.30E-01	5.00E-02	2.85E-02
	CAU	Aggregate Bin Unloading	3.30E-01	5.00E-02	2.85E-02
	CM	Central Mixer Loading	1.83E-02	2.67E-03	5.48E-03
	PCSP1	Portable Crushing and Screening Plant 1	2.33E-01	3.04E-02	3.04E-02
	PCSP2	Portable Crushing and Screening Plant 2	2.33E-01	3.04E-02	3.04E-02
	LS1	Limestone transfer to Primary Crusher Hopper	5.18E-02	8.00E-03	6.17E-03
	LS2	Primary Crushing and Associated Transfers In and Out	1.13E-01	1.69E-02	1.31E-02
	LS3	Primary Screening and Associated Transfers In and Out	4.10E-01	6.21E-02	4.79E-02
	LS4	Secondary Crushing and Associated Transfers In and Out	1.13E-01	1.69E-02	1.31E-02
	LS5	Secondary Screening and Associated Transfers In and Out	4.10E-01	6.21E-02	4.79E-02
	LS7	Limestone transfer to Ball Mill Feed Conveyor	5.18E-02	8.00E-03	6.17E-03
	LS8	Ball Mill Feed transfer to Ball Mill	5.18E-02	8.00E-03	6.17E-03
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	1.22E-02	1.89E-03	1.60E-03
	LS11	Fines Screening and Associated Transfers In and Out	9.68E-02	1.47E-02	1.25E-02
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	1.22E-02	1.89E-03	1.60E-03
	LSU	Pebble Lime Silo discharge to Lime Slaker	6.20E-04	6.20E-04	5.26E-04
	HRT001-HRT072	Haul Road[b]	9.09E-01	9.10E-02	9.11E-02
	HRN001-HRN022	Haul Road[b]	9.09E-01	9.10E-02	9.11E-02

a. Pounds per hour.

b. The Haul Road was represented in the model as a series of volume sources. The emission rates listed in this table represent each individual volume source.

Table 6. MODELED 1-HOUR CO, 8-HOUR CO, and ANNUAL NO_2 EMISSION RATES FOR CUMULATIVE NAAQS IMPACT ANALYSES (WORST-CASE MODELING SCENARIO, W1).				
Type of Source	**Source ID**	**Description**	**1-hour, 8-hour CO (lb/hr)[a]**	**Annual NO_2 (lb/hr)**
Point Sources	SB1	Sb Dryer (2.72 MMBtu/hr Propane-Fired)	2.23E-01	3.86E-01
	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.39E+00	8.27E-03
	CKD	Carbon Regeneration (Drum)	1.20E-01	1.20E-02
	CKB	Carbon Regeneration (Kiln)	1.85E-01	3.20E-01
	EDG1	Camp Emergency Generator (Mfr. Yr.	7.72E+00	1.61E-01

		>2007; diesel)		
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	7.72E+00	1.61E-01
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	7.72E+00	1.61E-01
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	1.54E+00	2.01E-02
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	8.20E-03	1.42E-02
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	4.10E-01	7.10E-01
	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	3.28E-01	5.68E-01
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	3.28E-01	5.68E-01
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	3.28E-01	5.68E-01
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	2.05E-02	3.55E-02
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	2.05E-02	3.55E-02
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	2.05E-02	3.55E-02
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	4.10E-02	7.10E-02
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	1.64E-01	2.84E-01
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	2.46E-01	4.26E-01
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	3.17E+00	1.44E+00
	LKC	PFR Shaft Lime Kiln Combustion	1.81E+00	2.66E+00
Volume Source	WEPBL	West End Pit Blasting	1.74E+03	3.90E+00

[a] Pounds per hour.

Table 7. MODELED 1-HOUR NO_2, 1-HOUR SO_2, AND 3-HOUR SO_2 EMISSION RATES FOR CUMULATIVE NAAQS IMPACT ANALYSES (WORST-CASE MODELING SCENARIO, B1).

Type of Source	Source ID	Description	1-hour NO_2 (lb/hr)[a]	1-hour, 3-hour SO_2 (lb/hr)
Point Sources	SB1	Sb Dryer (2.72 MMBtu/hr Propane-Fired)	3.86E-01	4.73E-02
	AC	Autoclave	0.00E+00	6.53E-01
	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	2.42E+00	2.95E-01
	CKD	Carbon Regeneration (Drum)	1.20E-02	0.00E+00
	CKB	Carbon Regeneration (Kiln)	3.20E-01	3.92E-02
	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0.00E+00	1.45E-02
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0.00E+00	1.45E-02
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0.00E+00	1.45E-02
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0.00E+00	2.90E-03
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.42E-02	1.74E-03
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	7.10E-01	8.69E-02
	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-	5.68E-01	6.95E-02

		Fired)		
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	5.68E-01	6.95E-02
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	5.68E-01	6.95E-02
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	3.55E-02	4.34E-03
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	3.55E-02	4.34E-03
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	3.55E-02	4.34E-03
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	7.10E-02	8.69E-03
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	2.84E-01	3.48E-02
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	4.26E-01	5.21E-02
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	1.69E+00	8.45E-03
	LKC	PFR Shaft Lime Kiln Combustion	3.13E+00	3.83E-01
Volume Source	BTBL	Bradley Tailings Blasting	4.68E+01	9.36E-02

a. Pounds per hour.

Table 8. CRITERIA POLLUTANT TOTAL MODELED EMISSION RATES (WORST-CASE MODELING SCENARIOS).

Pollutant	Averaging Time	Emissions[a]
CO	8 hours	1,775.50 lb/hr
	1 hour	1,775.50 lb/hr
NO_2	1 year	54.93 ton/yr
	1 hour	58.07 lb/hr
$PM_{2.5}$	1 year	135.23 ton/yr
	24 hours	781.69 lb/day
PM_{10}	24 hours	5,768.93 lb/day
SO_2	3 hours	1.97 lb/hr
	1 hour	1.97 lb/hr

a. Combined process, ancillary, and fugitive emissions modeled. Fugitive emissions vary by pit scenario. Maximum pit scenario emissions are shown.

Ozone (O_3) differs from other criteria pollutants in that it is not typically emitted directly into the atmosphere. O_3 is formed in the atmosphere through reactions of VOCs, NOx, and sunlight. Atmospheric dispersion models used in stationary source air permitting analyses cannot be used to estimate O_3 impacts resulting from VOC and NOx emissions from an industrial facility. O_3 concentrations resulting from area-wide emissions are predicted by using more complex airshed models such as the Community Multi-Scale Air Quality (CMAQ) modeling system. Use of the CMAQ model is very resource-intensive and DEQ asserts that performing a CMAQ analysis for a particular permit application is not typically a reasonable or necessary requirement for air quality permitting.

Addressing secondary formation of O_3 within the context of permitting a new stationary source has been somewhat addressed in EPA regulation and policy. As stated in a letter from Gina McCarthy of EPA to Robert Ukeiley, acting on behalf of the Sierra Club (letter from Gina McCarthy, Assistant Administrator, United States Environmental Protection Agency, to Robert Ukeiley, January 4, 2012):

. . . footnote 1 to sections 51.166(I)(5)(I) of the EPA's regulations says the following: "No de minimis air quality level is provided for ozone. However, any net emission increase of 100 tons per year or more of volatile organic compounds or nitrogen oxides subject to PSD would be required to perform an ambient impact analysis, including the gathering of air quality data."

"The EPA believes it unlikely a source emitting below these levels would contribute to such a violation of the 8-hour ozone NAAQS, but consultation with an EPA Regional Office should still be conducted in accordance with section 5.2.1.c. of Appendix W when reviewing an application for sources with emissions of these ozone precursors below 100 TPY."

DEQ determined it was not appropriate or necessary to require a quantitative source-specific O_3 impact analysis because allowable emission estimates of VOCs and NOx are below the 100 tons/year threshold.

3.1.2 TAPs Modeling Applicability and Modeled Emission Rates

A comparison of the applicable non-carcinogenic and carcinogenic screening emission levels (EL) for the TAP from IDAPA 58.01.01, Sections 585 and 586, respectively, with applicable facility-wide maximum potential TAP emissions for the highest-emitting scenario (W3) is provided in Table 9. Note that TAPs also classified as HAPs emitted from sources addressed by NSPS or NESHAP were not required to be evaluated for compliance with TAP increments in accordance with IDAPA 58.01.01.210.20.

Table 9. TAP MODELING APPLICABILITY DETERMINATION.

HAP/TAP	Emissions (lb/hr)			EL (lb/hr)		Determination
	(a)	(b)	Total	(c)	(d)	
1,3-Butadiene	--	--	--	--	2.4E-5	EL not exceeded
3-Methylchloranthrene	--	3.2E-8	3.2E-8	--	2.5E-6	EL not exceeded
Acetaldehyde	--	--	--	--	3.0E-3	EL not exceeded
Acrolein	--	--	--	1.7E-2	--	EL not exceeded
Antimony	--	--	--	3.3E-2	--	EL not exceeded
Arsenic	--	5.7E-6	5.7E-6	--	1.5E-6	Carcinogenic EL exceeded
Benzene	--	3.8E-5	3.8E-5	--	8.0E-4	EL not exceeded
Benzo(a)pyrene[e]	--	2.1E-8	2.0E-7	--	2.0E-6	EL not exceeded
Benz(a)anthracene[e]	--	3.2E-8				
Benzo(b)fluoranthene[e]	--	3.2E-8				
Benzo(k)fluoranthene[e]	--	3.2E-8				
Chrysene[e]	--	3.2E-8				
Dibenzo(a,h)anthracene[e]	--	2.1E-8				
Indenol(1,2,3-cd)pyrene[e]	--	3.2E-8				
Beryllium	--	2.3E-7	2.3E-7	--	2.8E-5	EL not exceeded
Biphenyl	--	--	--	1.0E-1	--	EL not exceeded
Cadmium	--	2.0E-5	2.0E-5	--	3.7E-6	Carcinogenic EL exceeded
Carbon disulfide	--	--	--	2.0E+0	--	EL not exceeded
Chromium	--	2.7E-5	2.7E-5	3.3E-2	--	EL not exceeded
Chromium (VI)	--	3.4E-7	3.4E-7	--	5.6E-7	EL not exceeded
Cobalt	--	1.5E-6	1.5E-6	3.3E-3	--	EL not exceeded
Cyanide	--	--	--	3.3E-1	--	EL not exceeded
Dichlorobenzene	--	2.1E-5	2.1E-5	3.0E+1	--	EL not exceeded
Formaldehyde	--	1.3E-3	1.3E-3	--	5.1E-4	Carcinogenic EL exceeded
Hexane	--	3.2E-2	3.2E-2	1.2E+1	--	EL not exceeded
Hydrogen Chloride	--	--	--	--	5.0E-2	EL not exceeded
Manganese	--	3.6E-5	3.6E-5	6.7E-2	--	EL not exceeded
Naphthalene	--	1.1E-5	1.1E-5	3.3E+0	--	EL not exceeded
Nickel	--	4.0E-5	4.0E-5	--	2.7E-5	Carcinogenic EL exceeded

Table 9. TAP MODELING APPLICABILITY DETERMINATION.						
HAP/TAP	Emissions (lb/hr)			EL (lb/hr)		Determination
	(a)	(b)	Total	(c)	(d)	
Phenol	--	--	--	1.3E+0	--	EL not exceeded
Phosphorus	--	8.2E-6	8.2E-6	7.0E-3	--	EL not exceeded
PAH (except 7-PAH) [e]	--	--	--	--	9.1E-5	EL not exceeded
Selenium	--	4.3E-7	4.3E-7	1.3E-2	--	EL not exceeded
Toluene	--	6.1E-5	6.1E-5	2.5E+1	--	EL not exceeded
Xylene	--	--	--	2.9E+1	--	EL not exceeded
Aluminum	57.9	6.5E-1	58.5	6.7E-1	--	Non-carcinogenic EL exceeded
Barium	6.5E-1	6.8E-3	6.6E-1	3.3E-2	--	Non-carcinogenic EL exceeded
Calcium Carbonate	11.4	2.24	13.7	6.7E-1	--	Non-carcinogenic EL exceeded
Calcium Oxide	--	7.0E-1	7.0E-1	1.3E-1	--	Non-carcinogenic EL exceeded
Copper	4.1E-3	5.3E-4	4.6E-3	6.7E-2	--	EL not exceeded
Cyclohexane	--	1.0E-3	1.0E-3	7.0E+1	--	EL not exceeded
Hydrogen Sulfide	--	9.0E-1	9.0E-1	9.3E-1	--	EL not exceeded
Iron	14.8	2.1E-1	15.0	6.7E-2	--	Non-carcinogenic EL exceeded
Molybdenum	8.1E-4	4.7E-4	1.3E-3	3.3E-1	--	EL not exceeded
Pentane	--	1.2E-1	1.2E-1	1.2E+2	--	EL not exceeded
Silver	4.1E-4	4.1E-4	8.2E-4	7.0E-3	--	EL not exceeded
Sulfuric Acid	--	2.03	2.03	6.7E-2	--	Non-carcinogenic EL exceeded
Thallium	8.1E-3	5.2E-4	8.7E-3	7.0E-3	--	Non-carcinogenic EL exceeded
Uranium	8.1E-3	5.2E-4	8.7E-3	1.3E-2	--	EL not exceeded
Vanadium	2.3E-2	8.4E-4	2.4E-2	3.0E-3	--	Non-carcinogenic EL exceeded
Trimethyl Benzene	--	1.1E-2	1.1E-2	8.2E+0	--	EL not exceeded
Tungsten	8.1E-3	5.2E-4	8.7E-3	3.3E-1	--	EL not exceeded
Zinc	2.9E-2	2.2E-3	3.1E-2	6.7E-1	--	EL not exceeded

a. Total HAP/TAP emissions for EL evaluation from mining (i.e., pits, blasting, haul roads, stockpiles and DRSF, access road, and underground exploration) and leaching. Emissions from sources addressed by NSPS/NESHAP are not included in the evaluation for modeling applicability.

b. Total HAP/TAP emissions for EL evaluation from processing and production (i.e., ore processing, ore concentration and refining, process heating, lime production, aggregate production, concrete production, HVAC, emergency power, fuel storage). Emissions from sources addressed by NSPS/NESHAP are not included in the evaluation for modeling applicability.

c. Non-carcinogenic EL from IDAPA 58.01.01 Section 585.

d. Carcinogenic EL from IDAPA 58.01.01 Section 586.

e. Polycyclic aromatic hydrocarbon (PAH). The group of seven PAH with a single EL are regulated as polycyclic organic matter (POM) equivalent in potency to benzo(a)pyrene as specified in IDAPA 58.01.01.586.

Table 9 shows that the SGP facility-wide potential TAP emissions exceed the respective EL for arsenic, cadmium, formaldehyde, nickel, aluminum, barium, calcium carbonate, calcium oxide, iron, sulfuric acid, thallium, and vanadium. Therefore, modeling was required for these 12 TAPs.

Table 10 lists the source-specific modeled emission rates for all 12 TAPs (worst-case modeling scenario: W5).

Table 10. MODELED TAP EMISSION RATES (WORST-CASE MODELING SCENARIO, W5).													
Type of Source	**Source ID**	**ALUM[a] (lb/hr)[b]**	**ARSE[c] (lb/hr)**	**BARI[d] (lb/hr)**	**CACA[e] (lb/hr)**	**CADM[f] (lb/hr)**	**CAOX[g] (lb/hr)**	**FORM[h] (lb/hr)**	**IRON (lb/hr)**	**NICK[i] (lb/hr)**	**SULF[j] (lb/hr)**	**THAL[k] (lb/hr)**	**VANA[l] (lb/hr)**
Point Sources	LS1L	2.33E-04	0	1.50E-06	0	0	7.63E-03	0	1.07E-04	0	0	5.16E-08	1.60E-07
	MILLS2L	2.33E-04	0	1.50E-06	0	0	7.63E-03	0	1.07E-04	0	0	5.16E-08	1.60E-07
	SB1	0	0	0	0	0	0	0	0	0	0	0	0
	SB2	0	0	0	0	0	0	0	0	0	0	0	0
	AC	2.31E-05	0	2.31E-05	2.31E-05	0	0	0	2.31E-05	0	2.03E+00	2.31E-05	2.31E-05
	ACB	0	0	3.06E-06	0	0	0	0	0	0	0	0	1.60E-06
	ACS1L	9.32E-04	0	5.98E-06	0	0	3.05E-02	0	4.27E-04	0	0	2.06E-07	6.39E-07
	ACS2L	9.32E-04	0	5.98E-06	0	0	3.05E-02	0	4.27E-04	0	0	2.06E-07	6.39E-07
	ACS3L	9.32E-04	0	5.98E-06	0	0	3.05E-02	0	4.27E-04	0	0	2.06E-07	6.39E-07
	ACS4L	4.66E-04	0	2.99E-06	0	0	1.53E-02	0	2.13E-04	0	0	1.03E-07	3.20E-07
	CKD	9.59E-05	0	9.59E-05	9.59E-05	0	0	0	9.59E-05	0	0	9.59E-05	9.59E-05
	CKB	0	0	9.73E-06	0	0	0	0	0	0	0	0	5.08E-06
	EW	9.59E-05	0	9.59E-05	9.59E-05	0	0	0	9.59E-05	0	0	9.59E-05	9.59E-05
	MR	9.59E-05	0	9.59E-05	9.59E-05	0	0	0	9.59E-05	0	0	9.59E-05	9.59E-05
	MF	9.59E-05	0	9.59E-05	9.59E-05	0	0	0	9.59E-05	0	0	9.59E-05	9.59E-05
	EDG1	0	0	0	0	0	0	0	0	0	0	0	0
	EDG2	0	0	0	0	0	0	0	0	0	0	0	0
	EDG3	0	0	0	0	0	0	0	0	0	0	0	0
	EDFP	0	0	0	0	0	0	0	0	0	0	0	0
	PV	0	0	4.31E-07	0	0	0	0	0	0	0	0	2.25E-07
	HS	0	0	2.16E-05	0	0	0	0	0	0	0	0	1.13E-05
	H1M	0	7.84E-07	1.73E-05	0	4.31E-06	0	2.94E-04	0	8.24E-06	0	0	9.02E-06
	H2M	0	7.84E-07	1.73E-05	0	4.31E-06	0	2.94E-04	0	8.24E-06	0	0	9.02E-06
	HM	0	7.84E-07	1.73E-05	0	4.31E-06	0	2.94E-04	0	8.24E-06	0	0	9.02E-06
	HAC	0	4.90E-08	1.08E-06	0	2.70E-07	0	1.84E-05	0	5.15E-07	0	0	5.64E-07
	HR	0	4.90E-08	1.08E-06	0	2.70E-07	0	1.84E-05	0	5.15E-07	0	0	5.64E-07
	HA	0	4.90E-08	1.08E-06	0	2.70E-07	0	1.84E-05	0	5.15E-07	0	0	5.64E-07
	HMO	0	9.80E-08	2.16E-06	0	5.39E-07	0	3.68E-05	0	1.03E-06	0	0	1.13E-06
	HTS	0	3.92E-07	8.63E-06	0	2.16E-06	0	1.47E-04	0	4.12E-06	0	0	4.51E-06
	HW	0	5.88E-07	1.29E-05	0	3.24E-06	0	2.21E-04	0	6.18E-06	0	0	6.76E-06
	PSL	0	0	0	0	0	0	0	0	0	0	0	0
	CS1L	0	2.90E-08	0	0	0	0	0	0	2.86E-07	0	0	0
	CS2L	0	2.90E-08	0	0	0	0	0	0	2.86E-07	0	0	0
	LS6	3.19E-03	0	2.05E-05	3.88E-02	0	0	0	1.46E-03	0	0	7.06E-07	2.19E-06
	LSBM	4.30E-02	0	2.76E-04	5.22E-01	0	0	0	1.97E-02	0	0	9.51E-06	2.95E-05
	LS9	7.54E-04	0	4.84E-06	9.16E-03	0	0	0	3.45E-04	0	0	1.67E-07	5.17E-07
	LK	2.07E-02	0	1.33E-04	2.51E-01	0	0	0	9.47E-03	0	0	4.58E-06	1.42E-05

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Table 10. MODELED TAP EMISSION RATES (WORST-CASE MODELING SCENARIO, W5).													
Type of Source	**Source ID**	**ALUM[a] (lb/hr)[b]**	**ARSE[c] (lb/hr)**	**BARI[d] (lb/hr)**	**CACA[e] (lb/hr)**	**CADM[f] (lb/hr)**	**CAOX[g] (lb/hr)**	**FORM[h] (lb/hr)**	**IRON (lb/hr)**	**NICK[i] (lb/hr)**	**SULF[j] (lb/hr)**	**THAL[k] (lb/hr)**	**VANA[l] (lb/hr)**
	LKC	0	0	9.51E-05	0	0	0	0	0	0	0	0	4.97E-05
	LCR	6.43E-03	0	4.12E-05	0	0	2.11E-01	0	2.94E-03	0	0	1.42E-06	4.41E-06
	LSL	1.40E-04	0	8.99E-07	0	0	4.59E-03	0	6.41E-05	0	0	3.10E-08	9.60E-08
Area Sources	WEP	5.59E+00	0	6.29E-02	1.10E+00	0	0	0	0	0	0	0	0
	UGEXP	2.49E-05	0	2.80E-07	4.91E-06	0	0	0	0	0	0	0	0
Line Sources	AR01	2.02E-02	0	2.28E-04	3.99E-03	0	0	0	0	0	0	0	0
	AR02	1.56E-02	0	1.75E-04	3.07E-03	0	0	0	0	0	0	0	0
	AR03	3.93E-02	0	4.43E-04	7.75E-03	0	0	0	0	0	0	0	0
	AR04	3.77E-02	0	4.25E-04	7.43E-03	0	0	0	0	0	0	0	0
Volume Sources	WEPBL	1.90E+00	0	2.14E-02	3.75E-01	0	0	0	4.88E-01	0	0	2.68E-04	7.50E-04
	WEDRSF	8.58E-01	0	9.66E-03	1.69E-01	0	0	0	2.20E-01	0	0	1.21E-04	3.38E-04
	OC1	1.04E-02	0	1.17E-04	2.04E-03	0	0	0	2.65E-03	0	0	1.46E-06	4.08E-06
	OC2	1.04E-02	0	1.17E-04	2.04E-03	0	0	0	2.65E-03	0	0	1.46E-06	4.08E-06
	OC3	1.04E-02	0	1.17E-04	2.04E-03	0	0	0	2.65E-03	0	0	1.46E-06	4.08E-06
	OC4	1.04E-02	0	1.17E-04	2.04E-03	0	0	0	2.65E-03	0	0	1.46E-06	4.08E-06
	OC5	1.04E-02	0	1.17E-04	2.04E-03	0	0	0	2.65E-03	0	0	1.46E-06	4.08E-06
	OC6	1.04E-02	0	1.17E-04	2.04E-03	0	0	0	2.65E-03	0	0	1.46E-06	4.08E-06
	OC7	8.87E-02	0	1.00E-03	1.75E-02	0	0	0	2.28E-02	0	0	1.25E-05	3.50E-05
	OC8	1.04E-02	0	1.17E-04	2.04E-03	0	0	0	2.65E-03	0	0	1.46E-06	4.08E-06
	OC9	4.90E-02	0	5.52E-04	9.66E-03	0	0	0	1.26E-02	0	0	6.90E-06	1.93E-05
	OC10	4.90E-02	0	5.52E-04	9.66E-03	0	0	0	1.26E-02	0	0	6.90E-06	1.93E-05
	OC11	4.90E-02	0	5.52E-04	9.66E-03	0	0	0	1.26E-02	0	0	6.90E-06	1.93E-05
	OC12	9.80E-02	0	1.10E-03	1.93E-02	0	0	0	2.51E-02	0	0	1.38E-05	3.86E-05
	OC13	1.14E-02	0	1.29E-04	2.25E-03	0	0	0	2.93E-03	0	0	1.61E-06	4.51E-06
	LS1U	1.13E-03	0	7.25E-06	0	0	3.70E-02	0	5.18E-04	0	0	2.50E-07	7.75E-07
	MILLS2U	1.13E-03	0	7.25E-06	0	0	3.70E-02	0	5.18E-04	0	0	2.50E-07	7.75E-07
	ACS1U	2.17E-03	0	1.39E-05	0	0	7.10E-02	0	9.94E-04	0	0	4.80E-07	1.49E-06
	ACS2U	2.17E-03	0	1.39E-05	0	0	7.10E-02	0	9.94E-04	0	0	4.80E-07	1.49E-06
	ACS3U	2.17E-03	0	1.39E-05	0	0	7.10E-02	0	9.94E-04	0	0	4.80E-07	1.49E-06
	ACS42U	2.17E-03	0	1.39E-05	0	0	7.10E-02	0	9.94E-04	0	0	4.80E-07	1.49E-06
	PSU	0	0	0	0	0	0	0	0	0	0	0	0
	CS1U	0	2.90E-08	0	0	0	0	0	0	2.86E-07	0	0	0
	CS2U	0	2.90E-08	0	0	0	0	0	0	2.86E-07	0	0	0
	CAL	1.56E-02	0	1.00E-04	0	0	0	0	7.14E-03	0	0	3.45E-06	1.07E-05
	CAU	1.56E-02	0	1.00E-04	0	0	0	0	7.14E-03	0	0	3.45E-06	1.07E-05
	CM	0	2.03E-06	0	0	4.86E-09	0	0	0	1.70E-06	0	0	0
	PCSP1	1.41E-02	0	9.06E-05	1.72E-01	0	0	0	6.47E-03	0	0	3.12E-06	9.69E-06

Table 10. MODELED TAP EMISSION RATES (WORST-CASE MODELING SCENARIO, W5).													
Type of Source	**Source ID**	**ALUM[a] (lb/hr)[b]**	**ARSE[c] (lb/hr)**	**BARI[d] (lb/hr)**	**CACA[e] (lb/hr)**	**CADM[f] (lb/hr)**	**CAOX[g] (lb/hr)**	**FORM[h] (lb/hr)**	**IRON (lb/hr)**	**NICK[i] (lb/hr)**	**SULF[j] (lb/hr)**	**THAL[k] (lb/hr)**	**VANA[l] (lb/hr)**
	PCSP2	1.41E-02	0	9.06E-05	1.72E-01	0	0	0	6.47E-03	0	0	3.12E-06	9.69E-06
	LS1	3.19E-03	0	2.05E-05	3.88E-02	0	0	0	1.46E-03	0	0	7.06E-07	2.19E-06
	LS2	5.75E-03	0	3.69E-05	6.98E-02	0	0	0	2.63E-03	0	0	1.27E-06	3.94E-06
	LS3	2.66E-02	0	1.71E-04	3.23E-01	0	0	0	1.22E-02	0	0	5.88E-06	1.82E-05
	LS4	5.75E-03	0	3.69E-05	6.98E-02	0	0	0	2.63E-03	0	0	1.27E-06	3.94E-06
	LS5	2.66E-02	0	1.71E-04	3.23E-01	0	0	0	1.22E-02	0	0	5.88E-06	1.82E-05
	LS7	3.19E-03	0	2.05E-05	3.88E-02	0	0	0	1.46E-03	0	0	7.06E-07	2.19E-06
	LS8	3.19E-03	0	2.05E-05	3.88E-02	0	0	0	1.46E-03	0	0	7.06E-07	2.19E-06
	LS10	7.54E-04	0	4.84E-06	9.16E-03	0	0	0	3.45E-04	0	0	1.67E-07	5.17E-07
	LS11	6.29E-03	0	4.03E-05	7.63E-02	0	0	0	2.88E-03	0	0	1.39E-06	4.31E-06
	LS12	7.54E-04	0	4.84E-06	9.16E-03	0	0	0	3.45E-04	0	0	1.67E-07	5.17E-07
	LSU	1.40E-05	0	8.99E-08	0	0	4.59E-04	0	6.41E-06	0	0	3.10E-09	9.60E-09
	HRT001-HRT072[m]	2.62E-01	0	2.95E-03	5.16E-02	0	0	0	6.71E-02	0	0	3.69E-05	1.03E-04
	HRN001-HRN022[m]	2.62E-01	0	2.95E-03	5.16E-02	0	0	0	6.71E-02	0	0	3.69E-05	1.03E-04

a. Aluminum.
b. Pounds per hour.
c. Arsenic.
d. Barium.
e. Calcium carbonate.
f. Cadmium.
g. Calcium oxide.
h. Formaldehyde.
i. Nickel.
j. Sulfuric acid.
k. Thallium.
l. Vanadium.
m. The Haul Road was represented in the model as a series of volume sources. The emission rates listed in this table represent each individual volume source.

3.1.3 Modeling Scenarios

As discussed in Section 2.1, conventional open-pit methods will be used to extract ore and DR from three pits: YPP, HFP, and WEP, and legacy tailings from BT. Ore will be hauled to the crushing area, and the DR will be moved to four DRSF: Yellow Pine (YPDRSF), Hangar Flats (HFDRSF), West End (WEDRSF), and Fiddle (FDRSF). The SGP site layout provided later in Figure 4 shows these locations.

Midas Gold plans for an up to three-year construction schedule to build mine site facilities and infrastructure, as well as the power transmission line, followed by 12 years of mining operations (i.e., LOM Years 1 through 12). Depending on the mine design and operating schedule, mining activity rates will vary temporally and spatially during the 12 years of mine production and operation. For example, ore production varies from approximately 6.8 MMton in LOM Year 1 (67% in YPP, 26% in WEP, and 7% in BT) to 9 MMton in LOM 3 (78% in YPP, 10% in BT, 7% in WEP, and 5% in HFP). Similarly, DR production varies from approximately 4.8 MMton in LOM Year 12 (100% in WEP) to 34 MMton in each of LOM Years 4 through 9, with varying distribution among the four DRSF for each LOM Year. The total material (ore and DR) production varies from approximately 12.5 MMton in LOM Year 12 to 42.7 MMton in LOM Year 4.

Similar to the material production, the distribution and hauling of DR to the four destinations (YPDRSF, HFDRSF, WEDRSF, FDRSF) also will vary for each LOM year. Depending on the material origin (pits and BT) and destination (crushing area and DRSF), material hauling distances also will vary for each LOM year.

Therefore, depending on material production rates and origin, DR destination, and hauling distances, mining emissions will vary spatially and temporally throughout the mine life. For permitting purposes, Midas Gold used a maximum production rate of 180,000 tons of material (ore and/or DR) per day, for an annual production rate of 65.7 MMton/yr. This annual production rate is more than 50% higher than the estimated maximum total material production rate of 42.7 MMton/yr.

In order to allow Midas Gold with operation flexibility and to capture variability in material origin and destination in the air quality analyses, several pit scenarios were developed for the SGP air quality analyses. Each pit scenario uses the maximum production rate of 180,000 ton/day in a single pit and uses a single material destination. Each pit has a dedicated ore scenario that assumes all material produced is ore and is hauled to the crusher area; and depending on mine design multiple DR destination scenarios each assuming all material produced is DR and is transported to a single DRSF. For example, most of the DR from HFP will be moved to HFDRSF and during LOM Years 2 through 10, but a fraction of this rock will be moved to FDRSF during LOM Years 3 and 8, and a fraction to YPDRSF during LOM Year 9. Therefore, in order to evaluate all hauling scenarios originating from HFP, the following four (one for ore hauling, three for DR hauling) HFP scenarios were modeled:

1. HFP Scenario 1 – 180,000 ton/day of ore produced and hauled to the crusher area
2. HFP Scenario 2 – 180,000 ton/day of DR produced and hauled to the FDRSF
3. HFP Scenario 3 – 180,000 ton/day of DR produced and hauled to the HFDRSF
4. HFP Scenario 4 – 180,000 ton/day of DR produced and hauled to the YPDRSF

Overall, 14 scenarios were modeled for $PM_{2.5}$ and PM_{10} analyses to cover all possible origin and destination combinations. Each modeling scenario included processing and ancillary source potential emissions. The multiple scenarios modeled for $PM_{2.5}$ and PM_{10} analyses are presented in Table 11. This table also shows the six origin/destination options that are not applicable to the SGP Project as denoted by

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"0 ton/day." These six scenarios are not feasible because the timing of the activity within the sequence of mine operations makes the scenarios logistically impossible.

Table 11. MODELING SCENARIOS FOR $PM_{2.5}$ AND PM_{10} ANALYSES.

Pit Scenario	Pit/Origin (ton/day)				Ore Destination (ton/day)	DR Destination (ton/day)			
	YPP	HFP	WEP	BT	STKP	FDRSF	HFDRSF	YPDRSF	WEDRSF
Y1	180,000	--	--	--	180,000	--	--	--	--
Y2	180,000	--	--	--	--	180,000	--	--	--
Y3	180,000	--	--	--	--	--	180,000	--	--
Y4	0	--	--	--	--	--	--	0	--
Y5	0	--	--	--	--	--	--	--	0
H1	--	180,000	--	--	180,000	--	--	--	--
H2	--	180,000	--	--	--	180,000	--	--	--
H3	--	180,000	--	--	--	--	180,000	--	--
H4	--	180,000	--	--	--	--	--	180,000	--
H5	--	0	--	--	--	--	--	--	0
W1	--	--	180,000	--	180,000	--	--	--	--
W2	--	--	180,000	--	--	180,000	--	--	--
W3	--	--	180,000	--	--	--	180,000	--	--
W4	--	--	180,000	--	--	--	--	180,000	--
W5	--	--	180,000	--	--	--	--	--	180,000
B1	--	--	--	180,000	180,000	--	--	--	--
B2	--	--	--	180,000	--	--	180,000	--	--
B3	--	--	--	0	--	0	--	--	--
B4	--	--	--	0	--	--	--	0	--
B5	--	--	--	0	--	--	--	--	0

Scenario Y4 is not applicable because the YPDRSF and the YPP are in the same area; therefore, the pit cannot be backfilled with development rock until after mining of the pit is completed. Scenarios Y5 and H5 are not applicable because the WEDRSF will only be utilized by the WEP because of its proximity; it is only accessible from the WEP. Scenarios B3, B4 and B5 are not applicable because the development rock from the BT will only be hauled to the HFDRSF because of its proximity. All other development rock storage facilities are significantly farther away from BT.

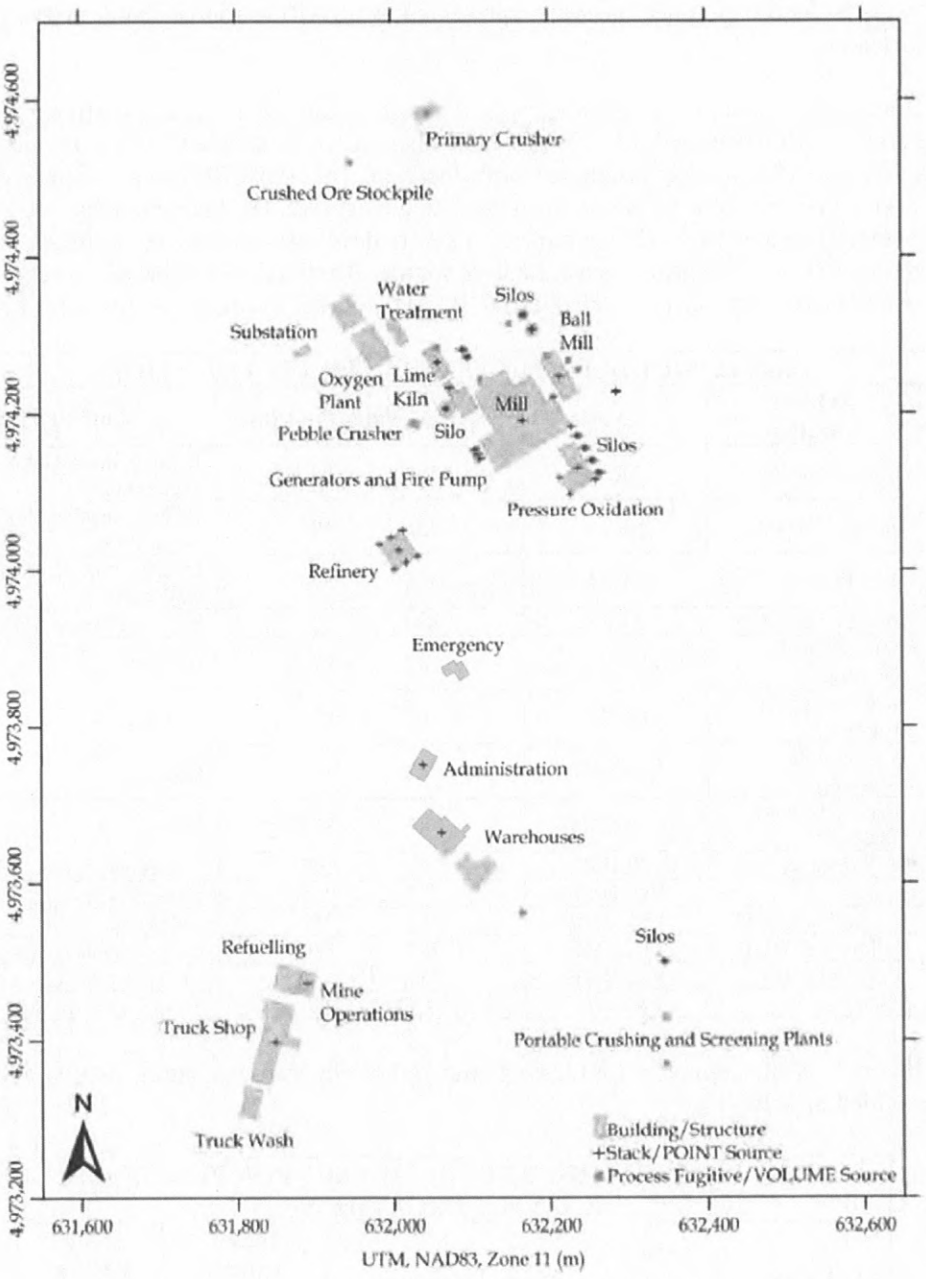
The fugitive CO, NO_2, and SO_2 emissions are limited to pits only, and they do not vary by ore and/or DR hauling and destinations. Therefore, for these pollutants, one scenario for each pit, including processing and ancillary source potential emissions, was modeled, i.e., scenarios Y1, H1, W1, and B1.

The TAP emissions are limited to processing and ancillary sources, so a single scenario was modeled for each applicable TAP analysis.

3.1.4 Processing, Refining, and Ancillary Sources

The processing, refining, and ancillary sources with exhaust stacks, such as baghouse-equipped sources, generators, process and building heaters, autoclave, retort, smelting furnace, carbon kiln, lime kiln, etc., were modeled as POINT sources. The process sources without exhaust stacks, such as material transfers, ore screening and crushing, etc., were modeled as VOLUME sources. A plot plan showing the processing and refining area buildings and sources is provided in Figure 3. Process and ancillary source model input parameters are provided later in Tables 15 and 16.

Figure 3. PROCESSING AND REFINING AREA BUILDING AND SOURCE LAYOUT.



3.1.5 Fugitive Sources: Blasting, Material Origin and Destination, and Underground Exploration Emissions

Blasting emissions were represented by a VOLUME source located inside a pit. Each material origin location (YPP, HFP, WEP, BT) was modeled as an AREA source and comprised appropriate emissions from drilling, material loading, dozing, and surface exploration. Ore destination (crusher area) was modeled as a VOLUME source and comprised ore unloading emissions. Each DR destination (FDRSF,

HFDRSF, YPDRSF, WEDRSF) was modeled as a VOLUME source comprising appropriate emissions from DR unloading, dozing, and wind erosion. Emissions from underground core sampling drilling (UGEXP) in the Scout prospect decline were represented by an AREA source characterized by the portal opening dimensions.

Model input physical characteristics for blasting and possible material origin and destination locations, and Scout portal are presented in Table 12. This table also shows the source type and associated dimensions for each of the modeled fugitive source/location. The VOLUME source dimensions for blasting provided in Table 12 were based on an estimated blast area. For the remaining AREA and VOLUME sources listed in Table 12, the dimensions were developed by reasonably fitting an equal-area rectangle within the actual footprint of each fugitive source. Blasting is not expected to occur in BT. However, blasting emissions were modeled in BT (BTBL) in order to streamline the permitting process.

Table 12. MODELED FUGITIVE ACTIVITY LOCATIONS.

Model ID	Activity Location	Type	Lateral Dimensions (m)	Emission Sources
YPP	Yellow Pine Pit	AREA	882 × 882	Drilling, loading, dozing, surface exploration
HFP	Hangar Flats Pit	AREA	491 × 491	Drilling, loading, dozing, surface exploration
WEP	West End Pit	AREA	376 × 376	Drilling, loading, dozing, surface exploration
BT	Bradley Tailings	AREA	820 × 420	Loading, dozing, wind erosion
YPPBL	Yellow Pine Pit (Blasting)	VOLUME	87 × 87	Blasting
HFPBL	Hangar Flats Pit (Blasting)	VOLUME	87 × 87	Blasting
WEPBL	West End Pit (Blasting)	VOLUME	87 × 87	Blasting
BTBL	Bradley Tailings (Blasting)	VOLUME	87 × 87	Blasting
STKP	PC Stockpile	VOLUME	229 × 229	Unloading, dozing, wind erosion
FDRSF	Fiddle DRSF	VOLUME	775 × 775	Unloading, dozing, wind erosion
HFDRSF	Hangar Flats DRSF	VOLUME	752 × 752	Unloading, dozing, wind erosion
YPDRSF	Yellow Pine DRSF	VOLUME	784 × 784	Unloading, dozing, wind erosion
WEDRSF	West End DRSF	VOLUME	533 × 533	Unloading, dozing, wind erosion
UGEXP	Scout Portal	AREA	4.9 × 4.9	Sample core drilling

The model input physical parameters for blasting, material origin and destination locations, and Scout portal are provided in Table 13.

Table 13. MODEL INPUT PARAMETERS FOR FUGITIVE ACTIVITY LOCATIONS.

Model ID	Base Elevation (m)	Release Height (m)	Initial Lateral Dispersion (m)	Initial Vertical Dispersion (m)
YPP	1,832.4	4.7	N/A	4.4
HFP	1,993.3	4.7	N/A	4.4
WEP	2,191.8	4.7	N/A	4.4
BT	2,011.7	4.7	N/A	4.4
YPPBL	1,717.2	15.0	20.2	7.0
HFPBL	1,890.6	15.0	20.2	7.0
WEPBL	1,994.0	15.0	20.2	7.0

BTBL	2,011.7	15.0	20.2	7.0
STKP	1,979.8	4.7	53.3	4.4
FDRSF	2,115.2	4.7	180.2	4.4
HFDRSF	2,079.8	4.7	174.8	4.4
YPDRSF	1,904.1	4.7	182.2	4.4
WEDRSF	2,376.5	4.7	124.1	4.4
UGEXP	2,018.0	0	N/A	0

The blasting physical parameters were developed from dimensions (provided in Table 12) based on blast area used in the emission calculation. The blasting release height is the midpoint of the blasting height (30 m).

The initial lateral and vertical dispersion dimensions for blasting were calculated per methods specified in (EPA 2018c) for a volume source not on or adjacent to a building, as:

$$Initial\ Lateral\ Dispesion = \frac{Width\ (87\ m)}{4.3}$$

$$Initial\ Vertical\ Dispesion = \frac{Height\ (30\ m)}{4.3}$$

For the pit and DRSF fugitive activity locations listed in Table 12, i.e., YPP, HFP, WEP, BT, FDRSF, HFDRSF, and WEDRSF, the release height was based on the haul truck height (weighted based on model-specific usage) and calculated using the recommendations provided in the Haul Road Workgroup Report (EPA 2012), as:

$$Release\ Height = \frac{Plume\ Top\ (Weighted\ Truck\ Height \times 1.7)}{2}$$

The applicable initial lateral dispersion for each VOLUME source was calculated from the respective shorter dimension and EPA-specified methods (EPA 2018c) (EPA 2016) as follows:

$$Initial\ Lateral\ Dispesion = \frac{Short\ Lateral\ Dimension}{2.15}$$

The applicable initial vertical dispersion for each AREA and VOLUME source was calculated from the respective vertical dimension and EPA-specified methods (EPA 2018c) (EPA 2016) as follows:

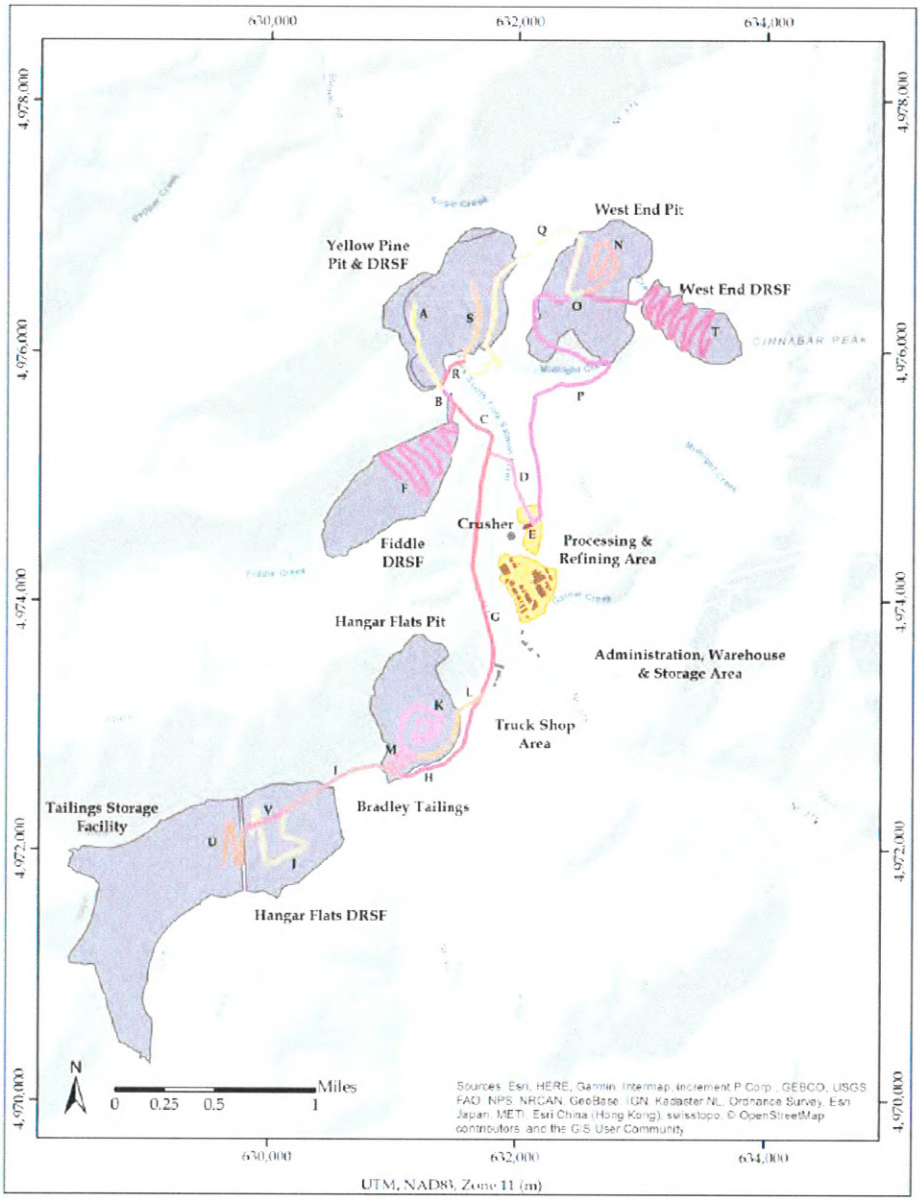
$$Initial\ Vertical\ Dispersion = \frac{Plume\ Top\ (Weighted\ Truck\ Height \times 1.7)}{2.15}$$

Scout portal was modeled as a surface-based AREA source with zero release height.

3.1.6 Fugitive Sources: Haul Roads

A representative haul road network for hauling material from inside the pit (or origin) to various destinations was developed for each pit scenario provided in Table 11. The haul road network is presented in Figure 4.

Figure 4. HAUL ROAD NETWORK AND SECTIONS.



As shown in Figure 4, the haul road network was divided into 22 sections, A through V. Each section was further divided into multiple segments with a length equal to twice the adjusted haul road width of 32.5 m (26 m road width plus 6 m (EPA 2012)). Each of the segments was characterized as an individual VOLUME source in the model, with a release height of 4.75 m (weighted-average truck height times 1.7, divided by 2 (EPA 2012)), an initial lateral dispersion of 15.1 m (adjusted road width divided by 2.15 (EPA 2012)), and an initial vertical dispersion of 4.42 m (weighted-average top-of-plume height divided by 2.15 (EPA 2012)). Material hauling emissions associated with each origin-destination route were assigned to each segment along the route based on estimated total emissions along the route and traffic distribution along each section, as provided in Table 14 for the four HFP scenarios.

Table 14. HAUL ROAD EMISSION DISTRIBUTION GRID FOR HFP SCENARIOS.					
Pit Scenario		**H1**	**H2**	**H3**	**H4**
Route: Origin-Destination		**HFP-STKP**	**HFP-FDRSF**	**HFP-HFDRSF**	**HFP-YPDRSF**
Segment Emission Denominator		96	148	87	115
Section	**No. of Segments**	**Traffic Distribution per Route**			
A	37	--	--	--	--
B	3	--	--	--	1
C	11	--	1	--	1
D	14	1	--	--	--
E	2	--	--	--	--
F	55	--	1	--	--
G	38	1	1	--	1
H	20	--	--	--	--
I	20	--	--	1	--
J	27	--	--	1	--
K	28	1	1	1	1
L	16	1	1	--	1
M	12	--	--	1	--
N	22	--	--	--	--
O	2	--	--	--	--
P	57	--	--	--	--
Q	49	--	--	--	--
R	6	--	--	--	1
S	13	--	--	--	1
T	72	--	--	--	--
U	19	--	--	--	--
V	7	--	--	--	--

The top row in Table 14 shows the pit scenarios, and the next two rows show hauling route and the associated segment emission denominator (SED) used to distribute segment emissions along each route. The remainder of Table 14 presents the number of segments for each road section (shown in Figure 4) and the associated traffic distribution factor for each route. The emission distribution for each applicable segment is illustrated in the following example.

For route: HFP–STKP (Hangar Flats pit to crusher stockpile), Figure 4 shows that material from HFP will be hauled to the crusher area following the route along Sections K, L, G, and D. All (100%) of the ore from HFP will travel on each of these sections; therefore, each of these sections has a traffic distribution factor of 1.0 for this route.

The SED for each route is the sum-product of the number of segments and traffic distribution for the applicable sections. The SED for the HFP–STKP route is calculated as:

$$SED_{(HFP-STKP)} = (28 \times 1) + (16 \times 1) + (38 \times 1) + (14 \times 1) = 96$$

Emissions for each section-segment were estimated by dividing the total emissions along the route by its SED and multiplying by the section distribution factor. For example, the emission rate for each of the 28 segments along Section K was calculated as:

$$Emission\ Rate - Section\ K_{(Segments\ 1-28)} = \frac{Total\ Emissions_{(HFP-STKP)}}{96} \times 1$$

3.1.7 Fugitive Sources: Burntlog Route Access Road

The access road portion within the operations boundary was characterized by a series of LINE sources laid along the actual route. Emissions associated along this access road include dust emissions generated from travel of maintenance equipment, light-duty pickup trucks and buses used for employee, visitor, and contractor transportation, and heavy-duty trucks used for cargo and services transportation. These sources were assigned a release height of 3 m and an initial vertical dispersion of 2.8 m. These release parameters were based on an estimated average vehicle height of 3.5 m, which is representative of an overall approximation of anticipated vehicle heights (grader – 3.7 m, heavy-duty truck – 3.6 m, and pickup truck – 3.2 m) and the AREA source parameterization recommendations provided in the Haul Road Workgroup Report (EPA 2012). The AERMOD emission input units for AREA source are grams per meter square. The access road emissions were evenly distributed along the road by dividing the total access road emissions by its total area, i.e., the Burntlog Route section within the operations boundary (2,950 m) multiplied by the road width (6.1 m).

3.1.8 Emission Release Parameters

Table 15 lists the emission release parameters, including stack height, exhaust temperature, exhaust velocity, and stack diameter for SGP's process and ancillary point sources in metric units (English units are in parentheses). Table 16 lists the emission release parameters for SGP's process and ancillary volume sources in metric units (English units are in parentheses). Emission release parameters were based on information provided in the application. Justification for emission release parameters is summarized in the next section.

Table 15. PROCESS AND ANCILLARY POINT SOURCE EMISSION RELEASE PARAMETERS IN METRIC UNITS (ENGLISH UNITS IN PARENTHESES).

Release Point	Description	UTM[a] Coordinates		Stack Height in m (ft)[c]	Stack Exhaust Temp. in K (°F)[d]	Stack Exhaust Velocity in m/sec (fps)[e]	Stack Diameter in m (ft)	Orient. Of Release[f]
		Easting-X in m[b]	Northing-Y in m					
LS1L	Mill Lime Silo #1 Loading	632,095	4,974,272	13.3 (43.7)	0.0 (-459.7)	18.1 (59.4)	0.15 (0.49)	D
MillS2L	Mill Lime Silo #2 Loading	632,090	4,974,282	13.3 (43.7)	0.0 (-459.7)	18.1 (59.4)	0.15 (0.49)	D
SB1	Sb Dryer (2.72 MMBtu/hr Propane-Fired)	632,231	4,974,183	45.7 (150.0)	455.4 (360.0)	6.9 (22.8)	0.30 (0.98)	D
SB2	Sb Bagging	632,208	4,974,221	45.7 (150.0)	0.0 (-459.7)	6.5 (21.2)	0.30 (0.98)	D
AC	Autoclave	632,229	4,974,096	23.5 (77.0)	364.3 (196.1)	7.4 (24.3)	1.52 (4.99)	D
ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	632,261	4,974,116	23.5 (77.0)	455.4 (360.0)	10.8 (35.6)	0.61 (2.00)	D
ACS1L	AC Lime Silo #1 Loading	632,267	4,974,124	17.4 (57.2)	0.0 (-459.7)	16.1 (52.8)	0.23 (0.75)	D
ACS2L	AC Lime Silo #2 Loading	632,257	4,974,140	17.4 (57.2)	0.0 (-459.7)	16.1 (52.8)	0.23 (0.75)	D
ACS3L	AC Lime Silo #3 Loading	632,248	4,974,156	17.4 (57.2)	0.0 (-459.7)	16.1 (52.8)	0.23 (0.75)	D
ACS4L	AC Lime Silo #4 Loading	632,238	4,974,171	14.5 (47.5)	0.0 (-459.7)	16.1 (52.8)	0.23 (0.75)	D
CKD	Carbon	632,013	4,974,051	16.8	338.7	5.1	0.15	D

Table 15. PROCESS AND ANCILLARY POINT SOURCE EMISSION RELEASE PARAMETERS IN METRIC UNITS (ENGLISH UNITS IN PARENTHESES).								
Release Point	**Description**	**UTM[a] Coordinates**		**Stack Height in m (ft)[c]**	**Stack Exhaust Temp. in K (°F)[d]**	**Stack Exhaust Velocity in m/sec (fps)[e]**	**Stack Diameter in m (ft)**	**Orient. Of Release[f]**
		Easting-X in m[b]	**Northing-Y in m**					
	Regeneration Kiln (Drum)			(55.0)	(150.0)	(16.6)	(0.49)	
CKB	Carbon Regeneration Kiln (Burners)	631,998	4,974,042	14.0 (46.0)	455.4 (360.0)	5.8 (18.9)	0.30 (0.98)	D
EW	Electrowinning Cells and Pregnant Solution Tank	631,983	4,974,033	16.8 (55.0)	310.9 (100.0)	24.2 (79.4)	0.30 (0.98)	D
MR	Mercury Retort	632,003	4,974,001	16.8 (55.0)	338.7 (150.0)	1.5 (5.1)	0.09 (0.30)	D
MF	Induction Melting Furnace	632,032	4,974,019	16.8 (55.0)	338.7 (150.0)	21.5 (70.6)	0.38 (1.25)	D
EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	634,274	4,972,050	2.1 (7.0)	866.5 (1,100.0)	29.7 (97.4)	0.46 (1.51)	D
EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	632,105	4,974,154	2.1 (7.0)	866.5 (1,100.0)	29.7 (97.4)	0.46 (1.51)	D
EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	632,109	4,974,148	2.1 (7.0)	866.5 (1,100.0)	29.7 (97.4)	0.46 (1.51)	D
EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	632,113	4,974,141	2.1 (7.0)	866.5 (1,100.0)	23.8 (78.0)	0.23 (0.75)	D
PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	632,216	4,974,118	20.7 (68.0)	455.4 (360.0)	1.6 (5.2)	0.12 (0.39)	D
HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	632,017	4,974,010	14.0 (46.0)	455.4 (360.0)	7.5 (24.8)	0.40 (1.31)	D
H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	632,287	4,974,227	2.1 (7.0)	455.4 (360.0)	6.0 (19.8)	0.40 (1.31)	D
H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	632,288	4,974,228	2.1 (7.0)	455.4 (360.0)	20.8 (68.3)	0.21 (0.69)	D
HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	632,168	4,974,191	43.0 (141.0)	455.4 (360.0)	28.3 (92.9)	0.09 (0.30)	D
HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	632,238	4,974,130	20.7 (68.0)	455.4 (360.0)	7.1 (23.3)	0.09 (0.30)	D
HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	632,008	4,974,026	14.0 (46.0)	455.4 (360.0)	7.1 (23.3)	0.09 (0.30)	D
HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	632,038	4,973,751	6.4 (21.0)	455.4 (360.0)	7.1 (23.3)	0.09 (0.30)	D

Table 15. PROCESS AND ANCILLARY POINT SOURCE EMISSION RELEASE PARAMETERS IN METRIC UNITS (ENGLISH UNITS IN PARENTHESES).								
Release Point	**Description**	**UTM[a] Coordinates**		**Stack Height in m (ft)[c]**	**Stack Exhaust Temp. in K (°F)[d]**	**Stack Exhaust Velocity in m/sec (fps)[e]**	**Stack Diameter in m (ft)**	**Orient. Of Release[f]**
		Easting-X in m[b]	**Northing-Y in m**					
HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	631,889	4,973,472	12.5 (41.0)	455.4 (360.0)	1.3 (4.3)	0.21 (0.69)	D
HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	631,848	4,973,398	12.5 (41.0)	455.4 (360.0)	5.2 (17.1)	0.21 (0.69)	D
HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	632,060	4,973,664	12.5 (41.0)	455.4 (360.0)	5.2 (17.1)	0.21 (0.69)	D
PSL	Prill Silos Loading (2 x 100 ton)	632,346	4,973,500	7.8 (25.5)	0.0 (-459.7)	18.1 (59.4)	0.15 (0.49)	D
CS1L	Cement/Shotcrete Silo #1 Loading	632,095	4,974,272	13.3 (43.7)	0.0 (-459.7)	24.1 (78.9)	0.15 (0.49)	D
CS2L	Cement/Shotcrete Silo #2 Loading	632,095	4,974,272	13.3 (43.7)	0.0 (-459.7)	24.1 (78.9)	0.15 (0.49)	D
LS6	Limestone transfer to Ball Mill Feed Bin	632,181	4,974,307	8.8 (29.0)	0.0 (-459.7)	0.001 (0.003)	0.30 (0.98)	D
LSBM	Limestone Ball Mill	632,215	4,974,248	21.3 (70.0)	0.0 (-459.7)	26.7 (87.5)	0.61 (2.00)	D
LS9	Limestone transfer to Kiln Feed Bin	632,169	4,974,325	8.8 (29.0)	0.0 (-459.7)	0.001 (0.003)	0.30 (0.98)	D
LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	632,057	4,974,265	45.7 (150.0)	449.8 (350.0)	26.4 (86.5)	0.61 (2.00)	D
LKC	PFR Shaft Lime Kiln Combustion	632,057	4,974,265	45.7 (150.0)	449.8 (350.0)	26.4 (86.5)	0.61 (2.00)	D
LCR	Lime Mill Crushing and associated transfers In and Out	632,073	4,974,233	15.2 (50.0)	0.0 (-459.7)	28.7 (94.3)	0.23 (0.75)	D
LSL	Pebble Lime Silo Loading via Bucket Elevator	632,069	4,974,206	8.8 (29.0)	0.0 (-459.7)	4.1 (13.4)	0.10 (0.33)	D

a. Universal Transverse Mercator.
b. m: meters.
c. ft: feet.
d. K: Kelvin; °F: degrees Fahrenheit.
e. m/sec: meters per second; fps: feet per second.
f. D: default (vertical, uninterrupted release); R: raincap; H: horizontal.
g. The exhaust temperature for the new silo was set to 0 K. This triggers AERMOD to use the actual temperatures from the meteorological data input files.

Table 16. PROCESS AND ANCILLARY VOLUME SOURCE EMISSION RELEASE PARAMETERS IN METRIC UNITS (ENGLISH UNITS IN PARENTHESES).						
Release Point	Description	UTM[a] Coordinates		Release Height in m (ft)[c]	Init. Horiz. Dim. in m (ft)	Init. Vert. Dim. in m (ft)
		Easting-X in m[b]	Northing-Y in m			
OC1	Loader Transfer of Ore to Grizzly	632,045	4,974,583	19.5 (64.0)	3.8 (12.3)	18.1 (59.5)
OC2	Grizzly to Apron Feeder	632,045	4,974,583	19.5 (64.0)	3.8 (12.3)	18.1 (59.5)
OC3	Apron Feeder to Dribble Conveyor	632,045	4,974,583	19.5 (64.0)	3.8 (12.3)	18.1 (59.5)
OC4	Apron Feeder to Vibrating Grizzly	632,045	4,974,583	19.5 (64.0)	3.8 (12.3)	18.1 (59.5)
OC5	Dribble Conveyor to Vibrating Grizzly	632,045	4,974,583	19.5 (64.0)	3.8 (12.3)	18.1 (59.5)
OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	632,045	4,974,583	19.5 (64.0)	3.8 (12.3)	18.1 (59.5)
OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	632,045	4,974,583	19.5 (64.0)	3.8 (12.3)	18.1 (59.5)
OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	631,947	4,974,520	10.9 (35.8)	0.2 (0.7)	10.2 (33.3)
OC9	Stockpile Transfers to Reclaim Conveyors	631,947	4,974,520	1.2 (4.0)	0.6 (1.9)	1.1 (3.7)
OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	631,947	4,974,520	1.2 (4.0)	0.6 (1.9)	1.1 (3.7)
OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	632,113	4,974,243	20.7 (69.0)	0.3 (0.9)	0.6 (1.9)
OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	632,028	4,974,187	3.0 (10.0)	2.3 (7.6)	2.8 (9.3)
OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	632,028	4,974,187	3.0 (10.0)	2.3 (7.6)	2.8 (9.3)
LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	632,095	4,974,272	1.4 (4.5)	0.1 (0.2)	0.1 (0.5)
MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	632,090	4,974,282	1.4 (4.5)	0.1 (0.2)	0.1 (0.5)
ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	632,267	4,974,124	1.4 (4.5)	0.1 (0.2)	0.1 (0.5)
ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	632,257	4,974,140	1.4 (4.5)	0.1 (0.2)	0.1 (0.5)
ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	632,248	4,974,156	1.4 (4.5)	0.1 (0.2)	0.1 (0.5)
ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	632,238	4,974,171	1.4 (4.5)	0.1 (0.2)	0.1 (0.5)
PSU	Prill Silos Unloading (2 x 100 ton)	632,346	4,973,500	1.4 (4.5)	0.1 (0.2)	0.1 (0.5)
CS1U	Cement/Shotcrete Silo #1 Unloading	632,095	4,974,272	1.5 (5.0)	5.1 (16.8)	1.4 (4.7)
CS2U	Cement/Shotcrete Silo #2 Unloading	632,095	4,974,272	1.5 (5.0)	5.1 (16.8)	1.4 (4.7)
CAL	Aggregate Bin Loading	632,095	4,974,272	1.5 (5.0)	5.1 (16.8)	1.4 (4.7)
CAU	Aggregate Bin Unloading	632,095	4,974,272	1.5 (5.0)	5.1 (16.8)	1.4 (4.7)
CM	Central Mixer Loading	632,095	4,974,272	1.5	5.1	1.4

Table 16. PROCESS AND ANCILLARY VOLUME SOURCE EMISSION RELEASE PARAMETERS IN METRIC UNITS (ENGLISH UNITS IN PARENTHESES).						
Release Point	Description	UTM[a] Coordinates		Release Height in m (ft)[c]	Init. Horiz. Dim. in m (ft)	Init. Vert. Dim. in m (ft)
		Easting-X in m[b]	Northing-Y in m			
				(5.0)	(16.8)	(4.7)
PCSP1	Portable Crushing and Screening Plant 1	632,348	4,973,429	2.1 (7.0)	13.1 (43.1)	2.0 (6.5)
PCSP2	Portable Crushing and Screening Plant 2	632,348	4,973,369	2.1 (7.0)	13.1 (43.1)	2.0 (6.5)
LS1	Limestone transfer to Primary Crusher Hopper	632,239	4,974,256	3.4 (11.3)	1.6 (5.2)	3.2 (10.5)
LS2	Primary Crushing and Associated Transfers In and Out	632,239	4,974,256	3.4 (11.3)	1.6 (5.2)	3.2 (10.5)
LS3	Primary Screening and Associated Transfers In and Out	632,239	4,974,256	3.4 (11.3)	1.6 (5.2)	3.2 (10.5)
LS4	Secondary Crushing and Associated Transfers In and Out	632,227	4,974,268	3.4 (11.3)	1.6 (5.2)	3.2 (10.5)
LS5	Secondary Screening and Associated Transfers In and Out	632,227	4,974,268	3.4 (11.3)	1.6 (5.2)	3.2 (10.5)
LS7	Limestone transfer to Ball Mill Feed Conveyor	632,181	4,974,307	1.1 (3.5)	0.1 (0.2)	0.4 (1.4)
LS8	Ball Mill Feed transfer to Ball Mill	632,200	4,974,273	8.5 (28.0)	0.3 (0.9)	0.6 (1.9)
LS10	Limestone transfer to Lime Kiln Feed Conveyor	632,169	4,974,325	1.1 (3.5)	0.1 (0.2)	0.4 (1.4)
LS11	Fines Screening and Associated Transfers In and Out	632,151	4,974,314	0.8 (2.5)	0.6 (1.9)	0.7 (2.3)
LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	632,056	4,974,285	20.7 (68.0)	0.3 (0.9)	0.6 (1.9)
LSU	Pebble Lime Silo discharge to Lime Slaker	632,069	4,974,206	1.1 (3.5)	0.1 (0.2)	0.4 (1.4)

a. Universal Transverse Mercator.
b. m: meters.
c. ft: feet.

3.1.9 Emission Release Parameter Justification

Modeled Process and Ancillary Point Sources

The pneumatic transfer silo loadings and bin transfers (LS1L, MillS2L, ACS1L, ACS2L, ACS3L, ACS4L, PSL, CS1L, CS2L, LS6, LSBM, LS9, LSL) were modeled as POINT sources with a 3-foot bin vent above standard silo height as release height. Exit velocity was estimated using the standard stack diameter and flow rates for similar sources (NDEP 2019) or 0.001 meter per second for horizontal exhaust. These sources were modeled with ambient exhaust temperature.

For propane-fired process (Sb1, ACB, CKB, PV, HS) and building heaters (H1M, H2M, HM, HAC, HR, HA, HMO, HTS, HW), exhaust flow rates were calculated using EPA Method 9 with 3% oxygen content and 15% moisture content. Standard stack diameters were selected based on the heater rating. The process heaters were modeled with a 10-foot stack above the building, whereas the building heaters were modeled with a release height of 1 foot above the respective buildings.

Similar source exhaust temperature, flow, and diameter from (NDEP 2017) were used for refinery sources, including the carbon regeneration kiln (CKD), electrowinning cells (EW), mercury retort (MR),

and induction furnace (MF). Each of these sources was modeled with a 10- foot stack above the refinery building.

For emergency generators (EDG1, EDG2, EDG3) and the fire pump (EDFP), the exhaust flow rates were calculated using EPA Method 9 with 9% oxygen content and 8% moisture content. Standard stack diameters were selected based on engine rating. Each engine was modeled with a 7-foot-high stack.

Antimony bagging (Sb2), autoclave (AC), lime kiln (LK) (common stack with kiln burner (LKC)), and lime crushing (LCR) were characterized with similar source parameters from (NDEP 2015b), (APT 2013), and (NDEP 2010). Each of these sources was modeled with a 10-foot stack above its respective building.

Release parameters for the process and ancillary point sources were appropriately documented and justified. DEQ's source-group analysis (Table 29 in Section 4.1.4) suggests that the process and ancillary point sources contribute a small amount to the modeled design concentrations.

Modeled Process and Ancillary Volume Sources

For the following VOLUME source characterization discussion, release height was estimated as half of the vertical length (for example, building height), initial vertical dispersion was calculated by dividing the vertical length by the applicable EPA-recommended constant (EPA 2018c) for a single VOLUME source (4.3), and initial lateral dispersion was determined using the lesser lateral dimension (for example, building width) divided by the applicable EPA-recommended constant (EPA 2018c) for the surface source or elevated source with a building (2.15).

The sources associated with the primary crusher building, including loader transfer (OC1), grizzly feeder (OC2), apron feeders (OC3, OC4), ore transfers (OC5, OC6), and primary crusher (OC7), were characterized by the primary crusher building dimensions: 128' high and 52.9' wide.

The stockpile height (71.6') and the conveyor width (3') were used to determine the VOLUME source parameters for the stockpile feed conveyor (OC8).

Tunnel exit dimensions (8' high and 8' wide) were used to estimate the VOLUME release parameters for the stockpile transfer points (OC9, OC10). The SAG mill feed conveyor transfer (OC11) was characterized by a building opening (4' high and 4' wide) at the mid-height (70') of the mill building.

Pebble crusher building dimensions (20' high and 32.7' wide) were used to characterize the pebble crusher-associated sources (OC12, OC13).

Silo/bin unloading sources (LS1U, Mill2SU, ACS1U, ACS2U, ACS3U, ACS42U, PSU) were characterized by a typical screw discharge feeder characteristic, i.e., 5' above the ground with a 1' diameter.

Aggregate transfer and handling sources (CS1U, CS2U, CAL, CAU, CM) were characterized by the aggregate stockpile dimensions: 20' high and 72.2' wide.

Each portable crushing and screening plant was characterized by typical portable crushing and screening plant dimensions: 14' high and 185' wide.

Sources associated with limestone crushing (LS1, LS2, LS3, LS4, LS5) were characterized by the associated crusher building dimensions: 22.6' high and 22.6' wide.

The crushed limestone/pebble lime transfers (LS7, LS10, LSU) were characterized by a typical screw discharge to a conveyor characteristic, i.e., 5' above the ground, 3' drop, and a 1' diameter.

The limestone ball mill feed discharge (LS8) was characterized by a building opening (4' high and 4' wide) at the mid-height (30') of the ball mill building.
The limestone fines screening (LS11) was characterized by screen dimensions: 5' drop and 8' wide.

The limestone kiln feed (LS12) was characterized by a building opening (4' high and 4' wide) at the mid-height (70') of the kiln building.

Model input source characterization for fugitive emissions is described in Sections 3.1.5 and 3.1.6. Fugitive activity locations and their respective dimensions are provided in Table 12 and associated release parameters are listed in Table 13.

Release parameters for the process and ancillary volume sources were appropriately documented and justified. DEQ's source-group analysis (Table 29 in Section 4.1.4) suggests that the process and ancillary volume sources contribute a small amount to the modeled design concentrations.

3.2 Background Concentrations

Background concentrations are used if a cumulative NAAQS impact analysis is needed to demonstrate compliance with applicable NAAQS.

3.2.1 Onsite Particulate Monitoring

To establish background ambient air conditions for the SGP area, Midas Gold developed an onsite monitoring program to collect site-specific meteorological parameters and determine ambient particulate matter ($PM_{2.5}$ and PM_{10}) concentrations at its Stibnite monitoring station.

In September 2015, Midas Gold submitted the data collected at the Stibnite monitoring station for the period of November 2013 through June 2015 to DEQ. After reviewing the data and associated quality control procedures, DEQ concluded that the $PM_{2.5}$ and PM_{10} data collected at the Stibnite monitoring station satisfied the applicable regulatory requirements and approved the data to be used for background concentrations in the SGP air quality analyses (DEQ 2015). In its conclusions, DEQ recommended that the $PM_{2.5}$ and PM_{10} background concentrations should be based on calendar year 2014 instead of the complete dataset (November 2013 through June 2015).

DEQ-approved $PM_{2.5}$ and PM_{10} background concentrations, in units of micrograms per cubic meter ($\mu g/m^3$), are provided in Table 17. For 24-hour PM_{10}, the design value is the *second-highest* 24-hour average concentration in a given year. However, review of the Meteorological and Air Quality Data Summary for the SGP Monitoring Network (Midas Gold 2015) indicates that the DEQ-approved background for 24-hour PM_{10} (37.0 $\mu g/m^3$) is the *first-highest* 24-hour average concentration measured in 2014 (DEQ 2015). Therefore, using the first-high instead of the second-high as background adds a layer of conservatism to the cumulative NAAQS impact analyses for 24-hour PM_{10}.

Table 17. DEQ-APPROVED $PM_{2.5}$ AND PM_{10} BACKGROUND CONCENTRATIONS FOR SGP.			
Pollutant	**Averaging Time**	**Background Concentration ($\mu g/m^3$)**	**Design Value Rank**
$PM_{2.5}$	1 year	3.5	Weighted average of quarterly means
	24 hours	15.0	98th percentile/8th high
PM_{10}	24 hours	37.0	Highest 1st high

3.2.2 Gaseous Pollutant Background Concentrations

With a few exceptions of very large facilities or facilities located in nonattainment areas, regulatory agencies do not require the collection of gaseous criteria pollutants, including CO, NOx (and/or nitrogen dioxide [NO_2]), O_3, and SO_2. For these gaseous pollutants, data collected at government-regulated monitoring stations located in settings similar to the project area in terms of terrain, land use, and proximity of emission sources are typically used to establish background concentrations.

To determine representative background concentrations of CO, NOx, O_3, and SO_2 for the SGP site, which is located in a remote rural area, the DEQ-maintained ambient monitoring network was reviewed by Air Sciences. This review revealed that DEQ only conducts limited trace monitoring for CO, NOx, O_3, and SO_2 in the Boise metropolitan area along the Interstate 84 corridor. Thus, the data collected at these monitors are exposed to high emissions from industrial, urban, and transportation sources (DEQ 2015a) (DEQ 2018). For this reason, the gaseous pollutant concentrations recorded at these urban monitoring locations were not considered to be representative of a rural area, like the SGP site.

The EPA-maintained monitoring stations (EPA 2018a) in Idaho and surrounding states also were reviewed by Air Sciences to determine representative gaseous pollutant background concentrations for the SGP site. This review also did not identify any representative monitoring station to establish background gaseous pollutant concentrations for the SGP site.

The DEQ-recommended (DEQ 2019) CO, NOx, O_3, and SO_2 background concentrations for the SGP air quality analyses in units of parts per billion (ppb) and $\mu g/m^3$, are provided in Table 18. These background concentrations were obtained from the Northwest International Air Quality Environmental Science and Technology Consortium (NW AIRQUEST; https://arcg.is/1jXmHH) online tool using the project site coordinates. These background air pollutant levels are based on regional-scale air pollution modeling of pollutants in Washington, Oregon, and Idaho, with modeling results adjusted according to available monitoring data.

Table 18. DEQ-RECOMMENDED GASEOUS POLLUTANT BACKGROUND CONCENTRATIONS FOR SGP.				
Pollutant	**Averaging Time**	**Background Concentration**		**Reference**
		(ppb)	**($\mu g/m^3$)**	
CO	8 hours	970	1,110	NW AIRQUEST, 2014-2017 design value
	1 hour	1,520	1,740	
NO_2	1 year	0.5	0.9	
	1 hour	2.3	4.3	
O_3 (for NO_2 modeling)	8 hours	55	107.9	
SO_2	3 hours	6.4	16.8	
	1 hour	4.7	12.3	

3.2.3 Medium-Traffic Pollutant Background Concentrations

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For additional information, background concentrations were obtained from NW AIRQUEST for the road section between mile markers 143 and 144 on Highway 55 passing through the town of McCall. This site (latitude 44.906° N, longitude 116.098° W) is approximately 38 miles west of the SGP. The annual average daily traffic count for this road section is over 10,000 vehicles per day. Table 19 provides the background concentrations for this medium-traffic site. Although these concentrations are not representative of the rural SGP area, they do provide additional information regarding the relative contribution of traffic emissions.

Table 19. MEDIUM-TRAFFIC BACKGROUND CONCENTRATIONS.

Pollutant	Averaging Time	Background Concentration		Reference
		(ppb)	($\mu g/m^3$)	
CO	8 hours	1,000	1,145	NW AIRQUEST, 2014-2017 design value, near McCall, ID (44.91°N, 116.10°W)
	1 hour	1,570	1,797	
NO_2	1 year	1.4	2.6	
	1 hour	7.6	14.3	
$PM_{2.5}$	1 year	--	5.1	
	24 hours	--	17.5	
PM_{10}	24 hours	--	60.1	
SO_2	3 hours	6.4	16.8	
	1 hour	4.7	12.3	

3.3 Impact Modeling Methodology

This section describes the modeling methods used by the applicant/consultant to demonstrate preconstruction compliance with applicable air quality standards.

3.3.1 General Overview of Impact Analyses

Air Sciences performed the project-specific air pollutant emission inventory and air impact analyses that were submitted with the application. The submitted information/analyses, in combination with results from DEQ's air impact analyses, demonstrate compliance with applicable air quality standards to DEQ's satisfaction, provided the facility is operated as described in the submitted application and in this memorandum.

Table 20 provides a brief description of parameters used in the modeling analyses.

Table 20. MODELING PARAMETERS.

Parameter	Description/Values	Documentation/Addition Description
General Facility Location	Stibnite, Idaho	The area is an attainment or unclassified area for all criteria pollutants.
Model	AERMOD	AERMOD with the PRIME downwash algorithm, version 19191.
Meteorological Data	Onsite and McCall, Idaho surface data; Boise, Idaho upper air data	See Section 3.3.5 of this memorandum for additional details of the meteorological data.
Terrain	Considered	1/3 arc second National Elevation Dataset (NED) was acquired from the USGS for the surrounding area. AERMAP version 18081 was used to process terrain elevation data for all buildings and receptors. See Section 3.3.6 for more details.
Building Downwash	Considered	Plume downwash was considered for the structures associated with the facility. BPIP-PRIME was used to evaluate building dimensions for consideration of downwash effects in AERMOD. See Section 3.3.7.
NOx Chemistry	Ozone Limiting	See Section 3.3.8.

	Method	
Receptor Grid	**SIL Analysis** A SIL analysis was not performed.	
	Cumulative NAAQS Impact Analysis The selection of receptors for use in the cumulative NAAQS impact analysis is as follows (see Section 3.3.12):	
	Boundary	25-meter (m) spacing
	Grid 1	50-m spacing, 0.25 kilometers (km) out
	Grid 2	100-m spacing, 0.25 km to 1.25 km out
	Grid 3	500-m spacing, 1.25 km to 5 km out
	Grid 4	1,000-m spacing, 5 km to 10 km out
	Hotspot	25-m spacing, 200-m × 200-m around highest model impacts
	TAPs Analysis The receptor network used in the cumulative NAAQS impact analysis was also used in the TAPs analysis.	

3.3.2 Modeling Protocol

A modeling protocol for the SGP analyses was submitted to DEQ prior to the application, on May 30, 2019. The protocol was submitted by Brown and Caldwell on behalf of Midas Gold. Conditional DEQ protocol approval was provided to Brown and Caldwell on June 27, 2019.

3.3.3 Modeling Methodology

Project-specific modeling and other required impact analyses were generally conducted using data and methods described in the *Idaho Air Quality Modeling Guideline* (DEQ 2013).

3.3.4 Model Selection

Idaho Air Rules Section 202.02 requires that estimates of ambient concentrations be based on air quality models specified in Appendix W. The refined, steady-state, multiple-source, Gaussian dispersion model AERMOD was promulgated as the replacement model for ISCST3 in December 2005. AERMOD retains the single straight-line trajectory of ISCST3, but it includes more advanced algorithms to assess turbulent mixing processes in the planetary boundary layer for both convective and stable stratified layers.

AERMOD version 19191 was used by Air Sciences for the modeling analyses to evaluate impacts of the facility. This version was the current version at the time the application was received by DEQ.

3.3.5 Meteorological Data

AERMOD requires an input of hourly meteorological data to estimate pollutant concentrations in ambient air resulting from modeled source emissions. These data are commonly obtained from National Weather Service (NWS) stations at airports throughout the state. Applicants select data from an airport site that is determined to be reasonably representative of the permitted site location. Collection of meteorological data from the permitted site is not typically required by DEQ for minor source permit applications. The collection of one year of onsite data is required for permitting projects subject to the Prevention of Significant Deterioration (PSD) program, which is triggered by larger non-fugitive emission quantities.

Site-specific hourly surface meteorological data were collected and used in air impact analyses for this project, as described in the submitted modeling report. These data were collected from January 1, 2014 through December 31, 2014 at the Stibnite monitoring station. They were collected for analyses supporting an Environmental Impact Statement (EIS) and the Idaho DEQ minor source permit.

The site-specific surface data were supplemented with the twice-daily upper-air data (all levels) collected at the National Weather Service (NWS) station in Boise, Idaho (WBAN 24131).

These meteorological datasets were processed with the most recent version (19191) of the AERMOD meteorological pre-processor, AERMET, to produce AERMOD-input-ready hourly surface and profile meteorological files. The default option of adjusted surface friction velocity (ADJ_U*) and the Bulk Richardson (BULKRN) method for boundary layer parameter calculations was used for this meteorological data processing.

Additionally, an alternative meteorological dataset was processed without using the BULKRN method (NON-BULKRN). This alternate processing used the onsite and upper air datasets discussed above, supplemented with the cloud-cover data collected at the NWS station in McCall, Idaho (WBAN 94182).

Both processing methods (BULKRN and NON-BULKRN) are considered default for regulatory modeling analyses. EPA Region X Regional Modeling Contact, Jay McAlpine, PhD, was consulted for guidance on which data processing procedure to require for the analyses supporting the Idaho PTC. The BULKRN method was used for air impact analyses supporting the EIS after consultation with EPA, DEQ, and the US Forest Service. EPA recommended (June 18, 2019, email from Jay McAlpine, EPA, to Kevin Schilling, DEQ) using the BULKRN method since "use of the onsite data best fulfills the Guidance, and ensures consistency with the EIS, but this should be looked upon as technical advice only and not a requirement of the EPA."

Compliance with all NAAQS was easily demonstrated using meteorological data processed by the NON-BULKRN method; however, a small number of receptors showed 24-hour PM_{10} violations when the meteorological data processed with BULKRN method was used. DEQ performed a weight of evidence analyses (see Section 4.1.4 of this memorandum) to further evaluate the confidence of NAAQS compliance, using sensitivity analyses of various model input variables and the meteorological data processed using the BULKRN method.

AERMET requires the input of three surface boundary layer parameters: midday Bowen ratio (B_o), midday albedo (r), and surface roughness length (z_o). These parameters are dependent on the land use and vegetative cover of the area being evaluated. The EPA-recommended model, AERSURFACE, was used to estimate these surface parameters for the Stibnite meteorological data processing. AERSURFACE uses 1992 National Land Cover Data to determine these surface characteristics.

The determination of B_o is dependent on ambient moisture conditions (i.e., wet, average, or dry). For this purpose, historic 30-year (1985–2014) precipitation data from the Taylor Ranch station in Idaho (the closest station from which this type of data is available) were used.

The 70th and 30th percentile values estimated from the 30-year precipitation data were used to assign a moisture class to each calendar month per the following scheme: monthly precipitation greater than the 70th percentile was considered "wet"; between the 70th and 30th percentiles was considered "average"; and less than the 30th percentile was considered "dry." The monthly season and moisture classifications and estimated r and B_o for 2014 Stibnite meteorological data processing are presented in Table 21.

Table 21. 2014 MONTHLY SEASON AND MOISTURE CLASSIFICATION, AND CALCULATED *r* AND B_O.

Month	Season	*r*	30-Year Precipitation	2014 Precipitation	Moisture Classification	*Bo*

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			Percentile (in)		(in)		
			30th	70th			
January	Winter	0.38	0.64	1.29	0.74	Average	0.50
February	Winter	0.38	0.40	0.81	0.99	Wet	0.50
March	Spring	0.13	0.83	1.23	2.33	Wet	0.34
April	Spring	0.13	1.11	1.57	0.99	Dry	1.57
May	Spring	0.13	1.43	2.23	0.74	Dry	1.57
June	Summer	0.13	1.17	1.80	1.32	Average	0.37
July	Summer	0.13	0.46	1.45	0.40	Dry	0.76
August	Summer	0.13	0.42	1.11	2.03	Wet	0.25
September	Fall	0.13	0.27	1.23	0.43	Average	0.87
October	Fall	0.13	0.59	1.69	1.75	Wet	0.35
November	Fall	0.13	0.72	1.44	3.73	Wet	0.35
December	Winter	0.38	0.64	1.16	0.83	Average	0.50

The seasonal z_o values in m for each 30-degree sector of the 1-km radius for the Stibnite monitoring station are provided in Table 22 (i.e., Sector 1 is 0° to 30° clockwise from the north, Sector 2 is 30° to 60° clockwise from the north, etc.).

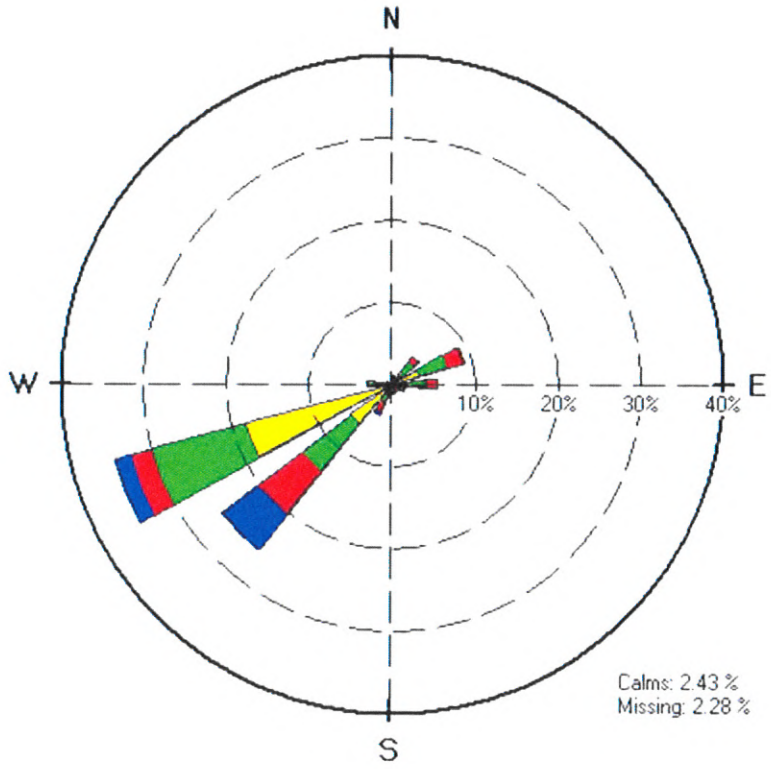
Table 22. CALCULATED SEASONAL z_O VALUES (m).

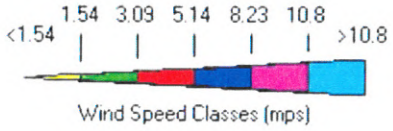
Sector	Winter	Spring	Summer	Fall
1	0.410	0.564	0.610	0.607
2	0.212	0.347	0.392	0.387
3	0.517	0.640	0.671	0.669
4	0.769	0.865	0.894	0.894
5	0.989	1.044	1.055	1.055
6	0.741	0.874	0.918	0.915
7	0.400	0.563	0.617	0.614
8	0.414	0.522	0.552	0.550
9	0.049	0.171	0.244	0.243
10	0.060	0.197	0.274	0.274
11	0.183	0.372	0.449	0.449
12	0.576	0.710	0.743	0.742

Winter = December, January, February
Spring = March, April, May
Summer = June, July, August
Fall = September, October, November

Wind frequency distribution for the 2014 Stibnite meteorological dataset is presented in Figure 5, and a map showing the location of the meteorological monitoring stations used for this meteorological data processing is presented in Figure 6.

Figure 5. WIND FREQUENCY DISTRIBUTION FOR 2014 SGP METEOROLOGICAL DATA (NON-BULKRN).

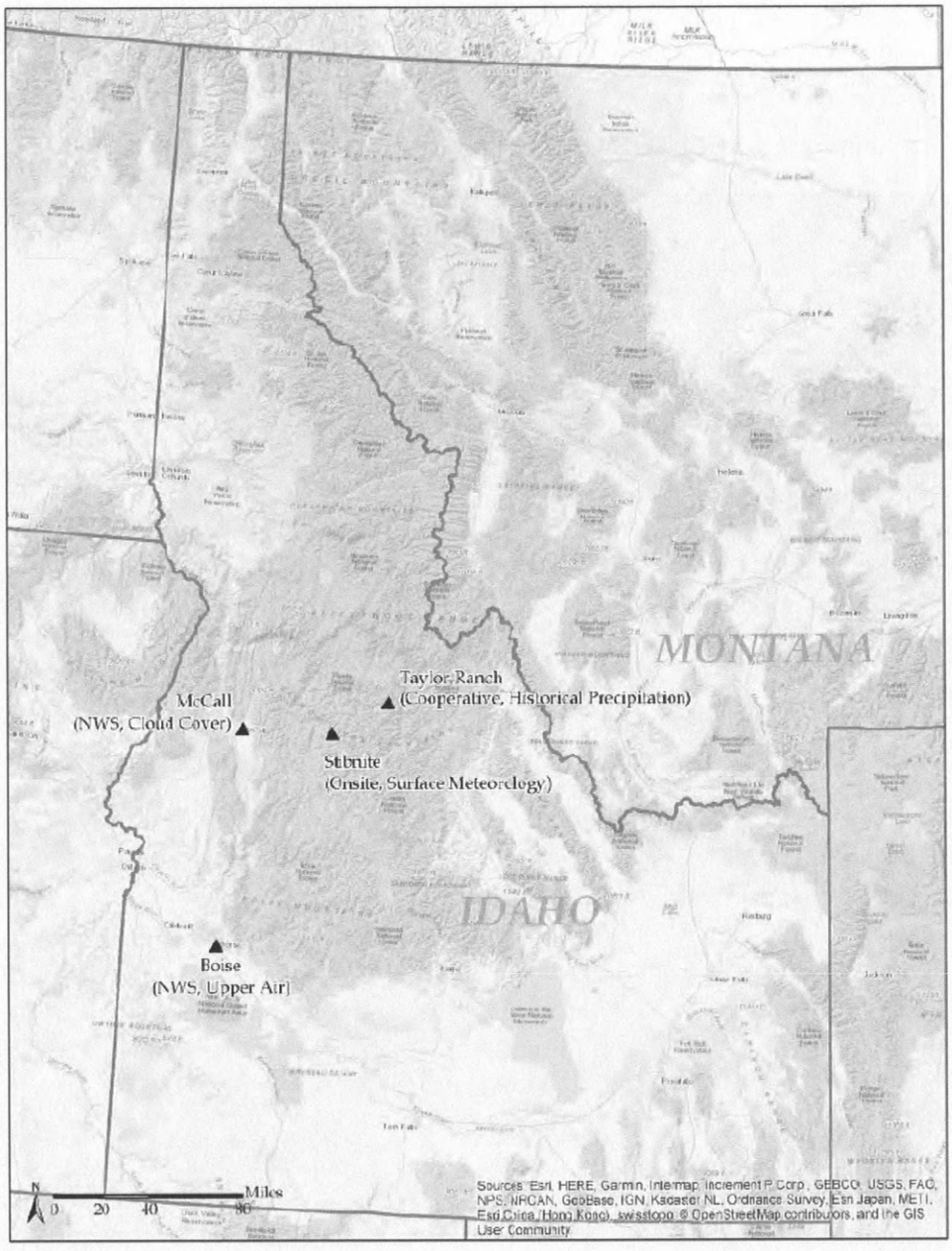




Note: Diagram of the frequency of occurrence of each wind direction.

Met File Type: AERMET SFC
File: STIBNITE_2014U.SFC

Figure 6. METEOROLOGICAL STATION LOCATIONS FOR SGP MODELING.



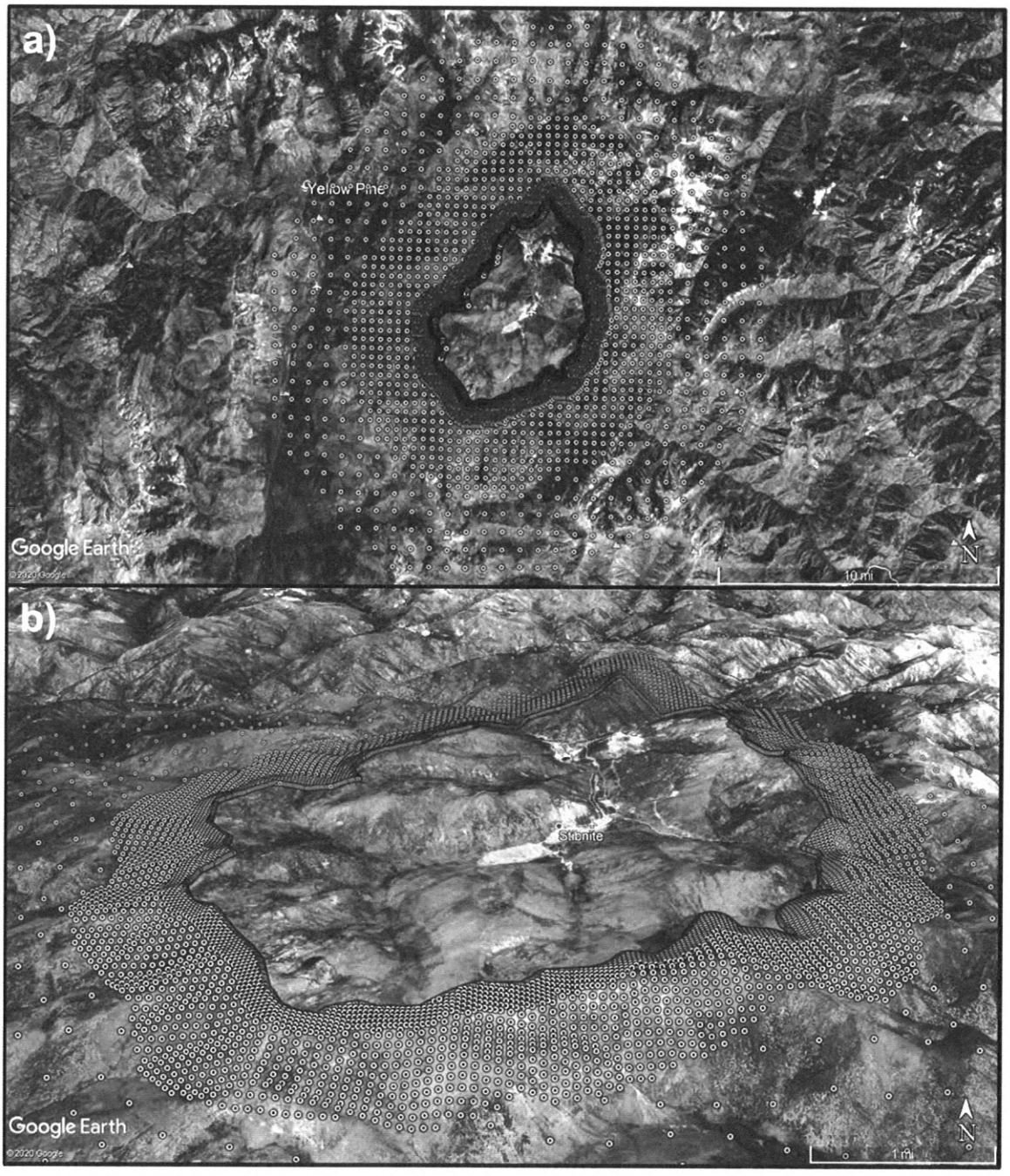
3.3.6 Effects of Terrain on Modeled Impacts

Submitted ambient air impact analyses used terrain data extracted from United States Geological Survey (USGS) National Elevation Dataset (NED) files.

The terrain preprocessor AERMAP version 18081 was used by Air Sciences to extract the elevations from the NED files and assign them to receptors in the modeling domain in a format usable by AERMOD. AERMAP also determined the hill-height scale for each receptor. The hill-height scale is an

elevation value based on the surrounding terrain which has the greatest effect on that individual receptor. AERMOD uses those heights to evaluate whether the emission plume has sufficient energy to travel up and over the terrain or if the plume will travel around the terrain. Figure 7a depicts the full receptor grid used in the modeling analyses and Figure 7b illustrates a close-up of Figure 7a, overlaid on a terrain image from Google Earth.

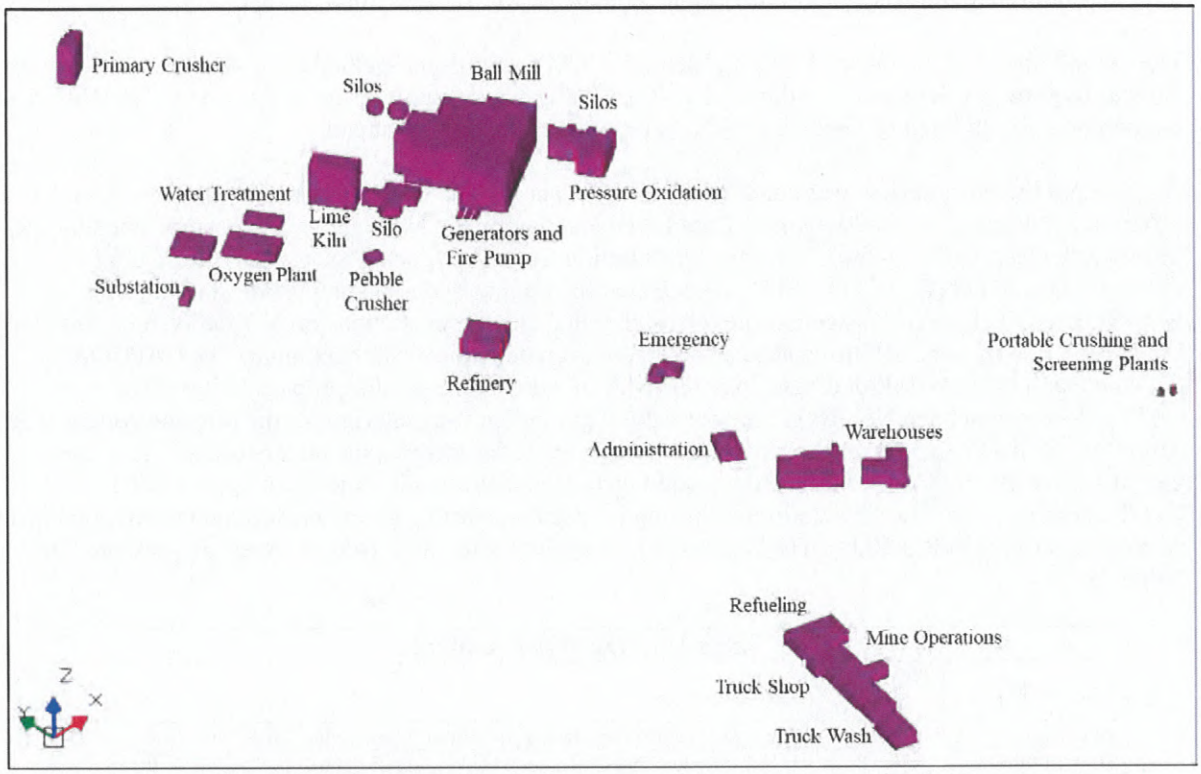
Figure 7. RECEPTOR GRID CENTERED AT THE SGP FACILITY.



3.3.7 Facility Layout and Downwash

Figure 3 shows the processing and refining area buildings and sources at the SGP facility. Figure 8 below depicts a three-dimensional view of Figure 3, as viewed from the southwest.

Figure 8. THREE-DIMENSIONAL VIEW OF PROCESSING AND REFINING AREA BUILDINGS AND SOURCES AT THE SGP FACILITY AS VIEWED FROM THE SOUTHWEST.



DEQ verified proper identification of the site location and the ambient air boundary by comparing a graphical representation of the modeling input file to aerial photographs on Google Earth (available at https://www.google.com/earth).

Potential downwash effects on emission plumes were accounted for in the model by using building dimensions and locations (locations of building corners, base elevation, and building heights). Dimensions and orientation of proposed buildings were used as input to the Building Profile Input Program for the Plume Rise Model Enhancements downwash algorithm (BPIP-PRIME version 04274) to calculate direction-specific dimensions and Good Engineering Practice (GEP) stack height information for input to AERMOD.

3.3.8 NOx Chemistry

The atmospheric chemistry of NO, NO_2, and O_3 complicates accurate prediction of NO_2 impacts resulting from NOx emissions. The conversion of NO to NO_2 can be conservatively addressed through the use of

several methods as outlined in a *2014 EPA NO_2 Modeling Clarification Memorandum* (EPA 2014). The guidance outlines a three-tiered approach:

- Tier 1 – assume full conversion of NO to NO_2 where total NOx emissions are modeled and modeled impacts are assumed to be 100 percent NO_2.
- Tier 2 – use an ambient ratio to adjust impacts from the Tier 1 analysis.
- Tier 3 – use a detailed screening method to account for $NO/NO_2/O_3$ chemistry such as the Ozone Limiting Method (OLM) or the Plume Volume Molar Ratio Method (PVMRM).

The default option of the Ozone Limiting Method (OLM), a third-tier method from 40 CFR 51, Appendix W, was used by Air Sciences to estimate the NO_2 1-hour and annual impacts for these analyses. The OLM method requires an input of in-stack NO_2/NOx ratio for each modeled source.

An in-depth literature review was conducted by Air Sciences to identify reasonable NO_2/NOx ratios for different combustion source categories. Based on this research, the NO_2/NOx ratio recommended for the heavy-duty diesel trucks in the California Air Pollution Control Officers Association (CAPCOA) Guidance Document (CAPCOA 2011) was selected for stationary diesel combustion sources. This NO_2/NOx ratio (11 percent) is conservatively higher than the diesel combustion NO_2/NOx ratio provided in the EPA ISR (In-Stack Ratio) database: 6 percent average, 9.8 percent maximum. The CAPCOA document and the EPA ISR database do not provide an NO_2/NOx ratio for propane boilers. The CAPCOA-recommended NO_2/NOx ratio for natural gas boilers was selected for the propane boilers. The natural gas boilers NO_2/NOx ratio is considered appropriate for the propane boilers because both are gaseous fuels with relatively similar combustion characteristics and are expected to have similar NO_2/NOx ratios. The NO_2/NOx ratio for blasting is based on blasting plume measurements provided in an Australian study (CSIRO 2008). The NO_2/NOx ratios used for the SGP NO_2 analyses are presented in Table 23.

Table 23. NO_2/NOx RATIOS.

Source Type	NO_2/NOx Ratio	Reference
Blasting	0.036	Commonwealth Scientific and Industrial Research Organization (CSIRO 2008)
Diesel Engines	0.11	CAPCOA Guidance Document, heavy-duty diesel trucks (CAPCOA 2011)
Propane Heaters	0.10	CAPCOA Guidance Document, natural gas boilers (CAPCOA 2011)

DEQ performed a sensitivity analysis using a Tier 2 screening method (ARM2), which is more conservative than OLM, and found that the SGP facility is safely below the 1-hour and annual NO_2 NAAQS. Results are summarized in Section 4.1.3.

3.3.9 Particulate Deposition

For $PM_{2.5}$ and PM_{10} analyses, default particulate modeling methods, including deposition (Method 1, to account for depletion due to particulate settling), were used. To account for particulate settling, AERMOD requires the following source-specific variables:

1. Mass-mean aerodynamic particle diameter (PARTDIAM) for each particle size bin
2. Mass fraction (MASSFRAX) for each particle size bin
3. Particle density (PARTDENS) for each particle size bin

REC 4248

TR 0933

A list of references that were used to develop the broad source category particle size bins and associated mass fractions was provided in the application. Midas Gold (Midas Gold 2017b) provided the ore and DR material densities. The diesel and propane combustion particulate densities were adopted from technical literature (UMN 2002) and (Khalizov et al. 2012), respectively. Densities for the remaining materials were obtained from the Engineering Toolbox (https://www.engineeringtoolbox.com/density-materials-d_1652.html). An average density was used when a material-specific density range was available.

For sources that were aggregated and modeled as activity locations, deposition parameters were selected for the dominant source within the activity location. For open-pits (YPP, HFP, WEP), approximately 90% of emissions were associated with drilling; therefore, drilling deposition parameters were assigned to these sources. Similarly, emissions from dozing accounted for over 70% of emissions in the DRSF (FDRSF, HFDRSF, WEDRSF) and BT; therefore, these sources were assigned deposition parameters based on a dozing particulate profile.

The deposition parameters including mass fractions, mass mean diameters, and densities for the different source categories/groups are provided in Table 24.

Table 24. DEPOSITION PARAMETERS BY SOURCE CATEGORY.

Source Category	Parameter	PM_{10}				$PM_{2.5}$	
		Bin 1	Bin 2	Bin 3	Bin 4	Bin 1	Bin 2
Haul Roads	Bin Upper Diameter (µm)	2.50	10.00	--	--	2.50	--
	Mass Fraction	0.10	0.90	--	--	1.00	--
	Mass Mean Diameter (µm)	2.50	10.00	--	--	2.50	--
	Density (g/cm^3) (YPP, HFP, WEP DR average)	2.46	2.46	--	--	2.46	--
Material Handling (Ore, DR, Limestone)	Bin Upper Diameter (µm)	2.50	5.00	10.00	--	2.50	--
	Mass Fraction	0.15	0.42	0.43	--	1.00	--
	Mass Mean Diameter (µm)	2.50	5.00	10.00	--	2.50	--
	Density (g/cm^3) (Ore)	Pit-specific, see Table 25.					
	Density (g/cm^3) (Ore and Waste)	Pit-specific, see Table 25.					
	Density (g/cm^3) (Limestone)	1.09	1.09	1.09	--	1.09	--
Baghouses	Bin Upper Diameter (µm)	2.50	6.00	10.00	--	2.50	--
	Mass Fraction	0.28	0.50	0.22	--	1.00	--
	Mass Mean Diameter (µm)	2.50	6.00	10.00	--	2.50	--
	Density (g/cm^3) (Ore)	Pit-specific, see Table 25.					
Diesel Engines	Bin Upper Diameter (µm)	1.00	2.50	6.00	10.00	1.00	2.50
	Mass Fraction	0.85	0.08	0.03	0.03	0.91	0.09
	Mass Mean Diameter (µm)	1.00	2.50	6.00	10.00	1.00	2.50
	Density (g/cm^3) (Diesel Combustion)	1.00	1.00	1.00	1.00	1.00	1.00
Heaters and Boilers	Bin Upper Diameter (µm)	1.00	2.50	6.00	10.00	1.00	2.50
	Mass Fraction	0.29	0.28	0.32	0.11	0.51	0.49
	Mass Mean Diameter (µm)	1.00	2.50	6.00	10.00	1.00	2.50
	Density (g/cm^3) (Propane Combustion)	1.24	1.24	1.24	1.24	1.24	1.24
Lime Loading and Unloading (Quick, Pebble)	Bin Upper Diameter (µm)	2.50	10.00	--	--	2.50	--
	Mass Fraction	0.15	0.85	--	--	1.00	--
	Mass Mean Diameter	2.50	10.00	--	--	2.50	--
	Density (g/cm^3) (Quick)	0.44	0.44	--	--	0.44	--
	Density (g/cm^3) (Pebble)	0.96	0.96	--	--	0.96	--
Lime Unloading (Quick, Pebble)	Bin Upper Diameter (µm)	2.50	10.00	--	--	2.50	--
	Mass Fraction	0.15	0.85	--	--	1.00	--
	Mass Mean Diameter (µm)	2.50	10.00	--	--	2.50	--
	Density (g/cm^3) (Quick)	0.44	0.44	--	--	0.44	--
	Density (g/cm^3) (Pebble)	0.96	0.96	--	--	0.96	--
Cement and Aggregate	Bin Upper Diameter (µm)	2.50	10.00	--	--	2.50	--
	Mass Fraction	0.15	0.85	--	--	1.00	--

Table 24. DEPOSITION PARAMETERS BY SOURCE CATEGORY.							
Source Category	**Parameter**	**PM_{10}**				**$PM_{2.5}$**	
		Bin 1	**Bin 2**	**Bin 3**	**Bin 4**	**Bin 1**	**Bin 2**
Loading and Unloading	Mass Mean Diameter (μm)	2.50	10.00	--	--	2.50	--
	Density (g/cm^3) (Cement)	1.44	1.44	--	--	1.44	--
	Density (g/cm^3) (Aggregate)	1.28	1.28	--	--	1.28	--
Prill Loading and Unloading	Bin Upper Diameter (μm)	2.50	10.00	--	--	2.50	--
	Mass Fraction	0.15	0.85	--	--	1.00	--
	Mass Mean Diameter (μm)	2.50	10.00	--	--	2.50	--
	Density (g/cm^3) (Prill)	0.84	0.84	--	--	0.84	--
Refining Processes	Bin Upper Diameter (μm)	1.00	2.50	6.00	10.00	1.00	2.50
	Mass Fraction	0.78	0.11	0.08	0.03	0.88	0.12
	Mass Mean Diameter (μm)	1.00	2.50	6.00	10.00	1.00	2.50
	Density (g/cm^3) (Diesel Combustion)	1.00	1.00	1.00	1.00	1.00	1.00
Portable Crushing and Screening Plant	Bin Upper Diameter (μm)	2.50	10.00	--	--	2.50	--
	Mass Fraction	0.13	0.87	--	--	1.00	--
	Mass Mean Diameter (μm)	2.50	10.00	--	--	2.50	--
	Density (g/cm^3) (YPP, HFP, WEP DR average)	2.46	2.46	--	--	2.46	--
Lime Kiln and Ball Mill	Bin Upper Diameter (μm)	2.50	10.00	--	--	2.50	--
	Mass Fraction (Kiln)	0.49	0.51	--	--	1.00	--
	Mass Fraction (Ball Mill)	0.36	0.64	--	--	1.00	--
	Mass Mean Diameter (μm)	2.50	10.00	--	--	2.50	--
	Density (g/cm^3)	1.09	1.09	--	--	1.09	--
Blasting and Drilling	Bin Upper Diameter (μm)	2.50	10.00	--	--	2.50	--
	Mass Fraction	0.06	0.94	--	--	1.00	--
	Mass Mean Diameter (μm)	2.50	10.00	--	--	2.50	--
	Density (g/cm^3) (Ore or DR)	Pit-specific, see Table 25.					
Dozing	Bin Upper Diameter (μm)	2.50	10.00	--	--	2.50	--
	Mass Fraction	0.55	0.45	--	--	1.00	--
	Mass Mean Diameter (μm)	2.50	10.00	--	--	2.50	--
	Density (g/cm^3) (DR)	Pit-specific, see Table 25.					

In order to account for variability in ore and DR densities for different pits, pit-specific densities were used for the ore and DR for each modeling scenario, with the following exception – for haul roads, access roads, and portable crushers, the average DR density from YPP, HFP, and WEP was used. Note that the BT density was excluded from those sources because the BT material will not be used for roads or construction. The pit-specific ore and DR densities are provided in Table 25.

Table 25. PIT-SPECIFIC ORE AND DEVELOPMENT ROCK DENSITIES FOR DEPOSITION.		
Pit	**Material**	**Density (g/cm^3)**
YPP	Ore	2.59
BT	Ore	2.00
HFP	Ore	2.59
WEP	Ore	2.68
YPP	DR	2.48
BT	DR	2.00
HFP	DR	2.34
WEP	DR	2.57
Average (YPP,HFP, WEP)	DR	2.46

3.3.10 Ambient Air Boundary

Ambient air is defined in Section 006 of the Idaho Air Rules as "that portion of the atmosphere, external to buildings, to which the general public has access."

Midas Gold will legally control the SGP, an active industrial site where mining activities will occur, such as heavy equipment operation. Most areas of the mine will require strict safety protocols and controlled access. Midas Gold has established an operations boundary to identify the area where public access will be excluded. Public access inside the operations boundary will be restricted for the life of the mine by physical barriers at points of potential access, including the current Stibnite Road point of entry and proposed site access via the Burntlog Route, as well as natural features of the landscape that prevent access. Consistent with the guidance provided in the EPA's draft revised policy on ambient air (EPA 2018b), public access control will include the following measures:

- Primary Access Points: The Stibnite Road (north) and Burntlog Route (south) access points will include locked gates. Guard shacks will be located at each gate to monitor all vehicle ingress/egress. Each gate also will include appropriate adjacent barriers (i.e., fencing, bollards, boulders, or other barriers) to prevent any vehicle from circumventing the gate and gaining site access. These primary access points are also controlled by adjacent natural features, such as streams and creeks, steep topography, and areas of thick vegetation and undergrowth that serve as natural barriers or impediments to access.

- Secondary Access Points: Other potential access points, such as secondary roadways and trails, will include posted signs warning the public against entry into the site. At these locations, boulders will be placed across the trail and at an appropriate width adjacent to the trail to prevent any vehicle from circumventing the barrier. These secondary access points also incorporate adjacent natural features, such as streams and creeks, steep topography, and areas of thick vegetation and undergrowth that serve as natural barriers or impediments to access. Some mine features, such as the TSF and process plant areas, will include perimeter fencing.

- Surveillance: Midas Gold security personnel will routinely patrol mine facilities and roadways for unauthorized individuals. In addition, all onsite personnel will be trained on the necessity of restricting public access to areas within the operations boundary. Any suspected trespassing by unauthorized individuals will be reported immediately to security, and trespassers will be escorted off the site.

In response to comments from local community citizens, Midas Gold will manage an access route to provide the general public with limited access through the SGP site between Stibnite Road at Sugar Creek and Thunder Mountain Road at Meadow Creek (shown in Figure 2). This route will be managed in accordance with the Stibnite Road Access Management Plan which is summarized as follows:

The proposed Stibnite Road access route through the SGP site is meant to provide controlled through-site access that is safe, provides travel-time comparable to current conditions and is consistent with the United States Forest Service travel management plan. The Stibnite Road access route extends from the north entry point southward to the Administration, Warehouse and Storage Area. Continuing southward, the Stibnite Road access route incorporates the Burntlog access road segment that occurs within the operations area and extends to the south entry point as shown on Figure 2. Midas Gold has the legal authority to control access to the Stibnite Road access route and would provide seasonal (non-winter conditions) access only. At the discretion of Midas Gold, additional access controls may occur during various phases of construction, during mine operations that present potential safely hazards such as blasting, due to inclement weather, or under any other circumstances that may present a threat to the protection of public or employee health and safety. Midas Gold has the legal and practical ability to

enforce its control over roadway access and to monitor traffic passing through the SGP site. Signage will be placed at the North Security Gate (near the bridge over Sugar Creek) and the South Security Gate (near the Stibnite Lodge) to provide information to travelers, and guard shacks will be located at each gate to monitor all vehicle ingress/egress. Persons wishing to traverse the SGP site on the Stibnite Road access route will be required to check in at the security gate to receive a safety briefing and to alert mine staff of their presence. Travelers will be required to check out upon exiting the site to ensure passage through the site in a safe and timely manner. Travelers will not be allowed to stop or loiter while traveling though the operations area. Along its full length, the Stibnite Road access route would have appropriate signage to direct travelers and would be separated from mine haul roads and areas of mine operations by fencing, berms, or gates to prevent travelers from straying from the route. When possible and to the degree practicable, anticipated public access restrictions will be communicated to the public in a timely manner so that they may plan appropriately. Receptors on the Stibnite Road access route were not included in the SGP air quality analyses as this road is not considered ambient air.

The worker housing facility will be located within the project operations boundary, near the south access security gate. This housing facility will be used strictly for accommodating employees, contractors, and official visitors, and it will not be accessible to the general public. Therefore, the atmosphere over the land occupied by the worker housing facility is not considered ambient air, and receptors were not placed at this location for the air quality analyses.

The operations boundary, shown in Figure 2 above and Figure 9 below, was used to define the ambient air boundary for air dispersion modeling purposes.

3.3.11 Nearby Co-Contributing Sources

If impacts of neighboring emission sources on receptors showing a significant impact from the sources subject to the permitting action are not adequately accounted for by the background concentration used, then emissions from those sources must be modeled. The nearest significant permitted facility to SGP is Tamarack Mill, located more than 75 kilometers (km) west. This facility is located too far away to cause a significant concentration gradient along the periphery of the SGP and was therefore not included in the cumulative impact analyses for SGP.

3.3.12 Receptor Network

DEQ determined that the receptor grid used in the submitted modeling analyses was adequate to resolve maximum modeled impacts.

The SGP air quality analyses were performed using the following receptor spacing and extents (Table 20):

- 25-m-spaced receptors placed along the ambient air boundary;
- 50-m-spaced receptors extending 250 m beyond the ambient air boundary;
- 100-m-spaced receptors extending 1 km beyond the 50-m-spaced receptors;
- 500-m-spaced receptors extending 5 km beyond the ambient air boundary; and
- 1-km-spaced receptors extending 10 km beyond the ambient air boundary.

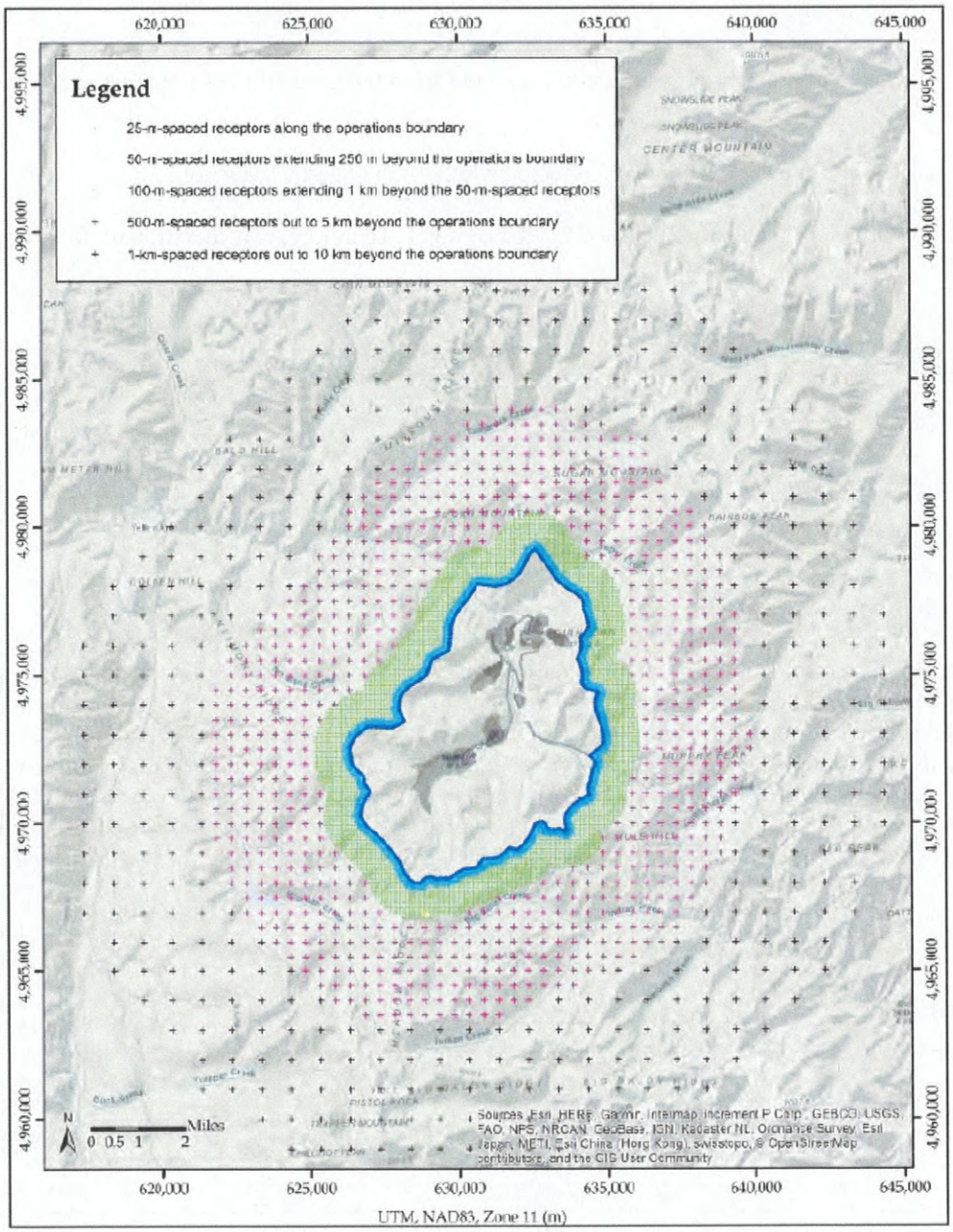
In addition, each highest modeled impact was evaluated further by performing a hot-spot analysis using a finer 25-m-spacing receptor grid. The modeling receptor grid is shown below in Figure 9. The full grid, along with the fenceline receptors, includes a total of 9,631 receptors. A SIL analysis was not conducted. The full receptor grid was used in the cumulative NAAQS impact and TAPs impact analyses.

REC 4252

TR 0937

The receptor grid used in the submitted modeling analyses met the minimum recommendations specified in the *Idaho Air Quality Modeling Guideline* (DEQ 2013), and DEQ determined that the receptor network was effective in reasonably assuring compliance with applicable air quality standards at all ambient air locations.

Figure 9. SGP AMBIENT AIR BOUNDARY AND MODELING RECEPTOR GRID.



3.3.13 Good Engineering Practice Stack Height

An allowable good engineering practice (GEP) stack height may be established using the following equation in accordance with Idaho Air Rules Section 512.03.b:

H = S + 1.5L, where:

H = good engineering practice stack height measured from the ground-level elevation at the base of the stack.

S = height of the nearby structure(s) measured from the ground-level elevation at the base of the stack.

L = lesser dimension, height or projected width, of the nearby structure.

Sources from the SGP facility are below GEP stack height. Therefore, consideration of downwash caused by nearby buildings was required.

4.0 NAAQS and TAPs Impact Modeling Results

4.1 Results for NAAQS Analyses

4.1.1 Significant Impact Level Analyses

A SIL analysis was not performed for the SGP project.

4.1.2 Cumulative NAAQS Impact Analyses

Table 26 provides results (highest of 14 scenarios) for the cumulative NAAQS impact analysis. It provides the model-predicted maximum design concentration (including the hot-spot analyses) and the associated modeling scenario, the background concentration, and the estimated total concentration (SGP impact plus background) for each pollutant-averaging time combination. A comparison of the estimated total concentrations with the applicable NAAQS is also provided in this table. For each pollutant and averaging period, two modeled design concentrations are listed, each corresponding to the meteorological data processed with (BULKRN) and without (NON-BULKRN, grey shading) the Bulk Richardson method.

Table 26. RESULTS FOR CUMULATIVE NAAQS IMPACT ANALYSES.

Pollutant	Averaging Time	Max. Conc.[a] ($\mu g/m^3$)[b]	Model Scenario	Back. Conc.[c] ($\mu g/m^3$)	Total Conc.[d] ($\mu g/m^3$)	NAAQS ($\mu g/m^3$)	Percent of NAAQS
Carbon monoxide	8 hours	6,218[e]	W1	1,110	7,328	10,000	73.3%
		3,516[f]	**W1**		**4,626**		**46.3%**
	1 hour	17,054	W1	1,740	18,794	40,000	47.0%
		9,467	**W1**		**11,207**		**28.0%**
Nitrogen dioxide	1 year	2.3	W1	0.9	3.2	100	3.2%
		1.4	**W1**		**2.3**		**2.3%**
	1 hour	116.7	B1	4.3	121.0	188	64.4%
		111.0	**W1**		**115.3**		**61.3%**
$PM_{2.5}$[g]	1 year	7.7	W5	3.5	11.2	12	93.3%

REC 4254

TR 0939

		4.2	W5		7.7		64.2%
	24 hours	18.6	W5	15.0	33.6	35	96.0%
		11.0	W5		26.0		74.3%
PM_{10}[h]	24 hours	121.5	W5	37.0[i]	158.5	150	105.7%[j]
		75.7	W5		112.7		75.1%
Sulfur dioxide	3 hours	1.8	B1	16.8	18.6	1,300	1.4%
		1.2	B1		18.0		1.4%
	1 hour	3.2	B1	12.3	15.5	196	7.9%
		2.7	B1		15.0		7.7%

a. Max. Conc. = maximum modeled design concentration.
b. Micrograms per cubic meter.
c. Back. Conc. = background concentration.
d. Total Conc. = total (modeled + background) concentration.
e. The first Max. Conc. value for each pollutant and averaging time represents results using the BULKRN meteorological data.
f. The second (grey-shaded) Max. Conc. value for each pollutant and averaging time represents results using the NON-BULKRN meteorological data.
g. Particulate matter with an aerodynamic diameter less than or equal to a nominal 2.5 micrometers.
h. Particulate matter with an aerodynamic diameter less than or equal to a nominal 10 micrometers.
i. For 24-hour PM_{10}, the design value is the *second-highest* 24-hour average concentration in a given year. However, the background value that was used in the modeling analyses represents the *first-highest* 24-hour average concentration measured in 2014. Therefore, using a larger background concentration adds a layer of conservatism to the calculated total impact for 24-hour PM_{10}.
j. Results for 24-hour PM_{10} with meteorological data processed using BULKRN show up to five hotspot receptors that exceed NAAQS. Refer to Section 4.1.4 of this modeling memo for a weight-of-evidence analysis demonstrating NAAQS compliance.

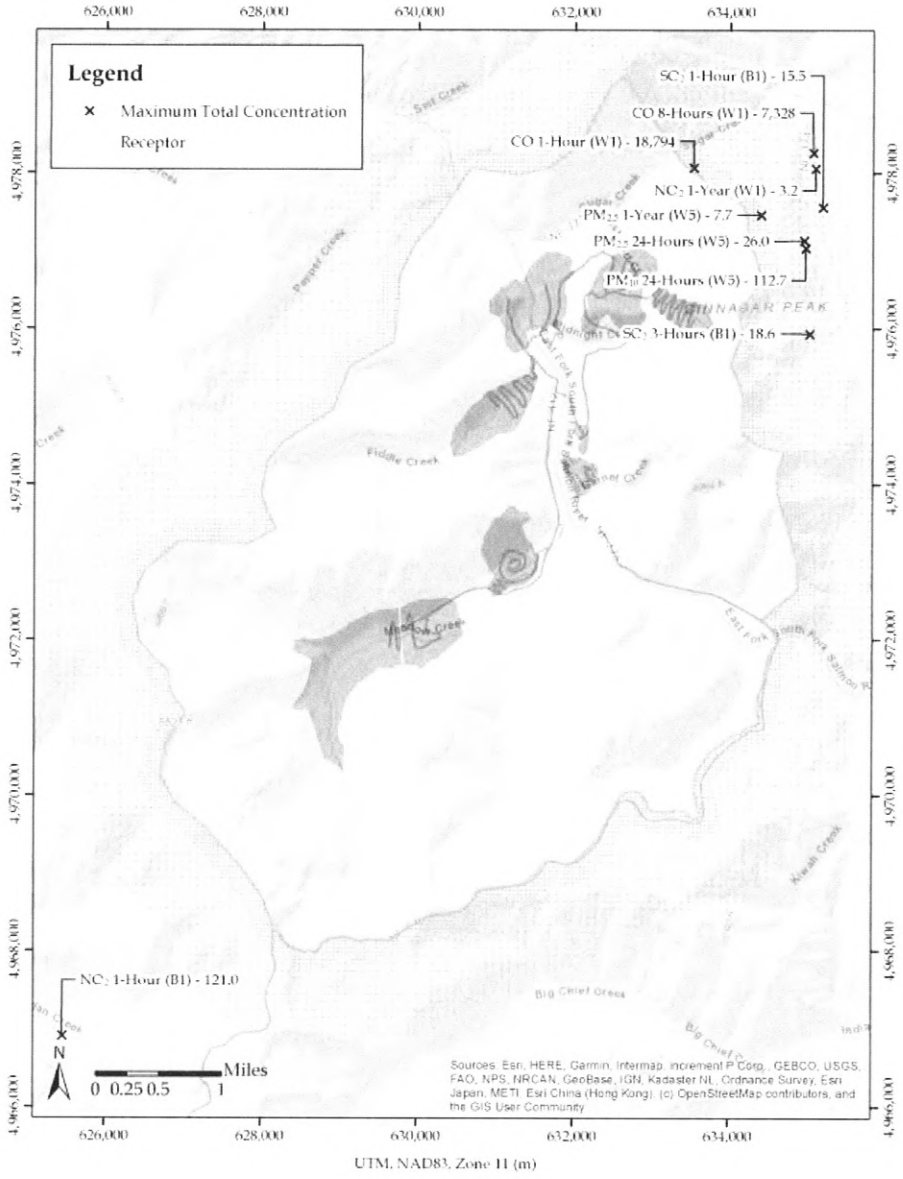
Table 26 shows that modeled concentrations derived using the BULKRN meteorological data are higher than the NON-BULKRN dataset. It also shows that the total (modeled + background) concentrations from the SGP cumulative impact analyses do not exceed the applicable NAAQS, except for when the BULKRN meteorological data are used in modeling 24-hour PM_{10} (total concentration is 105.7% of the 24-hour PM_{10} NAAQS).

PM_{10} modeling with the meteorological dataset processed with the BULKRN method shows up to five hotspot receptors for three modeling scenarios (W1, W3, and W5) with slight exceedance of NAAQS. Scenario W5 is the worst-case scenario, with a maximum total concentration of 158.5 $\mu g/m^3$ which exceeds the NAAQS of 150 $\mu g/m^3$. A weight-of-evidence analysis demonstrating PM_{10} NAAQS compliance is presented in Section 4.1.4 of this modeling memo.

The locations of the maximum impacts for each pollutant and averaging time are illustrated in Figure 10. The results presented in this figure include the hot-spot analyses conducted for each applicable pollutant-averaging time combination. For $PM_{2.5}$ and PM_{10}, the alternate meteorological data (NON-BULKRN) were used.

Modeling for ozone and secondary $PM_{2.5}$ were not performed for this minor stationary source. These analyses are typically associated with applications for major stationary sources. Nonetheless, taking the ratio of the VOC, NOx, and SO_2 emissions from the SGP facility by the emissions and resulting concentrations of O_3 and secondary $PM_{2.5}$ from EPA's modeled emission rates for precursors (MERPs) guidance yields estimated O_3 and secondary $PM_{2.5}$ concentrations of less than 1 ppb of O_3 and less than 0.1 $\mu g/m^3$ of $PM_{2.5}$ (24-hour and annual) for the SGP. These estimated concentrations have a negligible effect on compliance demonstration with the NAAQS.

Figure 10. SGP CUMULATIVE IMPACTS (µg/m³) AND LOCATIONS.



Higher background concentrations from McCall that include medium-traffic emissions provided in Section 3.2.3 were then combined with the SGP model-predicted maximum design concentrations to provide an additional level of conservatism in demonstrating compliance. These results are shown in Table 27. For $PM_{2.5}$ and PM_{10}, the alternate meteorological data (NON-BULKRN) were used. For the rest of the criteria pollutants, the BULKRN meteorological data were used.

Table 27. RESULTS FOR CUMULATIVE NAAQS IMPACT ANALYSES WITH MEDIUM-TRAFFIC BACKGROUND.							
Pollutant	**Averaging Time**	**Max. Conc.[a] (µg/m³)[b]**	**Model Scenario**	**Back. Conc.[c] (µg/m³)**	**Total Conc.[d] (µg/m³)**	**NAAQS (µg/m³)**	**Percent of NAAQS**
Carbon monoxide	8 hours	6,218	W1	1,145	7,363	10,000	73.6%
	1 hour	17,054	W1	1,797	18,851	40,000	47.1%
Nitrogen dioxide	1 year	2.3	W1	2.6	4.9	100	4.9%
	1 hour	116.7	B1	14.3	131.0	188	69.7%
$PM_{2.5}$[e]	1 year	4.2	W5	5.1	9.3	12	77.5%
	24 hours	11.0	W5	17.5	28.5	35	81.4%
PM_{10}[f]	24 hours	75.7	W5	60.1	135.8	150	90.5%
Sulfur dioxide	3 hours	1.8	B1	16.8	18.6	1,300	1.4%
	1 hour	3.2	B1	12.3	15.5	196	7.9%

a. Max. Conc. = maximum modeled design concentration.
b. Micrograms per cubic meter.
c. Back. Conc. = background concentration.
d. Total Conc. = total (modeled + background) concentration.
e. Particulate matter with an aerodynamic diameter less than or equal to a nominal 2.5 micrometers.
f. Particulate matter with an aerodynamic diameter less than or equal to a nominal 10 micrometers.

4.1.3 DEQ's Sensitivity Analyses for 1-hour and annual NO_2

DEQ performed a sensitivity analysis for 1-hour and annual NO_2 using a Tier 2 (ARM2) screening method. Minimum and maximum NO_2/NOx ratios of 0.5 and 0.9, respectively, were used. Results from DEQ's cumulative NAAQS impact analyses, summarized below in Table 28, indicate that the SGP facility is safely below the 1-hour and annual NO_2 NAAQS even when using a more conservative NO_2 screening method.

Table 28. RESULTS FOR DEQ'S NO_2 SENSITIVITY ANALYSES USING TIER 2 (AMBIENT RATIO METHOD 2) SCREENING METHOD.							
Pollutant	**Averaging Time**	**Max. Conc.[a] (µg/m³)[b]**	**Model Scenario**	**Back. Conc.[c] (µg/m³)**	**Total Conc.[d] (µg/m³)**	**NAAQS (µg/m³)**	**Percent of NAAQS**
Nitrogen dioxide	1 year	1.8	B1	0.9	2.7	100	2.7%
		1.8	H1		2.7		2.7%
		2.3	W1		3.2		3.2%
		1.8	Y1		2.7		2.7%
	1 hour	110.9	B1	4.3	115.2	188	61.3%
		73.0	H1		77.3		41.1%
		162.6	W1		166.9		88.8%
		59.8	Y1		64.1		34.1%

a. Max. Conc. = maximum modeled design concentration.
b. Micrograms per cubic meter.
c. Back. Conc. = background concentration.
d. Total Conc. = total (modeled + background) concentration.

4.1.4 DEQ's Weight-of-Evidence Analyses for 24-hour PM_{10}

This section describes a weight-of-evidence analysis that provides additional analytical information to evaluate the degree of NAAQS compliance confidence for 24-hour PM_{10}. NAAQS compliance was demonstrated in the submitted application using meteorological data processed with an EPA-approved method using regional cloud cover to calculate stability parameters rather than site-specific monitored solar radiation and measured temperature differences with height. Both methods are considered default for regulatory purposes, and modeling using this dataset shows that the facility is well below NAAQS.

As described in Section 4.1.2, PM_{10} modeling with meteorological dataset processed using the site-specific BULKRN method shows up to five hotspot receptors for Scenario W5 (the highest PM_{10} modeling scenario) that exceed NAAQS (150 $\mu g/m^3$). The hotspot receptors have a 25-meter grid spacing. Hotspot receptors that exceed 24-hour PM_{10} NAAQS have total (modeled + background) concentrations of 152.7, 154.3, 155.0, 155.7, and 158.5 $\mu g/m^3$. Locations of these receptors are illustrated in Figure 11. Figure 12 shows these receptors overlaid on Google Earth. As noted in Section 3.2.1 of this modeling memorandum, the design value for 24-hour PM_{10} is the *second-highest* 24-hour average concentration in a given year. However, the background value that was used in the modeling analyses (37.0 $\mu g/m^3$) represents the *first-highest* 24-hour average concentration measured in 2014. Therefore, using a larger background concentration adds another layer of conservatism to the calculated total impact for 24-hour PM_{10}. If the *second-highest* 24-hour average concentration (34.0 $\mu g/m^3$) were used in the modeling analyses, the number of receptors that exceed the 24-hour PM_{10} NAAQS is reduced from five to four.

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Figure 11. HOTSPOT RECEPTORS THAT EXCEED 24-HOUR PM_{10} NAAQS (SCENARIO W5, BULKRN METEOROLOGICAL DATA).

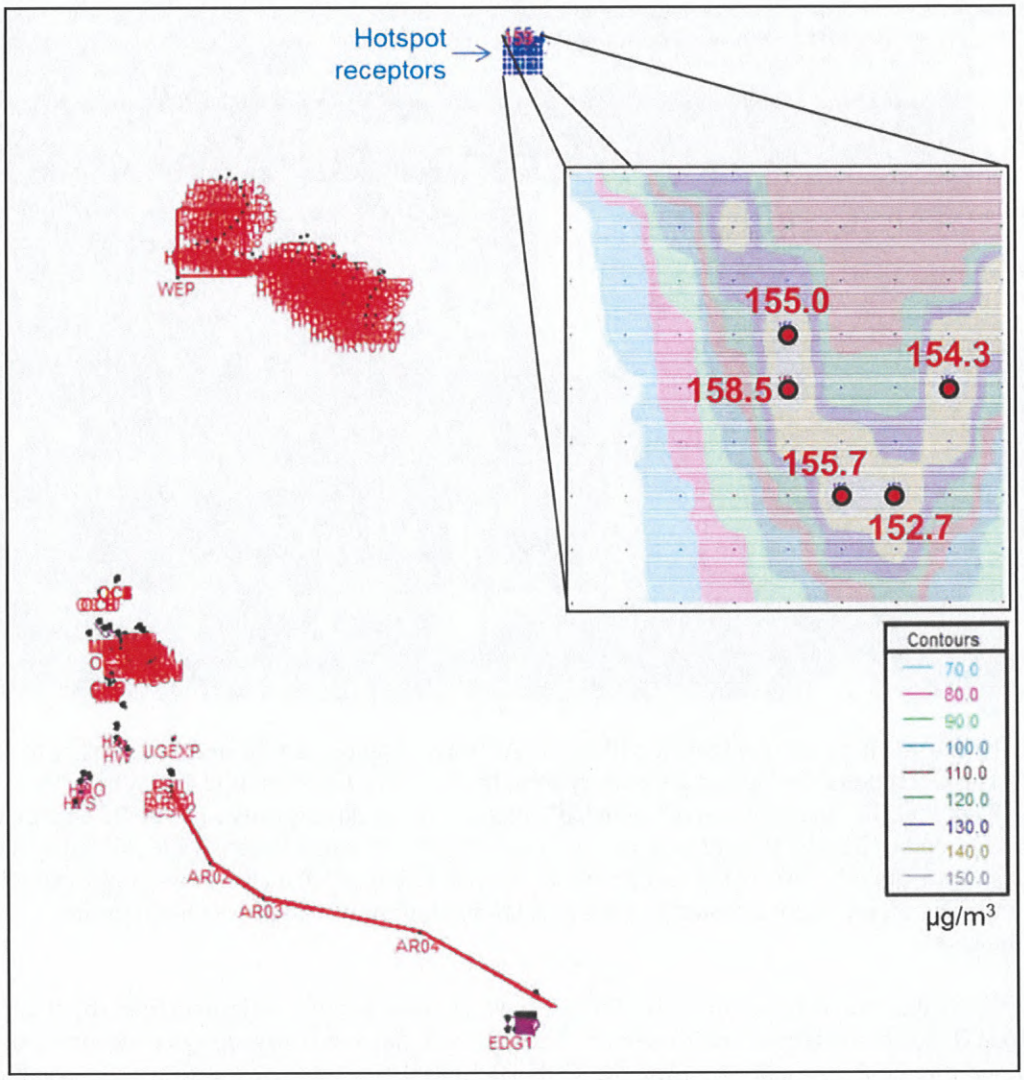
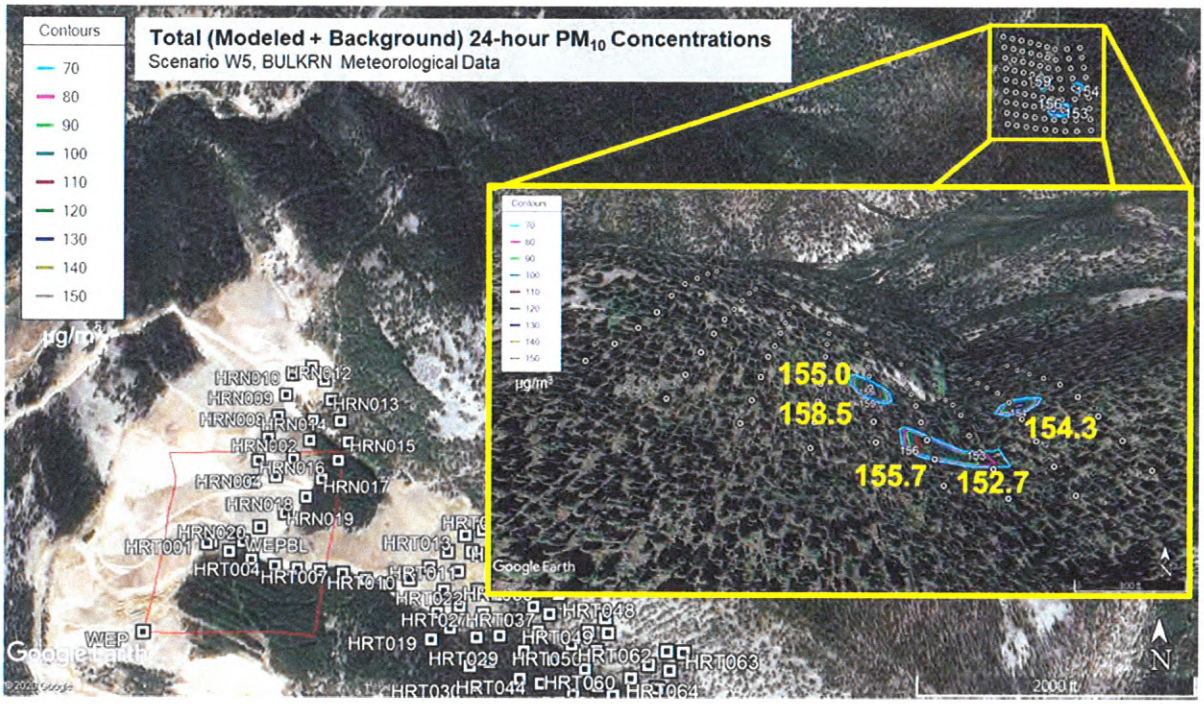


Figure 12. HOTSPOT RECEPTORS THAT EXCEED 24-HOUR PM_{10} NAAQS, OVERLAID ON GOOGLE EARTH IMAGE (SCENARIO W5, BULKRN METEOROLOGICAL DATA).



Figures 11 and 12 show that the modeled PM_{10} NAAQS exceedances are located northeast of the SGP facility. These receptors are located 2 km away from the center of the West End Pit (WEP). The AERMOD output files indicate that all modeled violations occur during winter (all modeled violations occur on December 23, 2014). Data provided in the SGP baseline study (Midas Gold 2017a) specify an average snow depth of 21-68 inches and an average precipitation of 6.0 inches at the project site during this period. Therefore, fugitive road dust emissions during high-modeled impact hours could be overestimated.

DEQ performed a source-group analysis (Table 29) which indicates that emissions from the WEP and the Haul Road (HR) are the largest contributors to the maximum modeled PM_{10} design concentrations. For comparison, source-group analyses using the NON-BULKRN meteorological data are also listed in Table 29.

Table 29. SOURCE-GROUP ANALYSES FOR 24-HOUR PM_{10} (SCENARIO W5).

Emission Source Group	Modeled Design Concentration (µg/m³)[a]	
	BULKRN	NON-BULKRN
ALL	121.5	75.7
West End Pit (WEP)	89.3	24.5
West End Pit Blasting (WEPBL)	1.94	1.81
West End Pit Development Rock Storage Facility (WEDRSF)	0.98	3.47
Haul Road (HR)	51.0	52.5
Access Road (ACCRD)	0.0064	0.0074
Underground Exploration (UGEXP)	0.00001	0.00001

Process & Ancillary Point Sources	0.23	0.76
Process & Ancillary Volume Sources	0.20	0.29

[a] Micrograms per cubic meter.

The six source groups listed in Table 29 that are related to mining activity and emissions (WEP, WEPBL, WEDRSF, HR, ACCRD, UGEXP) were examined further. Table 30 lists the daily modeled PM_{10} emissions (in pounds per day [lb/day]), grouped according to mining activity. Key assumptions for calculating the daily emissions are also listed in this table. Total modeled PM_{10} emission from mining activity for Scenario W5 is 3,336.76 lb/day. The contribution from each source group is listed in the second column of Table 30, and a pie chart is illustrated in Figure 13.

Table 30. KEY ASSUMPTIONS FOR CALCULATING DAILY MINING ACTIVITY EMISSIONS FOR 24-HOUR PM_{10} (SCENARIO W5).

Mining Activity	Emissions (lb/day)[a]
WEP (West End Pit)	**885.54**
Open Pit Drilling	
• Blasting 180,000 tons of material (DR) per day • Drilling 1,200 holes per day	811.20
Material Loading	
• Blasting 180,000 tons of material (DR) per day	18.00
Dozing	
• Dozers operating 144 hours per day • Surface material silt content of 6.9% • Material moisture content of 7.9%	54.20
Surface Exploration	
• Total wet drilling holes of 700 divided by 14 years • 50 holes per year	2.15
WEPBL (West End Pit Blasting)	**334.38**
Open Pit Blasting	
• Blasting 180,000 tons of material (DR) per day • Two blasts per day	334.38
WEDRSF (West End Pit Development Rock Storage Facility)	**57.12**
Material Unloading	
• Blasting 180,000 tons of material (DR) per day	2.88
Dozing	
• Six dozers operating 144 hours per day • Surface material silt content of 6.9% • Material moisture content of 7.9%	54.20
Wind Erosion	0.04
HR (Haul Road)	**2,050.34**
Onsite Hauling	
• Blasting 180,000 tons of material (DR) per day • One-way hauling distance of 3.07 miles • Total travel of 7,758 vehicle miles traveled (VMT) per day • Surface material silt content of 4% • Daily PM_{10} emission factor of 3.55 pounds per VMT • Control efficiency of 90% for chemical suppressant • Control efficiency of 33% for watering	1,842.97
Grading	
• Grader average speed of 6.5 mph • Three graders operating 72 hours per day • Control efficiency of 90% for chemical suppressant	60.51
Water Truck Travel	
• Two water trucks operating 48 hours per day	146.86

• Average truck speed of 15 mph • Surface material silt content of 4% • Daily PM_{10} emission factor of 3.04 pounds per VMT • Control efficiency of 90% for chemical suppressant • Control efficiency of 33% for watering	
ACCRD (Access Road) *Vehicle Travel* • Access road length of 1.6 miles (within project boundary) • Surface material silt content of 4% • Daily PM_{10} emission factor of 1.26 pounds per VMT • Control efficiency of 90% for chemical suppressant • Control efficiency of 33% for watering *Grading* • PM_{10} emission factor of 1.3 pounds per VMT • Control efficiency of 90% for chemical suppressant	**9.38** 9.17 0.21
UGEXP (Underground Exploration) *Underground Exploration* • Wet drilling 25 holes per year	**0.004** 0.004

[a] Pounds per day.

Figure 13. PIE CHART FOR DAILY MODELED PM_{10} EMISSIONS FROM MINING ACTIVITY (SCENARIO W5).

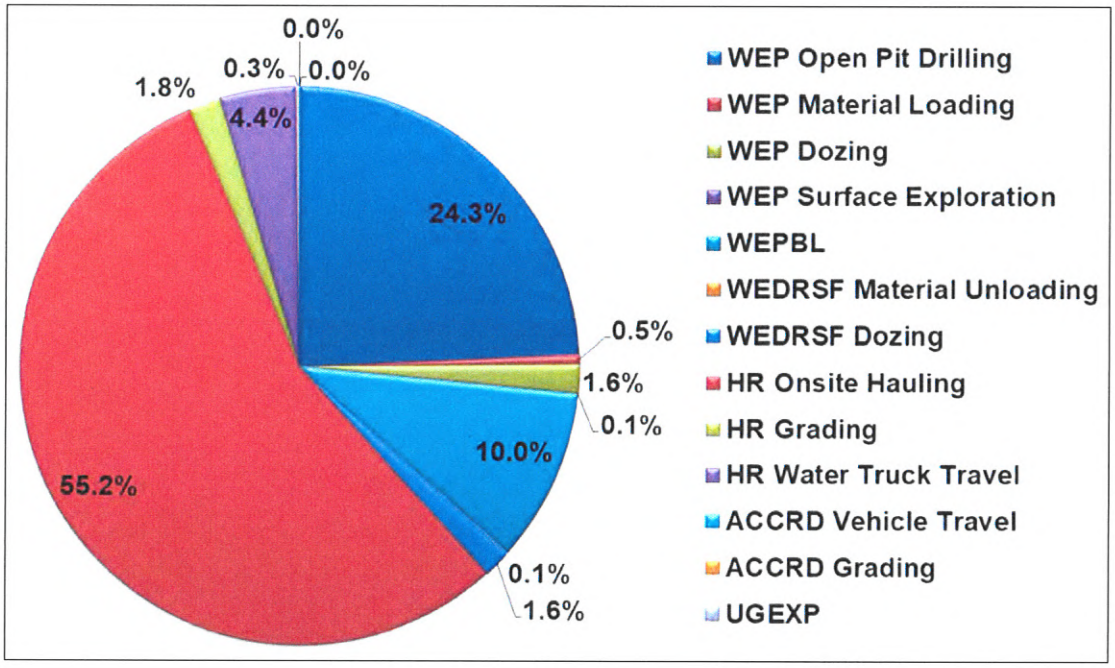


Figure 13 shows that onsite hauling on haul roads ("HR Onsite Hauling") accounts for 55.2% of the total daily PM_{10} emissions. Open pit drilling at the WEP ("WEP Open Pit Drilling") and blasting ("WEPBL") account for 24.3% and 10.0% of the daily PM_{10} emissions, respectively. Therefore, it is not surprising that HR, WEP, and WEPBL are associated with the highest modeled design concentrations in Table 29.

Table 31 shows the ten highest-ranked modeled 24-hour PM_{10} impacts from each emission source group. Note that for 24-hour PM_{10}, the design value is the *second-highest* 24-hour average concentration in a given year. Therefore, the second-high modeled value for source group ALL (121.5 $\mu g/m^3$) was summed

with the background concentration for comparison to NAAQS. The calculated total impact (modeled design value + background concentration) is conservative because the background value that was used in the cumulative NAAQS impact analyses (37.0 μg/m^3) represents the *first-highest* 24-hour average concentration measured in 2014.

Table 31. TEN HIGHEST-RANKED MODELED 24-HOUR PM_{10} IMPACTS IN μg/m^3 FROM DIFFERENT SOURCE GROUPS (SCENARIO W5, BULKRN METEOROLOGICAL DATA).

Rank	ALL[a]	WEP[b]	WEPBL[c]	WEDRSF[d]	HR[e]	ACCRD[f]	UGEXP[g]	PRCSPT[h]	PRCSVOL[i]
1ST	142.2	102.5	2.27	1.02	52.1	7.26E-03	1.00E-05	0.24	0.23
2ND	121.5	89.3	1.94	0.98	51.0	6.41E-03	1.00E-05	0.23	0.20
3RD	113.4	78.1	1.83	0.96	49.6	5.31E-03	1.00E-05	0.22	0.13
4TH	110.1	77.0	1.73	0.93	49.4	3.39E-03	1.00E-05	0.20	0.10
5TH	108.5	76.9	1.62	0.90	46.1	3.39E-03	1.00E-05	0.18	0.09
6TH	107.7	75.7	1.57	0.85	45.5	3.22E-03	1.00E-05	0.17	0.08
7TH	105.7	73.3	1.49	0.84	43.4	3.21E-03	0	0.16	0.08
8TH	105.6	72.3	1.30	0.77	42.9	2.91E-03	0	0.15	0.08
9TH	101.5	71.4	1.28	0.77	41.8	2.87E-03	0	0.15	0.08
10TH	99.8	71.2	1.23	0.76	41.8	2.56E-03	0	0.15	0.08

a. ALL = all emission sources.
b. WEP = West End Pit.
c. WEPBL = West End Pit Blasting.
d. WEDRSF = West End Pit Development Rock Storage Facility.
e. HR = Haul Road.
f. ACCRD = Access Road.
g. UGEXP = Underground Exploration.
h. PRCSPT = Process & Ancillary Point Sources.
i. PRCSVOL = Process & Ancillary Volume Sources.

Given a background of 37.0 μg/m^3 and a NAAQS of 150 μg/m^3, the critical modeled concentration threshold for any 24-hour PM_{10} NAAQS violation is therefore 113.0 μg/m^3. Table 31 shows that the third-high modeled value for source group ALL (113.4 μg/m^3) barely exceeds NAAQS. Fourth-high (and lower-ranked) modeled impacts, when added to the background concentration, are below NAAQS.

As discussed earlier in this section, HR Onsite Hauling, WEP Open Pit Drilling, and WEP Blasting are the three largest components of the total daily PM_{10} emissions. Therefore, it is not surprising that HR, WEP, and WEPBL are associated with the highest modeled concentrations among all source groups.

To investigate the potential culpability of each source group to the modeled 24-hour PM_{10} NAAQS violation, DEQ performed a culpability analysis using the MAXIFILE output option in AERMOD. The MAXIFILE option provides the receptor location and date of an impact. DEQ performed two MAXIFILE runs. In the first MAXIFILE simulation, the model was run using source group ALL. A threshold value (113.0 μg/m^3) equal to the NAAQS minus background was set. The output file provided a list of the receptors where the NAAQS is exceeded. In the second MAXIFILE simulation, the model was run using only the receptors identified by the first MAXIFILE run. Source groups were included in the second modeling simulation. A threshold value equal to the 24-hour PM_{10} SIL (5.0 μg/m^3) was set. The output file provided a date stamp for any day when a source group exceeds the SIL and potentially contributes to a violation of the NAAQS. A significant contribution to a NAAQS violation would be predicted to occur if the date stamps for source group ALL (from the first MAXIFILE run) and for a specific source group (from the second MAXIFILE run) matched.

DEQ's culpability analyses confirm that emission source groups HR and WEP are culpable for the 24-hour PM_{10} NAAQS exceedances. The date stamps indicate NAAQS violations during the winter season (January 6, January 15, and December 23). We show next that when modeled emissions are more-closely

representative of typical daily mining production rates for a high-production period (everything else held constant), the SGP facility is able to demonstrate compliance with 24-hour PM_{10} NAAQS at those few receptors showing a potential violation when using meteorological data processed with the BULKRN method. We also discuss next the implication of NAAQS violations occurring during the winter season.

As listed in Table 30, PM_{10} modeling simulation for Scenario W5 was based on a mining production rate of 180,000 ton/day of development rock. This corresponds to 65,700,000 ton/year, which is more conservative than the expected peak production rate of 42,692,000 ton/year (116,964 ton/day). To investigate the effect of a lower modeled mining production rate on design value concentrations, DEQ performed a modeling simulation ("DEQ Run 1") where mining production rate was assumed to be 120,000 ton/day instead of 180,000 ton/day, but all other model variables were held constant. This adjustment lowered the modeled daily emission rates for WEP, WEDRSF, and HR, which are summarized in Table 32. Because the modeled emission rates were lower, the modeled design concentrations were also lower. Results for DEQ's sensitivity analyses are summarized in Table 33.

Table 32. DAILY MINING ACTIVITY EMISSIONS USED IN DEQ'S SENSITIVITY ANALYSES FOR 24-HOUR PM_{10} (SCENARIO W5).

Mining Activity	Emissions (lb/day)[a]	
	Applicant's Submittal	DEQ Run 1
WEP (West End Pit)	**885.54**	**879.54**
Open Pit Drilling	811.20	811.20
Material Loading	18.00	12.00
Dozing	54.20	54.20
Surface Exploration	2.15	2.14
WEPBL (West End Pit Blasting)	**334.38**	**334.38**
Open Pit Blasting	334.38	334.38
WEDRSF (West End Pit Development Rock Storage Facility)	**57.12**	**56.15**
Material Unloading	2.88	1.92
Dozing	54.20	54.20
Wind Erosion	0.04	0.03
HR (Haul Road)	**2,050.34**	**1,436.50**
Onsite Hauling	1,842.97	1,229.13
Grading	60.51	60.51
Water Truck Travel	146.86	146.86
ACCRD (Access Road)	**9.38**	**9.38**
Vehicle Travel	9.17	9.17
Grading	0.21	0.21
UGEXP (Underground Exploration)	**0.004**	**0.004**
Underground Exploration	0.004	0.004
Total	**3,336.76**	**2,715.95**

[a] Pounds per day.

Table 33. RESULTS FOR DEQ'S SENSITIVITY ANALYSES FOR 24-HOUR PM_{10} (SCENARIO W5, BULKRN METEOROLOGICAL DATA).

Pollutant	Averaging Time	Max. Conc.[a] ($\mu g/m^3$)[b]	Model Scenario	Back. Conc.[c] ($\mu g/m^3$)	Total Conc.[d] ($\mu g/m^3$)	NAAQS ($\mu g/m^3$)	Percent of NAAQS
PM_{10}[e]	24 hours	111.5[f]	W5	37.0[g]	148.5	150	99.0%

[a] Max. Conc. = maximum modeled design concentration.
[b] Micrograms per cubic meter.

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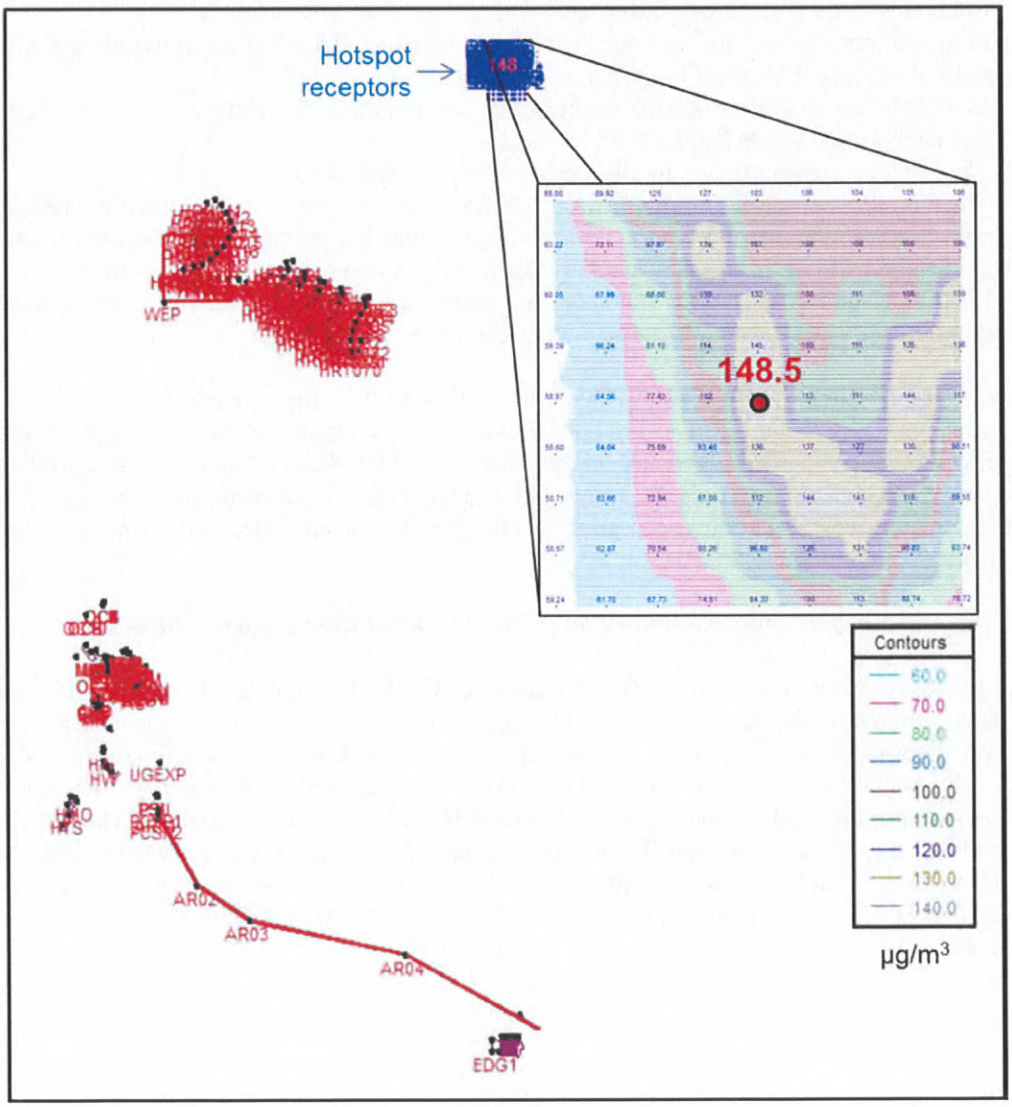
c. Back. Conc. = background concentration.
d. Total Conc. = total (modeled + background) concentration.
e. Particulate matter with an aerodynamic diameter less than or equal to a nominal 10 micrometers.
f. DEQ Run 1: mining production rate was modeled at 120,000 ton/day instead of 180,000 ton/day. Everything else was held constant.
g. For 24-hour PM_{10}, the design value is the *second-highest* 24-hour average concentration in a given year. However, the background value that was used in the modeling analyses represents the *first-highest* 24-hour average concentration measured in 2014. Therefore, using a larger background concentration adds a layer of conservatism to the calculated total impact for 24-hour PM_{10}.

Maximum modeled concentration for "DEQ Run 1", when summed with the background concentration, is lower than NAAQS thereby demonstrating NAAQS compliance. Total (modeled + background) concentrations for all hotspot receptors are depicted in Figure 14; maximum total impact is depicted by the red circle. The SGP facility complies with the 24-hour PM_{10} NAAQS when daily mining production rates closer to a more typical daily rate for a high-production period are used in the model, instead of a very conservative mining production rate, even when using site-specific BULKRN meteorological data.

Figure 14. RESULTS FOR DEQ'S SENSITIVITY ANALYSES SHOWING TOTAL (MODELED + BACKGROUND) 24-HOUR PM_{10} CONCENTRATIONS AT HOTSPOT RECEPTORS (SCENARIO W5, BULKRN METEOROLOGICAL DATA).



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Meteorological data processing with and without BULKRN are considered acceptable by EPA. However, the BULKRN meteorological data yielded higher modeled design values for the SGP facility than the meteorological data processed without the BULKRN method. DEQ's analyses suggest that when daily mining production rates closer to a more typical daily rate for a high-production period are used (everything else held constant), the SGP facility is able to demonstrate compliance with 24-hour PM_{10} NAAQS at those few receptors showing a potential violation when using meteorological data processed with the BULKRN method.

Maximum modeled design value 24-hour PM_{10} impacts, even with the use of more reasonably expected daily production rates, are still just under the 150 $\mu g/m^3$ NAAQS. As noted earlier in this section, these high values were observed during the winter season. During this period, not only are fugitive emissions minimized because of the higher moisture content of material handled or driven over, but background concentrations in such remote areas are generally much lower because of the absence of wildfires and dust-generating sources.

To summarize, DEQ considered the following assumptions and results in its weight-of-evidence analyses:

a. All modeled impacts are below NAAQS for meteorological data with stability parameters calculated by regional cloud cover data.
b. Modeled impacts over the 24-hour PM_{10} NAAQS using BULKRN meteorological data are limited to a small area and limited period of time.
c. Modeled 24-hour PM_{10} NAAQS exceedances are limited to the winter season, where emissions and background levels are likely overestimated.
d. The model assumes maximum allowable operations/emissions.
e. The model assumes minimum allowable controls on emissions. The permit would require at least 93% control of maximum potential fugitive emissions, but the fugitive emissions may in fact be controlled by more than that, especially during winter and periods of precipitation.
f. Finally, 24-hour PM_{10} background concentrations represent the maximum 1st high (instead of the maximum 2nd high) which is on the higher end of the distribution.

DEQ's weight-of-evidence analyses show that, considering all the collective conservative layers of the modeling analyses, modeling efforts using both site-specific and alternative meteorological datasets show acceptable impacts. DEQ is highly confident that operation of the SGP will not cause or contribute to a violation of NAAQS. This is based on: (1) the submitted application materials and analyses; (2) DEQ's supplemental analyses; and (3) the assumption that the facility is constructed and operated as described in the application and limited by the PTC.

4.1.5 DEQ's Sensitivity Analyses for a Lower Fugitive Road Dust Control Efficiency

Fugitive particulate emissions from roadways were estimated by the applicant to be controlled above 93%, which is an aggressive level of control. The high level of emission control was needed to demonstrate compliance with NAAQS. To investigate the effect of lower unpaved road emission control efficiency, DEQ performed a modeling simulation ("DEQ Run 2") where the control efficiency was set to 90%. The daily mining production rate was assumed to be 120,000 ton/day instead of 180,000 ton/day, but everything else was held constant. These adjustments lowered the daily modeled emission rates for WEP and WEDRSF, but increased the daily modeled emission rate for HR and the Access Road (ACCRD) (Table 34). Five receptors exceed the 24-hour PM_{10} NAAQS. Figure 15 shows the locations of these receptors.

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Table 34. DAILY MINING ACTIVITY EMISSIONS USED IN DEQ'S SENSITIVITY ANALYSES FOR 24-HOUR PM_{10} (SCENARIO W5).		
Mining Activity	**Emissions (lb/day)[a]**	
	Applicant's Submittal	**DEQ Run 2**
WEP (West End Pit)	**885.54**	**879.54**
Open Pit Drilling	811.20	811.20
Material Loading	18.00	12.00
Dozing	54.20	54.20
Surface Exploration	2.15	2.14
WEPBL (West End Pit Blasting)	**334.38**	**334.38**
Open Pit Blasting	334.38	334.38
WEDRSF (West End Pit Development Rock Storage Facility)	**57.12**	**56.15**
Material Unloading	2.88	1.92
Dozing	54.20	54.20
Wind Erosion	0.04	0.03
HR (Haul Road)	**2,050.34**	**2,114.24**
Onsite Hauling	1,842.97	1,834.53
Grading	60.51	60.51
Water Truck Travel	146.86	219.20
ACCRD (Access Road)	**9.38**	**13.90**
Vehicle Travel	9.17	13.69
Grading	0.21	0.21
UGEXP (Underground Exploration)	**0.004**	**0.004**
Underground Exploration	0.004	0.004
Total	**3,336.76**	**3,398.21**

[a] Pounds per day.

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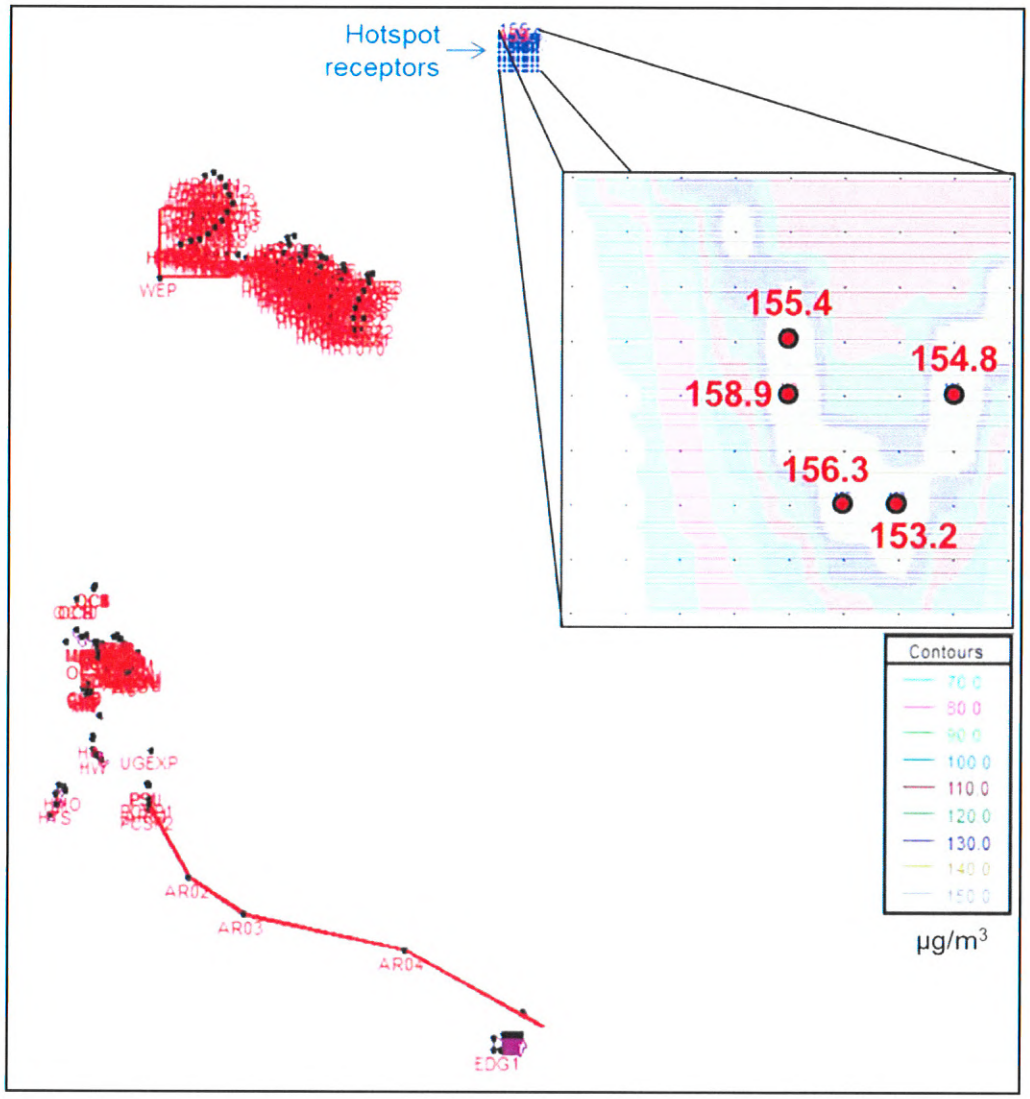
Figure 15. RESULTS FOR DEQ'S SENSITIVITY ANALYSES SHOWING HOTSPOT RECEPTORS THAT EXCEED 24-HOUR PM_{10} NAAQS, ASSUMING MINING PRODUCTION RATE OF 120,000 TONS PER DAY AND FUGITIVE ROAD DUST CONTROL EFFICIENCY OF 90% (SCENARIO W5, BULKRN METEOROLOGICAL DATA).



DEQ's sensitivity analyses suggest that a few hotspot receptors exceed the 24-hour PM_{10} NAAQS when the unpaved road control efficiency falls below 93% and the meteorological data processed with the BULKRN method is used. When the meteorological data processed without the BULKRN method is used, all the hotspot receptors demonstrate compliance with NAAQS at a 90% control efficiency and at both examined production levels:

- maximum impact at 120,000 ton per day: 73.9 $\mu g/m^3$ + 37.0 $\mu g/m^3$ = 110.9 $\mu g/m^3$.
- maximum impact at 180,000 ton per day: 84.6 $\mu g/m^3$ + 37.0 $\mu g/m^3$ = 121.6 $\mu g/m^3$.

While using alternative meteorological data processed without the BULKRN method safely demonstrates

compliance with NAAQS, using site-specific BULKRN meteorological data does not. Therefore, DEQ's modeling team recommends that the permit require an aggressive implementation of measures to achieve above 93% control efficiency for fugitive particulate emissions from roadways.

4.2 Results for TAPs Impact Analyses

The SGP TAP modeling results and their comparison with the applicable AACs/AACCs are provided in Table 35.

Table 35. RESULTS FOR TAPS IMPACT ANALYSES.

Toxic Air Pollutant	Averaging Time	Maximum Modeled Concentration ($\mu g/m^3$)[a]	Model Scenario	AAC[b] ($\mu g/m^3$)	AACC[c] ($\mu g/m^3$)	Percent of AAC/AACC
Arsenic	Annual	<1.00E-06	All	--	0.00023	<0.4%
Cadmium	Annual	0.00001	All	--	0.00056	1.8%
Formaldehyde	Annual	0.00064[d]	All	--	0.077	0.8%
Nickel	Annual	0.00002	All	--	0.042	0.05%
Aluminum	24-hour	27.454	W5	500	--	5.5%
Barium	24-hour	0.309	W5	25	--	1.2%
Calcium carbonate	24-hour	5.416	W5	500	--	1.1%
Calcium oxide	24-hour	0.208	All	100	--	0.2%
Iron	24-hour	7.037	W5	50	--	14.1%
Sulfuric acid	24-hour	0.470[d]	All	50	--	0.9%
Thallium	24-hour	0.00387	W5	5	--	0.1%
Vanadium	24-hour	0.0108	W5	2.5	--	0.4%

a. Micrograms per cubic meter.
b. Acceptable Ambient Concentration of a non-carcinogenic TAP.
c. Acceptable Ambient Concentration of a Carcinogenic TAP.
d. Deposition was not applied for formaldehyde and sulfuric acid (non-particulate TAPs).

Table 35 shows that the modeled TAP impacts from the SGP sources do not exceed the applicable AACs/AACCs. The locations of the maximum impacts for each TAP are presented in Figure 16.

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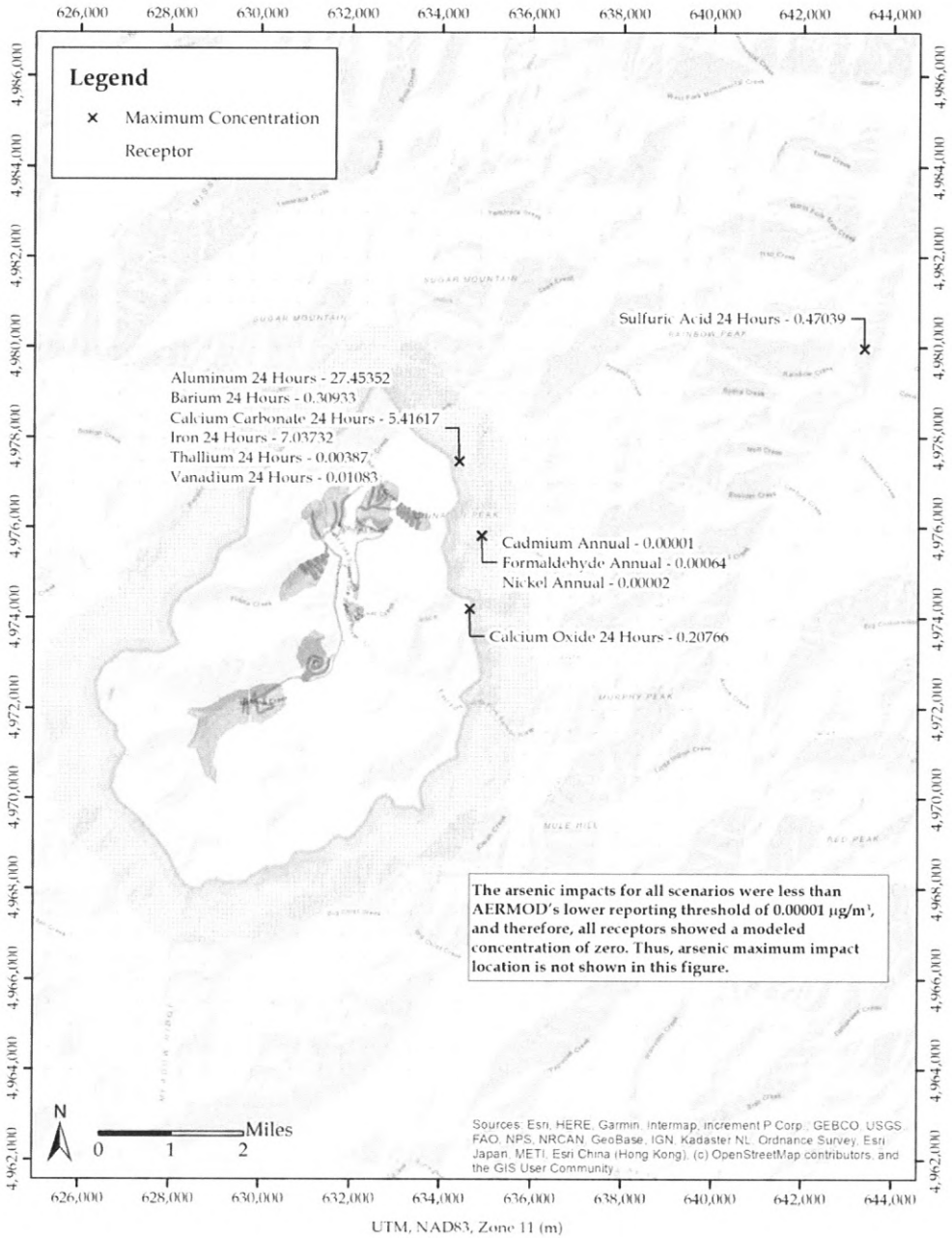
TR 0954

Figure 16. SGP TAP IMPACTS (µg/m³) AND LOCATIONS.



To investigate the effect of deposition on modeled TAP impacts, DEQ performed a sensitivity analysis where deposition was not applied in the model (Table 36). Results show that modeled TAP impacts for non-carcinogens are higher than when deposition is applied (Table 35). However, modeled TAP impacts are still well below AACs/AACCs even when deposition is not applied in the model. This result illustrates that deposition is not a critical factor for demonstrating compliance with TAP increments.

Table 36. RESULTS FOR DEQ'S SENSITIVITY ANALYSES FOR TAPS IMPACT MODELING (WITHOUT DEPOSITION).						
Toxic Air Pollutant	**Averaging Time**	**Maximum Modeled Concentration ($\mu g/m^3$)[a]**	**Model Scenario**	**AAC[b] ($\mu g/m^3$)**	**AACC[c] ($\mu g/m^3$)**	**Percent of AAC/AACC**
Arsenic	Annual	<1.00E-06	All	--	0.00023	<0.4%
Cadmium	Annual	0.00001	All	--	0.00056	1.8%
Formaldehyde	Annual	0.00064	All	--	0.077	0.8%
Nickel	Annual	0.00002	All	--	0.042	0.05%
Aluminum	24-hour	54.101	W5	500	--	10.8%
Barium	24-hour	0.610	W5	25	--	2.4%
Calcium carbonate	24-hour	10.670	W5	500	--	2.1%
Calcium oxide	24-hour	0.226	All	100	--	0.2%
Iron	24-hour	13.868	W5	50	--	27.7%
Sulfuric acid	24-hour	0.470	All	50	--	0.9%
Thallium	24-hour	0.00762	W5	5	--	0.2%
Vanadium	24-hour	0.0213	W5	2.5	--	0.9%

a. Micrograms per cubic meter.
b. Acceptable Ambient Concentration of a non-carcinogenic TAP.
c. Acceptable Ambient Concentration of a Carcinogenic TAP.

5.0 Conclusions

The information submitted with the PTC application, combined with DEQ's air impact analyses and the assumption that the facility is constructed and operated as described in the application and limited by the PTC, demonstrated to DEQ's satisfaction that emissions from the Stibnite Gold Project in Valley County, Idaho will not cause or significantly contribute to a violation of any applicable ambient air quality standard or TAP increment.

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APPENDIX F – SUBSECTION 210.20 INTERPRETATION OF ADDRESSED

STATE OF IDAHO
DEPARTMENT OF
ENVIRONMENTAL QUALITY

1410 N Hilton Street, Boise, ID 83706
(208) 373-0502

Brad Little, Governor
Jess Byrne, Director

Examples of How DEQ Interprets the Word "Addressed" in Subsection 210.20

For example, 40 CFR 63 Subpart 6J - National Emission Standards for Hazardous Air Pollutants for Industrial, Commercial, and Institutional Boilers Area Sources regulates HAP emissions from coal, biomass, and oil-fired boilers. However, the subpart specifically exempts gas-fired (i.e. natural gas-fired) boilers because EPA determined that HAP emissions from these sources were too inconsequential to be regulated by the Subpart. DEQ interprets this to mean EPA did "address" natural gas boiler HAP emissions by choosing to exempt them. Thus, HAP emissions that are also TAP emissions from coal, biomass, oil-fired boilers, and natural gas-fired boilers are not required to demonstrate compliance with IDAPA 58.01.01.210 per section 210.20.

For example, 40 CFR 63 Subpart ZZZZ - National Emissions Standards for Hazardous Air Pollutants for Stationary Reciprocating Internal Combustion Engines regulates HAP emissions from IC engines by regulating CO emissions as a surrogate for HAP emissions. Therefore, HAP emissions from IC engines are not directly regulated by the Subpart. DEQ interprets this to mean EPA "addressed" HAP emissions by regulating CO emissions as a surrogate. Therefore HAP emissions that are also TAP emissions from IC engines are not required to demonstrate compliance with IDAPA 58.01.01.210 per section 210.20.

For example, HAP/TAP emissions from lumber drying kilns were evaluated in promulgating 40 CFR 63 Subpart DDDD - National Emission Standard for Hazardous Air Pollutants: Plywood and Composite Wood Products (PCWP). This Subpart regulates major sources of HAP emissions and includes lumber drying kilns at PCWP manufacturing facilities and "at any other kind of facility" as affected sources, even though this subpart does not include any substantive requirements to control or limit emissions from the kilns. In developing Subpart DDDD EPA stated "…we know of no other lumber kilns that are controlled for HAP, and we know of no cost effective HAP controls for lumber kilns…" (see Fed. Reg. /Vol 68, No. 6/Thursday, Jan 9, 2003/Proposed Rules page 1285). DEQ interprets this to mean EPA "addressed" HAPS that are also TAPS for both major and minor sources of HAP emissions; and therefore, lumber kilns are not required to demonstrate compliance with IDAPA 58.01.01.210, per section 210.20.

For example, when EPA regulated Phosphoric Acid Manufacturing for new sources, only the wet-process phosphoric acid line, superphosphoric acid process line, phosphate rock dryer, and the phosphate rock calciner have specific emissions limits in the rule. However, other emissions sources at facility were also looked at but they were determined by EPA to be insignificant and were not regulated in the rule. Therefore, when EPA looks at a source category to regulate, all emissions sources associated with the source category are "addressed" whether EPA establishes specific emissions limits for the emissions sources or not.
In sum, the term "addressed" is interpreted to mean EPA (1) specifically regulated, (2) specifically regulated by a surrogate, (3) reviewed, or (4) evaluated, the HAP emissions that are also TAPs.

Please note that in all cases it is presumed that EPA evaluated the 187 HAPs when developing the emission standards for new, modified or existing stationary sources regulated by 40 CFR Part 63 Subparts. Therefore, in all cases IDAPA Toxic Air Pollutants that are not one of the 187 Hazardous Air Pollutants will still need to be evaluated for compliance with IDAPA 58.01.01 Section 210.

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Attorneys for Perpetua Resources Idaho, Inc.

BEFORE THE BOARD OF ENVIRONMENTAL QUALITY
STATE OF IDAHO

IN THE MATTER OF AIR QUALITY PERMIT TO CONSTRUCT P-2019.0047

NEZ PERCE TRIBE, IDAHO CONSERVATION LEAGUE, and SAVE THE SOUTH FORK SALMON,

Petitioner,

v.

IDAHO DEPARTMENT OF ENVIRONMENTAL QUALITY,

Respondent,

and

PERPETUA RESOURCES IDAHO, INC.

Intervenor-Respondent.

Case Docket No. 0101-22-01
OAH Case No. 23-245-01

EXPERT DECLARATION OF THERESA LOPEZ

PERPETUA RESOURCES EXHIBIT
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I, Theresa Lopez, hereby declare and affirm as follows:

1. My name is Theresa Lopez. I am employed by Tetra Tech, Inc. as a Principal Toxicologist.

2. In addition to this Declaration, I have prepared a supporting memorandum that further elaborates on my testimony (Memorandum). A copy is attached.

A. Qualifications and Experience

3. My curriculum vitae is attached as Attachment C to the Memorandum.

4. I received a Master of Science degree in Public Health from the University of Colorado in 1991 and a Bachelor of Science degree in Nutritional Science with a minor in Zoology from the University of Florida in 1989. My relevant areas of expertise include chemical risk assessment, human health risk assessment, regulatory toxicology, and exposure assessments.

5. I worked extensively in the areas of public health, epidemiology, human health risk assessment, toxicology, and occupational health and safety, representing both the public and private sector for over 32 years with Tetra Tech.

6. My work included a variety of human health risk assessment projects at the federal and state levels, as well as international work. I led the investigation and assessment of chemical releases and environmentally compromised sites such as former nuclear weapons plants, active and closing naval bases, Superfund Sites, and mining, commercial, and school sites.

7. My work includes assisting in risk assessments and remediation of former mining sites with heavy metal, pesticides, petroleum compounds and other chemicals; and risk assessments for proposed mines, hazardous waste release sites, and petroleum remediation in the United States and Canada. I prepared human exposure assessments for schools and recreational settings and assessed clean-up goals and remediation strategies for closed industrial, mining,

redevelopment, and other sites. These sites often include the consideration of native and indigenous peoples. I provided exposure and dose reconstruction for Oak Ridge Associated Universities to quantify radiation doses to former nuclear weapons workers.

8. Recent relevant work includes review of human exposures, livestock exposures, plant, and food ingestion pathways for the development of water quality standards for the Navajo Nation; technical support for the Agency for Toxic Substances and Disease Registry (ATSDR) to provide scientific advise and education on public health assessment methodologies, review of toxicity data, and probabilistic risk assessment methodology, and primary experiments, for example to assess uptake measurements of metals and PFAS from soil to common food plants; and peer review of chemical assessments for the Consumer Product Safety Commission. I author and review reports for Health Canada related to Existing Substances Risk Assessment Bureau mandates. For these projects I am often designated as lead toxicologist.

B. Scope of Review

9. I have been retained as an expert witness by Perpetua Resources Idaho, Inc. (Perpetua) in the above-captioned case, to address issues raised in the Final Order issued by the Board of Environmental Quality on May 9, 2024 and to evaluate the risks presented by emissions of arsenic from the Stibnite Gold Project (SGP). Specifically, I have been asked to evaluate:

a. Whether the Idaho Department of Environmental Quality (DEQ) used appropriate risk assessment methodology by adjusting the maximum modeled lifetime arsenic emissions from the SGP by 16/70 to reflect the operational life of the SGP;

b. Whether, as conditioned by the Air Quality Permit to Construct (PTC) issued to Perpetua, arsenic emissions from the SGP present a greater than 1 in 100,000 cancer risk; and

c. Whether DEQ's use of a five-year rolling average production limit to demonstrate compliance with T-RACT is protective of public health and the environment.

C. Summary of Opinions

10. Based on my review of the permitting record in this matter, the Declarations of Norka Paden, Kevin Schilling, and Kevin Lewis, and the documents cited in, and attached to, my Memorandum, I conclude as follows:

a. I conclude that the 16/70 calculation was consistent with good scientific methodology for assessing cancer risk and consistent with the applicable rules. DEQ appropriately calculated, and considered, the exposure duration of 16 years of SGP operational life when evaluating the risk posed by arsenic emissions from the SGP. Cancer risk cannot be evaluated without taking into consideration the length of time a potential receptor will be exposed to carcinogen.

b. The Rules for the Control of Air Pollution in Idaho (Air Rules), IDAPA 58.01.01, provide a default formula for calculating cancer risk from carcinogen emissions from stationary sources. The Air Rules, specifically Section 586, adopted EPA risk assessment information and methodology, which inherently requires consideration of exposure duration.

c. The use of a 10-times adjustment to the Acceptable Ambient Concentration for Carcinogens (AACC) when a project will operate for five years or less is an example of an adjustment of exposure duration when evaluating cancer risk and does not preclude adjustment for exposure duration when a project will operate for less than 70 years.

d. I conclude that the incremental increase in cancer risk caused by arsenic emissions from the SGP is 1 in 240,000, which is less than the acceptable risk of 1

in 100,000. This conclusion is based on the maximum modeled annual concentration of arsenic predicted for SGP operations, the operational life of the SGP established by conditions in the PTC, and risk assessment methodology established by EPA.

e. I conclude that the use of a five-year rolling average production limit to demonstrate compliance with T-RACT is sufficiently protective to ensure that the ambient concentration of arsenic from the SGP will not cause a cancer risk above 1 in 100,000.

f. The PTC includes both daily production limits and limits production from the SGP to 135,000 tons per year based on a five-year rolling average. EPA's risk assessment methodology evaluates the incremental increase in cancer risk for each incremental increase in carcinogen dose over the exposure duration. Use of a five-year rolling average ensures that a receptor's total exposure to arsenic caused by the SGP will not exceed a 1 in 100,000 cancer risk. Although there may be short term increases in production, and the ambient concentration of arsenic, these short-term increases will not, alone, cause unacceptable cancer risk.

D. Background

11. Arsenic comes in several forms and occurs naturally in soil and minerals. Arsenic can enter the atmosphere from wind-blown dust. Arsenic concentrations in soil are variable across the country, and when soil is disturbed arsenic can become airborne and be carried with dust particles. Since arsenic is naturally in the environment, everyone is exposed to some arsenic by eating food, drinking water, or breathing air. People normally ingest small amounts of arsenic from breathing air, drinking water, and eating food. Indeed, food is considered the largest source of arsenic exposure for humans.

12. EPA analyzes the long-term, or carcinogenic, health effects of arsenic through animal and worker studies. The arsenic inhalation unit risk (IUR) published by EPA in the Integration Risk Information System (IRIS) reflects many years of research and evaluation and was developed using a linear extrapolation method that assumes that any level of exposure carries a risk. Under a linear risk extrapolation method, the dose is cumulative over the duration of exposure and cancer risk increases linearly as the cumulative total dose increases. Exposure is assumed to occur over a lifetime, assumed to be 70 years. See Memorandum, Figure 1.

13. All IURs (including for arsenic) are based on an incremental lifetime risk of 1 in one million from exposure to 1 $\mu g/m^3$ of a substance continuously (24 hours day and 365 days/ year) over a lifetime of exposure (assumed to be 70 years). Importantly, this is an incremental risk that does not consider other, unrelated risks present over a lifetime.

14. DEQ adopted EPA's cancer risk values and risk assessment methodology when it promulgated the Air Rules for toxic air pollutants from stationary sources. IDAPA 58.01.01.586; Memorandum at 5-7; Memorandum, Attachment A, Idaho DEQ 1993 at 33.

15. The unit risk factor (URF) of 4.3E-03$\mu g/m^3$ for arsenic that DEQ adopted in IDAPA 58.01.01.586 is the IUR developed by EPA and reflected in the IRIS.

16. Similarly, the AACC that DEQ adopted in IDAPA 58.01.01.586 is taken from the IRIS database and is referred to by EPA as the "Air Concentration at Specific Risk Levels." The AACC is calculated by dividing the acceptable lifetime risk (1 in 1,000,000) by the URF. See Memorandum, Figure 1.

17. The AACC in Section 586 of the Air Rules reflects the ambient concentration of arsenic to which a person could be exposed 24 hours a day, 365 days a year, for a 70-year lifetime before the cancer risk level exceeds 1 in 1,000,000 (AACC = 0.00023$\mu g/m^3$).

18. The AACC does not represent an annual emission limit; it is the concentration that a person may be exposed to for a lifetime continuously, with an incremental risk of cancer of 1 in 1,000,000. *See* Idaho DEQ 1993 at 32.

19. Both the URF and AACC are derived using a linear risk extrapolation method, meaning that cancer risk from arsenic exposure increases linearly as the dose or exposure duration increases. See Memorandum at 4. Therefore, although the URF and AACC are based on lifetime exposure, the ultimate determinate of cancer risk is the cumulative dose, regardless of the timeframe over which that dose is delivered.

E. Opinions

DEQ Appropriately Adjusted the Exposure Duration of SGP to 16 Years Consistent with Permit Conditions Limiting the Project Life.

20. When considering carcinogenic exposure, a critical factor to determine the cancer risk is the exposure duration. Although the AACC assumes a 70-year constant exposure, where the exposure duration is less than 70 years, the exposure duration must be adjusted for an accurate risk calculation. In the case of the SGP, the maximum exposure duration is 16 years. Therefore, the cancer risk from the ambient concentration of arsenic caused by the SGP cannot be compared to the AACC (that assumes 70 years) without adjusting for exposure duration.

21. Comparing unadjusted emissions to the AACC would result in an over-estimation of cancer risk because the dose will not continue for the 70-year lifetime exposure assumed

in the development of the AACC. For an "apples to apples" comparison, evaluation of SGP emissions must be adjusted for the shorter exposure duration.

22. EPA provides the following formula to compare the exposure concentration from a project that operates for less than 70 years to the lifetime exposure concentration that would cause a specified cancer risk (shaded notes are presented by author for clarification):

Cair-adj=Cair x ET x 1day/24 hours x EF x ED/AT

Where:
$C_{air-adj}$ = Air Concentration adjusted for exposure
C_{air} = Concentration of contaminant in air (mg/m^3) (this is the modeled or measured annual air concentration)
ET = Exposure time (hours/day) (this is assumed to be 24 hours/day)
EF = Exposure frequency (days/year) (this is assumed to be 365 days/year)
ED = Exposure duration (years) (this is 16 years – the life of operations)
AT = Averaging time (days) (this is lifetime – 70 years x 365 days/year; it never changes for any carcinogen)

See Memorandum at 9-10.

23. DEQ used this formula when it determined the acceptable risk from the ambient arsenic concentration caused by SGP operations.

24. Using the highest modelled annual average arsenic concentration from the project of 0.00414 $\mu g/m^3$ (REC 716) the calculation of the air concentration adjusted for exposure from the SGP is as follows:

$$\left[0.00414\,\frac{\mu g}{m3}\,x\,24\,\frac{hours}{day}\,x\,\frac{1\,day}{24\,hours}\,x\,365\,\frac{days}{year}\,x\,16\,years\right] / \left[365\,\frac{days}{year}\,x\,70\,years\right] = 0.00095\,\frac{\mu g}{m3}$$

25. Using EPA methodology, as adopted by DEQ, the adjusted lifetime-exposure concentration from the SGP is 0.00095$\mu g/m^3$. This is the correct project-specific arsenic

concentration to compare to the T-RACT AACC of 0.0023 µg/ m^3 for a cancer risk of 1:100,000. *See* REC 716.

The Cancer Risk Caused by Arsenic Emissions from the SGP is 1-in-240,000 -- Less than the Acceptable Risk of 1-in-100,000.

26. The highest air concentration of arsenic from the project is below the acceptable lifetime risk established by the T-RACT AACC.

27. Once the ambient arsenic concentration has been adjusted from a lifetime exposure to a project specific duration, to provide an "apples-to-apples" comparison to the AACC, then that ambient concentration is used to determine the cancer risk from arsenic from SGP.

28. Calculation of the incremental increase in cancer risk from SGP arsenic emissions is as follows:

$$\frac{1}{100{,}000} T\text{–}RACT\ Risk\ x\ 0.00095 \frac{\mu g}{m3} C_{air-adj} \,/\, 0.0023 \frac{\mu g}{m3}\ T\text{–}RACT\ AACC$$
$$= 4.1E\text{–}6\ or\ \frac{1}{240{,}000} Actual\ Risk$$

29. The incremental increase in cancer risk from SGP arsenic emissions is 1 in 240,000, meaning that if 240,000 people are exposed to the maximum ambient arsenic air concentration from the SGP continuously over 16 years, then one excess cancer would probabilistically be expected to develop over a lifetime. This is less than 1 excess cancer in 100,000 people, which is the acceptable risk limit in the T-RACT AACC for SGP.

30. DEQ utilized the formulas described in paragraphs 24 and 28 to compare the risk of exposure to arsenic emissions from the SGP. This analysis is consistent with EPA methodology and provides an "apples to apples" comparison of risk between SGP emissions of 16 years and the AACC concentration that assumes exposure over 70 years.

31. DEQ's assessment ensured that the PTC, and the conditions imposed on SGP, would ensure that the cancer risk from SGP emissions would be less than 1-in-100,000.

32. Section 210.15 of the Air Rules is an example of the proper adjustment for exposure duration and does not preclude this adjustment in other circumstances for an "apples to apples" comparison, where the project life is limited to less than 70 years.

33. In its analysis, DEQ analogized the SGP exposure duration adjustment to the short-term adjustment factor for sources that operate for 5 years or less in Section 210.15 of the Air Rules. The Final Order expressed concern that the Air Rules do not explicitly allow for an adjustment for sources that will operate for more than 5 years but less than 70 years.

34. Section 210.15 of the Air Rules is an example of an appropriate adjustment for exposure duration. This is consistent with EPA's methods for risk assessment and reliance on the URFs and AACCs. Sections 210.02 and 210.03 allow DEQ to develop analyses using project specific information, such as exposure duration. In my opinion these rules cannot be read to impede DEQ's use of EPA's methods and scientific practices to perform an appropriate risk assessment under the Air Rules.

35. Adjusting exposure duration is necessary and proper from a scientific and toxicological standpoint to apply the AACCs accurately. Omitting this adjustment is contrary to common scientific practice and the intent of the Air Rules as reflect DEQ documents. Memorandum Attachment A, References, Idaho DEQ 1992 and Idaho DEQ 1993.

36. This is particularly true when comparing project specific risk to the AACC because the AACC, and the URF upon which it is based, assumes a 70 year (lifetime) exposure.

37. The AACCs are not annual average air concentration limits or standards.

38. Treating the AACC as an annual emission limitation or annual limit on ambient exposure concentration is inconsistent with the purpose and development of the AACC. The

AACC is an ambient concentration that if emitted over time (default 70 years) could result in a risk of cancer response.

39. Treating the AACC as an annual emissions limitation significantly lowers acceptable risk. If the T-RACT AACC of 0.0023 $\mu g/m^3$ for arsenic were based on a one-year exposure, then the risk represented by that value would be about 1-in-7,000,000.

40. The URF and the AACC derived from it represent the upper-bound excess lifetime cancer risk estimated to result from continuous exposure to a contaminant over a lifetime at an air concentration of 1 $\mu g/m^3$.

41. In other words, the AACC and T-RACT AACC represent the chemical-specific airborne concentration at which the risk to an individual if exposed all day, every day for a lifetime is 1-in-1,000,000 (AACC) or 1-in-100,000 (T-RACT AACC). Any other interpretation defies fundamental toxicological science used by the EPA in the development of IURs (URFs).

42. The AACC and T-RACT AACC do not represent the risk of a cancer response following a single exposure.

The Use of a Five-Year Rolling Average Production Limit to Demonstrate Compliance with T-RACT is Sufficiently Protective to Ensure that the Ambient Concentration of Arsenic from the SGP Will Not Cause a Cancer Risk Above 1-in-100,000.

43. Finally, use of a 5-year rolling average production limit is as protective as an annual production limit, for purposes of determining an acceptable cancer risk.

44. Cancer risk increases from cumulative long-term exposure, not short-term annual emissions. Cancer risk is assessed based on total cumulative dose over the exposure duration, as demonstrated in the Memorandum, Figure 1, column D.

45. As shown in Figure 1, a total dose of 0.16 $\mu g/m^3$ of arsenic would cause an increased cancer risk of 1-in-100,000. The risk does not change if this total cumulative dose occurs in 1 year, 5 years, 16 years, or 70 years. Therefore, the 5-year rolling average is as protective as an annual production limit.

46. The 5-year average production limit ensures that if production is above the limit in one year, then future production must be reduced below the limit. This ensures that the cumulative ambient arsenic concentration does not exceed the acceptable ambient concentration level for the defined risk.

47. The 5-year average production limit in the PTC ensures that the ambient arsenic concentration from the SGP over the project life (exposure duration of 16 years) results in an acceptable cancer risk under the Air Rules.

I declare under penalty of perjury under the laws of the United States that the foregoing is true and correct to the best of my knowledge, information, and belief.

DATED: August 30, 2024.

Theresa K. Lopez

Theresa Lopez, TetraTech

CERTIFICATE OF SERVICE

I hereby certify that on August 30, 2024, a true and correct copy of the **EXPERT DECLARATION OF THERESA LOPEZ** was served on the following:

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Memorandum in Support of Declaration: DEQ's Review of Risk for the Stibnite Gold Project

TETRA TECH, INC.

Author:	Theresa Lopez MSPH Tetra Tech, Inc.
Date:	August 30, 2024
Subject:	Memorandum in Support of Declaration: DEQ's Review of Risk for the Stibnite Gold Project

I. INTRODUCTION

This memorandum and my opinions address certain of the issues remanded by the Idaho Board of Environmental Quality (Board) in *In re Matter of Air Quality Permit to Construct* P-2019.0047 regarding the Idaho Department of Environmental Quality's (DEQ) issuance on June 17, 2022 of a permit to construct (PTC) to Perpetua Resources Idaho, Inc. for the Stibnite Gold Project (SGP). This memorandum concludes that, as issued, the PTC for the SGP is protective of public health and establishes conditions that ensure a less than 1 in 100,000 cancer risk from worst-case exposure to arsenic, applying established toxicological principles. This memorandum confirms that the DEQ properly interpreted and applied the toxic air pollutant (TAPs) rules (including the ambient TAP carcinogenic increments and the acceptable risk represented by Sections 161, 210.12 and 586 of the Rules for the Control of Air Pollution in Idaho, IDAPA 58.01.01 (IDAPA or the Air Rules)) consistent with scientific methods and EPA guidelines.

II. STATEMENT OF QUALIFICATIONS

Attached hereto as Attachment C is a copy of my curriculum vitae.

III. DOCUMENTS REVIEWED

To form the opinions expressed in this memorandum, I reviewed the following documents:

- Board's Final Order
- PTC, issued June 17, 2022
- Statement of Basis (SOB) for the PTC issued June 17, 2022
- References listed in Attachment A
- Expert Declaration of Kevin Lewis (Filed Aug. 30, 2024)
- Expert Declaration of Kevin Schilling (Filed Aug. 13, 2024)
- Expert Declaration of Norka Paden (Filed Aug. 13, 2024)

IV. OVERVIEW OF ISSUES REMANDED BY THE BOARD AND ADDRESSED BY THIS MEMORANDUM

In its *Final Order* dated May 9, 2024, the Board remanded this case to the Hearing Officer for the development of further evidence related to DEQ's risk assessment for the Acceptable Ambient Concentration for Carcinogens (AACC) for arsenic as set forth in Section 586 of the Air Rules. Specifically, the Board directed that on remand, the Hearing Officer address the following:

- DEQ's application of the project exposure duration of 16 years when assessing compliance with the AACC. Specifically, the Board indicated that "DEQ did not provide sufficient evidence in the form of an expert opinion from a toxicologist or other qualified expert regarding the cancer risk associated with the 16/70 adjustment."
- DEQ's use of a five-year rolling average for T-RACT that the Board concluded was not supported by sufficient evidence.
- The T-RACT analysis limiting the non-West End Pit production limit.

This memorandum supports my expert opinion on the first two issues.

- This memorandum explains the role of exposure duration, including the current state of scientific methods for assessing risk from inhalation exposure and U.S. Environmental Protection Agency (EPA) directives on the use of toxicity values and risk assessment.
- This memorandum addresses the use by DEQ of a project specific adjustment factor of 16/70 to account for the operational life of the SGP.
- This memorandum addresses the use of a short-term adjustment factor, provided for in IDAPA 210.15 of the Air Rules, allowing a 10-times adjustment to the AACC for short-term projects. This is an example of the use of exposure duration in risk assessment, and adjustment for exposure duration in other risk assessments is also appropriate.
- This memorandum clarifies that AACCs are not annual average air concentration limits or standards.
- This memorandum explains why the use of a 5-year rolling average production limit is equally protective as an annual production limit.

V. TOXICOLOGY, THE TAPs RULES, AND ARSENIC

Toxicology is the study of the adverse effects (called "responses") of exposures to chemicals (as well as other compounds) on biological systems (called "doses"). In toxicology, dose-response is critical to characterizing risk of experiencing adverse effects. A dose-response assessment is a mathematical relationship between the extent of a biological response in an organism (if any) to a substance at varying levels of exposure (i.e., concentration) for varying periods of time (i.e., the duration of the exposure). The goal of a dose-response assessment is to define an exposure threshold above which a substance may cause adverse effects. In other words, the goal is to define the rate at which adverse effects may be experienced as the dose (concentration and exposure) increases.

EPA uses established dose-response assessments for various chemicals to characterize both non-cancer and cancer risks. For carcinogens, these assessments result in inhalation unit risk (IUR) values and are set forth in the EPA Integrated Risk Information System (IRIS). EPA uses the IUR to develop ambient concentrations that reflect cancer risk levels from continuous exposure over a 70-year lifetime. These concentrations can be found in the EPA IRIS.

Based on my review of the relevant documents, in my opinion, the foundation of the TAPs rules is consistent with the scientific principles underlying dose-response assessments that are established by EPA. IDAPA 586 reflects EPA risk assessment methodology that prompts adjustment of the exposure duration to assess the dose-response risk assessment properly. DEQ appropriately

considered exposure duration when applying the TAPs rules to the PTC, consistent with the EPA assessments on which they are based. In this PTC, DEQ applied the Air Rules consistent with the best available scientific practices in establishing cancer risk levels, and evaluating the environmental and health risks of exposure to arsenic from the SGP:

A. DEQ interpreted and applied the TAPs Rules consistent with EPA's risk assessment methodology including accepted scientific principles governing toxicity values, exposure evaluations, and cancer risk.
B. Based on EPA methods and DEQ policies and methodologies, DEQ appropriately adjusted the exposure duration to 16 years from the assumed 70 years reflecting conditions in the PTC that limit the project life to 16 years; this adjustment was necessary for a scientifically defensible "apples to apples" comparison with the AACC.
C. The highest air concentration projections modelled for arsenic emissions from SGP are below the acceptable lifetime risk established by the T-RACT AACC in IDAPA 586 and 210.12, and therefore, the PTC authorizes risks that are acceptable for human health and the environment.
D. IDAPA 210.15 allows for a 10-times adjustment to the AACC when a project will operate for 5 years or less. This is an example of applying exposure duration when evaluating cancer risk. The Air Rules do not limit DEQ's analyses that follow EPA methodology and scientific principles for exposure duration adjustment in risk assessment for permits issued under the Air Rules.
E. Idaho's AACCs are not annual average air concentration limits or standards.

As described in the *Final Order*, the primary TAP of concern from the SGP is Arsenic. Arsenic comes in several forms, occurs naturally in soil and minerals, and volcanic eruptions are a source of arsenic. Arsenic can enter the atmosphere from wind-blown dust. Arsenic concentrations in soil are variable, as some areas having higher arsenic levels than others. When soil is disturbed arsenic can become airborne and carried with dust particles. Since arsenic is naturally in the environment, everyone is exposed to some arsenic by eating food, drinking water, or breathing air. People normally ingest small amounts of arsenic from breathing air, drinking water, and eating food. "Of these, food is usually the largest source of arsenic. The predominant dietary source of arsenic is seafood, followed by rice/rice cereal, mushrooms, and poultry." (ATSDR 2007)

Impacts of arsenic exposure are also well-studied. Arsenic presents risks of both noncarcinogenic (acute) and carcinogenic (long-term) health effects. Long-term, or carcinogenic, health effects are evaluated through animal or worker studies. EPA states that risk assessment is a scientific process that depends on 3 factors: (2024 - About Risk Assessment | US EPA)

1. **How much of a stressor is present** in an environmental medium (e.g., soil, water, air) over what geographic area,
2. **How much contact (exposure)** a person has with that environmental medium, and
3. **How it affects** the health of humans (e.g., **toxicity)**

EPA published toxicity values for both carcinogenic and noncarcinogenic health effects of arsenic (EPA 1984). These toxicity values are the result of many years of research and evaluation. The

carcinogenic toxicity values for arsenic via inhalation were developed by EPA using a linear extrapolation method that assumes that any level of exposure carries a risk. EPA stated: "It is assumed, unless evidence exists to the contrary, that if a carcinogenic response occurs at the dose levels used in a study, then responses at all lower doses will occur with an incidence that can be determined by an appropriate extrapolation model." (EPA 1984). The linear model used by EPA incorporated 4 different studies and resulted in the calculation of an IUR of 4.3Ex 10^{-3} per $\mu g/m^3$ for arsenic. According to EPA, the mode provides a plausible estimate of the upper limit of risk; the true risk could be considerably lower. The figure below is one of several created by EPA; a combined figure for all studies from which the IUR was calculated is not available. (EPA 1984).

Figure 1

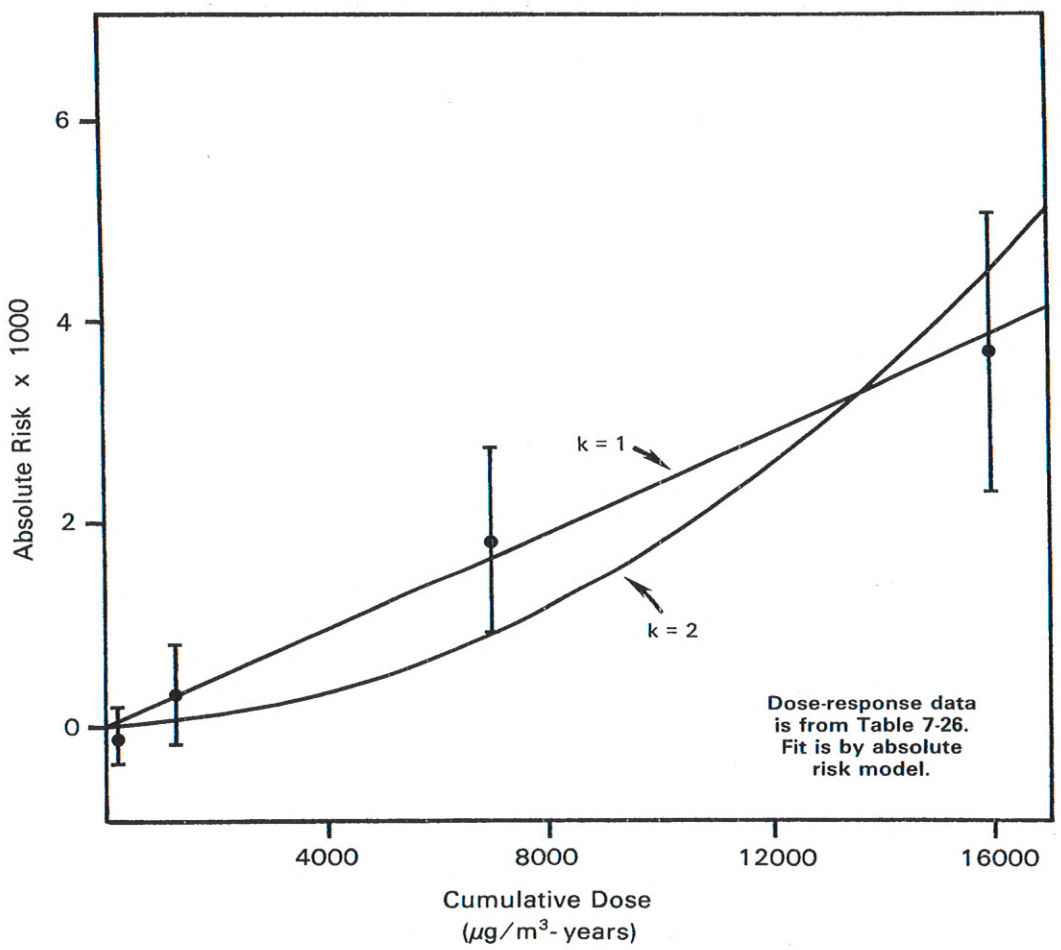

Figure 7-5. Absolute risks and 90% confidence limits for data of Higgins (1982).

The figure highlights EPA's scientific bases for risk assessment using the IUR for arsenic. The dose is cumulative. The exposure is assumed to occur over years. The IUR provides a measure of risk per unit exposure over a lifetime, assumed to be 70 years.

All IURs are based on an incremental lifetime risk of 1 in one million from exposure to 1 µg/m^3 of a substance continuously, every day over a lifetime of exposure (assumed to be 70 years). Importantly, this is an incremental risk considering unrelated risks present over a lifetime.[1]

VI. SUPPORT FOR OPINIONS INCLUDED IN DECLARATION

A. DEQ interpreted and applied the Air Rules to the SGP consistent with EPA's risk assessment methodology including accepted scientific principles governing toxicity values, exposure evaluations, and cancer risk.

DEQ adopted the EPA's values for assessment of risk in the TAPs rules. Correspondingly, DEQ adopted EPA's risk assessment methodology and underlying scientific principles governing those adopted values and risks. To interpret the Air Rules any other way would be to defy the science, toxicology, and application of these values established by EPA.

IDAPA 586 explicitly includes both a Unit Risk Factor (URF) and an Acceptable Ambient Concentration for Carcinogens (AACC) for each listed compound, including arsenic. Neither the URF (4.3E-03/µg/m^3) nor the AACC (2.3E-04 µg/m^3) for arsenic were developed by DEQ. EPA developed these values and published them in the IRIS (EPA 2024b), which is a database maintained by EPA (and only EPA). DEQ adopted these values into the TAPs Rules in 1993-1994. (Idaho DEQ 1992, Appendix 6; Idaho DEQ 1993)

DEQ adopted the URF directly from EPA's IUR, and the URF reflects the *cancer risk* based on continuous exposure to a concentration of 1 µg/m^3 of a particular compound over a lifetime. (Idaho DEQ 1992, Appendix 6; Idaho DEQ 1993). Separately, the AACC reflects that *ambient concentration* that would result in a 1 in 1 million risk of developing cancer assuming a constant exposure to that ambient concentration over a 70-year lifetime.

As noted above, the IUR represents the incremental increased cancer risk from a lifetime (70 years) inhalation exposure to a constant (24 hours/ day and 365 days/ year) dose concentration of 1 µg/m^3. In other words, the exposure duration is assumed within the IUR and the cancer risk assumes constant, lifetime (70 years) exposure. Because the IUR estimates cancer risk based on continuous

[1] The National Institute of Health (Cancer Statistics - NCI) states that approximately 40.5% of men and women in the US will be diagnosed with cancer at some point during their lifetimes (based on 2017–2019 data); that is roughly a risk of 4 persons in every 10 persons developing cancer over a lifetime. Risks of 1 in one million or one in 1 hundred thousand are very low. To put that risk in perspective, the National Oceanic and Atmospheric Association estimates that the chances of getting struck by lightning is much higher—1 in 15,300 in a lifetime (How Dangerous is Lightning? (weather.gov)

exposure to 1 µg/m^3 of a chemical over a lifetime (70 years), the IUR does not represent the lifetime risk of developing cancer after a single exposure.[2]

The URF in IDAPA 586 and the EPA IUR for arsenic are presented in Figure 1. EPA considers a lifetime to be 70 years. EPA recognizes that exposure duration is not always this long.

The AACC for each chemical is based on and derived from the EPA URF and a lifetime (70 years) exposure duration. The AACC is the identified risk divided by the URF. The AACC reflects the ambient concentration of arsenic to which a person could be exposed 24 hours a day, 365 days a year, for a 70-year lifetime before the identified cancer risk level is exceeded. The AACC value appears in EPA's IRIS database. EPA calls this value the "Air Concentration at Specific Risk Levels," and these levels assume a lifetime of 70 years and a constant exposure for 70 years.

Figure 1 illustrates: (A) risk level: (B) how the AACC is derived, (C) the AACC concentration, and (D) the ambient air concentration of arsenic that an individual would need to be exposed to for a full year to equal a full lifetime (70-year) exposure at a cancer risk expressed in the AACC (1 in 1,000,000).

Figure 2:
Inhalation Unit Risk — 4.3E-3 per (µg/m^3)
Extrapolation Method —absolute-risk linear model

A	B	C	D
Risk Level	**How AACC is derived *(risk level /URF)***	**AACC Concentration *(risk level/URF)***	**Annual Air Concentration equating to a 70-year constant exposure**
E-4 (1 in 10,000)	0.0001 / 4.3E-3	2.3E-2 µg/m^3	1.6 µg/m^3 (0.023 x 70 years)
E-5 (1 in 100,000)	0.00001 / 4.3E-3	2.3E-3 µg/m^3	0.16 µg/m^3 (0.0023 x 70 years)
E-6 (1 in 1,000,000)	0.000001 /4.3E-3	2.3E-4 µg/m^3	0.016 µg/m^3 (0.00023 x 70 years)

Source: Arsenic IUR from EPA [*Integrated Risk Information System (*Arsenic, inorganic (CASRN 7440-38-2) | IRIS | US EPA*), modified by adding Column B to illustrate how the AACC is derived and Column D showing the Annual Air Concentration equating to a 70-year constant exposure.]*

As illustrated, the risk in Column A may manifest when the annual air concentration shown in Column D is emitted 24 hours per day, 7 days per week, for 365 days in one year. One year of constant exposure at the levels in Column D is to equal the constant exposure of the AACC concentration in Column C, over 70 years.

DEQ applied the TAPs rules to the SGP consistent with EPA's risk assessment methodology including accepted scientific principles governing toxicity values, exposure evaluations, and cancer risk. The

[2] EPA IRIS defines Inhalation Unit Risk (called URF in the IDAPA 586 table) as: Inhalation unit risk (IUR) is an estimate of the increased cancer risk from inhalation exposure to a concentration of 1 µg/m^3 for a lifetime. The IUR can be multiplied by an estimate of lifetime exposure (in µg/m^3) to estimate the lifetime cancer risk.

worst case SGP annual air concentration is 0.00414 µg/m^3 (page 305 of 506 in the SOB dated 6/17/2022) and is significantly lower than the annual air concentrations in Column D. This means that if arsenic were emitted from SGP at the worst-case level (0.00414 µg/m^3) constantly for a single year, the dose would not equal the dose of the AACC level (Column C) over 70 years. The Board's concern that SGP could emit the equivalent of 70-year emissions in one year is not possible. I confirmed this conclusion applying EPA methods and common toxicology analyses.

DEQ also applied the TAPs rules to the SGP consistent with the agency's principles reflected in Idaho DEQ 1992 that explained the bases for the Board's adoption of the TAPs rules. The statements explain that EPA risk assessment methodology formed the foundation of the TAPs rules.[3] Specifically, the document directs use of refined modeling, consistent with guidance documents from EPA at the time, updated guidance on the use of URFs, and adjustments for exposure duration in the assessment of risk.

The statements explain the basis of the Board's adoption of the TAPS rules are consistent with DEQ's calculation of an exposure concentration, indicate that the AACCs are screening levels, allow for refined modeling as needed, and reference EPA as the source of URFs (and the AACCs) with the indication that their use should be consistent with EPA risk assessment guidance. The 1992 Meeting Packet refers to the AACCs (as well as all other TAPs values) as "screening levels." Specifically:

> The DEQ list of regulated air toxics is quite large in scope. However, this was not done to burden industry. Quite the contrary. It was done in order, to the maximum extent possible, provide industry with a ready reference to acceptable screening levels of these various compounds. This enables new sources to review their processes and see if controls, may be needed early on in the planning process, there by maximizing start up budget planning. In addition, it allows existing sources to review their emissions and see how they compare to the screening levels that DEQ considers reasonably protective of human health and the environment.

Appendix 6 describes that the exposure must be 24 hours/day for 70 years to interpret the risk associated with a URF or AACC properly. The appendix describes that the URFs in IDAPA 586 are the same as EPA's IURs, noting that the URF is the probability of developing excess cancers over a 70-year lifetime exposure to 1 µg/m^3 of a carcinogen expressed in terms of a screening emission level or an acceptable ambient concentration for a carcinogenic TAP. (Idaho DEQ 1992, Appendix 6).

Appendix 7 describes that URFs are applied to determine the risk to off-site receptors and that refined modeling is used to evaluate the risks. According to DEQ's statements in Appendix 7, refined modeling can include adjusting model parameters such as emission, topography, meteorology, or receptors. (Idaho DEQ 1992, Appendix 7).

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[3] This packet was first introduced in this proceeding when the Idaho Conservation League (ICL) submitted a declaration that included reference to a 1992 document titled "Meeting Packet: Idaho Department of Environmental Quality, Monday July 13, 1992" (Idaho DEQ 1992).

These adjustments are made in compliance with IDAPA 210.02 as described in a relevant rulemaking document (Idaho DEQ 1993, Comment 108, page 30).

DEQ's approach to implementing the TAP rules is rooted in rulemaking documents that express its intentions and authority to follow well established risk assessment methodologies adopted by EPA.

B. Based on methods consistent with EPA and DEQ policies and methodologies, DEQ appropriately adjusted the exposure duration to 16 years (16/70) consistent with conditions in the PTC limiting project life because this adjustment was necessary for a scientifically defensible "apples to apples" comparison with the AACC.

The values set forth in IDAPA 586 and applied by DEQ are based on EPA toxicological determinations and derived from EPA's IRIS database. DEQ's application of the AACCs to comply with the Air Rules conforms to EPA guidance for evaluating risk, including accounting for the appropriate exposure duration. As detailed in this section, DEQ appropriately conducted its analysis following EPA methodology by comparing modeled concentrations from the SGP to the arsenic AACC.

One of the critical considerations in evaluating risk is exposure duration. EPA's definition for IUR reads (emphasis added):

> Inhalation unit risk (IUR) is an estimate of the increased cancer risk from inhalation exposure to a concentration of 1 µg/m^3 for a lifetime. The IUR can be multiplied by an estimate of lifetime exposure (in µg/m^3) to estimate the lifetime cancer risk.[4]

The AACCs set forth in IDAPA 586 assume an estimate of lifetime cancer risk based on 70 years of constant exposure and a 70-year lifetime. The assumed exposure is 24 hours /day and 365 days /year for 70 years. In other words, at a specific risk level, say 1 in 1,000,000, a person can be exposed to the AACC level (0.00023 µg/m^3) of arsenic every day, 24 hours/day, for 70 years and will have a 1 in 1,000,000 risk of developing cancer. A project that is permitted to operate for 70 years or more would properly assume a 70-year lifetime exposure when comparing modeled concentrations against the AACC.

If 70 years is not the exposure duration, then adjustments to the exposure duration are necessary to appropriately evaluate the cancer risk, as directed by EPA and as intended by the Air Rules (Idaho DEQ 1993, Comment 108, p.30)[5]. For a project like SGP with a 16-year project life, the analysis is adjusted to reflect the actual exposure duration for an "apples to apples" comparison with the AACC.

In this case, the AACC (0.00023 µg/m^3) is based on an assumed 70-year exposure. The SGP exposure duration is shorter (16 years), so the cancer risk cannot be determined accurately by comparing the modeled exposure concentration (0.00414 µg/m^3) to the AACC. Comparing those emissions to the AACC would result in an over-estimation of cancer risk because the dose will not continue for the 70-year lifetime exposure assumed in the development of the AACC. For an "apples to apples" comparison, evaluation of SGP emissions must take into account the shorter exposure duration.

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[4] https://www.epa.gov/iris/basic-information-about-integrated-risk-information-system

[5] IDHW believes that the revised [IDAPA] Section 210. 02 Quantification of Emissions Rates and Ambient Concentrations, which allows site specific data gives adequate flexibility in compliance with toxic standards.

EPA guidance provides methodologies to assess risk, taking into consideration the exposure to an air concentration based on a formula for "air concentration adjusted for exposure." EPA guidance reflects this approach through a calculation methodology called the "adjusted air concentration" ($\mathbf{C}_{air\text{-}adj}$), which considers "the timeframe over which inhalation exposure occurs." (EPA 2009, EPA 2024a) (Exposure Assessment Tools by Routes - Inhalation | US EPA).

According to EPA, and as undertaken by DEQ, the exposure concentration must be adjusted for exposure duration to accurately reflect the exposure, associated dose, and resultant risk of cancer response. This adjustment allows for a correct ("apples to apples") comparison of exposure concentration to the AACC. This adjustment allows DEQ to evaluate whether the risk from actual exposure over the life of the project is acceptable under EPA methods and the AACCs.

DEQ followed this EPA methodology to assess the risk of arsenic emissions from the SGP.[6] The approach taken by DEQ for the SGP is set forth below (shaded notes are presented by author clarification):

$$\mathbf{Cair\text{-}adj = Cair \times ET \times 1day/24\ hours \times EF \times ED/AT}$$

Where:

$\mathbf{C}_{air\text{-}adj}$ = Air Concentration adjusted for exposure
$\mathbf{C}_{air}$ = Concentration of contaminant in air (mg/m^3) (this is the modeled or measured annual air concentration)
ET = Exposure time (hours/day) (this is assumed to be 24 hours/day)
EF = Exposure frequency (days/year) (this is assumed to be 365 days/year)
ED = Exposure duration (years) (this is 16 years – the life of operations)
AT = Averaging time (days) (this is lifetime – 70 years x 365 days/year; it never changes for any carcinogen)

EPA specifies that the first variable, concentration in air ($\mathbf{C}_{air}$) is either a measured or modeled value based on an annual average concentration. *For the SGP, DEQ used the highest modelled concentration after considering 14 different scenarios (0.00414 $\mu g/m^3$)*[7]

The temporal parameters in the equation include the following:

- Exposure time (**ET**) and exposure frequency (**EF**), which refer to the frequency with which the exposure occurs and might be provided in hours per day and days per year, respectively. *For the SGP DEQ used 24 hours/day for ET and 365 days/year for EF for the SGP review.*

[6] EPA established three calculations to assess risk properly. For completeness the additional EPA calculation methods for are presented in Attachment B.
[7] See Kevin Lewis Declaration

- Exposure duration (**ED**) is the amount of time that an individual or population is exposed to the contaminant being evaluated and is typically given in years. *For the SGP, DEQ used the 16-year life of mine ED reflected in enforceable PTC conditions.*
- Averaging time (**AT**) is the amount of time over which exposure is averaged and is equal to ED for assessing non-cancer risks. For chronic assessments (e.g., cancer), potential lifetime average daily dose (LADD) is calculated in which lifetime (LT, in days) is substituted for AT. *For the SGP, DEQ used 70 years, the default value, for the SGP review.*

Inclusion of a project-specific exposure duration in the calculation of the exposure concentration is essential for an accurate assessment of potential risks and for an appropriate comparison to the AACC to determine compliance with the Air Rules.

Using the highest modelled annual average arsenic concentration from the project of 0.00414 µg/m^3 (page 305 of 506 in the SOB dated 6/17/2022)[8] the calculation of the air concentration adjusted for exposure from the SGP is as follows:

$C_{air\text{-}adj}$ (Air Concentration adjusted for exposure) =

$$[\ C_{air}\ x\ ET\ x\ {}^{1}/_{24}\ x\ EF\ x\ ED\ ]\ /\ [\ AT\ ]\ =\ C_{air-adj}$$

$$\left[0.00414\,\frac{\mu g}{m3}\,x\,24\,\frac{hours}{day}\,x\,\frac{1\ day}{24\ hours}\,x\,365\,\frac{days}{year}\,x\,16\ years\right]\ /\ \left[365\,\frac{days}{year}\,x\,70\ years\right]\ =\ 0.00095\,\frac{\mu g}{m3}$$

In this analysis, the numerator (ET x EF x ED = 24 hours/day x 1 day/24 hours x 365 days/year x 16 years) reflects the exposure duration and the denominator of the equation (AT = 365 days/year x 70 years) reflects the 70-year averaging time for carcinogens. The resulting arsenic air concentration from the SGP adjusted for exposure risk review is 0.00095 µg/ m^3.

This approach follows the underlying rulemaking documents, including the authority noted in IDAPA 210.02. (Idaho DEQ 1993, Comment 108, p.30). DEQ appropriately adjusted the SGP evaluation to use 16 years (the actual exposure duration) because there can be no exposure to emissions beyond the life of mine. DEQ evaluated the highest annual air concentration modelled to determine the risk of a maximum 16-year exposure over a 70-year lifetime (modelled concentration x Exposure Duration (16 years)/70-year lifetime x URF. DEQ's approach followed EPA scientific principles, accepted risk assessment method, and foundational DEQ rulemaking documents.

C. The highest air concentration projections modelled for arsenic emissions from SGP are below the acceptable lifetime risk established by the T-RACT AACC listed in IDAPA 210.12 and 586, and therefore the risk from the SGP as permitted is protective of human health and the environment.

The calculated air concentration adjusted for exposure is 0.00095 µg/ m^3 -- this is the proper project-specific arsenic concentration to compare to the T-RACT AACC of 0.0023 µg/ m^3 for a cancer risk of 1:100,000 (see page 305 of 506 of the 6/17/2022 SOB).

This method is reflected in the permitting reviews to determine that the arsenic emissions risk was acceptable. Comparison to the T-RACT AACC is as follows:

[8] See Kevin Lewis declaration

$$\frac{1}{100{,}000} T\text{–}RACT\ Risk\ x\ 0.00095 \frac{\mu g}{m3} C_{air-adj} \ /\ 0.0023 \frac{\mu g}{m3}\ T\text{–}RACT\ AACC =$$

$$= 4.1E\text{–}6\ or\ \frac{1}{240{,}000} Actual\ Risk$$

This acceptable method provides an "apples to apples" comparison of SGP arsenic air concentrations to the AACC adjusted for T-RACT. This is the mathematical equivalent of 16-year emission rate of arsenic, plus 54 years of zero arsenic emissions, divided by 70 years to produce an annual exposure concentration that can be compared to the AACC.

DEQ's use of EPA toxicity values and risk assessment methodology in evaluating emissions from the SGP is consistent with IDAPA 586 because the same EPA toxicity values and risk assessment methodology formed the basis of the AACCs.

D. IDAPA 210.15 allows for a 10-times adjustment to the AACC when a project will operate for 5 years or less and is an example of DEQ's use of EPA's methods to achieve "apples to apples" analyses to compare with the AACC values.

IDAPA 210.15 provides that "[f]or short term sources, the applicant may utilize a short-term adjustment factor of ten (10). For a carcinogen, multiply either the applicable acceptable ambient concentration (AACC) or the screening emission rate, but not both, by ten (10), to demonstrate preconsturction compliance."

The *Final Order* held that the Air Rules do not explicitly authorize an adjustment for sources that will operate for more than 5, but less than 70 years. *Final Order* at 21. The Air Rules and IDAPA 210.15 should not be read to impede adjustment for exposure duration when a project will operate for less than 70 years. (Idaho DEQ 1993, Comment 108, p.30). An exposure duration is necessary and proper from a scientific and toxicological standpoint to apply the AACCs accurately. Omitting this adjustment is contrary to common scientific practice and the intent of the Air Rules as reflect DEQ documents (Idaho DEQ 1992 and Idaho DEQ 1993). Specifically the refernce from Petitioners reads:

> For short term sources (usually less than five years in duration), such as remediation projects, a probability of greater than one in a million risk (over 70 years) will generally be acceptable to account for the decreased term of exposure. It is not acceptable however, for exposed individuals to receive a full 70 year exposure during the life of a short term project. (Idaho DEQ 1992).

Unpacking this content may be helpful. First, the accepted scientific approach to determine risk is to calculate a lifetime average daily dose that includes the air concentration for the duration of exposure. In other words, to compare "apples to apples" an evaluator must adjust the default exposure duration (70 years) to the actual of exposure duration (16 years for SGP) then divide by 70 years to account for a lifetime-based URF. This is the proper method to determine "a probability of greater than one in a million risk (over 70 years)" as described.

Next, to expose individuals to "a full 70-year exposure" means that the AACC value is multiplied by 70 to derive the full exposure. See Figure 1 above. For arsenic emissions, the calculations follow:

- At a risk of 1E-6, using the AACC of 0.00023 µg/m^3 arsenic air concentration
  - 0.00023 µg/m^3 x 70 years = 0.016 µg/m^3
  - Exposure to 0.016 µg/m^3 air concentration every day for one year would expose an individual to the full 70-year exposure in one year.
- At a risk of 1E-5, using the T-RACT AACC of 0.0023 µg/m^3 air concentration
  - 0.0023 µg/m^3 x 70 years = 0.16 µg/m^3
  - Exposure to 0.16 µg/m^3 air concentration every day for one year would expose an individual to the full 70- year exposure in one year.

The AACC is not a one-year exposure limit and such an interpretation ignores both the definition of the URF and the definition of the AACC.

E. Idaho's AACCs are not annual average air concentration limits or standards.

The AACCs are distinct from annual average air concentrations and are not limits or standards. (Idaho DEQ 1993, Comment 31, page 10; Comment 111, page 32). One is an apple, the other an orange. The reference to an annual average concentration represents the longest period for which air concentrations are projected by air emission models, specifically AERMOD. Models only project concentration estimates over certain time periods of prediction (hourly, daily, monthly) within one year or over an annual duration. Models do not address exposure duration.[9]

The AACCs (derived from EPA's URFs) reflect exposure duration (i.e., 70-year lifetime) and present an acceptable constant dose of a contaminant over a known averaging time (70 years is the default averaging time for carcinogens). The AACC is the concentration that a person may be exposed to for a lifetime continuously, with an incremental risk of cancer of 1 in 1,000,000. The T-RACT AACC is the concentration that a person may be exposed to for a lifetime continuously, with an incremental increased risk of cancer of 1 in 100,000. The AACCs are not one-year limits. Compliance with IDAPA 586 is not based on comparing annual air concentrations from the model to an AACC. (Idaho DEQ 1993, Comment 111, page 32).[10]

Comparing an annual average concentration from a model to the AACC is not a risk evaluation and does not demonstrate acceptable risk. Nor is the annual average concentration predicted from modeling the same as an exposure concentration.[11]

DEQ understood and applied these distinct parameters properly in the PTC reviews for the SGP. For the SGP PTC, DEQ reviewed maximum daily emissions under 14 modeling scenarios that were each modeled for 365 days/year to produce an annual average arsenic concentration for each of the 14 scenarios. DEQ then used the highest annual average concentration—0.00414 µg/m^3—to conduct its risk evaluation calculations following EPA and DEQ guidance referred to above to compare to the AACC. This conservative approach assumed that the highest annual concentration modelled is

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[9] See Kevin Lewis Declaration

[10] In the design of this rule, the AAC relates to a stack emission rate. In the most prescribed sense, the AAC would be assured by a permit ted emission limit. This emission limit then might be guaranteed by some ample control technology design or perhaps an operational limit prescribed in the permit.

[11] See Kevin Lewis Declaration

emitted for all the years of operation at SGP. To demonstrate compliance with the arsenic AACC, DEQ adjusted the exposure duration as directed by EPA (methodology explained above) and the DEQ guidance referred to above. Based on the modeling and scientific risk evaluation methods, DEQ concluded that the maximum arsenic emissions from SGP would cause an increased cancer risk of less than 1 in 100,000. This use of the annual average concentration in DEQ's AACC risk evaluation followed appropriate scientific methods.

Treating the AACC as an annual emission limitation or annual limit on ambient exposure concentration would result in significantly lower acceptable risk from TAPS emissions than envisioned by the Air Rules. If the T-RACT AACC of 0.0023 $\mu g/m^3$ were based on a one-year exposure, then the risk represented by that value would be about 1 in 7,000,000. Using the EPA guidance for URFs, and assuming continuous exposure to the T-RACT AACC concentration for an exposure duration of 1 year, the $CA_{air\text{-}adj}$ is:

0.0023 $\mu g/m^3$ x 24 hrs/day x 365 days/yr x 1 yr / (70 yrs x 365 days/yr x 24 hrs/day) = 0.000033 $\mu g/m^3$

And the associated risk of developing cancer over a 70-year lifetime is:

0.0043 ($\mu g/m^3$) x 0.000033 $\mu g/m^3$ = 1.4 E-7 (about 1 in 7,000,000)

The AACC (and the URF it is based on) represent the upper-bound excess lifetime cancer risk estimated to result from continuous exposure to a contaminant over a lifetime at an air concentration of 1 $\mu g/m^3$. In other words, the AACC and T-RACT AACC represent the risk to an individual if exposed all day, every day for a lifetime to a concentration of 1 $\mu g/m^3$. The AACC and T-RACT AACC do not represent the risk of a cancer response following a single exposure. The latter interpretation defies fundamental toxicological science used by the EPA in the development of IURs (URFs).

F. The 5-year rolling average production limit will ensure that the ambient arsenic concentration caused by the SGP does not cause unacceptable cancer risk.

The *Final Order* expresses concern that the use of a 5-year rolling average production limit will allow for smoothing out of peak ambient concentrations of ambient arsenic and may not be equally protective of ambient air as the AACC limits set forth in IDAPA 586.

First, the AACC is not a limit based on my reading of the relevant documents cited in this memorandum, in particular Idaho DEQ 1992 and Idaho DEQ 1993. Second, in my opinion, for purposes of evaluating cancer risk, use of a 5-year rolling average production limit is as protective as an annual production limit.

As described earlier in the report, risk assessment evaluates the probable response to a particular dose of a carcinogen over time. Risks increase from cumulative long-term exposure, not short-term annual emissions. Risks are assessed based on total cumulative dose, as demonstrated in Figure 1, column D. As shown in Figure 1, a total cumulative dose of 0.16 $\mu g/m^3$ of arsenic would cause an increased cancer risk of 1 in 100,000. However, whether this dose occurs in 1 year, 5 years, 16 years, or 70 years, the risk would not change.

The 5-year average production limit ensures that if production is above the limit in one year, then future production must be reduced below the limit. This ensures that the cumulative ambient arsenic concentration does not exceed the acceptable ambient concentration level for the defined risk. The 5-year average production limit in the PTC ensures that the ambient arsenic concentration from the SGP over the project life (exposure duration of 16 years) results in an acceptable cancer risk under the Air Rules.

VII. CONCLUSIONS

Based on my review of the modeled emissions from the SGP, the Air Rules, and EPA risk assessment methodology, and relevant explanatory documents, arsenic emissions from the SGP will result in an increased cancer risk of less than 1 in 100,000. DEQ appropriately applied a project specific adjustment factor to account for exposure duration, consistent with established EPA risk assessment methodology. The permit issued to SGP, including the five-year rolling average production limit, represents acceptable risk confirmed by methods that follow EPA's approaches for using URF, IUR values in risk assessments.

ATTACHMENT A
References

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Idaho DEQ 1993. Idaho Department of Health and Welfare, Responses to Comments and Questions Submitted During a Public Comment Period and Public Hearings on the Proposed Repeal and Reissuance of Rules for the Control of Air Pollution in Idaho.

Idaho DEQ 2021. Guideline for Performing Air Quality Impact Analyses. Stationary Source Program AQ Division. Idaho Department of Environmental Quality, July.

Idaho DEQ 2018. Risk Evaluation Manual for Petroleum Releases. August 2018.

EPA 1984. Health Assessment Document for Inorganic Arsenic. Final Report March 1984. EPA/600-8-83-021F. Office of Health and Environmental Assessment.

EPA 2009. Risk Assessment Guidance for Superfund Volume I: Human Health Evaluation Manual (Part F, Supplemental Guidance for Inhalation Risk Assessment). EPA-540-R-070-002 OSWER 9285.7-82. January.

EPA 2022. Conducting a Human Health Risk Assessment | US EPA. Last updated June 22, 2022.

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EPA 2024c. Regional Screening Levels, May 2024. Available at Regional Screening Levels (RSLs) - Generic Tables | US EPA.

ATSDR 2007. Agency for Toxic Substances and Disease Registry. Toxicological Profile for Arsenic. U.S. Department of Health and Human Services. Public Health Service.

National Cancer Institute. 2024. Cancer Statistics – NCI.

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ATTACHMENT B

For completeness the additional EPA calculation methods for are presented here.

Method 2: Calculate the risk associated with the air concentration

The second option for correct use of the URF in the evaluation of project risk is to forward-calculate a risk from the modelled concentrations and using the IUR (URF) as shown in the "Equation 6" from EPA 2009 (below).

The EPA screening levels, associated risk calculator and several guidance documents published by EPA rely on the unit risk factor (again, called IUR by EPA and called URF in the Air Rules). For arsenic, the IUR is 0.0043/(µg/m^3)(from EPA 2024b and shown in IDAPA 58.01.01.586 as the URF). Exposure for inhalation is determined by the following equation for carcinogenic chemicals (EPA 2009), which necessarily relies upon an exposure time, frequency and duration to estimate dose. Exposure concentration (EC) is the parameter that is to be evaluated by use of the URF; Concentration in Air (CA) is the estimated contaminant concentration that is predicted by the model. The exposure concentration is the equivalent to the adjusted air concentration described in Method 1.

From EPA 2009, Risk Assessment Guidance for Superfund, Part F. Page 14

EC = (CA x ET x EF x ED)/AT **(Equation 6)**

Where:
EC (µg/m^3) = exposure concentration;
CA (µg/m^3) = contaminant concentration in air;
ET (hours/day) = exposure time;
EF (days/year) = exposure frequency; ED
(years) = exposure duration; and
AT (lifetime in years x 365 days/year x 24 hours/day) = averaging time

The EC is then multiplied by the URF to calculate incremental lifetime risk.

Using the SGP highest modeled air concentration for arsenic of 0.00414 µg/m^3:

Exposure Concentration (µg/ m^3) =

[CA x ET x EF x ED] / [AT] = EC

$$\left[0.00414\,\frac{\mu g}{m3}\,x\,24\,\frac{hours}{day}\,x\,365\,\frac{days}{year}\,x\,16\,years\right] / \left[70\,years\,x\,365\,\frac{days}{year}\,x\,24\,\frac{hours}{day}\right] = 0.0095\,\frac{\mu g}{m3}$$

Then, the Exposure Concentration (EC) x IUR (or URF) estimates the risk:

$$0.00095\,\frac{\mu g}{m3}\,EC\;x\;0.0043\left(\frac{\mu g}{m3}\right)^{-1}\,IUR = 4.1E{-}6\;or\;\frac{1}{240{,}000}\,Risk$$

Method 3: Adjust the AACC to reflect the Project Duration

The same calculation can be re-arranged to estimate a screening concentration in air, as shown in Table 4 from EPA 2009 (below).

TABLE 4

RECOMMENDED PROCEDURE FOR CALCULATING RISK-BASED SCREENING CONCENTRATIONS FOR CONTAMINANTS IN AIR

	Cancer Risk-Based	Hazard-Based[1]
Step 1: Select Target Levels	Select target cancer risk (e.g., 1 x 10^{-6}).	Select target HQ (e.g., 1).
Step 2: Identify Toxicity Value[2]	Identify inhalation cancer potency value (e.g., IUR). If none exists, proceed with hazard-based screening level calculation.	Identify inhalation reference value (e.g., RfC) to match exposure scenario (acute, subchronic, or chronic). If none exist, proceed with cancer screening level calculation.
Step 3: Calculate CA	Using target cancer risk from Step 1 along with the receptor- and scenario-specific exposure parameter values, calculate CA; the following equation is recommended: CA = (AT x Target Risk)/(IUR x ET x EF x ED)	Using target HQ from Step 1 along with the receptor- and scenario-specific exposure parameter values, calculate CA; the following equation is recommended: CA = (AT x Target HQ x RfC x 1000 µg/mg)/(ET x EF x ED)
Step 4: Select Screening Concentration	Select minimum of predicted cancer risk- and hazard-based values as screening concentrations.[3] Repeat for each receptor/scenario combination of interest.	

[1] Hazard-based screening concentrations are typically derived from reference values such as RfCs. These values may be available for non-cancer effects but may include cancer, if a nonlinear MOA is thought to operate for a chemical. [2] If no inhalation toxicity value is available for a chemical, contact STSC for further direction on how to proceed.

[3] Screening levels estimated from the equations presented in Step 3 could yield concentrations that exceed the maximum possible vapor concentration for a chemical. In such cases, it may be useful to calculate the maximum possible vapor concentration of the pure contaminant at the temperature of interest, using the following formula: C_{max} = S x H x 10^3 L/m^3, where S = solubility at 25° C (or temperature of interest) and H (unitless) = Henry's Law Constant at 25° C (or temperature of interest). This equation is based on an established relationship (see, for example, Schwartzenbach et al. 1993), that allows the Henry's Law Constant to be estimated as the ratio of a compound's vapor pressure and aqueous solubility for compounds that are slightly to moderately soluble in water. When the dimensionless Henry's Law constant, H, is used, the relationship described above can be used to calculate the vapor concentration of a saturated solution of a given compound, assuming equilibrium between the vapor and aqueous phases.

Note: MOA = Mode of Action, which refers to the way in which a chemical exerts a health effect.

In Step 3 of this table AT is averaging time as described in "Equation 6" from EPA 2009 or 70 years x 365 days for carcinogens (note - for noncarcinogens only, AT is equal to the Exposure Duration) (source: EPA RSLs 2024c, EPA Risk Assessment Guidance for Superfund 2009).

As shown in Step 3 the third option for assessing risk is to adjust the screening value (here, the AACC) to reflect the project-specific exposure duration. The default exposure duration assumed in the AACC is 70 years. The AACC values represent a concentration in air (CA) for a 24 hour/day, 365 day/year, and for 70-years of exposure (using both a lifetime exposure duration and lifetime for averaging time). At a T-RACT risk of 1:100,000 the calculation of the T-RACT AACC is as follows, using the equation in Step 3 of EPA guidance (2009):

$$[\ AT\ x\ \text{Target Risk}] / \left[\ \text{IUR}\ x\ \text{ET}\ \left(\frac{\text{hours}}{\text{day}}\right) x\ {}^{1\ day}/_{24\ hours}\ x\ \text{EF}\ x\ \text{ED}\ \right] = CA$$

$$specifically$$

$$\left[70\ years\ x\ 365\ \frac{days}{year}\ x\ {}^{1}/_{100{,}000}\right] / \left[4.3E{-}3/\frac{\mu g}{m3}\ x\ 24\ \frac{hours}{day}\ x\ \frac{1\ day}{24\ hours}\ x\ 365\ \frac{days}{year}\ x\ 70\ years\right] =$$

$$= 0.0023\ \frac{\mu g}{m3}\ Screening\ concentration, CA_{70-year\ ED}$$

The adjustment used by DEQ for the exposure duration reflects the 16-year life of the mine (i.e., there can be no operations related exposure after operations cease). Accordingly, the appropriate AACC for this project is:

$$[\ AT\ x\ \text{Target Risk}] / \left[\ \text{IUR}\ x\ \text{ET}\ x\ {}^{1\ day}/_{24\ hours}\ x\ \text{EF}\ x\ \text{ED}\ \right] = CA$$

specifically,

$$\left[70\ years\ x\ 365\ \frac{days}{year}\ x\ {}^{1}/_{100{,}000}\right] / \left[4.3E{-}3/\frac{\mu g}{m3}\ x\ 24\ \frac{hours}{day}\ x\ \frac{1\ day}{24\ hours}\ x\ 365\ \frac{days}{year}\ x\ 16\ years\right] =$$

$$= 0.0102\ \frac{\mu g}{m3}\ Screening\ concentration, CA_{16-year\ ED}$$

The adjusted AACC of 0.0102 µg/m^3 is used to compare the highest annual average concentration from the modeling without further adjustment to determine the risk. In this case it would be:

$$\frac{1}{100{,}000}\ Target\ Risk\ x\ 0.00414\ \frac{\mu g}{m3}\ C_{air}\ /\ 0.0102\ \frac{\mu g}{m3}\ CA_{16-year\ ED} =$$

$$= 4.1E{-}6\ or\ \frac{1}{240{,}000}\ Actual\ Risk$$

Using Method 1 (presented in the memorandum) or Method 2 or 3 presented here, the same estimate of lifetime risk is obtained, which for this project is 4.1E-6.

ATTACHMENT C

TETRA TECH

Theresa K. Lopez, MSPH
Principal Toxicologist

EXPERIENCE SUMMARY

Ms. Lopez has worked extensively in public health, epidemiology, human health risk assessment, toxicology, and occupational health and safety, representing both the public and private sector for over 30 years. She has been a task manager for a variety of human health risk assessment projects, including developing a disease burden reduction model for the optimized placement of infrastructure. She has led investigation and assessment of chemical releases and environmentally compromised sites such as former nuclear weapons plants, active and closing naval bases, and mining, commercial, and school sites. Ms. Lopez has worked extensively for federal, State, Provincial, and private clients. Her work includes assisting in remediation of former mining sites in the United States (US) and Canada with heavy metal, pesticides, TPH and other chemicals of concern; and risk assessments for proposed mines, hazardous waste release sites, and TPH remediation in the US and Canada. She has prepared human exposure assessments for schools and recreational settings, and assessed clean-up goals and remediation strategies for closed industrial, mining, redevelopment, and other sites. These sites often include the consideration of native and indigenous peoples.

In addition, she has provided exposure and dose reconstruction for Oak Ridge Associated Universities to quantify radiation doses to former nuclear weapons workers. She provided the exposure assessment information and mathematical evaluation for the development of a computer-based mouthing exposure tool for Health Canada which involved comparative evaluation of equations selected from a variety of countries and multi-national interest groups (including Japan, European Chemicals Agency, US, and UK). Currently, Ms. Lopez is performing the human health risk assessments involving both radionuclide and chemical impacts, modeling of indirect exposure pathways, TPH evaluations, and exposure assessments for private clients and US and international regulatory agencies, as well as providing scientific peer reviews and authoring reports for Health Canada related to the Existing Substances Risk Assessment Bureau mandates.

EMPLOYMENT HISTORY

Tetra Tech, Inc., Senior Toxicologist, 1997–present

PRC Environmental Management (NKA Tetra Tech EMI), Senior Toxicologist/Toxicology Group Leader, 1992–1997

University of Colorado Health Science Center, Student/Professional research Assistant, 1989-1992.

EDUCATION

MS, Public Health, University of Colorado, 1991

BS, Nutritional Science (Zoology minor), University of Florida, 1989

AREAS OF EXPERTISE

- Human Health Risk Assessment
- Chemical Risk Assessment
- Radiological Risk Assessment
- Regulatory toxicology
- Risk-based Remediation
- Public Health
- Epidemiology
- Guidance Development
- Exposure Assessments

TRAINING/CERTIFICATIONS

- Qualified Person, Site Assessment Chapter and Corrective Action Plan Chapter, Saskatchewan
- FEMA Emergency Response Training IS-00005.a, 230.d, and00029

PROFESSIONAL AFFILIATIONS

Society for Risk Analysis

Society for Environmental Toxicology and Chemistry

RELEVANT EXPERIENCE

Peer Review of Chemical Assessments, Consumer Product Safety Commission (2022-present). Program manager and lead toxicologist for peer review of chemical and nanomaterial risk assessments developed for and by the Consumer Product Safety Commission. Current project is the review of class-based assessment for organic flame retardants. The peer review will include response to charge questions as well as commentary on the approach and case study to evaluate scientifically defensibility, thoroughness, and accuracy.

Navajo EPA Ambient Water Quality Standards. **(8/2018 – present)**. Provided a review of existing ambient water standards and calculated health-based standards for the Navajo Nation based on human exposures, livestock exposures, plants, and food ingestion pathways. The report will be the basis of Navajo EPA water standards for surface water bodies and specifically the San Juan River within the Navajo Nation boundaries.

Technical Support Services, Agency for Toxic Substances and Disease Registry (ATSDR) (US-Nationwide). (12/2016-present). Managing a contract with ATSDR to provide ad-hoc scientific advice on a variety of public health assessment issues, including chemical toxicity, public health, environmental risk assessment and education and

outreach activities as needed. Projects to date have involved being a subject matter expert in public health assessments methodology, review of minimal risk levels and toxicity data used by ATSDR, and reviewing EPA databases (including the TRI) for potential uses in public health evaluation and outreach as well as providing technical support for ATSDR's soilSHOP outreach (a lead poisoning prevention program). The most current project involves measuring uptake of metals and PFAS from soil to common food plants.

Arizona Department of Environmental Quality. Phoenix AZ. (11/2019 – present). Providing toxicology and risk assessment review of reports submitted to ADEQ for approval under the Voluntary Cleanup Program, as well as conducting site-specific risk assessments for historic mining sites to facilitate remediation. Reviewing a variety of submitted reports for former industrial facilities and release sites throughout Arizona.

Toxicological Literature Reviews and Summaries, Health Canada. Ottawa, Ontario. (1/2015-present) Provided literature search and summary for various chemicals and exposures. A specific example include a literature review and data summary for 36 organic flame retardants and 45 salicylates. A literature search was conducted for each chemical in these two efforts, and summaries of material ranged from a few pages to over 120 pages per chemical depending on the amount of literature identified. Both carcinogenic and noncarcinogenic endpoints were included in the search, and endpoints included acute toxicity (single exposure), short-term toxicity (2 to 89 days), subchronic toxicity (90 days to 1 year), chronic toxicity (more than 90 days), carcinogenicity, reproductive and development toxicity, genotoxicity, endocrine effects, immune system, sensitization, and irritation. In addition, a data extraction project for ultrafine particles was also undertaken, reviewing health outcomes for human exposure to ultrafine particles in over 130 epidemiological papers.

Peer Review of Screening Assessment Reports (SARs), Health Canada. Ottawa Ontario. (1/2015 – present) Providing peer review of screening assessment reports for a variety of chemicals in consumer products for the Existing Substances Risk Assessment Bureau under the Chemicals Management Plan. Reviews include a literature search, review of identified literature, qualitative and quantitative exposure assessments, toxicity assessment, calculation of margins of exposure for each exposure pathway, and recommendations on the methodology used to assess the chemicals. Over 50 reviews have been conducted to date.

Peer Review of New Assessment Methodologies, State of the Science Reports, and Occupational Exposure Guidelines, Health Canada, Ottawa, Ontario (4/2017-present). Providing peer review of new assessment methodology reports (including *in silico* learning and transcriptomics), State of the Science (including PFAS compounds and Vitamin A) , and Occupational Exposure Guidelines (STOT RE for carbon black) for Health Canada under the Chemicals Management Plan and Hazardous Products Regulations.

Review of Proposed Drinking Water Guidelines, Health Canada, Ottawa, Ontario (8/2021- 12/ 2023). Providing peer review of six drinking water guidelines, focused on health-based standards and toxicological concerns, for several inorganic and organic chemicals under the Chemical Management Plan for the Water and Air Quality Bureau (WAQB). The reviews included verification of toxicological information, calculation of a guideline, and other technical issues relevant to water guideline development.

Exposure Assessment Studies, Health Canada, Ottawa, Ontario 4/2017-present). Provided peer review of exposure assessment reports, including internal backgrounders on body weight, drinking water intake rates, inhalation rates, and soil/dust intake rates, dermal surface area, and breast milk and formula intake. Collected literature and provided detailed reports for Health Canada on vapor recovery systems and air quality, chemical exposure in nail salon settings. Created and implemented consumer product surveys for hand sanitizer, automobile products, certain arts and crafts products, paint remover and essential oils. The hand sanitizer project was published while the paint remover and essential oil surveys are currently in progress. The automobile products and arts and craft product surveys remained internal to Health Canada but follow-up work may be planned.

UNICEF WASH Program, Pacific Island Countries. (4/2024-present). Assessed current disease burden rates for Solomon Islands including diarrheal disease and other water-related illness to determine economic benefits from placement of water and sanitation infrastructure improvements. The public health evaluation identified areas with potentially the highest rates of diarrheal disease and the reduction in disease burden that can be achieved by providing chlorinated water supplies and sanitation systems. The model that was created also can estimate disease reduction through reduced flooding and drainage improvements. A mathematical model was developed for this effort that included weighting factors to account for poverty and age, and different percentages for infrastructure improvements, to estimate disease and mortality reduction from the provision of disinfected water and sanitation infrastructure.

Relative Risk Ranking Model for Sanitary System Overflow Diversions, Metro Vancouver. (3/2024 – present). A model was developed for the relative risk to humans and ecological receptors from 5 options for based on options developed for consideration. This evaluation considered several inputs to evaluate potential risks to receptors from the overflow to conveyances, surface water, and eventually the bays surrounding Metro Vancouver. This is was not a quantitative risk assessment but rather a relative ranking of the risks associated with each option. Inputs to the model included overflow volume, distance to conveyance from overflow, distance to receiving body, dilution, chemical/bacterial measurements, and percent paved area surrounding conveyance. Special status ecological receptors in the areas of interest were identified, as well as human uses of the land and communities of special consideration. A ranked score was created for each option, under the broad categories of logistical, ecological risk, human health, and chemical inputs.

Public Health Assessment and Disease Burden Reduction, Millennial Challenge Corporation, Timor-Leste. (1/2020 - 9/2022). Assessed current disease burden rates for Dili, Timor Leste, including diarrheal disease and other water-related illness to determine areas that will achieve greatest disease burden reduction from proposed infrastructure improvements. The public health evaluation identified areas with potentially the highest rates of diarrheal disease and the reduction in disease burden that can be achieved by providing chlorinated water supplies, sanitation systems, and drainage improvements to reduce flooding. These improvements may be implemented individually or together, depending on the area. A mathematical model was developed for this effort that included weighting factors to account for poverty, age, and gender differences in the population.

Development of Biomonitoring Equivalents for Glyphosate and Ethylene Thiourea (1/2021-12/2023). In partnership with Summit Toxicology, gathered biomonitoring data, regulatory information, and adsorption, distribution, metabolism and excretion (ADME) data for these two pesticides. Data were used to develop biomonitoring equivalents and manuscripts have been developed documenting the results (one has been published and the other has been submitted).

City of Campbell River, British Columbia, Canada. (1/2023-present). Performing human health and ecological risk assessment for soil and groundwater with PFOS and PFOA impacts from firefighting training at an airport. Exposure pathways include drinking water, soil contact, and impacts to off-site freshwater bodies.

Human Health and Ecological Risk Assessment, Duck Lake, British Columbia. (4/2018-11/2018). Conducted a human health and ecological risk assessment of a former railway right-of-way using. The intent of the risk assessment was to document any potential risks associated with legacy polycyclic aromatic hydrocarbon residue from Site use as a railway, and the community plans to redevelop the right-of-way into a multi-use recreational trail. Site was submitted for closure and redevelopment in November 2018 based on the risk assessment findings.

Human Health and Ecological Risk Assessment, Aitchelitz, BC. (7/2021-7/2023). Conducting a human health and ecological risk assessment of a former industrial operations area. The intent of the risk assessment was to document any potential risks associated with current and legacy buried wastes and petroleum releases from the area, including any discharge of groundwater to the Aitchelitz Creek and use of groundwater as a drinking water source. As well, ecological effects in the Aitchelitz Creek were evaluated, particularly for endangered species.

Human Health and Ecological Risk Assessment, Kitsumkalum, BC. (3/2018 – 3/2019). Conducted a human health and ecological risk assessment of a former industrial and woodmill operations area. The intent of the risk assessment was to document any potential risks associated with legacy buried wood waste and petroleum releases from the area, including any discharge of groundwater to the Kitsumkalum River and use of groundwater as a drinking water source. The community planned to redevelop a portion of the Site for industrial re-use, while a portion was being considered for residential redevelopment. The Site was submitted for closure and redevelopment in March 2019 based on the risk assessment findings.

Human Health and Ecological Risk Assessment, Wei Wai Kum First Nation (WWK), Myra Fall Mine (MFM) and Indigenous Services Canada (ISC), Campbell River BC. (2021-2022). Providing human health and ecological risk assessment for Wei Wai Kum First Nations for this former port area located on Vancouver Island. Chemicals of potential concern include metals and PAHs, with a particular concern regarding marine life in the area and food chain exposures.

Evaluation of Human Toxicity Data for PFAS and PCBs to Determine Applicability to Marine Mammals, British Columbia Ministry of Environment and Climate Change (BMOECC). (9/2020-3/2021). Vancouver, British Columbia. Provided BCMOECC and federal agencies with a methodology and example of how data developed for the assessment of human toxicity could be extrapolated for use in protecting the endangered

Southern Resident Killer Whale population, as well as other marine mammals. Specific chemicals of interest were PCBs and PFAS.

San Juan River Risk Assessment, Utah Department of Environmental Quality. (2/2017 – 3/2018). Task leader for the human health and agricultural risk assessments of the San Juan River. Evaluating impacts of heavy metals (including arsenic) from the Gold King Mine release to residents, ranchers, farmers, and other users of the San Juan River water. Providing data evaluation including comparisons to background values, assessment of data from tributaries to the San Juan River, as well calculating exposure point concentrations. Providing assessment of current and future risks, including consideration of regulatory levels as well as site- and receptor-specific exposure parameters to fully evaluate potential long-term impacts of the release on receptors and the eventual deposition of impacted sediment in Lake Powell.

Exposure Assessment for Nanoform Cerium Oxide Silver, Titanium Dioxide and Zinc Oxide, National Industrial Chemicals Notification and Assessment Scheme, Australian Government Department of Health and Ageing. (11/2012 – 6/2013). Provided an exposure assessment of the public to nanoform cerium oxide, silver, titanium dioxide, and zinc oxide present in consumer products. Assessed both qualitative and quantitative measures of exposure, based on a range of nanomaterial content and use of consumer products. For each nanomaterial, provided current information on commercial uses, sources, synthesis methods, characterization, potential exposure routes, toxicokinetics, and environmental fate and transport, as well as addressing data gaps where information was not found. Developed exposure scenarios for each of the four nanomaterials, including exposure to workers, the public (consumers), and the environment, and provided estimates of exposure to the extent possible. Identified data gaps that introduced uncertainty into the estimates or prevented a quantitative estimate of exposure, including that the toxicity of nanomaterials may be related to the number of particles rather than mass of particles present, and that measures of exposure based on mass of material may therefore underestimate potential toxic effects.

Use of Biomonitoring Data and Biomonitoring Equivalents in Risk Assessment, Health Canada, Ottawa, Ontario. (1/2015-7/2015). Prepared a report for Health Canada regarding the current use and application of biomonitoring data and biomonitoring equivalents (BE) in regulatory settings as well as considerations for varying types of pharmacokinetic data used to interpret biomonitoring data for various matrices. Authored chapters defining BEs as the translation of screening exposure guidelines or criteria to chemical- and biological media-specific concentrations that can be used interpret biomonitoring results for specific chemicals in a health risk context. Provided an overview of its application in regulatory risk assessment as well as considerations for varying pharmacokinetic data in both animals and humans, and described international efforts in biomonitoring of several chemicals, including perfluorinated compounds, mercury, lead, 2,4-D, and phthalates. In addition, the report contains a discussion of how pharmacokinetic data can be used to interpret biomonitoring data for regulatory risk assessment of industrial chemicals under the Chemicals Management Plan.

Peer Review of Personal Care Products (PCP) Module III, Assessment of Exposures to Chemicals in Personal Care Products for the Hair. Health Canada, Ottawa, Ontario. (12/2014-4/2015). Provided a peer review for the Existing Substances Risk Assessment Bureau (ESRAB) - Healthy Environments and Consumer Safety Branch (HECSB) of the proposed Health Canada methodology for assessing consumer exposure to chemicals in hair care products, including an evaluation of recommended default exposure parameters for all receptors and a literature review to determine if additional applicable data were available for use in the effort.

Peer Review of OECD Documents, Health Canada Risk Assessment Bureau, Ottawa, Ontario. (8/12-8/13). Performed peer reviews of regulatory and advisory health summary documents for Health Canada for the Organization for Economic Co-Operation and Development (OECD) Cooperative Chemicals Assessment Meeting No. 4 (CoCAM 4). Peer review included verification of health effects data reported in IUCLID Dossier, Screening Information Data Set (SIDS) Initial Assessment Reports, and SIDS Initial Assessment Profiles documents.

Mouthing Exposure in Young Children: In Silico Tool. Health Canada, Ottawa, Ontario. (11/2013-7/2014). Designed exposure assessment and mathematical models for 26 separate equations to assess chemical exposure to children through mouthing of various consumer products. Provided a variety of algorithms that may be used with default or user-specified parameters to assess mouthing exposures in children from birth to 8 years of age. Identified mathematical approaches and modeling tools from a targeted search of the scientific literature, as well as various government sources, using on-line search engines and established medical information search tools and included a discussion of the circumstances and modulating factors surrounding an attempt at assessing object-to-mouth exposures in children as well as limitations to assessing such exposure. Also authored the user's guide to accompany the computer-based model that included description of mathematical similarities and differences in assessing exposure to non-food substances through direct mouthing, hand-to-mouth behavior, and swallowing as

well as compiling exposure data to provide users with a range of parameter values to assess chemical intake.

Human Health and Ecological Risk Assessment, Cantung Mine site, Northwest Territories, Canada. (3/2017-present). Lead human health and ecological risk assessor for this closed tungsten mine. Providing a detailed quantitative assessment of potential human exposure to metals, petroleum hydrocarbons, and other chemicals of concern at this site, including exposures through hunting, fishing, and gathering of plants as traditional food sources given the remote location and First Nations traditional land uses. Provided assessment of direct exposures including soil ingestion, particulate inhalation, dermal contact with impacted soil and tailings; and ingestion and incidental contact with surface water. Provided a detailed background comparison for metals in soils that will be used to guide soil remediation.

Risk Assessment, Public Works and Government Services Canada, Tulita NWT and Fort Reliance, NWT, and Yellowknife, NWT. (9/2017-3/2018). Currently performing human health and ecological risk assessment for petroleum hydrocarbon releases at three sites in Canada related to previous spills and releases at Royal Mounted Canadian Police detachments and Crown-owned residences. Provided methodology and risk calculations to evaluate indoor air exposure, soil exposure, groundwater impacts, and ecological receptor exposure.

Confidential Maryland Redevelopment Site, Baltimore Maryland. (3/2022 – 7/2022). Conducted a multimedia, Site-Specific Risk Assessment for redevelopment of a former electrical manufacturing facility located in Baltimore, Maryland. Using soil, groundwater and soil vapor data, evaluated the potential risk to future residential, commercial, and recreational receptors for Chemicals of Potential Concern (COPCs) included PCBs, chlorinated compounds, petroleum compounds, metals (including lead), and PAHs. Working collaboratively with the Maryland Department of the Environment, the risk assessment was completed in accordance with voluntary cleanup guidance and provided a health-protective path forward to redevelopment.

Risk Assessment, Beazer, L.A. Paint Site, Vernon, California. (5/2014 – present). Performing a human health risk assessment for vapor intrusion to indoor air from soil gas and groundwater data at historical release site, including paint manufacturing process solvents and petroleum products. Providing risk calculations and correlation of soil, soil gas, and groundwater data to provide multiple lines of evidence to assess potential risks from site reuse and redevelopment. Working cooperatively with both State and local regulators involved in this risk assessment process to address concerns and obtain site closure.

Indoor Air Risk Assessment, Lockheed Martin Corporation, Palo Alto, California. (9/2016-10/2021). Risk assessor for ongoing monitoring and assessment of soil vapor plume for solvent release site for Lockheed Martin Corporation (LMC) in Palo Alto, California. Provide updates of indoor air modeling and risk assessment every 6 months using soil gas data collected from 3 impacted areas.

Risk and Dose Assessment, American Jewish University, Simi Valley, California. (2/2016-5/2018). Performed a review of historic data and risk assessments conducted for the site. Evaluated the potential for the AJU campus, which is downgradient of the Santa Susana Field Laboratory (SSFL), to receive storm water discharge, groundwater, and air-dispersed particulates from former operations at the SSFL. Reviewed AJU and SSFL data related to release of metals, dioxins, perchlorate, polycyclic aromatic hydrocarbons, and TCE, as well as radionuclides. Evaluated historic data and recently collected data to determine if any risks currently exist to patrons of the AJU campus. Conducted site evaluation involving tracing potential migration pathways of contaminants from origin to the campus, and review of soil, sediment, surface water, groundwater, and food data, as well as gamma survey results. Evaluation of impacts to the campus relied upon establishing background and ambient conditions that could influence sampling results, including the effects of forest fires and releases from other facilities in the surrounding urban areas. Exposure evaluation included delineating areas of specific use on the campus, as well as the types of activities, exposure durations, and populations that have access to the areas. Currently providing technical and scientific support as needed.

Human Health Criteria Development using 2000 Human Health Criteria Methodology for U.S. EPA. (Nationwide). (2/2015-5/2018) Supported EPA in updating the human health ambient water quality criteria for 94 chemicals published in late 2014 and researched bioaccumulation factors (BAFs) using EPA's 2000 *Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health* and its 2003 *Technical Support Document Volume 2: Development of National Bioaccumulation Factors*. Conducted a systematic review of peer-reviewed available literature and peer-reviewed public toxicology databases to obtain data to update the BAFs, as well as conducting research of peer reviewed sources to update the relative source contribution (RSC) values used in the 2014 criteria. Also helped provide exposure information to support relative source contribution values using the decision tree in EPA's 2000 Methodology and is currently assisting in producing BAFs and AWQC for 24 metals (including arsenic) and persistent organic pollutants.

Policy Briefings and Update to Human Health Ambient Water Quality Criteria Methodology Document for U.S. EPA (Nationwide). (9/14-1/15). Assisted in reviewing toxicological information, exposure factors, relative source contributions, and bioaccumulation potential of the contaminants included in this project. Provided technical input to the methodology recommendations that included recommendations for using human surveillance data as an input in the development of human health criteria, identification of exposure factors, and determination of exposure factors to appropriately assess minority and low-income populations engaged in subsistence fishing practices. Reviewed the use of NHANES data for determining fish consumption rates for this project and provided technical review of several issue papers and briefings discussing options for calculating different exposure factors, use of probabilistic methods for deriving criteria, and developing technically defensible approaches for filling critical data gaps.

Computer Program to Evaluate Risks from Residential Indoor Water Use, Agency for Toxic Substances and Disease Registry (ATSDR). (6/15-8/17). Assisted in providing exposure and risk assessment support in the development of a desk top computer application to assess potential risks associated with volatile organics and other compounds from the use of contaminated groundwater for showering, bathing, and other household residential uses. Provided input to the assessment of inhalation and dermal exposures, as well as consideration of background exposure concentrations in ambient air. Performed detailed QA/QC of the model through numerous test runs of each exposure scenario for various chemicals and concentrations. Reviewed EPA databases, including the TRI, to determine if a component could be added to this program to incorporate anthropogenic sources to address background concentrations.

Human Health and Ecological Risk Assessment, Treasury Metals, Goliath Mine, Ontario. (6/2014-6/2016). Provided oversight of the Screening Level Risk Assessment (SLRA) for a Proposed Mine Site in Ontario in support of the Environmental Impact Statement, which included a preliminary human health risk assessment and assessment of ecological health risks associated with potential exposures to dust, tailings, waste rock, and mine effluent in the operational and post-closure phases of the proposed mine. Performed the human health risk assessment using guidance from Health Canada, and relied upon site assessment and chemical of concern selection performed using guidance from Environment Canada's Federal Contaminated Sites Action Plan (FCSAP) and Canadian Council of Ministers of the Environment (CCME) as well as Ontario's Provincial Water Quality Objectives (PWQO) and CCME's Water Quality Guidelines. Performed a country foods risk assessment to determine risks from exposures through food items harvested from the proposed mining site during both the operational period and post-closure phases, focusing on mercury and lead. Also attended three public meetings on behalf of the mine proponent to discuss human health risk concerns with the community and First Nations members.

Human Health Risk and Dose Assessment Review, United States Forest Service, Sundance, Wyoming. (1/2014-6/2015). Provided a review of the radiological dose from rare earth mining at this proposed mine site. Performed radiological and nonradiological human health risk assessment for the proposed mine based on the Plan of Operations and baseline studies to date, including soil, ore, air, and water data. Provided calculations and predicted risks and hazards from the estimated heavy metal releases from mining operations combined with ore concentrations, rare earth recovery rates, transportation concerns, and radiological dose. Assigned estimated risks to both the operational and post-closure site conditions as determined in the Plan of Operations as part of this predictive risk assessment. The reports are under consideration as part of the Environmental Impact Statement (EIS) process and permitting processes related to mining and radiological material handling.

Human Health Risk Assessment of Metals and Radionuclides, United States Forest Service, Riley Pass, South Dakota.). (4/2015 – 1/2018). Reevaluated 2006 risk assessment and risk-based cleanup goals for arsenic, molybdenum, copper, radium-226, uranium, and thorium at a former uranium mine. The risk-based cleanup goals focus on site-specific receptors as determined by the U.S. Forest Service and land use patterns of Native Americans for the site. In addition, reevaluated food ingestion pathways related to hunting and ranching in developing updated risk-based goals. Currently, providing risk assessment input to the clean-up actions being performed at the Site.

Risk-based Remediation Goal Calculations, State of Montana, Grant Kohrs Remediation Site. (12/2014-2/2015). Calculated site-specific remediation concentrations for soil to remediate heavy metals, including arsenic, from former mining releases at a currently used recreational area. Evaluation and calculations involved identifying site-specific exposure parameters for different areas of the site based on usage patterns of different occupational and recreational receptors, and were used by the State to guide remediation of the site.

Human Health Risk Assessment, Ross Adams Uranium Mine, Newmont Mining, Prince of Wales Island, Alaska. (8/2009 – 6/2016). Responsible for human health screening evaluation of data from inactive mines, mine roads, shoreline area, and surrounding marine area. Environmental media of interest include soil, surface water,

stream sediment, and marine sediment. Determined the background dataset and selected chemicals of potential concern (COPCs) for different media and locations throughout the mine area; the selected COPCs (uranium, thorium, arsenic, and lead) formed the basis of both the human health and ecological risk evaluations. Included food ingestion pathways related to hunting and gathering activities in the risk assessment for both terrestrial and marine foods. Evaluated historical data to provide recommendations for future sampling and analysis, as well as to define the conceptual site model to be used to assess human health risks.

Human Health Risk Assessment of Lead Exposures, Confidential Client, Former Mining Site, Colorado. (2011). Conducted a risk assessment for school-aged children exposed to lead in soils from historical mining activity. Results of the risk assessment determined the acceptability of continuing to use the site for a school, as well as the need for any alteration in plans to renovate and expand the existing school grounds.

Human Health Risk assessment in Support of Permitting, Sheep Mountain Uranium Mine, Titan Uranium, Jeffrey City, Wyoming. (2011). Responsible for input regarding impacts to human health in application for NRC license, including portions of the Environmental Report regarding public and occupational health impacts from the preferred alternative. Assisted health physicists in incorporating information from their evaluations into appropriate sections of the Technical Report and Environmental Report that were submitted to the NRC.

Environmental Sampling QAPP, Cameco, Wyoming. (2011). Prepared a draft Quality Assurance Project Plan (QAPP) for the Smith Ranch-Highland Uranium Project (SR-HUP) facility that included environmental sample collection and laboratory procedures for environmental samples. Report included data quality assurance procedures, quality control specifications, and other technical activities that assure that the data collected at SR-HUP meet appropriate data objectives and protocol per NRC guidance.

Screening Level Evaluation of an Off-site Relocation of the Large Tailings Pile, Homestake Mining Company, Grants Site. (2012). Compiled and evaluated of costs and risks associated with moving a large tailings pile from the Site to an off-site location. The purpose of the report was to explore costs, efforts, and regulatory requirements to be met under the alternatives of continuing with the current remediation and reclamation strategy or a hypothetical move of the tailings pile to a location outside of the San Andres Aquifer basin and the Village of Milan. For costing purposes, a distance of 30 miles for relocation was chosen in this evaluation. Costs, impacts, and potential risks of the off-site removal were evaluated to assist in long-term remediation decisions.

TENORM Dose Assessment, Waste Management of Colorado. (9/2017-5/2018). Provide radiation dose assessment for 2 landfills and one solidification plant in Colorado. Used site-specific inputs to provide dose assessment for current workers and future hypothetical resident farmers at the Sites, and to support alternative disposal limits for technologically enhanced naturally occurring radioactive material (TENORM).

Human Health Risk Assessment, American Bumper and Plating, Missoula, Montana. (2/2015-2/2016). Responsible for calculating risks and hazard indices associated with residual metal impacts in soils for potential current and future receptors. Evaluation included site-specific exposure pathways of soil ingestion, dermal contact, and inhalation of particulates by adult and child receptors, as well as an evaluation of the acceptability of lead concentration in soil for each of the four areas of the Site that were sampled and, in some cases, remediated.

Review of Subsurface Vapor Intrusion Model and Risk Assessment, Lockheed Martin Corporation, Torrance, California. (2011). On behalf of LMC, conducted an internal review of a human health risk assessment for the site related to subsurface vapor intrusion from a large, heterogeneous groundwater plume in several hydrogeologic formations. Identified potential issues surrounding the vapor intrusion modeling used, as well recommending a revision of the selection of chemicals of concern. Identified potential issues for LMC from calculating risks associated with non-detected chemicals and recommended a different approach to assessing non-detect data.

Human Health Risk Assessment, Department of Toxic Substances Control, Los Angeles, California. (2/2010 – 5/2010). Assisted in conducting a human health risk assessment for Chatsworth Park South, a park owned by the City of Los Angeles that had residual contamination from former skeet shooting activities. Assessment included metals related to dissolved lead pellets and PAHs from clay pigeons in shallow soil. The risk assessment will be used to guide remediation activities to re-open the facility.

Human Health Risk Assessments, Los Angeles Unified School District, Los Angeles, California. (2005-2010). Task leader for conducting risk assessments for proposed school sites in the greater Los Angeles Area. Environmental contamination assessed varied by site, but included petroleum products, pesticides, and heavy metals. In general, soil was the medium of interest and both direct and indirect exposure pathways were of concern. Provided risk assessments that focused on school-based and residential receptors to conform to California

guidance. In some cases, investigations were required at existing schools; in these cases, provided an evaluation of indoor exposure to impacted air or dust to current receptors. Data from these projects was shared with Department of Toxic Substances Control to establish a regional background concentration of arsenic in soil, which is still in regulatory use in the greater Los Angeles area.

Radiation Dose Reconstruction, Oak Ridge Associated Universities, Various Sites. (2003-2009). Reviewed historical documents and estimated potential occupational medical radiation exposures at former nuclear weapons facilities as part of the U.S. Department of Labor's Energy Employees Occupational Illness Compensation Program Act (EEOICPA). Duties included site research of former nuclear facilities and reconstruction of occupational medical practices at each facility that would contribute to worker radiation exposures. Dose reconstruction project at former nuclear weapon facilities was conducted as part of CDC's National Institute for Occupational Safety and Health program to facilitate their response to concerns of DOE workers and contractors requesting compensation for radiation-related cancers resulting from work-related exposure.

Human Health Risk Assessments, Naval Air Station Moffett, Naval Air Station Alameda, Naval Air Station Lemoore, Naval Air Weapons Station China Lake, Naval Auxiliary Landing Field Crows Landing, Naval Fuel Depot Point Molate, and Naval Station Treasure Island, California. (1996-2000). Task Leader for Risk Assessment of propellants, explosives, jet fuel, diesel, and gasoline releases to soil and groundwater and the potential to migrate to surface waters. Integrated ASTM Risk based Corrective Action (RBCA) processes and the California RWQCB's guidance documents, developed methods for screening potentially hazardous components. Method proved to be cost effective by allowing use of all data collected and decreasing the cost of confirmation sampling. Successfully negotiated site specific approach to evaluating volatilization into buildings, resulting in lower site specific air concentrations and cost savings by avoiding expensive air sampling. Site specific environmental conditions were used to demonstrate an increased rate of degradation of the components.

Human Health Risk Assessments, Naval Air Station Lemoore, Naval Air Station Alameda, Naval Air Weapons Station China Lake, Naval Air Station Moffett and Naval Auxiliary Landing Field Crow's Landing, California. (1996-2000). Task Manager for oversight of human health risk assessments and statistical programs, including evaluation of exposure scenarios and pathways; validation of toxicity values and calculated risks; negotiation of appropriate exposure areas based on current and future land use plans for the base and surrounding communities; statistical evaluation of several data acts; selection of chemicals of concern from combined data sets; and estimation of risks using several data aggregation methods. Evaluated exposure concerns including migration of contaminants from soil to groundwater and surface water. Chemicals of concern included chlorinated pesticides, herbicides, volatile organic chemicals, semi-volatile organic chemicals, metals (including arsenic), TPH, dioxins, furans, and perfluorinated compounds. Provided risk analyses of many different environmentally contaminated areas, including landfills, pesticide/herbicide storage, mixing, and application areas, industrial complexes, artillery ranges, and areas impacted by runoff or groundwater infiltration from these sites. Developed confirmation sampling plans for several sites based on grid sampling patterns and statistical methodology, as well as deriving risk-based concentrations for remediation and compliance studies involving PCBs, pesticides, and explosives.

Technical Support for Human Health Risk Assessments, U.S. Environmental Protection Agency. (1992-1996). Provided technical support on epidemiology, public health, and statistical issues to EPA's RCRA/CERCLA program as part of a technical enforcement support (TES) contract. Conducted technical reviews of human health risk assessment documents submitted to EPA to evaluate compliance with CERCLA guidelines. Also reviewed work plans, technical memoranda, and risk assessments submitted to EPA regarding RFETS. Provided oversight for RFETS, and assisted EPA in the development of Monte Carlo simulations for the site. Acted as EPA's representative in negotiating all phases of risk assessments for Rocky Flats, including sampling procedures, data evaluation, exposure scenarios and pathways, chemical intake assumptions and risk characterization. RFETS risk assessments included radionuclides and nonradioactive chemicals such as heavy metals, polycyclic aromatic hydrocarbons, and solvents. Also provided technical oversight in EPA Region VIII include F.E. Warren Air Force Base in Wyoming; Tooele Army Depot in Utah; and Hill Air Force Base in Utah. Project Manager and provided technical oversight for human health and ecological risk assessments at Amoco Mandan Refinery, a RCRA site in EPA Region VIII.

PUBLICATIONS

Peer-Reviewed Journal Articles

Hays, S., C. Kirman, J. Flippin, **T.K. Lopez.** Biomonitoring Equivalents for Ethylene Thiourea. Regulatory Toxicology and Pharmacology 150 (2024) 105618.

Hays, S., C. Kirman, J. Flippin, **T.K. Lopez.** Biomonitoring Equivalents for Glyphosate. Regulatory Toxicology and Pharmacology 144 (2023) 105481.

Lopez T.K., K. Jones, A. Roseberry-Lincoln, A. Zidek, L. MacKinnon, L. Marro. Adult and children's use of Hand sanitizer during a pandemic - an observational study. Journal of Exposure Science and Environmental Epidemiology, September 24, 2022. DOI 10.1038/s41370-022-00479-w.

Lopez, T.K., J.A. Marshall, S.M. Shetterly, J. Baxter, R.F. Hamman, 1995. Ethnic Differences in Micronutrient Intake in a Rural Biethnic Population. American Journal of Preventive Medicine, 11:301 305.

Marshall J.A., **T.K. Lopez**, S.M. Shetterly, J. Baxter, and R.F. Hamman, 1995. Association of Education Level with Atherogenic Diets in Rural Biethnic Population. American Journal of Preventive Medicine, 11:294 300.

Baxter J., R.F. Hamman, **T.K. Lopez**, et al., 1993. Excess Incidence of Known Non Insulin Dependent Diabetes Mellitus (NIDDM) in Hispanics Compared with Non Hispanic Whites in the San Luis Valley, Colorado. Ethnicity and Disease, 3(1):11 21.

Conference Presentations

Session Lead and Presenter, 2024. "The Intersection of Human Health and Environmental Risk Assessment: A One- Health Perspective." Society for Environmental Toxicology and Chemistry. Fort Worth, Texas, October 20-24, 2024.

Poster Presentation, 2022. Society for Risk Analysis Annual Meeting, Tampa, Florida, December 4-8, 2022. "**Optimization of Infrastructure Placement Using a Novel Disease Burden Reduction Model Using Public Health Data to Save Lives through Informed Engineering Design."**

Platform Presentation, 2019. Society for Environmental Toxicology and Chemistry, Helsinki, Finland. May 29, 2019, **"Applying a "One Health" Approach to the Assessment of PFAS: Opportunity to Prevent Unintended Consequences."**

Poster Presentation, 2018. Society for Environmental Toxicology and Chemistry, Sacramento, CA, November 6, 2018. **"Applying a "One Health" Approach to the Assessment of PFAS."**

Poster Presentation, 2017. Society for Risk Analysis Annual Meeting, Arlington, VA, December 11-13, 2017. **"Alternate Approach to Deriving Metals Bioaccumulation Factors in Fish."**

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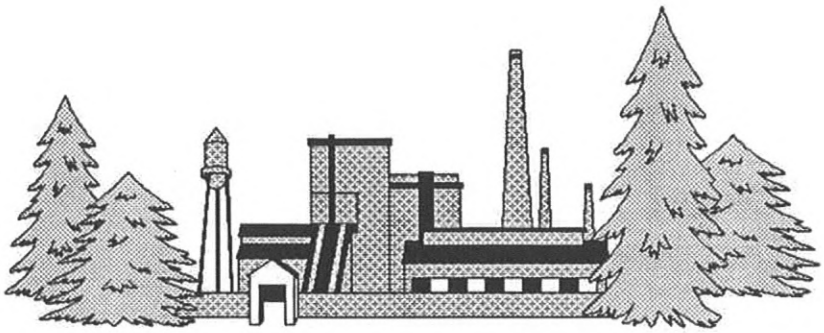
IDAHO DIVISION of

ENVIRONMENTAL QUALITY



MONDAY, JULY 13, 1992

Our Goal for Air Toxics Policy/Rule Making:

To protect the public health and the environment from the harmful effects of toxic air pollutants (TAP) per our responsibilities set forth in IDAPA 16.01.1011,01 and 1601.1952,02. and provide regulated industries with a reasonable, flexible, minimally burdensome framework with which to work.

Our Goal for this meeting:

To successfully negotiate air quality rules revisions that will satisfy the regulated industries need to have reasonable, flexible regulations that do not place an unwarranted impediment to their ability to do business in Idaho, while at the same time providing adequate protection to the public from the harmful effects of TAP. We hope that these revisions will provide industry with an awareness of what DEQ considers harmful and provide the basis for a straight forward and efficient permitting process.

Brief History of the DEQ TAP List

The DEQ TAP list (hereafter referred to as the list), was conceived as part of the New Source Review Policy, which was a response to the need to control the emissions of airborne toxic chemicals in the absence of effective EPA regulations. NESHAP (National Emmision Standards for Hazardous Air Pollutants, §122 of the 1970 Clean Air Act) had proven to be an ineffective means of of controling TAP as only seven pollutants were ever regulated after 17 years of the NESHAPS program.

It was the position of the DEQ that given the resources that we had available to us, that we would only attempt to hold the line on air quality and try to insure that new sources of air pollution did not "injure or unreasonably affect human or animal life or vegetation." One of the principal ways that we chose to do this was the development of a comprehensive list of TAP and, where possible, health based emissions limits and or acceptable ambient concentrations.

Our list was developed from a combination of sources. We surveyed what other states were doing and found that New Mexico had the most logical, straight approach to air toxics. The New Mexico list was chosen as the basis for our own TAP list. In addition, we looked at the Occupational Health and Safty Administration (OSHA), American Conference of Government and Industrial Hygenests (ACGIH) and National Institute for Occupational Safty and Health (NIOSH) occupational exposure limits (OEL) and threshold limit values (TLV) for non-carcinogens. For carcinogens we looked at the

data from the International Agency for Research on Cancer (IARC) and the Carcinogen Assesment Group of the EPA (CAG). In addition, we reviewed data from the Agency for Toxic Substances and Disease Registry of the Public Health Service. As many who have received periodic updates know, we have tried to continuously refine the list to reflect new data and to correct inaccuracies.

The DEQ list of regulated air toxics is quite large in scope. However, this was not done to burden industry. Quite the contrary. It was done in order, to the maximum extent possible, to provide industry with a ready reference to acceptable screening levels of these various compounds. This enables new sources to review their processes and see if controls, may be needed early on in the planning process, there by maximixing start up budget planning. In addition, it allows existing sources to review their emissions and see how they compare to the screening levels that the DEQ considers reasonably protective of human health and the environment. Please see appendix 6 for the derivation of emissions limits (EL) and acceptable ambient concentrations (AALC).

DEQ Position on the EPA "198" List

The EPA list of 189 compounds to be regulated represents a political process by the congress, rather than being put together by any environmental agency. This list is inadequate in and of it self to protect the air quality of Idaho or other specific location in the nation. This opinion is based on the following:

* The EPA 189 list is not an attempt to protect people or the environment of any specific area but a compromise list to address some of the major nation-wide sources of air pollution. The original proposed list contained 224 compounds, including ammonia and hydrogen sulfide which were later removed. We do not believe that this nation-wide effort can be effectively applied to Idaho and be adequate to address the unique Idaho situation. All along, EPA admitted that their agenda was not to protect all communities completely, rather their intent and design has been to address only pollutants and source catagories that are national in scope.

* The EPA 189 list does not include all the well documented carcinogens that have been assigned unit risk factors[1], let alone most possible and suspected carcinogens as listed in DEQ Appendix A2 of the New Source Review Policy. State and local agencies need to have the flexibility to protect public health by regulating the emission into the air of these very dangerous compounds should they be present locally.

* From only a partial inventory, we have found that there are currently being emitted into the ambient air of Idaho three known or suspected carcinogens which are not addressed by the EPA 189 list. In addition there are about 35 non-carcinogens of varying toxicity levels currently being emitted or being reviewed for new source permits.

* While it is not possible to predict the future, in a fast growing state like Idaho it is very reasonable to assume that new industries will be moving to Idaho as our work force expands with new residents. In addition, as environmental regulations in California and other states become more restrictive, Idaho will look more attractive to many of these regulated industries. This is already occurring in Nevada. While we certainly want the jobs and incomes that these industries may represent, just as certainly, we do not want to become a "toxic magnet" for polluting industries that other states don't want.

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[1] Unit Risk Factors for a known or suspected carcinogen describes the possibility of developing excess cancers over a 70 year lifetime of exposure to 1 microgram per cubic meter of that substance.

* Title III of the Clean Air Act Amendments of 1990 (CAAA) requires EPA to publish a list of source categories and then promulgate maximum achievable control technology (MACT) for the first 40 categories. MACT standards are then required for the rest of the categories on a phased in schedule. Even if this time schedule was adhered to, the first MACT standards would not be available before November of 1992. Without its own TAP policy or rules and regulations, Idaho is thus without any appropriate air toxics regulation until EPA is finished. EPA is already late in publishing the first source category list.

* If a particular source in Idaho is not addressed in the first 40 source categories, the DEQ could be unable to address toxic emissions from that source no mater how toxic the emissions might be or in what quantity the emissions may be emitted until EPA finally promulgates MACT standards. Given the past history of EPA deadlines, this is a very real concern. Even if EPA adhered to all deadlines, some sources would conceivably still be able to emit unregulated toxics until the year 2000, if that source was in the last group to have standards promulgated. It should also be noted that not all sources are covered by these MACT standards. As a consequence, sources not covered by this MACT standard would be essentially unregulated in Idaho. Further, the majority of covered sources are associated with surface coating and manufacturing of the regulated chemicals, while fore most sources of TAP in Idaho, the TAP in question is used in or produced as a by-product of their processes.

* Finally, Congress itself apparently felt that this list was not final. Congress required the EPA to periodically review the list and add pollutants "...which present or may present ...a threat of adverse human health effects (including but not limited to, substances which are known to be, or may be reasonably be anticipated to be, carcinogenic, mutagenic, teratogenic, neurotoxic, which cause reproductive dysfunction, or which are acuity or chronically toxic) or adverse environmental effects..." The EPA 189 list should be considered to be a starting point for toxics regulations.

* It is not the intent of DEQ to require sources to do an emissions inventory of every compound on the DEQ list. It is quite reasonable to assume that any source, including the small sources, be familiar with their own processes. There are common, readily available sources of information, such as Material Safty Data Sheets (MSDS)[2] that will assist a source

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[2] MSDS provides data concerning the nature and concentrations of hazardous or toxic components of substances used by a source. These sheets are available from the manufacturers of all compounds with hazardous or toxic components.

to ascertain what compounds can be reasonably assumed to be present in their process. They then need only inventory those compounds that can reasonably assumed to be emitted. In addition, the DEQ will be happy to assist sources in identifying potential TAP.

Some Options for Discussion

Option 1: Maintain current situation.
Pros: Would, of course, make DEQ happy; require no further legislation; all ready in place and functional.
Cons: Could make several in industry unhappy; may be seen as burdensome by industry; a policy is not as clear as a standard.

Option 2: Go with Maximum Achievable Control Technology (MACT) as per the 1990 CAAA or Best Available Control Technology (BACT) or Lowest Achievable Emissions Reduction (LAER) or Adaqualtly Demonstrated Control Technology (ADCT) or some other control technology based standard.
Pros: No EL or AALC; single consistent standard.
Cons: MACT/BACT etc. difficult to define: must be industry and chemical specific; lack flexibility esp. for relatively "clean" industries; no provision for new pollutants; may not adequately protect human health and the environment, esp. in the case where MACT/BACT has not been defined for various toxic chemicals.

Option 3: Regulate EPA "189 List" only
Pros: Would reduce the list in size; could possibly speed up permitting process
Cons: Not protective enough of human health and the environment; lacks flexibility; would not address many pollutants that are commonly emitted by modern industry; no provision for new pollutants; somewhat pointless as the EPA is already doing it; could complicate and slow the permitting process by increasing public comment over pollutants not covered.

Option 4: Regulate EPA "189 list" plus currently known TAP
Pros: list would be somewhat shorter and simpler;
Cons: no provision for adding new pollutants; could require more extensive and costly emissions inventories.

Option 5: Regulate EPA "189 List" plus any thing that has been identified elsewhere as toxic, hazardous or a carcinogen
Pros: Would be comprehensive; would regulate only pollutants that have been demonstrated to be of concern; would be similar to current policy, require little or no new legislation;
Cons: Could be a large list; May be seen as burdensome by some in industry; no provision for adding pollutants.

Option 6: Develop a series of "source specific" TAP lists
Pros: Would be easier for specific industries to know what to report on; A number of useful references available See Appendix 9.
Cons: Could require emissions inventories of some regulated industries; no provision for variation among industries of the same type; MSDS will not reflect bi-product compounds.

Option 7: Options 1 and 3 through 6 with the addtion of a method out side of DEQ to add TAP to lists. (Pros and Cons would, of course depend on the method for adding to the list, but in general, a board or review panel of some sort seems to be a common notion.)
Pros: Would provide DEQ with industry input on additions to lists; would provide DEQ with industry input on standards; would provide DEQ and industry with input by public interest groups;
Cons: Could slow down the process of adding new toxics and there for probably slow down the permitting process because of the public particapation process; could cause a political battle over the structure of the addition process; could convert the health based process for additions to list into a political one; depending on the make up of the committee/board, could be less protective of the public health.

Appendix 1

The following are known or possible carcinogens that have a URF but are not listed by EPA on the list of 189 toxics but are listed on Appendix A2 (carcinogens)

Aldrin* insecticide
Bis(2-chloroethyel)ether solvent
chloromethane methyl chloride
DDT insecticide, most uses banned; used for Tussock moth
1,2-dibromoethane solvent chemical industry
1,1-dichloroethane solvent
1,2-dichloroethane degreaser, ore flotation, solvent, paint, finish removers
1.1-dichloroethylene solvent
Dieldrin* insecticide
diethylstilbestrol synthetic estrogen
dimethylnitrosamine solvent
heptachlor epoxide insecticide
hexachlorodibenzo-p-dioxin (1:2 mixture) Possible. herbicide, a contaminant, poison
hydrazine sulfate mineral analysis, determination of arsenic in metals, fungicide, fumigant
3-methylcholanthrene biochemical research
N-nitroso-n-butylamine**
N-nitrosopyrrolidine**
pronamide herbicide
reserpine antihypertensive [lowers blood pressure], tranquilizer
thiourea photography, analytical reagent chemical intermediate

* part of current permit analysis at INEL Chem. Lab.
** no reference located
Benzo(a)pyrene, dibenz(a,h)anthracene, chrysene and other polynuclear aromatic hydrocarbons can be regulated under polycyclic organic mater (POM) which, as a category, is listed on the EPA list of 189.

Only two of these chemicals are currently under review. However, many of these chemicals are solvents which would seem to have the potential for use in industries common to Idaho (light manufacturing, electronics and so forth).

Appendix 2

The following are carcinogenic substances that are or have been reviewed in conjunction with permit applications in Idaho. These substances are not on the EPA 189 list but are on Appendix A2 (carcinogens):

Aldrin and **Dieldrin** as noted above
dimethyl sulfide from craft pulping black liquor

Appendix 3

The following are non-carcinogenic substances that are or have been reviewed in conjunction with permit applications in Idaho. These substances are not on the EPA 189 list but are on Appendix A1 (non-carcinogens): Note: many of these compounds are on the EPA Extremely Hazardous substances list, and the Community Right to Know list.

hydrogen sulfide: rotten eggs smell, human poison by inhalation, severe irritant, violent reaction with various metals & chemicals
methyl mercaptan: poison by inhalation,
turpentine: toxic by inhalation, irritant, experimental tumorigen
methanol: toxic by inhalation, experimental teratogen, reproductive effects, human mutagenic data.
fluorine: toxic by inhalation, irritant, mutagenic data
aluminum: possible cause of pulmonary fibrosis by inhalation
copper: tumorigen, teratogen, experimental reproductive effects
iron: potentially toxic by inhalation (arc welders lung)
magnesium: toxic by inhalation
zinc: relatively nontoxic
terphenyl: little toxicological data available
nitric acid: poison, corrosive, experimental teratogen and reproductive effects
isophorone diiysocyanate: poison by inhalation,
methyl ethyl ketone peroxide: moderately toxic by inhalation, experimental tumorigen
cyclohexanone: moderately toxic by inhalation, irritant
acetone: moderately toxic by various routes, irritant
hydrogen peroxide, 90%: moderately toxic by inhalation, skin contact, corrosive irritant, experimental tumorigen, suspected carcinogen
dimethyl disulfide: poison by inhalation
dimethyl sulfide: volitile liquid, gas odorant, solvent

Appendix 4

The following are non-carcinogenic substances that are or have been listed on the Toxic Release Inventory (TRI)[3] for Idaho. These substances are not on the EPA 189 list but are on Appendix A1 (non-carcinogens). Note: many of these compounds are on the EPA Extremely Hazardous substances list, and the Community Right to Know list.

sodium hydroxide: corrosive irritant, mutagenic data
methanol: toxic by inhalation, experimental teratogen, reproductive effects, human mutagenic data.
nitric acid: poison, corrosive, experimental teratogen and reproductive effects
hydrofluoric acid: human poison by inhalation, corrosive irritant, experimental teratogenic, reproductive effects, mutagenic data
chlorine: Moderately toxic by inhalation, irritant, human mutagenic data
ammonia: experimental poison by inhalation, irritant, mutagenic data
phosphoric acid: human poison, corrosive irritant
copper: tumorigen, teratogen, experimental reproductive effects
Methylene diphenyl diisocyanate (MDI): poison by inhalation, irritant, mutagenic data
Freon 113: most uses will be fazed out by 1995
ammonium sulfate: moderately toxic by several routes
ammonium nitrate: powerful allergen
zinc compounds: relatively nontoxic
barium compounds: low toxicity
hydrochloric acid: poison by unspecified route, mildly toxic by inhalation, corrosive irritant
manganese compounds: toxic by inhalation

The following substances are non-carcinogenic substances that are being reviewed in conjunction with permit applications or field inspections. These substances are not on the EPA 189 or currently on the DEQ list. ***This points out the need to be able to respond to changing circumstances.***

Acenaphthylene: irritant, mutagenic data
Amino functional Siloxane: organosilicon oxide polymer, mild to severe irritant
Busan 1127D (2-(thiocyanomethylthio)benzothiazole): mist is considered moderatly to highly toxic.
Carbitol Acetate (2-(2-Ethyoxyethoxy) Ethyl Acetate): solvent and placticizer
dimethyl disulfide: poison by inhalation

---

[3] The TRI is a report of all emissions of compounds required to be disclosed under SARA Title III.

Appendix 5

The following are examples of sources now existing in Idaho that have air releases of substances not on the EPA 189 list:

American Micro systems Inc.
Basic American Foods
Blount Industries
Borden Inc. Dairy
Del Monte Foods USA #130
Deming Industries
Fiberglass Systems Inc.
FMC Corp.
Gustafson
Hewlett Packard
IBP Inc.
INEL
J.R. Simplot
J.R. Simplot Food Di.
John E. Quinn
Kerr McGee Vanadium Facility
Kraft Inc.
MIcron Technology
Monsanto
N.A Degerstrom Inc.
Nu-West Industries Inc
Ore-Ida Foods
Peabody Spunstrand
Penford Products Co.
Pondarosa Paint Mfg. Inc.
Post Falls Particalboard
Potlatch
Spears Manufacturing Inc.
Unitech Composites Inc.
Zilog

Appendix 6

In developing emissions limits for new permitted facilities, the Idaho DEQ uses the terms Unit Risk Factors and Threshold Limit Values. The following is an explanation of these terms and how they are used.

UNIT RISK FACTOR

A unit risk factor (URF) is used to describe the possibility of developing excess cancers over an average 70 year lifetime. This is based on being exposed to concentration of one microgram of a carcinogenic (cancer causing) substance in one cubic meter ($1\ ug/m^3$) of air over 70 years. The term excess cancers means cases of cancers in excess of what would be normal for a given population. For example, if there was normally 5 cases of a given type of cancer in Anytown USA before a given exposure to some substance and 7 after the exposure, there would be 2 excess cancers.

Inhalation URFs are developed for carcinogenic substances by the EPA. Each URF represents months of research and often years of policy process. Teams of toxicologists gather toxicological data for each known or suspected carcinogen. The available data are then rated or point factored per the quality of the research involved. A URF is then a probability statement derived from this process. Each URF proposed by EPA is extensively reviewed and debated in public by scientists, health officials and industry representatives. Every URF represents a consensus of the best science and health opinion of the potency of a given carcinogen.

URFs are usually expressed as a number times 10 to some negative power. For example, benzene, an organic hydrocarbon found in various petroleum products and cigarette smoke has a unit risk factor of 8.3×10^{-6}. This means that are 8.3 chances in one million of getting cancer if a person is exposed to $1\ \mu g/m^3$ 24 hours a day for 70 years.

Another example would be asbestos. Asbestos has a URF of 2.3×10^{-1}. That means that if exposed to $1\ ug/m^3$ concentration for 70 years, the chances of getting cancer would be .23 in 10.

Within IAQB New Source Review (NSR) policy, URFs are used to calculate acceptable ambient levels for a given carcinogen. IAQB generally establishes that an ambient concentration which causes no more excess cancers than one in a million (1×10^{-6}) is acceptable. Once an acceptable ambient level is established, IAQB can then back calculate via engineering equations to an acceptable emission rate (in pounds per hour) for a given stack.

THRESHOLD LIMIT VALUE

Threshold Limit Value (TLV) is a time weighted exposure limit developed by the Occupation and Safety Administration or the American Council of Government Industrial Hygienists. This value is used to limit the exposure of informed workers to a given toxic substance in the work place. The value is based on exposure of adult males working an eight hour shift. The DEQ uses TLV information to screen proposed new source emissions levels. The DEQ divides the TLV first by a value of 10 due to the fact that an ambient air exposure of a carcinogen means people are usually living under that exposure longer than eight hours out of 24. This value is then again divided by 10 to compensate for the fact that not everyone who is potentially exposed is an adult male. Other people may be more sensitive. The TLV thus is divided by a total of 100 for use in setting an acceptable ambient level.

For example, the TLV for cyanide is 5 milligrams per cubic meter (mg/m^3). An acceptable ambient level under DEQ policy would be 5 divided by 100 or 0.05 mg/m^3. For another example, the TLV for Lindane (an insecticide) would be 0.5 mg/m^3 concentration. The acceptable ambient level would be 0.5 divided by 100 or 0.005 mg/m^3. As with carcinogens, the TLV derived acceptable ambient levels are used by the DEQ engineers to back calculate an acceptable stack emission rate for any proposed new source.

EL and AAL(C) as listed in the TAP list are *screening levels*, not standards. If a proposed source, at any level of review is shown to be under the screening level for the TAP in question then the source goes forward in the permitting process. If, on the other hand, the source is shown to likely exceed the screening level, then there is a number of options such as further analysis or enhanced controls that can be pursued. See: Idaho DEQ Procedures for Modeling Impacts of Toxic Air Emissions and Assessing Associated Risk Appendix 7, and the General Summary of DEQ's New Source Review Policy for Toxic Air Pollutants, Appendix 8 for a more complete discussion of this topic.

APPENDIX 7

DRAFT

Idaho DEQ Procedures for Modeling Impacts of Toxic Air Emissions and Assessing Associated Risk

Procedures for modeling the dispersion of air emissions are consistent for criteria pollutants and toxics.

Emissions are calculated for the specific operation, with EPA's AP-42 as the standard guidance document. Impacts for any toxic air pollutant (TAP) emitted in potentially significant amounts are estimated through a three tiered evaluation approach, using the Division of Environmental Quality (DEQ) TAP list and models approved by EPA for regulatory use.

The emissions screening levels as listed on the DEQ TAP list are a quick way to determine if modeling is needed. If a toxic air pollutant has the maximum potential to be emitted at levels below the screening emission level, the proposed emission is typically approved by the DEQ.

If the maximum potential emissions are above the screening levels, then modeling is performed. The models most commonly used for the first modeling run are TSCREEN and SCREEN for single emission points, or ISC with worst case meteorological data for multiple emission points. In "screening modeling", quantified emissions and stack (or fugitive) data are required, as well as distance to property boundary or, with DEQ approval, an off site receptor. Estimates of off site concentrations of the pollutant(s) are output by the model, which assumes a variety of worst case dispersion conditions. Model output is typically in one hour averages. Persistence factors are usually used to estimate worst case impacts for other averaging periods. Unit risk factors are then applied to translate the predicted off site concentrations to determine risk to those exposed.

If, after "screening modeling", unacceptable risks still are shown to be possible, refined modeling may be done. Refined modeling replaces many worst case assumptions in screening modeling with actual conditions. In refined modeling, a more realistic three dimensional simulation of emissions, topography, meteorology, and receptors is supplied. Actual on site meteorological data typically helps the applicant, since the alternative is a worst case meteorological data file like that used in screening modeling. The most commonly used models are ISC, COMPLEX1, and FDM. Refined modeling provides the most detailed and accurate assessment of potential air quality impacts.

After ambient concentrations are determined, these ambient levels are, in the case of known or suspected carcinogens (TAP list Appendix A2), converted to annual concentrations using persistence factors as mentioned above. They are then multiplied by the EPA

unit risk factor (URF) to obtain a risk level. A risk level of one in a million is generally considered acceptable for a long term or permanent emissions source. The acceptable ambient levels for a carcinogen (AALC) listed in the TAP list Appendix A2 reflect this one in a million risk level for carcinogens with established URFs.

For short term sources (usually less than five years in duration), such as remediation projects, a probability of greater than one in a million risk (over a 70 years) will generally be acceptable to account for the decreased term of exposure. It is not acceptable however, for exposed individuals to receive a full 70 year exposure during the life of a short term project. In addition, first impacts at receptor sites farther from the source than property boundaries may be considered for short duration projects.

For non-carcinogens (TAP list Appendix A1) the risk assessment procedures are similar. Ambient concentrations are compared with 1/100 of the published American Council of Government and Industrial Hygienists (ACGIH) Occupational Exposure Limits (OEL) or other ambient standard adopted by the DEQ in the absence of a published ACGIH OEL.

The 1/100 factor was derived to accommodate two levels of extrapolation of potential risk to the general public:

1. ACGIH factors assume an eight hour exposure; source exposures are generally continuous (24 hrs.).

2. ACGIH factors are derived from historical data that comes essentially from a work force of healthy adult males.

Thus we have used an uncertainty factor of 100 (10X for each of the above conditions) to accommodate the more sensitive populations.

In the absence of any published URF or OEL. the acceptable ambient concentration will be considered the detection limit unless it can be demonstrated to the satisfaction of the DEQ that an ambient level higher than the detection limit will not have an adverse effect on human health or the environment. In such cases we have allowed the toxicological profiles of like chemicals or compounds to be substituted for the unknowns.

General Summary of Idaho Air Quality Bureau's New Source Review Policy for Toxic Air Pollutants

Regulation Summary

January 1991

Toxic substances within ambient air are regulated in Idaho by IDAPA 16.01.1011,01. Toxic Substances, which states:

> *Any contaminant which is by its nature toxic to human or animal life or vegetation, but is not specifically controlled elsewhere in Idaho Department of Health and Welfare Rules and Regulations, Title 1, Chapter 1, "Rules and Regulations for the Control of Air Pollution in Idaho," shall not be emitted in such quantities or concentrations as to alone, or in combination with other contaminants, injure or unreasonably affect human or animal life or vegetation. As information becomes available, limits will be specified for concentration of toxic materials in the ambient air and emission limits will be set accordingly.*
>
> *(1-24-69)*

Any new source of air pollutants (including toxic pollutants) not specifically covered by the thirteen (13) specific New Source Performance Standards is regulated by IDAPA 16.01.1952,02 Sources Not Specifically Regulated which states:

> *Sources not specifically regulated under Idaho Department of Health and Welfare Rules and Regulations Sections 01.1955 through 01.1999 shall achieve the greatest degree of emission reduction that has been adequately demonstrated.*
>
> *(1-1-75)*

Idaho Air Quality Bureau (IAQB) has developed a method for permitting new sources of toxic air pollutants consistent with our responsibilities and authority under the Rules and Regulations for the Control of Air Pollution in Idaho. For that method, IAQB compiled a list of toxic air pollutants (TAP) and screening level emission limits for those substances.

Permit Decisions

If the Bureau finds that an eight-hour average ambient concentration of a toxic air pollutant will likely not exceed one hundredth (.01) of the OEL for non carcinogens, or is below detection levels for a compound without an OEL or URF, the Bureau shall grant the permit.

Similarly, if the Bureau can substantiate that ambient concentrations due to emissions of known or suspected carcinogens are not likely to cause excess cancers of more than one in a million (10^{-6}) then the bureau shall grant a permit.

If potential new source emissions are shown to likely cause ambient concentrations:

1. in excess of 1/100 of the OEL or

2. which could cause cancers in excess of one in one hundred thousand (10^{-5}) or

3. which exceed minimum detection levels for TAP without an OEL or URF,

the Bureau may grant the permit if the applicant implements the best available control technology (BACT) for that source or pollutant and after considering other factors.

If the TAP screening level is shown to likely be exceeded the Bureau will make a final decision considering the following factors:

(a) the health and environmental assessment prepared by the applicant (if one is required by the Bureau);

(b) the nature of the toxic air pollutant and the susceptibility and proximity of the human population;

(c) other health and environmental impacts associated with the anticipated level of exposure.

The Bureau may grant a permit for a new source to emit carcinogens which are likely to cause excess cancers between 1/100,000 and 1/1,000,000 (between 10^{-5} and 10^{-6}) after the applicant proves that additional controls would be a severe hardship.

Appendix 9

Samples of Industry Specific TAP Emissions Data for an Example Industry; the Asphalt Paving Mixtures and Block Industry, SIC Code 2951

This appendix contains excerpts from:

Toxic Air Pollutant Emission Factors - A Compilation for Selected Air Toxic Compounds and Sources, Second Edition EPA-450/2-90-011

Toxic Air Pollutant/Source Crosswalk - A screening tool For Locating Possible Sources Emitting Toxic Air Pollutants, Second Edition EPA 450/2-89-017

Compilation of Air Pollution Emission Factors, AP-42 Fourth Edition September 1985 Volume I Stationary Point And Area Sources. (While this document is not specifically for TAP, the emission factors for VOC's can be useful for calculations and it is a standard reference.

MSDS for the same industry.

United States
Environmental Protection
Agency

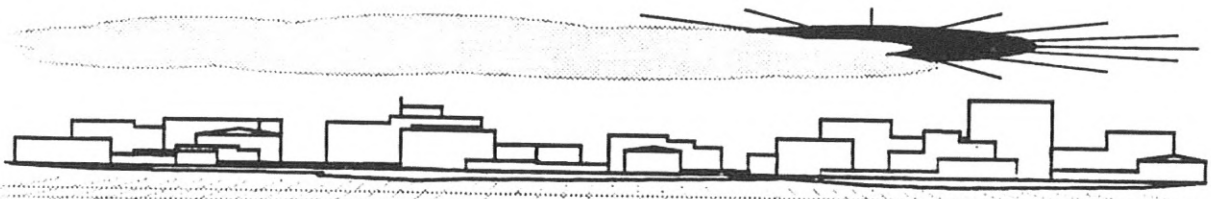
Office of Air Quality
Planning And Standards
Research Triangle Park, NC 27711

EPA-450/2-90-011
October 1990

AIR

EPA

TOXIC AIR POLLUTANT EMISSION FACTORS - A COMPILATION FOR SELECTED AIR TOXIC COMPOUNDS AND SOURCES, SECOND EDITION



REC 4338

TR 1023

SIC	SIC Code Description	SCC Code	Associated Pollutants
2951	Asphalt paving mixtures and blocks		ACETALDEHYDE (27); ACETATE, METHYL (29); ACETONE (27,28); ALUMINUM OXIDE (27); AMMONIA (21,22,23,27,29); ANILINE, 3-NITRO- (28); ANTHRACENE (27); ANTIMONY (27); ASBESTOS (21,22,23,27,28,29); ASPHALT (22); BENZENE (20,21,23,27,28,29); BENZENE, CHLORO- (28); BENZENE, ETHYL- (27,28); BENZENE, HEXACHLORO- (22,28); BENZIDINE (28); BENZO(A)PYRENE (21,23,28); BIPHENYL (27); BUTANETHIOL, N- (28); 1-BUTANOL (27); BUTYRALDEHYDE (26); CHLORINE (27); CHROMIUM (21,23,27,29); CUMENE (27); CYCLOHEXANE (27,28); DIBUTYL PHTHALATE (27); DIOCTYL PHTHALATE (27); EPOXY RESINS (25); ETHANE, CHLORO- (27); ETHANE, 1,2-DICHLORO- (27); ETHANE, 1,1,1-TRICHLORO- (21,22,23,28,29); ETHANOL, 2-ETHOXY-, ACETATE (22); ETHYLENE (27); ETHYLENE GLYCOL (27); ETHYLENE OXIDE (27); FORMALDEHYDE (20,21,22,26,28,29); FORMAMIDE, N,N-DIMETHYL- (28); FURAN, DIBENZO- (27); FURAN, 1,2,3,6,7,8-HEXACHLORODIBENZO- (27); FURAN, 1,2,3,7,8,9-HEXACHLORODIBENZO- (27); HEPTANE (22); HEXANE (22); HYDROGEN CHLORIDE (27,28); ISOPROPANOL (27); KEROSINE (29); LEAD (27); MANGANESE (29); MERCURY (23,29); METHANOL (27); METHYL ETHYL KETONE (21,22,27,28); METHYL ISOBUTYL KETONE (27); METHYLISOCYANATE (21,22,23,29); NAPHTHALENE (21,24,27,28); NICKEL (29); N-OCTYL PHTHALATE (27); 2-PENTANOL, 4-METHYL- (29); PHENOL, 2,4-DICHLORO- (27); POLYCYCLIC ORGANIC MATTER (21,23,26,29); POLYETHYLENE GLYCOL (25); POLYVINYL CHLORIDE LATEX (28); PROPYLENE (27); SODIUM HYDROXIDE (27); SORBITAN, MONO-9-OCTADECENOATE, POLY(OXY-1,2-ETHANDIYL) (2)- (29); STYRENE (28); SULFURIC ACID (21,22,27,28); TETRACHLOROETHYLENE (22,28); THALLIUM COMPOUNDS (28); TOLUENE (20,21,22,23,27,28,29); XYLENE, M- (27); XYLENE, O- (27); XYLENE, P- (27); XYLENES (MIXED ISOMERS) (27,28); ZINC COMPOUNDS (27)
		3-05-002	BUTYRALDEHYDE (26); FORMALDEHYDE (26)
		3-05-002-01	BENZENE (20); FORMALDEHYDE (20); POLYCYCLIC ORGANIC MATTER (26); TOLUENE (20)
		3-05-002-03	NAPHTHALENE (21,24)
		3-05-002-05	POLYCYCLIC ORGANIC MATTER (26)

United States
Environmental Protection
Agency

Office of Air Quality
Planning And Standards
Research Triangle Park, NC 27711

EPA-450/2-89-017
December 1989

AIR

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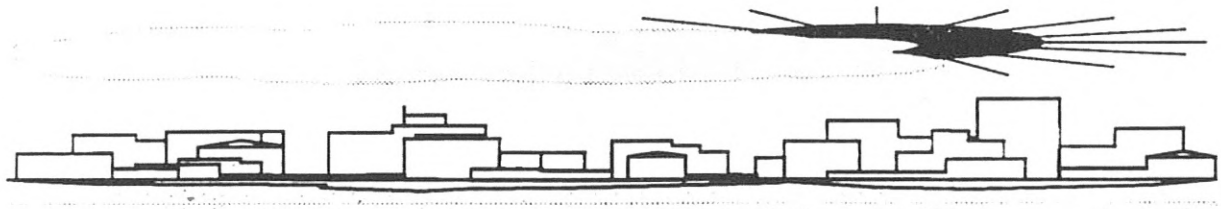
TOXIC AIR POLLUTANT/SOURCE CROSSWALK - A SCREENING TOOL FOR LOCATING POSSIBLE SOURCES EMITTING TOXIC AIR POLLUTANTS, SECOND EDITION



REC 4340

TR 1025

INDUSTRIAL PROCESS	SIC CODE	EMISSION SOURCE	SCC CODE	POLLUTANT	CAS NUMBER	EMISSION FACTOR	NOTES	REFERENCE
Asphaltic concrete production	2951	Plant stack	305002	Magnesium	7439954	8.8 x 10E-9 lb/ton concrete	Controlled (unspecified) from a single plant, mean of 2 values, range is 4.4 x 10E-9 - 1.32 x 10E-8 lb ton	170
Asphaltic concrete production	2951	Plant stack	305002	Magnesium	7439954	2.96 x 10E-7 lb/ton concrete	Uncontrolled from a single plant, mean of 2 values, range is 2.05 x 10E-7 - 3.87 x 10E-7 lb/ton	170
Asphaltic concrete production	2951	Plant stack	305002	Manganese	7439965	3.02 x 10E-10 lb/ton concrete	Controlled (unspecified) from a single plant, average of 2 values, range is 1.63 x 10E-10 - 4.4 x 10E-10 lb/ton	170
Asphaltic concrete production	2951	Plant stack	305002	Manganese	7439965	5.72 x 10E-9 lb/ton concrete	Uncontrolled from a single plant, average of 2 values, range is 3.3 x 10E-9 - 8.1 x 10E-9 lb/ton	170
Asphaltic concrete production	2951	Plant stack	305002	Mercury	7439976	<1.1 x 10E-9 lb/ton concrete	Controlled (unspecified) from a single plant, average of 2 values, range is 8.8 x 10E-10 - 1.3 x 10E-9	170
Asphaltic concrete production	2951	Plant stack	305002	Mercury	7439976	<2.07 x 10E-9 lb/ton concrete	Uncontrolled from a single plant, average of 2 values, range is 1.5 x 10E-9 - 2.6 x 10E-9	170
Asphaltic concrete production	2951	Plant stack	305002	Nickel	7440020	1.48 x 10E-10 lb/ton concrete	Controlled (unspecified) from a single plant, avg. of 2 values, range is 1.44 x 10E-10 - 1.51 x 10E-10 lb/ton	170
Asphaltic concrete production	2951	Plant stack	305002	Nickel	7440020	7.7 x 10E-10 lb/ton concrete	Uncontrolled from a single plant, avg. of 2 values, range is 6.6 x 10E-10 - 8.8 x 10E-10 lb/ton	170
Asphaltic concrete production	2951	Plant stack	305002	Vanadium	7440622	1.87 x 10E-9 lb/ton concrete	Controlled (unspecified) from a single plant, avg. of 2 values, range is 1.76 x 10E-9 - 1.98 x 10E-9	170
Asphaltic concrete production	2951	Plant stack	305002	Vanadium	7440622	<3.9 x 10E-9 lb/ton concrete	Uncontrolled from a single plant, avg. of 2 values, range is 1.98 x 10E-9 - 5.7 x 10E-9	170
Asphaltic concrete production	2951	Plant stack	305002	Vanadium	7440622	8.00E-7 g/ton concrete	Controlled (unspecified) from a single plant	170
Asphaltic concrete production	2951	Plant stack	305002	Zinc	7440666	5.5 x 10E-10 lb/ton concrete	Controlled (unspecified) from a single plant, avg. of 2 values, range is 4.4 x 10E-10 - 6.6 x 10E-10 lb/ton	170
Asphaltic concrete production	2951	Plant stack	305002	Zinc	7440666	1.98 x 10E-9 lb/ton concrete	Uncontrolled from a single plant, avg. of 2 values, range is 1.76 x 10E-9 - 2.2 x 10E-9 lb/ton	170
Automobile carburetor manufacture	3592	Manual plating cleaning tanks		Sodium hydroxide	1310732	0.03 lb/hr/ft2 tank	Developed by State agency and plant personnel, assume NaOH is 5.7% soln.	158
Automotive products use		End use		Xylenes (mixed isomers)	1330207	2000 lb/ton xylene consumed	Engineering judgement	77
Bagasse combustion	0133	Industrial boilers	10201101	Polycyclic organic matter		179.7 lb/10E12 Btu heat input	2 boilers each w/ multicyclone vented to 1 common stack. Represents both gaseous & particulate POM	114
Bagasse combustion	0133	Industrial boilers	10201101	Polycyclic organic matter		99.9 lb/10E12 Btu heat input	Average of 2 (17.2-48.9), multicyclone, represents both gaseous and particulate POM.	114

TR 1026
REC 4341
1C/14PRINT

TR 1027

INDUSTRIAL PROCESS	SIC CODE	EMISSION SOURCE	SCC CODE	POLLUTANT	CAS NUMBER	EMISSION FACTOR	NOTES	REFERENCE
Asphaltic concrete production	2951	Plant stack	305002	Aluminum	7429905	1.2 x 10E-7 - 2.67 x 10E-7 lb/ton concrete	Uncontrolled from a single plant	170
Asphaltic concrete production	2951	Plant stack	305002	Aluminum	7429905	1.76 x 10E-9 - 5.1 x 10E-9 lb/ton concrete	Controlled (unspecified) from a single plant	170
Asphaltic concrete production	2951	Plant stack	305002	Beryllium	7440417	2.50 x 10E-11 lb/ton concrete	Uncontrolled from a single plant, avg. of 2 values, range is 2.1 - 2.9 x 10E-11 lb/ton	170
Asphaltic concrete production	2951	Plant stack	305002	Beryllium	7440417	1.98 x 10E-12 lb/ton concrete	Controlled (unspecified) from a single plant	170
Asphaltic concrete production	2951	Plant stack	305002	Butyraldehyde	123728	0.0024 lb/ton concrete	Based on limited test data, cyclone/wet scrubber control	97
Asphaltic concrete production	2951	Plant stack	305002	Cadmium	7440439	2.46 x 10E-10 lb/ton concrete	Controlled (unspecified) from a single plant, avg. of 2 values, range is 5.24 x 10E-11 - 4.4 x 10E-10 lb/ton	170
Asphaltic concrete production	2951	Plant stack	305002	Cadmium	7440439	1.82 x 10E-10 lb/ton concrete	Uncontrolled from a single plant, avg. of 2 values, range is 1.81 x 10E-10 - 1.83 x 10E-10 lb/ton	170
Asphaltic concrete production	2951	Plant stack	305002	Calcium	7440702	1.73 x 10E-5 lb/ton concrete	Uncontrolled from a single plant, avg. of 2 values, range is 1.03 x 10E-5 - 2.42 x 10E-5 lb/ton	170
Asphaltic concrete production	2951	Plant stack	305002	Calcium	7440702	2.76 x 10E-7 lb/ton concrete	Controlled (unspecified) from a single plant, avg. of 2 values, range is 1.72 x 10E-7 - 3.81 x 10E-7 lb/ton	170
Asphaltic concrete production	2951	Plant stack	305002	Calcium	7440702	3.3 x 10E-11 lb/ton concrete	Controlled (unspecified) from a single plant	170
Asphaltic concrete production	2951	Plant stack	305002	Chromium	7440473	1.24 x 10E-10 lb/ton concrete	Controlled (unspecified) from a single plant. Avg. of 2 values, range is 7.57 x 10E-11 - 1.71 x 10E-10 lb/ton	170
Asphaltic concrete production	2951	Plant stack	305002	Chromium	7440473	1.21 x 10E-9 lb/ton	Uncontrolled from a single plant, avg. of 2 values, range is 1.10 x 10E-9 - 1.32 x 10E-9 lb/ton	170
Asphaltic concrete production	2951	Plant stack	305002	Formaldehyde	50000	0.00015 lb/ton concrete	Based on limited test data, cyclone/wet scrubber control	97
Asphaltic concrete production	2951	Plant stack	305002	Iron	15438310	3.72 x 10E-7 lb/ton concrete	Uncontrolled from a single plant, avg. of 2 values, range is 2.22 x 10E-7 - 5.21 x 10E-7 lb/ton	170
Asphaltic concrete production	2951	Plant stack	305002	Iron	15438310	4.73 x 10E-9 lb/ton concrete	Controlled (unspecified) from a single plant, avg. of 2 values, range is 3.08 x 10E-9 - 6.38 x 10E-9 lb/ton	170
Asphaltic concrete production	2951	Plant stack	305002	Lead	7439921	3.98 x 10E-11 lb/ton	Controlled (unspecified) from a single plant, avg. of 2 values, range is 3.7 x 10E-11 - 4.25 x 10E-11 lb/ton	170
Asphaltic concrete production	2951	Plant stack	305002	Lead	7439921	9.9 x 10E-10 lb/ton concrete	Uncontrolled from a single plant, average of 2 values, range is 8.8 x 10E-10 - 1.1 x 10E-9 lb/ton	170

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INDUSTRIAL PROCESS	SIC CODE	EMISSION SOURCE	SCC CODE	POLLUTANT	CAS NUMBER	EMISSION FACTOR	NOTES	REFERENCE
Asphalt (hot mix) production	2951	Drum mix plant	30500205	Polycyclic organic matter		7.18 x 10E-5 lb/ton asphalt produced	Knock out box, using recycled feed	114
Asphalt (hot mix) production	2951	Drum mix plant	30500205	Polycyclic organic matter		3.38 x 10E-5 lb/ton asphalt produced	Knock out box and venturi scrubber, using recycled feed	114
Asphalt (hot mix) production	2951	Drum mix plant	30500205	Polycyclic organic matter		4.42 x 10E-5 lb/ton asphalt produced	Knock out box	114
Asphalt (hot mix) production	2951	Drum mix plant	30500205	Polycyclic organic matter		2.7 x 10E-5 lb/ton asphalt produced	Knock out box and venturi scrubber	114
Asphalt distribution/use	5032	Entire process		Benzene	71432	0.077 lb/ton asphalt applied	Benzene assumed to be 9.6% of THC	92
Asphalt distribution/use	5032	Entire process		Formaldehyde	50000	0.004 lb/ton asphalt applied	Formaldehyde assumed to be 0.5% of THC	92
Asphalt distribution/use	5032	Entire process		Polycyclic organic matter		0.0008 lb/ton asphalt applied	POM assumed to be 0.1% of THC	92
Asphalt production		Entire process		Formaldehyde	50000	0.00015 lb/ton asphalt produced	Control uncertain	94
Asphalt roofing material production	2952	Asphalt blowing still	30500101	Polycyclic organic matter		0.0304 lb/ton asphalt blown	Uncontrolled	114
Asphalt roofing material production	2952	Asphalt blowing still	30500101	Polycyclic organic matter		9.6 x 10E-5 lb/ton asphalt blown	Afterburner	114
Asphalt roofing material production	2952	Asphalt blowing still	30500101	Polycyclic organic matter		4.2 x 10E-6 lb/ton asphalt blown	Fume incinerator	114
Asphalt roofing material production	2952	Asphalt blowing still	30500101	Polycyclic organic matter		1.16 x 10E-5 lb/ton asphalt blown	Process heater furnace	114
Asphalt roofing material production	2952	Asphalt blowing still	30500101	Polycyclic organic matter		0.0096 lb/ton asphalt blown	Stack baffles, represents particulate POM	114
Asphalt roofing material production	2952	Saturator	30500103	Polycyclic organic matter		4.2 x 10E-4 lb/ton produced	Uncontrolled	114
Asphalt roofing material production	2952	Saturator	30500103	Polycyclic organic matter		1.92 x 10E-4 lb/ton produced	ESP controlled	114
Asphalt roofing material production	2952	Saturator	30500103	Polycyclic organic matter		6.6 x 10E-4 lb/ton produced	Uncontrolled	114
Asphalt roofing material production	2952	Saturator and asphalt storage tanks	30500103	Polycyclic organic matter		0.042 lb/ton produced	High velocity air filter	114

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INDUSTRIAL PROCESS	SIC CODE	EMISSION SOURCE	SCC CODE	POLLUTANT	CAS NUMBER	EMISSION FACTOR	NOTES	REFERENCE
Asbestos product fabrication	3292	Floor tile		Asbestos	1332214	1.0 lb/ton asbestos produced	Controlled	33
Asbestos product fabrication	3292	Friction material production		Asbestos	1332214	6 lb/ton asbestos produced	Controlled	33
Asbestos product fabrication	3292	Grinding brake shoes		Asbestos	1332214	465 fibers/cc air/g asbestos machined	Average of test results	22
Asbestos product fabrication	3292	Sawing asbestos cement sheet		Asbestos	1332214	1838 fibers/cc air/g asbestos machined	Average of test results, cut-off wheel saw	22
Asbestos product fabrication	3292	Sawing asbestos cement sheet		Asbestos	1332214	305 fibers/cc air/g asbestos machined	Average of test results, toothed blade saw	22
Asbestos product fabrication	3292	Sawing asbestos millboard		Asbestos	1332214	647 fibers/cc air/g asbestos machined	Average of test results, toothed blade saw	22
Asbestos product fabrication	3292	Textiles		Asbestos	1332214	40 lb/ton asbestos produced	Uncontrolled	33
Asbestos product fabrication	3292	Textiles		Asbestos	1332214	2 lb/ton asbestos produced	Controlled	33
Asbestos product usage		Brake linings		Asbestos	1332214	10 lb/ton asbestos produced	Uncontrolled	33
Asbestos product usage		Construction industry		Asbestos	1332214	26 lb/ton asbestos produced		33
Asbestos product usage		Insulating cement		Asbestos	1332214	26 lb/ton asbestos produced	Controlled	33
Asbestos product usage		Steel fireproofing		Asbestos	1332214	10 lb/ton asbestos produced	Controlled	33
Asbestos textiles manufacturing	3292	Entire process		Asbestos	1332214	63.7 lb/ton asbestos consumed	Calculated average uncontrolled factor, calculated range 26.7-88.8	100
Asbestos textiles manufacturing	3292	Entire process		Asbestos	1332214	3.54 lb/ton asbestos consumed	Calculated average controlled factor, calculated range 0.026-35.5	100
Asbestos-reinforced plastics manufacturing	3292	Entire process		Asbestos	1332214	930.8 lb/ton asbestos consumed	Calculated average uncontrolled factor, calculated range 0.96-2000	100
Asbestos-reinforced plastics manufacturing	3292	Entire process		Asbestos	1332214	5.70 lb/ton asbestos consumed	Calculated average controlled factor, calculated range 9.66 x 10-5 - 200	100
Ascorbic acid production	2833	Plantwide emissions	301060	Chloroform	67663	4.92 x 10E5 lb/yr	Based on one facility (30 million lb/yr production)	160
Asphalt (hot mix) production	2951	Batch mix plant, rotary dryer and mixer	30500201	Polycyclic organic matter		3.94 x 10E-5 lb/ton asphalt produced	Cyclone and wet scrubber, virgin feed material	114

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Office of Air Quality Planning and Standards
Research Triangle Park, North Carolina 27711

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4.5 CUTBACK ASPHALT, EMULSIFIED ASPHALT AND ASPHALT CEMENT

4.5.1 General[1-3]

Asphalt surfaces and pavements are composed of compacted aggregate and an asphalt binder. Aggregate materials are produced from rock quarries as manufactured stone or are obtained from natural gravel or soil deposits. Metal ore refining processes produce artificial aggregates as a byproduct. In asphalt, the aggregate performs three functions. It transmits the load from the surface to the base course, takes the abrasive wear of traffic, and provides a nonskid surface. The asphalt binder holds the aggregate together, preventing displacement and loss of aggregate and providing a waterproof cover for the base.

Asphalt binders take the form of asphalt cement (the residue of the distillation of crude oils) and liquified asphalts. To be used for pavement, asphalt cement, which is semisolid, must be heated prior to mixing with aggregate. The resulting hot mix asphalt concrete is generally applied in thicknesses of from two to six inches. Liquified asphalts are (1) asphalt cutbacks (asphalt cement thinned or "cutback" with volatile petroleum distillates such as naptha, kerosene, etc.) and (2) asphalt emulsions (nonflammable liquids produced by combining asphalt and water with an emulsifying agent, such as soap). Liquified asphalts are used in tack and seal operations, in priming roadbeds for hot mix application, and for paving operations up to several inches thick.

Cutback asphalts fall into three broad categories: rapid cure (RC), medium cure (MC), and slow cure (SC) road oils. SC, MC and RC cutbacks are prepared by blending asphalt cement with heavy residual oils, kerosene-type solvents, or naptha and gasoline solvents, respectively. Depending on the viscosity desired, the proportions of solvent added generally range from 25 to 45 percent by volume.

Emulsified asphalts are of two basic types. One type relies on water evaporation to cure. The other type (cationic emulsions) relies on ionic bonding of the emulsion and the aggregate surface. Emulsified asphalt can substitute for cutback in almost any application. Emulsified asphalts are gaining in popularity, because of the energy and environmental problems associated with the use of cutback asphalts.

4.5.2 Emissions[1,2]

The primary pollutants of concern from asphalts and asphalt paving operations are volatile organic compounds (VOC). Of the three types of asphalts, the major source of VOC is cutback. Only minor amounts of VOC are emitted from emulsified asphalts and asphalt cement.

VOC emissions from cutback asphalts result from the evaporation of the petroleum distillate solvent, or diluent, used to liquify the asphalt cement. Emissions occur at both the job site and the mixing plant. At the job site, VOCs are emitted from the equipment used to apply the asphaltic product and from the road surface. At the mixing plant, VOCs are released during mixing and stockpiling. The largest source of emissions, however, is the road surface itself.

For any given amount of cutback asphalt, total emissions are believed to be the same, regardless of stockpiling, mixing and application times. The two major variables affecting both the quantity of VOC emitted and the time over which emissions occur are the type and the quantity of petroleum distillate used as a diluent. As an approximation, long term emissions from cutback asphalts can be estimated by assuming that 95 percent of the diluent evaporates from rapid cure (RC) cutback asphalts, 70 percent from medium cure (MC) cutbacks, and about 25 percent from slow cure (SC) asphalts, by weight percent. Some of the diluent appears to be retained permanently in the road surface after application. Limited test data suggest that, from rapid cure (RC) asphalt, 75 percent of the total diluent loss occurs on the first day after

application, 90 percent occurs within the first month, and 95 percent in three to four months. Evaporation takes place more slowly from medium cure (MC) asphalts, with roughly 20 percent of the diluent being emitted during the first day, 50 percent during the first week, and 70 percent after three to four months. No measured data are available for slow cure (SC) asphalts, although the quantity emitted is believed to be considerably less than with either rapid or medium cure asphalts, and the time during which emissions take place is expected to be considerably longer (Figure 4.5-1). An example calculation for determining VOC emissions from cutback asphalts is given below:

Example: Local records indicate that 10,000 kg of RC cutback asphalt (containing 45 percent diluent, by volume) was applied in a given area during the year. Calculate the mass of VOC emitted during the year from this application.

To determine VOC emissions, the volume of diluent present in the cutback asphalt must first be determined. Because of density of naptha (0.7 kg/l) differs from that of asphalt cement (1.1 kg/l), the following equations should be solved to determine the volume of diluent (x) and the volume of asphalt cement (y) in the cutback asphalt:

$$10{,}000 \text{ kg cutback asphalt} = (\text{x liter, diluent}) \cdot \left(\frac{0.7 \text{ kg}}{\text{liter}}\right) + (\text{y liter, asphalt cement}) \cdot \left(\frac{1.1 \text{ kg}}{\text{liter}}\right)$$

and

$$\text{x liter, diluent} = 0.45\ (\text{x liter, diluent} + \text{y liter, asphalt cement})$$

From these equations, the volume of diluent present in the cutback asphalt is determined to be about 4900 liters, or about 3400 kg. Assuming that 95 percent of this is evaporative VOC, emissions are then: 3400 kg x 0.95 = 3200 kg (i.e., 32% by weight, of the cutback asphalt eventually evaporates).

These equations can be used for medium cure and slow cure asphalts by assuming typical diluent densities of 0.8 and 0.9 kg/liter, respectively. Of course, if actual density values are known from local records, they should be used in the above equations rather than typical values. Also, if different diluent contents are used, they should also be reflected in the above calculations. If actual diluent contents are not known, a typical value of 35 percent may be assumed for inventory purposes.

In lieu of solving the equations in the above example, Table 4.5-1 may be used to estimate long term emissions from cutback asphalts. Table 4.5-1 directly yields long term emissions as a function of the volume of diluent added to the cutback and of the density of the diluents and asphalt cement used in the cutback asphalt. If short term emissions are to be estimated, Figure 4.5-1 should be used in conjunction with Table 4.5-1.

No control devices are employed to reduce evaporative emissions from cutback asphalts. Asphalt emulsions are typically used in place of cutback asphalts to eliminate VOC emissions.

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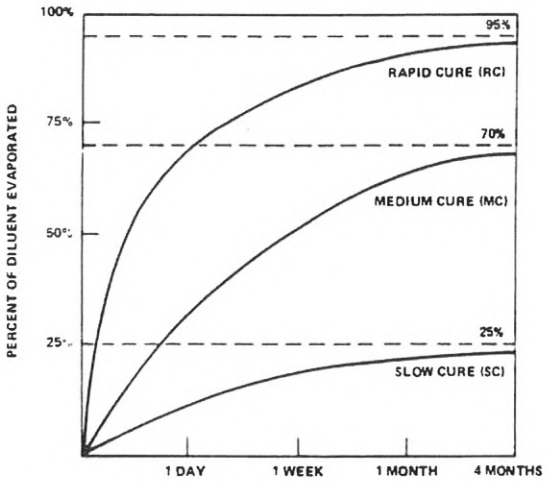

Figure 4.5-1. Percent of diluent evaporated from cutback asphalt over time.

TABLE 4.5-1. EVAPORATIVE VOC EMISSIONS FROM CUTBACK ASPHALTS AS A FUNCTION OF DILUENT CONTENT AND CUTBACK ASPHALT TYPE[a]

EMISSION FACTOR RATING: C

Type of Cutback[b]	Percent, by Volume, of Diluent in Cutback[c]		
	25%	35%	45%
Rapid cure	17	24	32
Medium cure	14	20	26
Slow cure	5	8	10

[a]These numbers represent the percent, by weight, of cutback asphalt evaporated. Factors are based on References 1 and 2.

[b]Typical densities assumed for diluents used in RC, MC and SC cutbacks are 0.7, 0.8 and 0.9 kg/liter, respectively.

[c]Diluent contents typically range between 25-45%, by volume. Emissions may be linearly interpolated for any given type of cutback between these values.

References for Section 4.5

1. R. Keller and R. Bohn, *Nonmethane Volatile Organic Emissions from Asphalt Cement and Liquified Asphalts*, EPA-450/3-78-124, U.S. Environmental Protection Agency, Research Triangle Park, NC, December 1978.

2. F. Kirwan and C. Maday, *Air Quality and Energy Conservation Benefits from Using Emulsions To Replace Asphalt Cutbacks in Certain Paving Operations*, EPA-450/2-78-004. U.S. Environmental Protection Agency, Research Triangle Park. NC, January 1978.

3. David W. Markwordt, *Control of Volatile Organic Compounds from Use of Cutback Asphalt*, EPA-450/2-77-037, U.S. Environmental Protection Agency, Research Triangle Park. NC, December 1977.

REC 4349

TR 1034

M A T E R I A L S A F E T Y D A T A S H E E T

IDAHO ASPHALT SUPPLY INC.
Nampa, Idaho

CRS-1, CRS-2, CRS-2f, CRS-2h

MATERIAL IDENTIFICATION

Chemical Name: Cationic Rapid Set Asphalt Emulsion
Manufacturer: Idaho Asphalt Supply Inc.
Address: P.O. Box 966, Nampa, Id. 83651
Hazard Rating (NFPA)
Health: 1
Fire: 0
Reactivity: 0
Special: None

CAS Registry No. N/A
Date Prepared; 5/1 /89

Hazard Rating Scale:
0 - Minimal 3 - Serious
1 - Slight 4 - Severe
2 - Moderate

HAZARDOUS INGREDIENTS

Ingredients	CAS #	Percent	PEL	STEL	TLV
Asphalt cement	8052-42-4	65-70%	N/A	10mg/m	5mg/m
Naptha	8032-32-4	0-3%	100ppm	N/A	400ppm
Emulsifier	TSCA	0.15-0.5%	N/A	N/A	N/A

PHYSICAL DATA

Boiling Point - 212f
Vapor Pressure - <1
Vapor Density - >0.062
Specific Gravity @ 60f - 1.025 to 1.06
Melting Point - N/A
Evaporation Rate - <1
Solubility in water - up to 100%
Appearance and Odor - Viscous brown to black liquid ; odor of amines and hydrocarbons

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FIRE AND EXPLOSIVE DATA

Flash Point - N/A
Autoignition Temperature NFPA - N/A
Extinguishing Media - CO2, Class "B" extinguisher, foam and water fog.
Special Fire Fighting Procedures - Avoid breathing vapors, wear self-contained breathing apparatus.
Unusual Fire Explosion Hazards - DO NOT heat material above 212f to avoid generating excessive steam pressure.

REACTIVITY DATA

Stable: X Unstable:

Conditions to Avoid	-	DO NOT HEAT ABOVE 212f, Ignition sources.
Incompatible Materials	-	Avoid strong oxidizing agents
Hazardous Decomposition Products	-	Combustion may form CO2, CO, and sulfur oxide.
Hazardous Polymerization	-	Will not occur.

HEALTH HAZARD DATA

Route of Exposure	Primary Route	Signs and Symptoms
Inhalation	[X]	Use with good ventilation. May cause respiratory tract irritation
Skin Absorption	[ ]	No significant symptoms indicative of skin absorption expected.
Skin Irritation	[X]	Will cause burns when product is hot. May cause dermatitis and acne like lesions on prolonged exposure.
Ingestion	[ ]	May cause nausea and diarrhea.
Eye Contact	[X]	Will burn and irritate.

Listed as Carcinogen? Not listed by NTP, IARC, or OSHA.

EMERGENCY FIRST AID

Inhalation:	Remove to fresh air. Give oxygen or artificial respiration as needed Obtain medical attention promptly.
Eye Contact:	Flush eyes with low pressure water for at least 15 minutes and obtain medical attention immediately.
Skin Contact:	If product is hot, cool with cold water. Otherwise wash thoroughly with soap and water.
Ingestion:	Call physician. Do not induce vomiting.

PROTECTIVE EQUIPMENT / CONTROL MEASURES

Respiratory Protection:	Avoid breathing vapors in confined spaces. NIOSH approved respirators may be required if TLV's are exceeded.
Eye Protection:	Use safety glasses, goggles or face shields.
Skin Protection:	Use rubber gloves, coveralls and impervious footwear.
Engineering controls:	Local exhaust ventilation may be required to meet exposure standards in confined areas.
Handling Precautions:	Avoid heating over 212f.

SPILL AND DISPOSAL

Spill or Release:	Stop release, prevent flow from entering sewers or public waters. Allow to cool. Recover large spill. Let product cure or soak up with sand on smaller spills.
Waste Disposal Method:	Handle in accordance with federal, state and local regulations.

DISCLAIMER

Some of the information presented and conclusions drawn herein are from sources other than direct test data on the product itself. The information in this MSDS was obtained from sources which we believe reliable. However, the information is provided without any warranty, expressed or implied, regarding its correctness.

The condition or methods of handling, storage, use and disposal of the products are beyond our control and may be beyond our knowledge. For this and other reasons, we do not assume responsibility and expressly disclaim liability for loss, damage or expense arising out of or in any way connected with the handling, storage, use or disposal of the product.

This MSDS was prepared and is to be used only for this product. If the product is used as a component in another product, this MSDS information may not be applicable.

This MSDS has been prepared in accordance with the requirements of the OSHA Hazardous Communication Standard (29 CFR 1200)

MATERIAL SAFETY DATA SHEET

IDAHO ASPHALT SUPPLY INC.
(Hauser), Post Falls, ID

LMCRS-2, LMCRS-2h, CRS-2R

RECEIVED
JUN 26 1992
DIV. OF ENVIRONMENTAL QUALITY
PERMITS & ENFORCEMENTS

MATERIAL IDENTIFICATION

Chemical Name: Cationic Rapid Set Asphalt Emulsion
Manufacturer: Idaho Asphalt Supply Inc.
Address: P.O. Box 966, Nampa, Id. 83651
Hazard Rating (NFPA)
Health: 1
Fire: 0
Reactivity: 0
Special: None

CAS Registry No. N/A
Date Prepared: 5/19/89

Hazard Rating Scale:
0 - Minimal 3 - Serious
1 - Slight 4 - Severe
2 - Moderate

HAZARDOUS INGREDIENTS

Ingredients	CAS #	Percent	PEL	STEL	TLV
Asphalt cement	8052-42-4	57-68%	N/A	10mg/m	5mg/m
Naptha	8032-32-4	0-3%	100ppm	N/A	400ppm
Elastomers	126-99-8	1.5-3%	10ppm	N/A	20ppm
Emulsifier	TSCA	1-3%	N/A	N/A	N/A

PHYSICAL DATA

Boiling Point - 212f
Vapor Pressure - <1
Vapor Density - >0.062
Specific Gravity @ 60f - 1.025 to 1.06
Melting Point - N/A
Evaporation Rate - <1
Solubility in water - up to 100%
Appearance and Odor - Viscous brown to black liquid ; odor of amines and hydrocarbons

FIRE AND EXPLOSIVE DATA

Flash Point - N/A
Autoignition Temperature NFPA - N/A
Extinguishing Media - CO2, Class "B" extinguisher, foam and water fog.
Special Fire Fighting Procedures - Avoid breathing vapors, wear self-contained breathing apparatus.
Unusual Fire Explosion Hazards - DO NOT heat material above 212f to avoid generating excessive steam pressure.

REACTIVITY DATA

Stable: X Unstable:

Conditions to Avoid	-	DO NOT HEAT ABOVE 212f, Ignition sources.
Incompatible Materials	-	Avoid strong oxidizing agents
Hazardous Decomposition Products	-	Combustion may form CO2, CO, and sulfur dioxide.
Hazardous Polymerization	-	Will not occur.

HEALTH HAZARD DATA

Route of Exposure	Primary Route	Signs and Symptoms
Inhalation	[X]	Use with good ventilation. May cause respiratory tract irritation
Skin Absorption	[ ]	No significant symptoms indicative of skin absorption expected.
Skin Irritation	[X]	Will cause burns when product is hot. May cause dermatitis and acne like lesions on prolonged exposure.
Ingestion	[ ]	May cause nausea and diarrhea.
Eye Contact	[X]	Will burn and irritate.

Listed as Carcinogen? Not listed by NTP, IARC, or OSHA.

EMERGENCY FIRST AID

Inhalation:	Remove to fresh air. Give oxygen or artificial respiration as needed Obtain medical attention promptly.
Eye Contact:	Flush eyes with low pressure water for at least 15 minutes and obtain medical attention immediately.
Skin Contact:	If product is hot, cool with cold water. Otherwise wash thoroughly with soap and water.
Ingestion:	Call physician. Do not induce vomiting.

PROTECTIVE EQUIPMENT / CONTROL MEASURES

Respiratory Protection:	Avoid breathing vapors in confined spaces. NIOSH approved respirators may be required if TLV's are exceeded.
Eye Protection:	Use safety glasses, goggles or face shields.
Skin Protection:	Use rubber gloves, coveralls and impervious footwear.
Engineering controls:	Local exhaust ventilation may be required to meet exposure standards in confined areas.
Handling Precautions:	Avoid heating over 212f.

SPILL AND DISPOSAL

Spill or Release:	Stop release, prevent flow from entering sewers or public waters. Allow to cool. Recover large spill. Let product cure or soak up with sand on smaller spills.
Waste Disposal Method:	Handle in accordance with federal, state and local regulations.

DISCLAIMER

Some of the information presented and conclusions drawn herein are from sources other than direct test data on the product itself. The information in this MSDS was obtained from sources which we believe reliable. However, the information is provided without any warranty, expressed or implied, regarding its correctness.

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This MSDS has been prepared in accordance with the requirements of the OSHA Hazardous Communication Standard (29 CFR 1200)

MATERIAL SAFETY DATA SHEET

IDAHO ASPHALT SUPPLY INC.
Nampa, Idaho

MC Cutbacks

MATERIAL IDENTIFICATION

Chemical Name: Medium Cure Cutback Asphalts
Manufacturer: Idaho Asphalt Supply Inc.
Address: P.O. Box 966, Nampa, Id. 83651
CAS Registry No. N/A
Date Prepared: 5/19/89

Hazard Rating (NFPA)
Health: 2
Fire: 2
Reactivity: 0
Special: None

Hazard Rating Scale:
0 - Minimal 3 - Serious
1 - Slight 4 - Severe
2 - Moderate

HAZARDOUS INGREDIENTS

Ingredients	CAS #	Percent	PEL	STEL	TLV
Asphalt cement	8052-42-4	60-90%	N/A	10mg/m	5mg/m
Benzene	100-14-1	>0.1%?	N/A	25 ppm	10ppm
No.1 Fuel	8032-32-4	40-10%	100ppm	N/A	400ppm

PHYSICAL DATA

Boiling Point - > 300f
Vapor Pressure - < 1
Vapor Density - > 1
Solubility in water - No
Specific Gravity @ 60f - 0.90 to 1.10
Melting Point - N/A
Evaporation Rate - <1
Appearance and Odor - Black liquid or solid. Odor of hydrocarbons.

FIRE AND EXPLOSIVE DATA

Flash Point - > 100f TOC
Autoignition Temperature NFPA - N/A
Extinguishing Media - CO2, Class "B" extinguisher, foam or water fog.
Special Fire Fighting Procedures - Avoid breathing vapors. Avoid subsurface penetration with water; may cause foaming or frothing which could spread hazard
Unusual Fire Explosion Hazards - None

REACTIVITY DATA

Stable: X Unstable:

Conditions to Avoid	-	Ignition sources.
Incompatible Materials	-	Avoid strong oxidizing agents
Hazardous Decomposition Products	-	Combustion may form CO2, CO, and sulfur dioxide.
Hazardous Polymerization	-	Will not occur.

HEALTH HAZARD DATA

Route of Exposure	Primary Route	Signs and Symptoms
Inhalation	[X]	Use with good ventilation. May cause respiratory tract irritation
Skin Absorption	[ ]	No significant symptoms indicative of skin absorption expected.
Skin Irritation	[X]	Will cause burns when product is hot. May cause dermatitis and acne like lesions on prolonged exposure.
Ingestion	[ ]	May cause nausea and diarrhea.
Eye Contact	[X]	Will burn and irritate.

Listed as Carcinogen? Not listed by NTP, IARC, or OSHA.

EMERGENCY FIRST AID

Inhalation:	Remove to fresh air. Give oxygen or artificial respiration as needed Obtain medical attention promptly.
Eye Contact:	Flush eyes with low pressure water for at least 15 minutes and obtain medical attention immediately.
Skin Contact:	If product is hot, cool with cold water. Otherwise wash thoroughly with soap and water.
Ingestion:	Call physician. Do not induce vomiting.

PROTECTIVE EQUIPMENT / CONTROL MEASURES

Respiratory Protection:	Avoid breathing vapors in confined spaces. NIOSH approved respirators may be required if TLV's are exceeded.
Eye Protection:	Use safety glasses, goggles or face shields.
Skin Protection:	Use rubber gloves, coveralls and impervious footwear
Engineering controls:	Local exhaust ventilation may be required to meet exposure standards in confined areas.
Handling Precautions:	Storage tanks and trucks must be emptied, cooled, ventilated, and tested for absence of vapors before allowing personel entry.

SPILL AND DISPOSAL

Spill or Release:	Stop release, prevent flow from entering sewers or public waters. Allow to cool. Recover large spill. Let product cure or soak up with sand on smaller spills.
Waste Disposal Method:	Handle in accordance with federal, state and local regulations.

DISCLAIMER

Some of the information presented and conclusions drawn herein are from sources other than direct test data on the product itself. The information in this MSDS was obtained from sources which we believe reliable. However, the information is provided without any warranty, expressed or implied, regarding its correctness.

The condition or methods of handling, storage, use and disposal of the products are beyond our control and may be beyond our knowledge. For this and other reasons, we do not assume responsibility and expressly disclaim liability for loss, damage or expense arising out of or in any way connected with the handling, storage, use or disposal of the product.

This MSDS was prepared and is to be used only for this product. If the product is used as a component in another product, this MSDS information may not be applicable.

This MSDS has been prepared in accordance with the requirements of the OSHA Hazardous Communication Standard (29 CFR 1200)

M A T E R I A L S A F E T Y D A T A S H E E T

IDAHO ASPHALT SUPPLY INC.
Nampa, Idaho

CMS-2, CMS-2h, CMS-2s, CMS-2R

MATERIAL IDENTIFICATION

Chemical Name: Cationic Medium Set Asphalt Emulsion
Manufacturer: Idaho Asphalt Supply Inc.
Address: P.O. Box 966, Nampa, Id. 83651
Hazard Rating (NFPA)
Health: 1
Fire: 1
Reactivity: 0
Special: None

CAS Registry No. N/A
Date Prepared; 5/19/89

Hazard Rating Scale:
0 - Minimal 3 - Serious
1 - Slight 4 - Severe
2 - Moderate

HAZARDOUS INGREDIENTS

Ingredients	CAS #	Percent	PEL	STEL	TLV
Asphalt cement	8052-42-4	60-70%	N/A	10mg/m	5mg/m
Benzene	100-14-1	>0.1%?	N/A	25 ppm	10ppm
Naptha	8032-32-4	5-15%	100ppm	N/A	400ppm
Emulsifier	TSCA	0.15-0.5%	N/A	N/A	N/A

PHYSICAL DATA

Boiling Point - 212f
Vapor Pressure - <1
Vapor Density - >0.062
Specific Gravity @ 60f - 1.025 to 1.06
Melting Point - N/A
Evaporation Rate - <1
Solubility in water - up to 100%
Appearance and Odor - Viscous brown to black liquid ; odor of amines and hydrocarbons

FIRE AND EXPLOSIVE DATA

Flash Point - N/A
Autoignition Temperature NFPA - N/A
Extinguishing Media - CO2, Class "B" extinguisher, foam and water fog.
Special Fire Fighting Procedures - Avoid breathing vapors, wear self-contained breathing apparatus.
Unusual Fire Explosion Hazards - DO NOT heat material above 212f to avoid generating excessive steam pressure.

REACTIVITY DATA

Stable: X Unstable:

Conditions to Avoid	-	DO NOT HEAT ABOVE 212f, Ignition sources.
Incompatible Materials	-	Avoid strong oxidizing agents
Hazardous Decomposition Products	-	Combustion may form CO2, CO, and sulfur dioxide.
Hazardous Polymerization	-	Will not occur.

HEALTH HAZARD DATA

Route of Exposure	Primary Route	Signs and Symptoms
Inhalation	[X]	Use with good ventilation. May cause respiratory tract irritation
Skin Absorption	[ ]	No significant symptoms indicative of skin absorption expected.
Skin Irritation	[X]	Will cause burns when product is hot. May cause dermatitis and acne like lesions on prolonged exposure.
Ingestion	[ ]	May cause nausea and diarrhea.
Eye Contact	[X]	Will burn and irritate.

Listed as Carcinogen? Not listed by NTP, IARC, or OSHA

EMERGENCY FIRST AID

Inhalation:	Remove to fresh air. Give oxygen or artificial respiration as needed Obtain medical attention promptly.
Eye Contact:	Flush eyes with low pressure water for at least 15 minutes and obtain medical attention immediately.
Skin Contact:	If product is hot, cool with cold water. Otherwise wash thoroughly with soap and water.
Ingestion:	Call physician. Do not induce vomiting.

PROTECTIVE EQUIPMENT / CONTROL MEASURES

Respiratory Protection:	Avoid breathing vapors in confined spaces. NIOSH approved respirators may be required if TLV's are exceeded.
Eye Protection:	Use safety glasses, goggles or face shields.
Skin Protection:	Use rubber gloves, coveralls and impervious footwear.
Engineering controls:	Local exhaust ventilation may be required to meet exposure standards in confined areas.
Handling Precautions:	Avoid heating over 212f.

SPILL AND DISPOSAL

Spill or Release:	Stop release, prevent flow from entering sewers or public waters. Allow to cool. Recover large spill. Let product cure or soak up with sand on smaller spills.
Waste Disposal Method:	Handle in accordance with federal, state and local regulations.

DISCLAIMER

Some of the information presented and conclusions drawn herein are from sources other than direct test data on the product itself. The information in this MSDS was obtained from sources which we believe reliable. However, the information is provided without any warranty, expressed or implied, regarding its correctness.

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This MSDS has been prepared in accordance with the requirements of the OSHA Hazardous Communication Standard (29 CFR 1200)

M A T E R I A L S A F E T Y D A T A S H E E T

IDAHO ASPHALT SUPPLY INC.
Nampa, Idaho

CSS-1, CSS-1H

MATERIAL IDENTIFICATION

Chemical Name: Cationic Slow Set Asphalt Emulsion
Manufacturer: Idaho Asphalt Supply Inc.
Address: P.O. Box 966, Nampa, Id. 83651
CAS Registry No.: N/A
Date Prepared: 7/1/89

Hazard Rating (NFPA)

Health:	1
Fire:	0
Reactivity:	0
Special:	None

Hazard Rating Scale:
0 - Minimal - Serious
1 - Slight - Severe
2 - Moderate

HAZARDOUS INGREDIENTS

Ingredients	CAS #	Percent	PEL	STEL	LV
Asphalt cement	8052-42-4	57-68%	N/A	10mg/m	mg/m
Emulsifier	TSCA	1-3%	N/A	N/A	N/A

PHYSICAL DATA

Boiling Point - 212f
Vapor Pressure - <1
Vapor Density - >0.062
Specific Gravity @ 60f - 1.025 to 1.06
Melting Point - N/A
Evaporation Rate - <1
Solubility in water - up to 100%
Appearance and Odor - Viscous brown to black liquid ; odor of amines and hydrocarbons

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FIRE AND EXPLOSIVE DATA

Flash Point - N/A
Autoignition Temperature NFPA - N/A
Extinguishing Media - CO2, Class "B" extinguisher, foam and water fog.
Special Fire Fighting Procedures - Avoid breathing vapors, wear self-contained breathing apparatus.
Unusual Fire Explosion Hazards - DO NOT heat material above 212f to avoid generating excessive steam pressure.

REACTIVITY DATA — Stable: X — Unstable:

Conditions to Avoid	-	DO NOT HEAT ABOVE 212f, Ignition sources.
Incompatible Materials	-	Avoid strong oxidizing agents
Hazardous Decomposition Products	-	Combustion may form CO2, CO, and sulfur dioxide.
Hazardous Polymerization	-	Will not occur.

HEALTH HAZARD DATA

Route of Exposure	Primary Route	Signs and Symptoms
Inhalation	[X]	Use with good ventilation. May cause respiratory tract irritation
Skin Absorption	[ ]	No significant symptoms indicative of skin absorption expected.
Skin Irritation	[X]	Will cause burns when product is hot. May cause dermatitis and acne like lesions on prolonged exposure.
Ingestion	[ ]	May cause nausea and diarrhea.
Eye Contact	[X]	Will burn and irritate.

Listed as Carcinogen? — Not listed by NTP, IARC, or OSHA.

EMERGENCY FIRST AID

Inhalation:	Remove to fresh air. Give oxygen or artificial respiration as needed Obtain medical attention promptly.
Eye Contact:	Flush eyes with low pressure water for at least 15 minutes and obtain medical attention immediately.
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Ingestion:	Call physician. Do not induce vomiting.

PROTECTIVE EQUIPMENT / CONTROL MEASURES

Respiratory Protection:	Avoid breathing vapors in confined spaces. NIOSH approved respirators may be required if TLV's are exceeded.
Eye Protection:	Use safety glasses, goggles or face shields.
Skin Protection:	Use rubber gloves, coveralls and impervious footwear.
Engineering controls:	Local exhaust ventilation may be required to meet exposure standards in confined areas.
Handling Precautions:	Avoid heating over 212f.

REVISION #1

LABEL INFORMATION

Chemical name: Asphalt Cements
Common name: Penetration Graded Asphalt AASHTO M-20;
Viscosity Graded Asphalt AASHTO M-226.

DANGER! VAPOR HARMFUL
DO NOT INTRODUCE WATER

Keep away from flames and other sources of ignition
Stable unless moisture is introduced
Extinguishing media - CO_2 or Class 'B' extinguisher
DO NOT APPLY WATER
Avoid breathing vapors. May contain low concentrations of hydrogen sulfide. Wear self-contained breathing apparatus when fire fighting. May cause dermatitis and acne lesions on prolonged and repeated exposure. Can cause severe burns when hot material contacts unprotected skin. Wear chemical resistant gloves, goggles or face shield, long sleeve shirt and pants. Use NIOSH approved respirator if TVL's are exceeded.

FIRST AID

Inhalation - Remove victim to fresh air. Start artificial resuscitation if necessary. Call a physician.

Eyes - Flush eyes with water for at least 15 minutes. Call a physician.

Skin- If hot material contacts skin, place affected part in cold water. Have a physician remove material or for small amounts use mineral oil for removal.

Ingestion - If ingested call a physician.

For further information refer to data sheet for Asphalt Cements.

Farmers Union Central Exchange, Inc. (CENEX)
P. O. Box 909
Laurel, Montana 59044
Telephone: (406)628-4311 or (406)628-4518

REVISION #1

FARMERS UNION CENTRAL EXCHANGE, INC.
P.O. Box 909, Laurel, Montana 59044

Asphalt Cements
Quick Identifier

MATERIAL SAFETY DATA SHEET

The information contained herein is based on data considered accurate, however, no warranty is expressed or implied regarding the accuracy of these data or the results to be obtained from the use thereof. Vendor assumes no responsibility for injury to vendee or third person proximately caused by the material if reasonable safety procedures are not adhered to as stipulated in the data sheet. Additionally, vendor assumes no responsibility for injury to vendee or third persons proximately caused by abnormal use of the material even if reasonable safety procedures are followed. Furthermore, vendee assumes the risk in his use of the material.

SECTION 1 GENERAL

Manufacturer's Name: Farmers Union Central Exchange, Inc. (CENEX)

Emergency Telephone No. 406/628-4518 | Information Telephone No. 406/628-4311

Chemical Name: Asphalt Cements | Date Prepared: 9/20/85

Chemical Family: Petroleum Asphalt Cements

Common Name(s): Penetration graded asphalt AASHTO M-20; Viscosity graded asphalt AASHTO M-22(

SECTION 2 HAZARDOUS INGREDIENTS/IDENTITY

This product, when heated above the softening point, may contain low concentrations of hydrogen sulfide. This gas, at low concentrations, may be irritating to eyes, skin and respiratory tract.

OSHA PEL: Petroleum Asphalt Cement Not Available

ACGIH TLV'S: Asphalt Cements - 5mg/m^3 Fumes; STEL - 10mg/m^3

SECTION 3 PHYSICAL/CHEMICAL CHARACTERISTICS

Boiling Point	Above 1050°F	Specific Gravity	1.02-1.06
Vapor Pressure	<1	Melting Point	Unknown
Vapor Density	>1	Evaporation Rate	Unknown

Solubility in Water: No

Appearance and Odor: Black semi-solid thermoplastic material; odor of hydrocarbon.

Becomes liquid above 90-130°F

SECTION 4 FIRE AND EXPLOSION HAZARD DATA

Flash Point in Degrees F (Method Used)	Above 325°F COC (D-92)	Flammable Limits in air % by volume	LEL Unknown	UEL Unknown

Extinguishing Media: CO_2 and Class 'B' extinguisher

Special Fire Fighting Procedures: Avoid breathing vapors, wear self-contained breathing apparatus. DO NOT APPLY WATER.

Unusual Fire and Explosion Hazards: Flammable at temperatures above 500°F.

DO NOT MIX WITH WATER.

SECTION 5 REACTIVITY DATA

Stability	Unstable		Conditions to Avoid	Stable unless moisture is introduced
	Stable	X		Flames and other sources of ignition

Incompatability (Materials to Avoid): Water, hydrocarbon solvents, strong oxidizing agents

Hazardous Decomposition Products: Fumes, smoke, carbon monoxide in the case of incomplete combustion

Hazardous Polymerization	May Occur	REC 4365	Conditions to Avoid	
	Will Not Occur	X		

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SECTION 6 HEALTH HAZARDS

Acute Will cause severe burns if hot material contacts unprotected skin.

Chronic Respiratory tract irritation

Signs & Symptoms of Exposure May cause dermatitis and acne like lesions on prolonged and repeated exposure to dust or vapors.

Medical Conditions Generally Aggravated by Exposure Respiratory disease and infection; cardiovascular diseases

Chemical Listed as Carcinogen or Potential Carcinogen	National Toxicology Program	Yes		IARC	Yes		OSHA	Yes	
		No	X		No	X		No	X

ROUTES OF ENTRY WITH EMERGENCY & FIRST AID PROCEDURES

1. Inhalation Remove victim to fresh air. Start artificial resuscitation if necessary. Call a physician.
2. Eyes Flush eyes with water for at least 15 minutes. Call a physician.
3. Skin If hot material contacts skin, place affected part in cold water. Have a physician remove material or for small amounts use mineral oil for removal.
4. Ingestion If ingested call a physician.

SECTION 7 SPECIAL PRECAUTIONS

Precautions to be Taken in Handling and Storing Never introduce water when hot. Avoid skin exposure to hot material. Avoid breathing vapors in confined spaces. Avoid sources of ignition.

Shipping Information DOT ID #NA1999 - No Placard Required

Steps to be Taken in Case Material is Spilled or Released In case of spillage allow to cool and pick up when solid or semi-solid. Have proper extinguishing media present.

Waste Disposal Methods Handle in accordance with federal, state and local regulations.

SECTION 8 CONTROL MEASURES

Ventilation 1. Local Exhaust 2. Mechanical — If possibility of vapor or fume accumulation exists, utiliz explosion proof ventilating equipment, to avoid toxic or explosive concentrations.

Protective Gloves Chemical Resistant

Eye Protection Goggles or Face Shield

Respiratory Protection (Specify Type) Use appropriate NIOSH approved respirator if TLV's are exceeded.

Other Protective Clothing or Equipment Long sleeve shirt and pants to minimize skin contact.

Work & Hygienic Wash exposed skin with soap and water after work periods and before

DRAFT

Idaho Division of Environmental Quality

Air Permitting Screening Policy for Air Strippers used in the Cleanup of Petroleum Contaminated Groundwater

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This policy is designed to quickly identify air stripper cleanups of petroleum contaminated ground water which pose limited risk to the public through the air pathway, and to expedite the approval for such air emissions. This policy is designed to work together with DEQ's Screening Model and Risk Assessment Procedures For Air Quality Permitting of Vapor Extraction Systems and Air Stripping Used for Leaking Underground Storage Tank Cleanup. Version 1.0 of that document is being updated to include this screening policy for air stripping.

The policy is implemented through a simple question and answer form (a copy of which follows), which conservatively estimates the significance of the emissions given the distance to the nearest property boundary or receptor. Sources with relatively insignificant emissions, as determined by answering the questions on the form and documented as required on the form, are offered DEQ review and final action within two weeks of the date of receipt. This significantly accelerates DEQ turnaround time to expedite the cleanup, since the timeline on processing air permit applications is typically 90 days or more.

For the purposes of this policy, a sensitive receptor is defined as any building or location occupied or frequented by persons who, due to age, infirmity or other health based criteria as defined by the Division of Environmental Quality, may be more susceptible to the deleterious effects of a toxic air pollutant(s) than the general population. Examples of sensitive receptors include but are not limited to: elementary and secondary schools, licensed day care centers, playgrounds and parks, hospitals, clinics and nursing homes.

The existence of a sensitive receptor within 500 feet of the proposed action will not necessarily result in a permit denial, but will trigger tighter DEQ scrutiny of risks to the surrounding population.

This screening policy does not supersede any other DEQ policies or requirements, but instead complements existing DEQ policies by identifying low risk sources, removing them from the standard air permit workload, and accelerating their review. Sources not approvable through this screening policy still may be approvable through the DEQ air quality permitting program. In those cases, a more thorough risk assessment will be required and DEQ review will remain on traditional timelines.

DRAFT

AIR PERMIT SCREENING TEST FOR AIR STRIPPING PETROLEUM CONTAMINATED WATER

Company/facility name _____
Facility address _____

A. PRESENCE OF SENSITIVE RECEPTORS

Is the proposed air stripping site located within 500 feet of a sensitive recepto: defined in the attached Air Permitting Screening Policy for Air Strippers used i Cleanup of Petroleum Contaminated Ground water?

YES _____ NO _____

B. CALCULATE UNCONTROLLED BENZENE LEVELS IN AIR EMISSIONS

1. Flow rate of water into Air Stripper in gallons per minute. The proposed flow must have DEQ approval. The proposed flow rate must be sufficient to adequ control, contain, and remove the petroleum contamination. Please a documentation verifying DEQ approval of the proposed flow rate.

_____ gal./min

2. Convert flow rate to liters per minute.
Multiply line 1 by 3.785. _____ l/min.

3. Determine Benzene concentration in ground water.

Is free product present in any ground water well associated with this petroleum release site? YES _____ NO _____

a. If you marked YES, you must conduct a pilot test to determine expected be concentrations. See the attached "Directions for Conducting a Pilo Determine Benzene Concentrations in Ground Water" for more informatio the benzene concentration here.

Benzene concentration from pilot test = _____ ppb (ug,

b. If you marked NO and free product is <u>not</u> present in any well, determine benzene concentration in the ground water by one of the following two met

i. Enter the Benzene concentration from a ground water well with the hi benzene concentration. Use only the most recent analysis.

Benzene concentration from single well = _____ ppb (ug,

ii. Conduct a pilot test to determine benzene concentrations following directions of the attached "Directions for Conducting Pilot a Tes Determine Benzene Concentrations in Ground Water."

Benzene concentration from pilot test = _____ ppb (ug,

4. Calculate benzene flow rate to air stripper.
Multiply line 2 by line 3a or 3b, whichever is appropriate. _____ ug/min.

5. Convert uncontrolled benzene air emission rate from ug/min to lbs/day. Multiply line 4 by 3.18E-6. _____ lbs./day

B. CALCULATION OF MAXIMUM ALLOWABLE BENZENE EMISSION RATE

6. a. Distance to nearest property line. _____ ft
b. Distance to nearest offsite structure serving as a workplace or residence _____ ft

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7. **Allowable Benzene emission level.**

a. Divide Line 6a by 100. _____
b. Divide line 6b by 200. _____
c. Enter the larger of line 7a or Line 7b _____
d. Enter the value 1.5 or the result from 7c, whichever is smaller. _____ lbs./day

The result in line 7d is the maximum allowable benzene emission rate for the proposed stripping operation at this site. Is the uncontrolled emission rate for benzene in li less than the maximum allowable benzene emission level in line 7d?

Yes ____ Control of benzene air emissions shall not be required. You ay skip Sec C. of this form and proceed directly to Section D. Document all data ent and enclose complete set of most recent water sampling results, a site map c to scale showing monitoring wells, and your monitoring plan. Send them with form to Division of Environmental Quality, Permits and Enforcement Program, N. Hilton, Boise, ID 83706.

No ____ Control of benzene air emissions shall be required. Call (208) 334-5898 review air quality permit requirements or proceed to the following page complete questions on emissions controls.

C. **CALCULATE CONTROLLED BENZENE LEVELS IN AIR EMISSIONS**
(please complete lines 1 to 7 before proceeding with this section)

8. Describe the type of emissions control you propose to use.
_____
_____
_____

9. Control Efficiency (0 < eff. < 1) 0.

10. 1.0 - Control Efficiency 0.

11. Enter uncontrolled benzene air emission rate from line 7 on reverse side. _____ lbs/day

12. Controlled benzene emissions Multiply lines 10 and 11. _____ lbs/day

Is the controlled emission rate for Benzene in line 12 less than the maximum allow Benzene emission rate calculated in line 7d?

Yes ____ Document all data entries and enclose complete set of most recent water samp results, a site map drawn to scale showing monitoring wells, your monitc plan, and documentation on the control equipment (manufacturer's specificatic its application at the proposed site, and its efficiency if credit is take emission controls through this process. Send them with this form to Div: of Environmental Quality, Permits and Enforcement Program, 1410 N. Hilton, Bc ID 83706.

No ____ Call (208) 334-5898, to review air quality permit requirements with DEQ staff

D. **SIGNATURE AND CONTACT INFORMATION**

Applications approved through this process will be required to document emissions rat DEQ during the initial two months of operation. Emissions rates exceeding those calcu above may result in further emissions limitations. DEQ may, in its sole discretion, rec modification to any project plans in order to protect public health.

_____ _____
Signature of preparer

DRAFT

(____)_____ Phone number REC 4371

DRAFT

Directions for Conducting a Pilot Test to Determine Benzene Concentrations in Ground Water (Air Stripping)

Benzene emission rates in air associated with air stripping operations are estimated using a benzene concentration in ground water. These data are then used to determine whether air emissions from the air stripping equipment require controls. The Division of Environmental Quality (DEQ) has determined that a short-term, full-scale pumping test with ground water sampling is an appropriate method for determining the benzene concentration in ground water in some cases. This procedure is required for determining benzene concentrations in ground water when free product is present in monitoring or recovery wells. It is also an acceptable, but not required, method of determining benzene concentrations when free product is not present.

For purposes of this guidance, the term "pilot test" shall mean the process of pumping ground water from the contaminated subsurface in the area targeted for remediation. Water samples shall be collected for laboratory analysis to determine benzene concentrations prior to treatment by the air stripping equipment. The criteria contained herein are designed specifically as a means of determining the concentration of benzene in pumped ground water. It may be possible to modify an aquifer test (designed to determine subsurface hydraulic parameters) conducted during site investigation work to obtain the same data. Alternatively, it may be appropriate to design or modify the pilot test so that subsurface hydraulic parameters are determined along with the expected benzene concentration.

Note that DEQ does not require air stripping equipment to be installed prior to conducting the pilot test. The pilot test may be conducted at any time within the site investigation as long as the benzene concentration is not likely to increase appreciably over time and site conditions are expected to be comparable between the time of sampling and cleanup. The criteria to be followed in performance of an acceptable pilot test are:

- Pumping shall take place from recovery well(s) expected to be used in the full-scale cleanup.

- The pumping rate shall be the same rate used in the full-scale cleanup. Usually, the pumping rate is approved by DEQ

REC 4372

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through submission of a written cleanup plan. The pumping system shall operate continuously at the desired rate for a minimum of two (2) hours and a maximum of twelve (12) hours. Upon completion of pumping, one (1) grab sample shall be collected and analyzed for benzene, toluene, ethylbenzene, and xylenes (BTEX).

- One (1) duplicate sample shall be collected and analyzed for BTEX. Duplicate sample analyses must result in a relative percent difference (RPD) of 25% or less.

- Samples shall be collected from the pumping system at a location representative of inflow to the air stripper but after any preliminary treatment equipment (i.e., oil/water separators, etc.).

- The laboratory analysis method must be an EPA-approved method and must have a lower detection limit of no greater than one (1) ug/l (ppb). Sampling must be conducted in accordance with the RCRA Ground Water Monitoring Technical Enforcement Guidance Document (National Water Well Association, 1986) or equivalent.

- Contaminated water generated during the pilot test must be treated or disposed of in a safe and acceptable manner. On-site storage prior to treatment system completion is acceptable as long as all applicable regulations and ordinances are followed. The treatment and disposal of all generated wastes are the sole responsibility of the person(s) conducting the pilot test.

C. List appropriate soil sample analytical results from excavated contaminated soil. Samples collected shall be representative of the respective stockpiled PCS. If the petroleum is not gasoline or fuel oil, attach separate table.

col.1 Stockpile volume (yd^3)	col.2 Sample I.D.	col.3 Sample type TPH-Gas TPH-Diesel	col.4 Grab or composite sample?	col.5 Sample TPH (ppm)	col.6 Average TPH per stockpile	col.7 Multiply average TPH (col. 6) by stockp volume (col. 1)
_____	_____	_____	_____	_____		
	_____	_____	_____	_____		
	_____	_____	_____	_____		
	_____	_____	_____	_____		
	_____	_____	_____	_____	_____	_____
_____	_____	_____	_____	_____		
	_____	_____	_____	_____		
	_____	_____	_____	_____	_____	_____
_____	_____	_____	_____	_____		
	_____	_____	_____	_____		
	_____	_____	_____	_____	_____	_____

sum of col. 1 _____ sum of col. 7 = _____

Note: Copies of lab results and chain of custody forms must be included.

IV. **Screening test for air emissions.**

A. Calculate average TPH for all PCS to be treated.

1. Enter TOTAL TPH x VOL. (sum of col. 7) here. _____
2. Enter TOTAL VOLUME (sum of col. 1) here. _____
3. Calculate AVERAGE TPH. Divide line 1 (TOTAL TPH x VOL.) by line 2 (TOTAL VOLUME) and enter quotient here. _____

B. Refer to table 2 to determine setback requirement based upon the TOTAL VOLUME and AVERAGE TPH values calculated above. Enter the setback requirement here. _____

Note: If the setback requirement is greater than the distance to the nearest building or residential property line appearing in line II.D, then the land-treatment proposal will not be approved under this expedited format and further review of the land-treatment proposal will be required.

V. **Include the following figures:**

A. Copy of county soil survey map (if the county has been mapped) with copies of the interpretation tables or sheets. CLEARLY MARK location of site on the soil map.

B. Map with exact land treatment site location marked.

VI. **Proposed end use of PCS:** _____

_____

_____

****

_____
Applicant's signature

_____ ( ) _____
Date Telephone

Consultant (or other) preparing this form

Company name_____

Street_____

City, zip_____

Telephone_____

DRAFT

REC 4374

TR 1059

DRAFT

OFFSET DISTANCES FOR LANDFARMING GASOLINE PETROLEUM CONTAMINATED SOIL

(Distances given in feet)

TOTAL PETROLEUM HYDROCARBON CONCENTRATIONS (PPM)

CUBIC YARDS OF MATERIAL	150	200	250	300	350	400	500	600	700	800	900	1000	1200	1400	1500	1600	1800	2000	2200	2400	2600	2800	3000	3500	4000
50	50	50	50	50	50	50	50	50	50	50	53	60	74	87	94	100	113	125	137	148	160	170	181	206	229
100	50	50	50	50	50	50	50	53	65	76	87	98	119	140	149	159	177	195	212	229	244	260	274	309	343
150	50	50	50	50	50	50	57	72	87	101	116	129	156	181	193	205	227	249	270	290	310	329	355	396	436
200	50	50	50	50	50	52	70	89	106	123	140	156	187	216	230	243	270	295	319	343	367	390	412	462	511
250	50	50	50	50	51	62	83	104	124	143	161	179	214	247	262	278	308	336	364	392	420	445	470	530	588
300	50	50	50	50	59	71	95	117	139	160	181	201	239	275	292	309	343	379	408	437	466	495	523	590	656
350	50	50	50	53	66	79	104	128	150	171	191	210	244	301	320	339	376	412	448	485	522	562	603	719	858
400	50	50	50	59	73	88	115	142	167	192	216	239	284	326	347	367	407	445	482	517	552	587	621	703	781
450	50	50	50	65	80	95	125	153	180	207	232	257	304	350	372	394	437	477	516	555	593	630	667	755	839
500	50	50	54	70	87	103	134	164	193	220	247	273	324	373	397	420	464	508	550	591	632	672	711	804	894
550	50	50	58	76	93	110	142	174	204	234	262	290	343	395	420	444	491	537	582	626	669	712	753	852	947
600	50	50	62	81	99	116	151	184	215	246	276	305	361	417	442	469	517	566	614	660	706	750	794	898	998
650	50	50	66	86	104	123	159	193	226	258	289	320	381	436	464	490	543	594	644	693	741	788	833	943	1047
700	50	50	70	90	110	129	165	202	237	270	303	335	396	453	481	509	562	613	663	711	757	801	843	942	1028
750	50	53	74	95	115	135	174	211	247	282	315	352	414	475	505	534	592	648	703	756	808	859	909	1026	1141
800	50	56	76	99	120	141	181	219	257	293	328	365	430	493	525	555	615	674	731	786	840	893	945	1069	1186
850	50	59	81	104	125	147	188	228	265	304	340	376	446	512	544	576	638	699	758	816	872	927	980	1108	1230
900	50	62	85	108	130	152	195	236	275	314	352	389	461	530	563	596	661	724	785	845	903	959	1015	1147	1273
950	50	64	88	112	135	158	201	244	285	325	364	403	476	547	582	616	683	748	811	873	933	991	1048	1185	1315
1000	50	67	92	116	140	163	209	251	294	335	375	415	491	564	600	635	705	772	837	901	962	1023	1081	1222	1356
1050	50	70	95	120	144	168	214	259	302	345	386	426	506	581	618	655	726	795	862	928	991	1053	1114	1259	1397
1100	50	72	99	124	149	173	220	266	311	355	398	439	520	596	636	673	747	818	887	954	1020	1083	1146	1295	1436
1150	50	75	101	127	153	178	226	274	319	364	409	451	536	614	653	692	767	840	911	980	1048	1113	1177	1330	1476
1200	50	77	104	131	157	183	232	281	328	374	420	463	549	630	670	710	787	862	935	1006	1075	1142	1207	1365	1514
1250	51	80	107	135	161	187	238	288	336	383	430	474	562	646	687	728	807	884	959	1031	1102	1171	1238	1399	1552
1300	53	82	110	138	165	192	244	295	344	393	440	486	575	662	704	745	827	905	982	1056	1129	1199	1267	1432	1589
1350	55	84	113	142	169	197	250	301	352	402	450	497	588	677	720	763	846	926	1005	1081	1154	1226	1297	1465	1626
1400	56	87	116	145	173	201	255	306	360	411	459	508	602	692	736	780	865	947	1027	1105	1180	1254	1325	1496	1662
1450	58	89	119	148	177	206	261	315	368	420	470	519	615	707	752	797	884	969	1049	1129	1206	1281	1354		
1500	60	91	122	152	181	210	266	321	375	428	479	529	627	722	766	813	902	988	1071	1152	1231	1307	1382		

REC 4375

TR 1060

DRAFT

OFFSET DISTANCES FOR LANDFARMING DIESEL CONTAMINATED SOIL

(Distances given in feet)

TOTAL PETROLEUM HYDROCARBON CONCENTRATIONS (PPM)

CUBIC YARDS OF MATERIAL	150	200	250	300	350	400	500	600	700	800	900	1000	1200	1400	1500	1600	1800	2000	2200	2400	2600	2800	3000	3500	4000
50	50	50	50	50	50	50	50	50	50	50	53	60	74	87	94	100	113	125	137	148	160	170	181	206	229
100	50	50	50	50	50	50	50	53	65	76	87	98	119	140	149	159	177	195	212	229	244	260	274	300	300
150	50	50	50	50	50	50	57	72	87	101	116	129	156	181	193	205	227	249	270	290	300	300	300	300	300
200	50	50	50	50	50	52	70	89	106	123	140	156	187	216	230	243	270	295	300	300	300	300	300	300	300
250	50	50	50	50	51	62	83	104	124	143	161	179	214	247	262	278	300	300	300	300	300	300	300	300	300
300	50	50	50	50	59	71	95	117	139	160	181	201	239	275	292	300	300	300	300	300	300	300	300	300	300
350	50	50	50	53	66	79	104	128	150	171	191	210	244	300	300	300	300	300	300	300	300	300	300	300	300
400	50	50	50	59	73	88	115	142	167	192	216	239	284	300	300	300	300	300	300	300	300	300	300	300	300
450	50	50	50	65	80	95	125	153	180	207	232	257	300	300	300	300	300	300	300	300	300	300	300	300	300
500	50	50	54	70	87	103	134	164	193	220	247	273	300	300	300	300	300	300	300	300	300	300	300	300	300
550	50	50	58	76	93	110	142	174	204	234	262	290	300	300	300	300	300	300	300	300	300	300	300	300	300
600	50	50	62	81	99	116	151	184	215	246	276	300	300	300	300	300	300	300	300	300	300	300	300	300	300
650	50	50	66	86	104	123	159	193	226	258	289	300	300	300	300	300	300	300	300	300	300	300	300	300	300
700	50	50	70	90	110	129	166	202	237	270	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300
750	50	53	74	95	115	135	174	211	247	282	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300
800	50	56	78	99	120	141	181	219	257	293	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300
850	50	59	81	104	125	147	188	228	268	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300
900	50	62	85	108	130	152	195	236	275	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300
950	50	64	88	112	135	158	201	244	285	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300
1000	50	67	92	116	140	163	208	251	294	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300
1050	50	70	95	120	144	168	214	259	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300
1100	50	72	98	124	149	173	220	266	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300
1150	50	75	101	127	153	178	226	274	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300
1200	50	77	104	131	157	183	232	281	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300
1250	51	80	107	135	161	187	239	288	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300
1300	53	82	110	138	165	192	244	295	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300
1350	55	84	113	142	169	197	250	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300
1400	56	87	116	145	173	201	255	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300
1450	58	89	119	148	177	206	261	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300
1500	60	91	122	152	181	210	266	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300

REC 4376

TR 1061

Idaho Department of Health and Welfare

Responses to Comments and Questions Submitted
During a Public Comment Period and Public Hearings
on the Proposed Repeal and Reissuance of
Rules for the Control of Air Pollution in Idaho

INTRODUCTION

The Notice of Proposed Rules for the Idaho Department of Health and Welfare's proposed repeal and reissuance of the Rules for the Control of Air Pollution was published in the Administrative Bulletin on September 3, 1993. The public comment period for the proposed rules was held from September 3, 1993 through October 8, 1993. Hearings were held in Coeur d'Alene, Pocatello and Boise, Idaho on September 30, October 5 and October 7, 1993, respectively. In addition, the portions of the proposed rules addressing toxic air pollutants were released for public comment in accordance with the old Administrative Procedures Act from March 12, 1993 through April 21, 1993. Hearings were held in Idaho Falls, Coeur d'Alene, Pocatello, Lewiston, Twin Falls and Boise, Idaho on April 6, March 23, March 24, March 24, March 25 and March 29, respectively.

IDHW is proposing a repeal and reissuance of the chapter due primarily to the extensive renumbering, restructuring and reformatting requirements of the Administrative Rules Coordinator. Most sections of the rules are not substantively affected by this rulemaking, and thus, comments regarding such sections are not considered to be substantive.

Substantive public comments which concern the proposed rulemaking have been summarized below. Each comment is followed by the Department's response. Some comments have been combined and paraphrased in order to eliminate duplication and provide a clearer summary. Each response to a comment discusses only the facts necessary to address the comment.

GENERAL COMMENTS

Comment #1: The State's proposed permitting rule is extremely restrictive; and we believe the State permit program should deviate as little as possible from the federal permitting program, in order to avoid inconsistent liabilities and to protect Idaho from possible loss of primacy.

IDHW Response: Many sections of 40 CFR Part 70 are left to the discretion of the implementing state. The Department has incorporated the basic frame work from 40 CFR Part 70 into these rules while designing an operating permit program that meshes with existing Idaho programs. The Department has incorporated the legislated directive to take advantage of the flexibility authorized in the Clean Air Act into these rules.

Comment #2: The proposed permitting regulations also lack implementing detail. The implementation of these regulations provides the "teeth" to the permitting process.

- **How are PTC/PSDs to be "rolled" into the operating permits?**
- **What is the schedule for submittal of permit applications?**
- **What is the schedule for approval of permit applications?**
- **What is the schedule for reissuing permits after initial approval?**
- **What is the recommended format for permit application?**
- **When will permit application forms be provided?**

IDHW Response: The Department has reworked the Tier I rules in response to this and other similar comments. The final rules have been rearranged to improve the logical organization and to clarify the procedures and requirements of the Tier I operating permit program.

Comment #3: The portions of the rules addressing toxic air pollutants are too complex and confusing.

IDHW Response: The rules have been changed in response to this comment. The rules have been revised and reorganized for the sake of clarity.

Comment #4 : The lists are too broad.

IDHW Response: The rules have not been changed in response to this comment. IDHW has attempted to regulate common industrial chemicals for which there is adequate data and for which there may be a reasonable anticipation of exposure to the public. There are currently millions of industrial chemicals in use. There is health data on about 70,000. IDHW is currently proposing to regulate less than 600 non-carcinogenic chemicals and less than 100 carcinogenic chemicals. Lacking a comprehensive emissions inventory, it is impossible to develop a list of regulated substances that take into account only those substances actually emitted at this time in Idaho. Processes change, and new business start so this sort of a "snapshot in time" list of chemicals becomes problematic if not impossible. Finally, if we do not have a reasonable program to control TAP in Idaho, both present and future, we run the risk of becoming a "toxic magnet" for businesses desiring to move to a more unregulated area.

After receiving similar comments after the withdrawn toxics rulemaking we reviewed the proposed list with such comments in mind and removed a number of compounds that we agreed did not materially add to the protection of the public health or the environment. It is IDHW's position that the TAP lists as currently compiled are a reasonable compromise between the need of industry to do business and the need to protect human health and the environment.

Comment #5 : The regulatory levels are too stringent.

IDHW Response: The rules have not been changed in response to this comment. IDHW has attempted to strike a balance between the needs of industry to do business and the need to protect human health and the environment. We believe that IDHW formula for figuring ambient and emissions levels for both carcinogen and non-carcinogens alike is reasonable and strikes the above noted balance. Finally, when compared to the ambient levels of other states, the ambient levels developed and adopted by IDHW are within regulatory norms.

Comment #6: The proposed regulations require too much IDHW involvement in the permitting process. Deminimis levels should be provided and department approved language should be eliminated.

IDHW Response: The rules have not been changed in response to this comment. The proposed rules and the rules as proposed for adoption already provide "deminimis levels" for permits to construct. If the source is not otherwise required to obtain a permit to construct, emissions of toxic air pollutants that are below the screening emissions levels are exempted without further action by the owner or operator of the source and emissions of toxic air pollutants that are above the screening emissions levels but below the acceptable ambient concentrations are exempted upon sending notice of the emissions to IDHW. If the source is otherwise required to obtain a permit to construct, emissions of toxic air pollutants that are below the screening emissions level are analyzed quickly. Emissions that are above the screening emissions level may be analyzed using several methods.

Deletion of the language requiring approval by IDHW would eliminate IDHW's oversight responsibility and allow the owners and operators of sources to decide for themselves whether they should receive a permit.

Comment #7: IDHW should adopt rules requiring an applicant to demonstrate compliance with the National Environmental Policy Act (NEPA) and DOE Orders in order to receive an air quality permit. Also recommend procedures for ensuring compliance with NEPA and DOE Orders.

IDHW Response: The rules have not been changed in response to this comment. IDHW believes that the Board of Health and Welfare may not be authorized by the air quality provisions of the Environmental Protection and Health Act to adopt rules requiring an applicant to demonstrate compliance with NEPA and DOE Orders in order to receive an air quality permit.

Comment #8: **Include a table of contents.**

IDHW Response: The form of the rules is dictated by the Office of the Administrative Rules Coordinator (ARC). The ARC does not publish a table of contents in the Administrative Bulletin, however, a table of contents for the final rules will be available in other publications and services.

Comment #9: **By restructuring and streamlining the federal regulation as a state rule, the requirements of 40 CFR 70.1(b), 70.7(b), and 70.7(c)(iii) that a source have and comply with a Title V permit has been omitted. In order for the Idaho operating permit program to be approvable, it must clearly require that all the affected sources must have an operating permit and must operate in compliance with that permit.**

IDHW Response: The Department has modified the rules in response to this comment. A prohibition has been added in Section 301.

Comment #10: **The existing Idaho rules regarding confidentiality of business information are too broad and may provide prohibit the public release of information on emissions or other materials in a permit application. In order for the Idaho operating permit program to receive full approval, these confidentiality rules must be revised to be consistent with the requirements of §114(c) of the Clean Air Act and 40 CFR 70.4(b)(3)(vii).**

IDHW Response: The Department has modified the rules in response to this comment. Section 126 has been modified to match a change in Idaho statute effective January 1, 1994. The change requires a person to certify that the information designated as confidential qualifies in accordance with Idaho Code 39-111.

Comment #11: **Although it is acceptable for Idaho to forego adopting phase II acid rain permitting requirements at this time (provided the Governor commits to timely adoption and submittal of rules for phase II permits), Idaho must adopt at this time all of the Title V permit provisions which relate to Title IV (acid rain) sources. The Title V provisions are necessary to address the potential need to permit some Title IV affected sources (e.g., new units, opt-in units) under Title V prior to the effective date of Phase II permits.**

IDHW Response: The Department believes the modifications to Sections 300 through 399 have addressed this comment. Responses to specific comments on Acid Rain provisions can be found in later sections of this document.

Comment #12: The rules do not address interstate contributions to air pollution.

IDHW Response: The rules have not been changed in response to this comment. This is beyond the scope of this rulemaking.

Comment #13: Some concern was expressed over the cost to regulate the substances on our appendices.

IDHW Response: The rules have not been changed in response to this comment. Under the current rule addressing toxic substances, IDHW has been regulating a broader list of chemicals than is regulated by the toxic air pollutants carcinogenic and noncarcinogenic increments. IDHW expects the costs per source to decrease as a result of this rulemaking.

Comment #14: It is unfair that these rules apply only to new sources.

IDHW Response: The rules have not been changed in response to this comment. The new portions of the rules addressing toxic air pollutants apply only to the net emissions increases from new and modifying sources of toxic air pollutants. It is common for new rules to "grandfather" existing sources and exempt them from compliance with the new rule. The existing portions of the rules regulating toxic substances will be applicable to all sources of toxic substances, including existing sources. The toxic substances rule will be implemented through the Tier II operating permit program on a case-by-case basis.

Comment #15: It will be nearly impossible for sources, especially small ones to identify what may come out of their stack.

IDHW Response: The rules have been changed in response to this comment. New section 210.01 has been added to provide information regarding how to identify toxic air pollutants emitted by the source.

Comment #16: IDHW has inadequate resources to enforce the requirements of the permit to construct program in general, and the new rules addressing toxic air pollutants in particular.

IDHW Response: The rules have not been changed in response to this comment. Under the current rule addressing toxic substances, IDHW has been effectively regulating a broader list of chemicals than is regulated by the toxic air pollutants carcinogenic and noncarcinogenic increments. IDHW expects to receive adequate

resources to implement and enforce the proposed rules addressing toxic air pollutants.

Comment #17: **Any rules more stringent than the federal regulations must be approved by the legislature which may cause Idaho to have only the EPA minimums.**

IDHW Response: The rules have not been changed in response to this comment. Idaho Code § 39-118B states in part "...that where EPA adopts or has adopted a specific standard, emission limitation or control technology requirement under the clean air act a more stringent standard, emission limitation or control technology requirement promulgated by the board shall not become effected until specifically approved by statute." The terms "specific standard," "specific emission limitation" and "specific control technology requirement" limit the scope of the section, and thus, the section is not applicable to "any state rule" as suggested by the commenter. In addition, the rules addressing toxic air pollutants are not more stringent than any such federal provision and will not need statutory approval to become effective.

Comment #18: **Does EPA have to approve state air toxics rules?**

IDHW Response: The rules have not been changed in response to this comment. With few exceptions, Idaho's air quality programs are adopted and implemented under state authorities. Federal approval of state air quality programs is only necessary to avoid federal sanctions and obtain federal benefits. The toxic air pollutant program is not mandated by the federal Clean Air Act and IDHW does not expect to submit them to EPA for federal approval.

Comment #19: **The IDHW makes its permitting decisions based only on the data that the source provides.**

IDHW Response: The rules have not been changed in response to this comment. IDHW conducts a thorough engineering review of all data submitted by the applicant. This data is checked for completeness and accuracy. A permit is issued only after IDHW engineers, meteorologists and other professionals are satisfied that the data submitted are complete and accurate. Furthermore follow up source testing and other appropriate methods for demonstrating actual and continuing compliance are required in permits.

Comment #20: **It was suggested that IDHW determine T-Ract for source categories. Additionally, the question was asked, how will IDHW know what control technology is available for each regulated chemical.**

IDHW Response: The rules have not been changed in response to this comment. Industries in Idaho are dissimilar enough in process to make this very difficult.

Any given control technology will control more than one specific substance. There is substantial literature available on what technologies control what categories of substances. IDHW will work with the applicants on a case by case basis to identify T-RACT.

Comment #21: A few commenters suggested that the IDHW restrict its new source review policy to the list of 189 substances listed in Section 112 of Title Three of the 1990 Clean Air Act Amendments (CAAA).

IDHW Response: The rules have not been changed in response to this comment. It is the position of the IDHW that this is not in the best interests of the people of Idaho for a number of reasons.

First, the EPA 189 list is not an attempt to protect people or the environment of any specific area but a compromise list to address some of the major nation-wide air pollution source types of air pollution. The EPA and congress have both reiterated that they do not wish negatively impact current state air toxics programs. The original proposed list contained 224 compounds, including ammonia and hydrogen sulfide which were later removed as the result of the political process. We do not believe that this nation-wide effort can be effectively applied to Idaho and be adequate to address the unique Idaho situation.

The EPA 189 list does not include all the well documented carcinogens that have been assigned unit risk factors. State and local agencies need to have the flexibility to protect public health by regulating the emission of TAP into the air.

While it is not possible to predict the future, in a fast growing state like Idaho it is very reasonable to assume that new industries will be moving to Idaho as our work force expands with new residents. In addition, as environmental regulations in California and other states become more restrictive, Idaho will look more attractive to many of these regulated industries. While we certainly want the jobs and incomes that these industries may represent, just as certainly, we do not want to become a "toxic magnet" for polluting industries that other states don't want.

Title III of the Clean Air Act Amendments of 1990 (CAAA) requires EPA to publish a list of source categories and then promulgate maximum achievable control technology (MACT) for the first 40 categories. MACT standards are then required for the rest of the categories on a phased in schedule. If a particular source in Idaho is not addressed in the first 40 source categories, the IDHW without TAP rules, could be unable to address toxic emissions from that source no mater how toxic the emissions might be or in what quantity the emissions may be emitted until EPA finally promulgates MACT standards. Given the past history of EPA deadlines, this is a very real concern. Even if EPA adhered to all

deadlines, some sources would conceivably still be able to emit unregulated toxics until the year 2000, if that source was in the last group to have standards promulgated. It should also be noted that not all sources are covered by these MACT standards. As a consequence, sources not covered by this MACT standard would be unregulated for air toxics in Idaho.

Finally, Congress itself apparently felt that this list was not final. Congress required the EPA to periodically review the list and add pollutants "...which present or may present ...a threat of adverse human health effects (including but not limited to, substances which are known to be, or may be reasonably be anticipated to be, carcinogenic, mutagenic, teratogenic, neurotoxic, which cause reproductive dysfunction, or which are acuity or chronically toxic) or adverse environmental effects..."

COMMENTS ON SPECIFIC SECTIONS OF THE PROPOSED RULES

SECTION 100

Comment #22: **There should be a general exemption from all air quality rules for agriculture and agriculture-related industries. This suggestion was made in the context of several definitions.**

IDHW Response: The rules have not been changed in response to this comment. Most agricultural activities and services are exempted from permit to construct requirements, including those addressing toxic air pollutants. Federal statutes and regulations mandate which sources of total suspended particulates and other air pollutants will be required to obtain Tier I operating permits. Except as prohibited by statute, it is appropriate to retain the ability to review all agricultural practices through the Tier II operating permit program. In addition, many of the definitions identified by the commenter have not been substantively changed by this rulemaking. IDHW does not consider it appropriate to respond to comments concerning aspects of the rules that were not substantively addressed in this rule making, but only renumbered, reformatted and restructured as required by The Administrative Rules Coordinator for this rule making.

Comment #23: **Section 100. DEFINITIONS. Definitions of the term "emissions allowable under the permit," must be added to comply with the requirements of Title V of the Act and 40 CFR Part 70.**

IDHW Response: The Department has incorporated a definition of this term into Section 103 of the final rules.

Comment #24: **Section 100.03. Definitions of Actual Emissions. The phrase added in subpart "6" appears to unnecessarily limit when**

permitted emission rates may be considered actual emissions and should be deleted.

IDHW Response: The Department has not modified the rules in response to this comment. This phrase was added to clarify under what circumstances the Department could consider permitted emission rates to be equivalent to actual emissions.

Comment #25: Section 100.03. Actual Emissions. The phrase "January of the current year or the date on which an application for a permit was filed" must be changed to "a particular date". There are many provisions in the permit rules where the actual emissions of a stationary source or emissions unit will need to be determined for some date in the past and this provision would not allow or provide for that determination.

IDHW Response: The Department has made the suggested modification.

Comment #26: Section 100.06 Agricultural Activities and 100.07 Agricultural Field. As drafted, the definition applies only to the agricultural activities "at the point of cultivation," which immediately exempts all animal husbandry activities. The definition should include all agricultural activities. Revised language was suggested. For Agricultural Field, the phrase for commercial sale should be deleted.

IDHW Response: The rules have been changed in response to this comment. IDHW agrees that these definitions need revision but had concerns with the specific language suggested. The rules now define the term "agricultural activities and services". The Definition of "agricultural field" has been deleted.

Comment #27: Section 100.08. Affected States. This definition should be revised to refer to the State of Idaho and not to any "State in which a Tier I permit...".

IDHW Response: The Department has modified this section of the rules in response to this comment.

Comment #28: Section 100.08. Air Pollutant. The use of the term "air pollutant' is likely to cause some confusion with the term "air contaminant," as used in the Idaho Code Section 39-103.04. Revised language was suggested.

IDHW Response: The rules have not been changed in response to this comment. The definition of "air pollutant/air contaminant" in the rules is consistent with the language and intent of the Environmental Protection and Health Act, Idaho Code §§ 39-101 et

seq., and the federal Clean Air Act, 42 U.S.C. §§ 7401 et seq., so that Idaho may obtain and retain federal delegation of several air quality programs.

Comment #29: **Section 100.11. Air Pollutant. This definition must be revised to cover every pollutant regulated under the federal Clean Air Act, not just those covered by the Idaho Act and these rules.**

IDHW Response: The Department has modified this section of the rules in response to this comment.

Comment #30: **Section 100.12. Air Pollution. This definition should use the term "air pollutant," not "contaminant" since only "air pollutant" is defined herein.**

IDHW Response: The Department has incorporated the suggested modification into the rules.

Comment #31: **Section 100.15 Definition of Ambient Air quality Standards and Violations. There is no definition of the term "ambient air quality standard." The definition of "ambient air quality violation" suggests that any locality may set standards which would them be enforced by IDHW. There may be some confusion with the Air Toxic Increments being assumed to be "air quality standards."**

IDHW Response: The rules have not been changed in response to this comment. Local entities may be able to adopt emission standards or ambient air quality standards depending upon the powers and duties that they have been granted by the Idaho Constitution and Idaho Code. If a local entity adopts such standards, IDHW is required to determine whether a proposed source complies with the standard before issuing a permit to construct. This type of determination is usually accomplished by asking the local entity to certify that the proposed source complies with the local standard. IDHW would probably include terms or conditions in the permit to construct that are relevant to the local standard, and thus, a violation of the local standard would probably also be a violation of the permit to construct. Although IDHW could enforce the permit to construct term directly, in most cases the local entity would take the lead in the matter and initiate an enforcement action.

The Toxic Air Pollutant Carcinogenic and Noncarcinogenic Increments are expressed in terms of an ambient air concentration, but they are not ambient air quality standards.

Comment #32: Section 100.16. Allowance. Note that this definition uses the term "affected unit" which either needs to be defined or replaced with the term "Phase II unit."

IDHW Response: The Department has incorporated the suggested modification into the rules.

Comment #33: In Section 100.16 "Unit" is not defined. Replace "unit" with "emissions unit."

See response to comment #32(the comment above).

Comment #34: Section 100.19. Applicable Requirement. This definition must be revised in a number of ways in order to meet the requirements of Title V:

(1) The parenthetical phrase in the opening sentence must be revised to indicate that applicable requirements are only those that have been promulgated or approved by EPA. Rules promulgated by Idaho that have not been approved by EPA are not applicable requirements for purposes of Title V of the Act.

IDHW Response: The Department has modified this section in response to this comment.

Comment #35: Section 100.19. (2) Subsection (a) must be revised to include any standard or requirement promulgated by EPA under Title I of the Clean Air Act.

IDHW Response: The Department has modified this section in response to this comment.

Comment #36: Section 100.19. (3) Subsection (b) must be revised to include terms and conditions in preconstruction permits issued by EPA under Title I (there are permits issued by EPA before Idaho's preconstruction review program was approved by EPA). Furthermore, the clause beginning with "solely excluding..." must be deleted since this definition by its own terms, only applies to Tier I sources.

IDHW Response: The Department has modified this section in response to this comment. The Department has maintained the clarification that terms and conditions relevant only to toxic air pollutants are not applicable requirements.

Comment #37: Section 100.19. (4) Subsection (c) should be revised to refer to all provisions under section 111 of the Act, such as 40 CFR Part 62.

IDHW Response: The Department has modified this section in response to this comment.

Comment #38: Section 100.19. (5) Subsection (d) should be revised to refer to all provisions under section 112 of the Act, such as 40 CFR Part 63.

IDHW Response: The Department has modified this section in response to this comment.

Comment #39: Section 100.19. (6) Subsection (f) must be revised to reference any monitoring requirements promulgated under Section 504(b) of the Act.

IDHW Response: The Department has modified this section in response to this comment.

Comment #40: Section 100.19. (7) Subsection (h) must be revised to avoid any possible confusion in combing the references to 42 U.S.C. §§ 7511b(e) and (f). We suggest the phrase "and tank vessels" be added after the words "consumer and commercial products."

IDHW Response: The Department has incorporated the suggested modification in the rules.

Comment #41: Section 100.19. (8) Subsection (i) must be revised to include reference to Title VI of the Act since future Title VI requirements could be promulgated under provisions other than 40 CFR. Part 82.

IDHW Response: The Department has modified this section in response to this comment.

Comment #42: Section 100.19. (9) An additional subsection must be added, consistent with the EPA regulations, to include any national ambient air quality standard or increment or visibility requirement under part C of Title I of the CAA as applied to temporary sources.

IDHW Response: The Department has added a section to the rules in response to this comment.

Comment #43: Section 100.25. Best Available Control Technology (BACT). This definition must be revised to include reference to 40 CFR Part 63, since all National Emission Standards for Hazardous Air Pollutants are not included in 40 CFR Part 61.

IDHW Response: The Department has modified this section in response to this comment.

Comment #44: Section 100.26. Collection Efficiency. The term "contaminant" should be changed to "air pollutant."

IDHW Response: The Department did not modify the rules in response to this comment. However, the definition of air pollutant has been modified.

Comment #45: Section 100.39. Designated Representative. This definition must be revised to use the term "affected unit", not just "unit". Also it must be consistent with the definition in EPA's Acid Rain regulations. "Unit" is not defined. Replace "unit" with "emissions unit.

IDHW Response: The Department has modified this section to clarify that a "unit" is a "phase II unit".

Comment #46: Section 100.39. Effective Dose Equivalent. While this definition is taken directly from the Code of Federal Regulations, it could be written more clearly. Different language was suggested.

IDHW Response: The rules have not been changed in response to this comment. Changing the definition would adversely affect the regulatory scheme for radionuclides from sources regulated under 40 CFR Part 61 or 40 CFR Part 63 since the emission standards for such air pollutants are based on "effective dose equivalent" as defined in the federal regulations.

Comment #47: 100.51. Excess Emissions. The definition is not tagged to stationary sources nor are time limits given. Suggest that the language be clarified and appropriate exemptions included in the rule.

IDHW Response: The rules have not been changed in response to this comment. The definition does not need to reference "stationary sources" or "time limits." The term is only used in the context of provisions regulating stationary sources and there is no time limit associated with the term.

Comment #48: Section 100.45. Emission Standard. This definition must be revised to include any requirement established by the EPA, not just the Department. Again, this definition must also reference 40 CFR Part 63 to cover all of the National Emission Standards for Hazardous air pollutants.

IDHW Response: The Department has modified this section in partial response to this comment. The Department will incorporate future federal requirements into these rules in accordance with state rule-making procedures.

Comment #49: Section 100.46. Definition of Environmental Remediation Source. Sources, which are not remediating oil or hazardous wastes, but which generate Air toxics should be included in the definition.

IDHW Response: IDHW has looked at this definition and has revised it by taking out the reference to hazardous materials. This was done because of potential conflicts with RCRA regulations. However Section 210.12 Specialized Method E: Department Approved methods can be used to allow review of a non-petroleum remediation project that may generate emissions of a toxic air pollutant. IDHW believes that this will remove potential RCRA conflicts while allowing flexibility in permitting non-petroleum remediation sources.

Comment #50: Section 100.47. Emission Unit. This definition must be expanded to indicate that it does not alter or affect the definition of the term "unit" for purposes of title IV of the Clean Air Act.

IDHW Response: The Department has incorporated the suggested modification in the rules.

Comment #51: Sections 100.47., 100.137. and 100.142. The definitions of Emissions unit, Source and Stationary Source all seem to be talking about the same thing. Choose one and use it throughout the rules.

IDHW Response: The rules have not been changed in response to this comment. This comment will, however, be considered when IDHW drafts future rulemakings regarding air quality.

Comment #52: Section 100.63. Hazardous Air Pollutant. This definition must be revised to include the pollutants listed in or pursuant to section 112(b) of the Clean Air Act. These pollutants are "hazardous air pollutants" even though they may not yet be subject to a standard under section 112.

IDHW Response: The Department has modified this section in response to this comment.

Comment #53: Section 100.68. Insignificant Activities. This definition is not used in the text of the rules and needs to be referenced therein to implement the concept. This approach is important to maintain a manageable program that is well understood by both the agency and public. New definition language was suggested.

IDHW Response: The Department has not modified this section in response to this comment. However, a subsection has been added to Section 314 that does incorporate the term "insignificant activities". This term was added to the rules solely for use in the Tier I operating permit program.

Comment #54: Section 100.71. Insignificant Activities. The item for space heating must include a size cutoff so that large central heating systems are not inappropriately exempted from permit requirements.

IDHW Response: The Department has modified this section in response to this comment.

Comment #55: Section 100.75, 100.76 Major Facility and Modifications. One commenter questioned the import of the changes to these definitions in the proposed rules. Another commenter stated that Section 100.75.b.ii and Section 100.76.c are not consistent.

IDHW Response: The Department modified the rules in response to this comment and the following comment. The Department has returned the existing definition of Major Facility. This definition is consistent with the definition of Major Modification.

A second definition of Major Facility has been placed in the new Section 103 "Definitions for the Purposes of Sections 300 through 399".

Comment #56: Section 100.75. Major Facility. This definition must be revised in a number of ways:

(1) Either the term "facility" must be used instead of "stationary source" or the definition must be substantially revised to conform with the EPA definition of "major stationary source".

(2) In subsection (a) the term "hazardous regulated air pollutant" must be changed to simply "hazardous air pollutant" and the provisions allowing EPA to establish lesser quantities for some pollutants and alternatives for radionuclides must be added.

(3) In subsection (b), the term "stationary source" must be changed to "facility," and paragraph (ii) must be revised to cover all regulated pollutants, not just those covered by the standards to comply with 50 CFR 51.166, and reference to 40 CFR Part 63 must be included. Note that this provision is now inconsistent with the

definition of "major modification" in that this definition exempts all "fugitive emissions" whereas the definition of "major modification" only exempts "fugitive dust."

IDHW Response: The Department has modified this section in response to this comment.

Comment #57: Section 100.76. Major Modification. Subsection c. must be revised to include reference to 40 CFR Part 63 in order to cover all sources regulated under section 112 of the Clean Air Act.

IDHW Response: The Department has incorporated the suggested modification into the rules.

Comment #58: Section 100.79. Member of the Public. The definition of "member of the public" as it applies to the regulation of radionuclide emissions should be amended to mean "any human being who is in any public access area, who receives the maximum potential dose exposure."

IDHW Response: The rules have not been changed in response to this comment. Changing the definition would adversely affect the regulatory scheme for radionuclides from sources regulated under 40 CFR Part 61 or 40 CFR Part 63 since the emission standards for such air pollutants are based on the effective dose equivalent for a "member of the public" as defined in the federal regulations.

Comment #59: Section 100.94. Nonattainment Area. The proposed change in this definition makes the basis for the designation less clear, and the parenthetical appears to extend the traditional reach of a non-attainment area.

This definition must be revised to include reference to Section 107(d) of the Clean Air Act. Although the state can add additional areas, it must consider as nonattainment all areas designated by EPA under section 107(d).

IDHW Response: The Department has modified this section in response to these comments.

Comment #60: Section 100.102. Process or Process Equipment. Delete the word "whatever" from the definition.

IDHW Response: The Department did not modify the rules in response to this comment.

Comment #61: The change in definition of PM-10 Emissions might be interpreted to also imply a change in reference method. We do not

support such a change, particularly in this manner. We would appreciate the opportunity to discuss the intended import of this change or the deletion of the proposed language.

IDHW Response: The Department did not change the rules in response to this comment. This definition was updated to match the federal definition of PM-10.

Comment #62: Section 100.105. Phase II Source and 100.106. Phase II Unit. These definitions must either be made consistent with the definitions of the EPA terms "affected source" and "affected unit" or replaced with those terms and their definitions.

IDHW Response: The Department has modified this section in response to this comment.

Comment #63: Section 100.110. Potential to Emit/Potential Emissions. This definition must be revised to include "facilities" as well as stationary sources since it is used primarily to determine if a facility is major. Second, the provision ensuring that this term will not alter or affect the term "capacity factor" used in title IV of the Clean Air Act must be added.

IDHW Response: The Department has modified this section in response to this comment.

Comment #64: Section 100.112. PPM (parts per million). The term "contaminant" should be changed to "air pollutant."

IDHW Response: The Department did not modify this section in response to this comment. See the definition of Air Pollutant.

Comment #65: Section 100.118.a.xx. One commenter made three related suggestions regarding the definition of "significant" as it applies to radionuclide emissions from sources regulated under 40 CFR Part 61 or 40 CFR Part 63. The commenter suggested that there should be a clearer determination of how the Department determines PSD so that a source knows whether to submit a PSD application; the designation of any radionuclide emission as significant, if total facility-wide emissions exceed an EDE of 3 mrem/yr, is overly conservative, and not based on any known scientific reasoning or regulatory precedence; and the definition should include only those radionuclide emissions that result in an EDE of at least 0.1 mrem/yr (NESHAP below-regulatory-concern level) if total facility-wide emissions are maintained below the NESHAP standard of 10 mrem/yr. Another commenter suggested that the existing definition of "significant" should not be amended, and thus, "any" amount of radionuclides would remain a "significant" emission.

IDHW Response: The rules have not been changed in response to these comments. The rules delineate application and permit to construct requirements based upon whether a proposed source is "major" and whether the proposed source is, or is located at, a facility with a potential to emit 250 tons or more of any air pollutant. If the proposed source is located at an existing major facility, it is a "modification" and the definition of "major modification" is based upon whether the proposed source has a net "significant" increase in emissions. The definition of "significant" is based on specified amounts of listed air pollutants. Therefor, an applicant should refer to the definition of "significant" and to whether the facility has the potential to emit 250 tons of air pollutants to determine what application information is required and what type of permit review will be conducted.

The regulatory scheme for radionuclides included in the definition of "significant" reflects many aspects of the federal scheme, but is also designed to meet the needs of the State of Idaho. It reflects a balancing of diverse and complex public, governmental and industry interests.

Comment #66: Section 100.118.b. One commenter suggested that Section 100.118.b be deleted because of his understanding of the provisions. He states that prior to these proposed regulations, this provision had relatively little impact since it only applied to pollutants regulated by the Clean Air Act and that now that there is no distinction between an air contaminant and pollutant in Idaho's regulations, this provision defines emission of any pollutant regulated by either the Clean Air Act or Idaho's regulations as significant.

IDHW Response: The rules have been changed in response to this comment. Without confirming the commenter's reasoning, IDHW has amended the section so that toxic air pollutants will not be "significant" emissions.

Comment #67: Section 100.118.a. The phrase "or any radionuclide emission rate, if the Department determines that Section 205 shall apply" should be deleted.

IDHW Response: The rules have been changed in response to this comment. The phrase was deleted.

Comment #68: Section 100.118.b. Prior to these proposed regulations, this provision had relatively little impact since it only applied to pollutants regulated by the Clean Air Act. Now that there is no distinction between an air contaminant and pollutant in Idaho's regulations, this provision defines emission of any pollutant regulated by either the Clean Air Act or Idaho's

regulations as significant. It is recommended that Section 100.118.b. be deleted.

IDHW Response: The rules have been changed in response to this comment. Without confirming the commenter's reasoning, IDHW has amended the section so that toxic air pollutants will not be "significant" emissions.

Comment #69: Section 100.131. Significant. Subsection (b) must be revised to include the phrase "or facility" since potential to emit applies to facilities as well as sources.

IDHW Response: The Department has incorporated the suggested modification in the rules.

Comment #70: Section 100.131. A TIER II Source. If the Tier I Source and Tier II Source are going to define the two types of permits, there should be a definition of each and more descriptive names.

IDHW Response: The Department has modified the rules in partial response to this comment. Section 302 has been moved to the general definition section of the rules. The Department has not defined "Tier II Source" in these rules. However, Section 401 describes which facilities are affected by the Tier II operating permit rules.

Comment #71: SectionS 100.146-149. These four definitions are used in many general schema for environmental calculations. Many of the conclusions are directly applicable to normal practice of agriculture and should be exempted.

IDHW Response: Agricultural activities and services are specifically exempt for new source review for toxic air pollutants.

Comment #72: One commenter noted that the rules appear to be incorporating Clean Air Act Section 114 Letter Authority by rule in Section 122 of the proposed rules. The commenter does not support this action and suggests that it is not required for an approvable Title V Program. The commenter also questions IDHW's legislative authority for the action and suggests that Section 122 be totally deleted.

IDHW Response: The rules have not been changed in response to this comment. This rulemaking is not limited to rules required for approval of the Tier I operating permit program. The Environmental Protection and Health Act grants the Board of Health and Welfare adequate authority to adopt Section 122.

Section 122 is an important aspect of this rulemaking. It will provide IDHW with the ability to obtain certain types of information from specified persons as necessary to develop, implement and enforce Idaho's air quality programs. It will drastically increase the efficiency and effectiveness of several of Idaho's air quality programs, including enforcement and the development and implementation of the area plans for the nonattainment areas. The State of Idaho and the public face severe sanctions if the nonattainment areas are not brought into attainment by the federally mandated deadlines. In addition, the United States Environmental Protection Agency's (EPA) ability to request information is very similar to the ability provided by Section 122. Section 122 will allow IDHW to request information directly from industry and other members of the public, and thus, IDHW will be able to collect necessary information without contacting or involving EPA.

Comment #73: **Section 123. Certification of Documents. It appears that neither the federal regulations nor the Clean Air Act require notarization on all forms, documents, progress report, monitoring data, test data, and other information to be submitted. Requiring notarization in the proposed rules is overly burdensome and unnecessary.**

IDHW Response: The rules have been changed in response to this comment. The phrase requiring notarization has been deleted and a section requiring all documents to be truthful, accurate and complete has been added to accomplish the same goal as notarization.

Comment #74: **New Section 100. Permit Successions. It would be useful in administration of the air quality program to establish by regulation the relationship between permits to construct and operating permits (both Tier I and Tier II). Section 150, a new proposal, attempts to define this relationship.**

IDHW Response: The Department did not make the suggested modification to the rules. However, the Department has modified Section 209.06 (now 209.05) to clarify how the permit to construct program interacts with the Tier I operating permit program. Section 401 describes how a Tier II operating permit can be used to net out of the Tier I operating permit program.

Comment #75: **Section 100.161. Toxic Substances. Referring to the listed acceptable ambient impact levels as ambient air quality standards (those levels that cannot be exceeded, regardless of the source) is confusing and conflicts with what IDHW indicated the toxics regulations would apply to. The definition of these limits to the increase in ambient concentrations should be changed to more**

clearly indicate that they are ambient increments, similar to PSD increments.

IDHW Response: The rules have been changed in response to this comment. The Department has incorporated the suggested modification into the rules.

Comment #76: Section 100.161. Toxic Substances. Other sections of the regulations deal more specifically with emissions of toxics. This section is unnecessary since the other regulations are more specific and should be deleted.

IDHW Response: The rules have not been changed in response to this comment. This sections contains the definition of toxic substances on which the other sections are based. In addition this section allows the IDHW the option of addressing a situation that may present a threat to public health or the environment by imposing a Tier II operating permit. IDHW believes that this section is basic to the state's efforts to protect the environment and human health by controlling toxic air pollutants.

Comment #77: Section 161. TOXIC SUBSTANCES. The structure of this provision is confusing. Paragraphs .02 and .03 should be subparagraphs under the provision in paragraph .01 (i.e. delete the number .01, and renumber .02 and .03 to .01 and .02, respectively).

IDHW Response: The rules have been changed in response to this comment. This Section has been rewritten to be clearer.

Comment #78: Section 121.01. This paragraph should be clarified to specify that the schedule prepared by the source is a "proposed" compliance schedule.

IDHW Response: The rules have been changed in response to this comment. The Department has incorporated the suggested modification into the rules.

Comment #79: Section 130. UPSET CONDITIONS, BREAKDOWN. This provision is not approvable as a part of the Idaho SIP as it fails to comply with the requirements of the Clean Air Act for violations of applicable SIP emission limits.

IDHW Response: The Department did not modify the rules in response to this comment.

Comment #80: Sections 140 through 149. VARIANCES et seq. These sections are not approvable as revisions to the Idaho SIP. First,

EPA does not approve "variances" to Idaho rules. EPA can approve revisions to the Idaho SIP which have been adopted by the Department and submitted to EPA, including variances that the Director has granted pursuant to this provision. As such, this section must be revised significantly. Furthermore, the variance provisions must either be inapplicable to Title V sources, or the rules must clarify that a variance must be accomplished through a revision to the source's Title V permit.

IDHW Response: The Department has replaced "EPA" with "Department" to correct this section. Sections 300 through 399 have been revised to clarify the requirements that apply to facilities affected by the Tier I operating permit program.

Comment #81: Section 141.02. Petitions. It is unclear what the term "petitioner and other..." refers to. Modified language is suggested.

IDHW Response: The Department has modified this section in response to this comment.

Comment #82: Section 145.03 Authorization of Hearing. Suggested that this section could be more clearly worded.

IDHW Response: The Department has modified this section to clarify that the Department, not EPA, may authorize a hearing. The suggested modification has been incorporated into the rules.

SECTION 200

Comment #83: Section 200 Procedures & Requirements for Permits to Construct. The proposed rules do not contain guidelines as to how the State of Idaho will develop MACT standards, if the EPA misses its deadline to develop MACT standards (Section 112 (j) of the Clean Air Act). As a result, we recommend that the Department issue guidance on how they will determine MACT standards, if and when the EPA does not meet its deadline, these Procedures should be developed through rulemaking.

This incrementalism approach will end up costing industry more to comply because they will go ahead with an addition, approved under a new source review permit but then have to make major modifications to that new source as part of the operating permit later on.

IDHW Response: The rules have not been changed in response to this comment. As EPA finalizes its various implementations procedures for §112(g) and 112(j) IDHW will respond appropriately. Until these federal rules and guidance are done, IDHW considers it inappropriate to attempt to develop rules by trying to guess what

EPA might do. When IDHW develops its responses to federal requirements IDHW will comply with all state and federal guidelines for public participation.

IDHW has built in a high degree of flexibility onto these rules in order to assist industry in complying with required controls. However, given the unsettled nature of new source MACT, IDHW has chosen to defer this issue until EPA finalizes and promulgates regulations in this area.

Comment #84: Section 201. Put the original effective date (January 24, 1969) into the regulation to eliminate any confusion as to what date it is.

IDHW Response: The rules have been changed in response to this comment. The phrase "after the original effective date of Sections 200 et seq." was deleted.

Comment #85: Section 201. Permit to Construct Applicability. As stated in previous comments to the Department on an earlier draft of these proposed revisions, the changes to the permit to construct rules which are being made to incorporate the hazardous air pollutant sources will adversely impact the currently-approved SIP provisions for criteria pollutant sources. If adopted as currently proposed, EPA would be required to disapprove these rules and the Idaho permit to construct program.

As discussed in my letter of June 29, 1993 (copy attached), the proposed revisions to the permit to construct applicability provision will not be approvable as revisions to the Idaho SIP for a number of reasons.

(1) The new exemptions for Category I, II, III, and IV sources inappropriately relaxes the currently approved SIP, and fails to comply with the requirements of section 110(a)(2)(C) of the Clean Air Act and 40 CFR Part 51, Subpart I of EPA regulations. Specifically, the four categories are not mutually exclusive and therefore would allow a source to be exempted under one provision where another provision would require a permit.

IDHW Response: The Department has not modified the rules in response to this comment. Categories I through III specifically require that the source not cause or significantly contribute to a violation of an ambient air quality standard. Category IV sources are either already exempted from obtaining permits to construct in the currently effective rules or are activities that the Department has historically not regulated.

The exemptions were not designed to be mutually exclusive. If a source qualifies under any of the categories, it is exempt from obtaining a permit to construct. The Department carefully examined sources and activities that have been exempted from obtaining a permit to construct in the past. This information was used to develop the categories in these rules.

Comment #86: (2) Broad discretionary exemptions such as 201.01.g., 202.02.d.i., etc. are not approvable.

IDHW Response: The Department has modified the rules in partial response to this comment. However, the Department has exercised discretion to exempt sources from obtaining a permit to construct under existing rules (16.01.01012,02.h). The Department is not aware of any concern expressed by EPA in its use of the discretion allowed by this rule.

Comment #87: (3) Section 201.02.a. exempts all major sources by using the term "Not."

IDHW Response: The Department has modified this section in response to this comment.

Comment #88: (4) The reference in 201.03. to "Section 200 et seq." should be changed to 201.03 since the source need not verify compliance with all of Sections 200 to 299, only the provisions of 201.03.a. through d.

IDHW Response: The Department has modified this section in response to this comment.

Comment #89: (5) In subparagraph (vi), the phrase "agricultural activities and services" is used, whereas the definition section defines only "agricultural activities." Also, the clarification of what are not agricultural activities (i.e. manufacturing, bulk storage and handling for resale or formulating any listed chemical) should be moved to the definition section unless this exempted activity is intended to be narrower than all "agricultural activities"

IDHW Response: The Department has modified the definition of Agricultural Activities.

Comment #90: (6) The permit to construct applicability provisions must ensure that all new, modified, or reconstructed stationary sources subject to any standard under sections 111 or 112 of the Clean Air Act are required to obtain a permit to construct. Idaho's Title V operating permit program cannot be approved unless it demonstrates that it can implement and enforce all of the requirements of sections 111 and 112 for subject sources, including the requirements for preconstruction review and initial source compliance determinations.

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IDHW Response: The Department has not modified the rules in response to this comment. The Department is committed to updating the rules in accordance with future federal rule-making.

Comment #91: Sections 201.01.f, 201.02.d.i, 201.03.d.ii: Category I, II, and III Sources. The State requirements should be consistent with the Federal NESHAP requirements in 40 CFR 61.96 Applications to Construct or Modify.

IDHW Response: The rules have not been changed in response to this comment. The regulatory scheme for radionuclides reflects many aspects of the federal scheme, but is also designed to meet the needs of the State of Idaho. It reflects a balancing of diverse and complex public, governmental and industry interests.

Comment #92: Section 201.02.iii-iv. Each of these sections represent the use of equipment essential to some phases of agriculture. These engines are potentially used in remote or populated locations. As such, an agricultural exempted may be appropriate.

IDHW Response: An agricultural activities and services exemption is provided for in Section 220 Category IV exemption

Comment #93: Section 201.03.d. Pilot Plants. Pilot plants pose a serious potential risk of radiation exposure. and should not have any exclusions from PTC requirements.

IDHW Response: The rules have not been changed in response to this comment. To qualify for an exemption, pilot plants may have no emissions of a radionuclide for which a National Emission Standard for Hazardous Air Pollutant (NESHAP) exists. The IDHW considers this adequately protective.

Comment #94: Section 201.04. Each of the above sections would be more clearly defined and interpreted if an agricultural exemption consistent with Idaho Environmental Protection and Health Act, Idaho Code Sections 39-101 et seq. (1993), which is clearly incorporated into this rule making.

IDHW Response: An agricultural activities and services exemption is provided for in Section 220 Category IV exemption

Comment #95: Section 201.04.c Permits to Construct, Category IV Exemptions. Section viii. needs to be expanded to allow the Director to exempt sources other than "equipment." This will allow the concept of "insignificant activities" which was earlier defined

but never used in the text of the rule, to be compiled into a publicly available list. This would allow the list to be compiled over time in a less expensive fashion than listing all insignificant sources in the rule. The additions list should be published annually in the Idaho Administrative Bulletin.

IDHW Response: The Department has modified this section in partial response to this comment. It should be noted that Insignificant Activities have been defined solely for the purposes of the Tier I operating permit program.

Comment #96: Section 201.04.c. Grain storage and handling facilities do not always fit cleanly under the agricultural exemption for a number of reasons.A new section should be added to exempt Country Grain Elevators under the 1 million bushel PSD size in PM-10 attainment areas.

IDHW Response: The Department has not modified the rules in response to this comment. Because there are no enforceable limits on the potential to emit from these facilities, the Department cannot exempt them from the requirement to obtain a permit to construct.

Comment #97: Section 202. APPLICATION PROCEDURES. The phrase "by the owner or operator" should be replaced with "in accordance with Section 123" now that section 123 sets out who must be the certifying official for permits to construct. Furthermore, Section 202.01.c. should be expanded to include a reference to 205.07

IDHW Response: The Department has incorporated the suggested modification into the rules.

Comment #98: Section 203. The old Section 203 stated that IDHW shall conduct a T-Ract evaluation for specific sources within 180 days, while Section 209 requires that a proposed permit be issued or denied within 60 days after the permit is declared complete. Recommended that the time frame in Section 209 take precedence.

IDHW Response: The rules have been changed in response to this comment. New Section 210.07 provides the applicant with two alternative procedures and timelines. Under Section 210.07.a, the applicant will submit the information regarding T-RACT in her initial application and IDHW will issue a permit action in accordance with the timelines in Section 209. Under Section 210.07.b, the applicant may supplement her application and the timelines in Section 209 will be reinitiated when a complete supplemental application is received.

Comment #99: Section 202.b.viii. Application Procedures. The list of Ambient concentrations is hard to read.

IDHW Response: The rules have not been changed in response to this comment. The form of the rules is dictated by the Office of the Administrative Rules Coordinator.

Comment #100: Section 203.03.c and d Adjustment Factors. Incorporate language to allow use of the adjustment factors for applicability determinations.

IDHW Response: The rules have not been changed in response to this comment. This concept is inherent in the language of the existing section.

Comment #101: Section 203.03 through 05. Recognize that these provisions for new and modified air toxics sources do not meet the requirements of section 112(g) of the Clean Air Act. When EPA's regulations to implement section 112(g) are promulgated, Idaho will have to substantially revise and tighten these requirements.

IDHW Response: The rules have not been changed in response to this comment. The IDHW rules concerning toxic air pollutants are for the control of toxic air pollution from new and modified sources and were not drafted with the intent of mirroring potential federal regulations. Additionally, the EPA has not finalized its guidance on §112(g) yet so IDHW believes that this comment is premature. As EPA promulgates further 112(g) guidance, IDHW will propose legislation to respond to these future federal requirements. IDHW acknowledges that this may entail extensive revisions of these rules.

Comment #102: Section 203.04. T-RACT. Best Available Control Technology (BACT) should not be changed to Reasonably Available Control Technology for Toxics (T-RACT). Some thought that T-RACT should not be available in non-attainment areas. (There were multiple comments expressing this sentiment)

IDHW Response: The rules have not been changed in response to this comment. The change from BACT in the old TAP policy to RACT in the proposed rules will allow a greater degree of flexibility, both economic and technological, in complying with the various emissions and ambient levels of the toxic air pollution (TAP) regulations. BACT is a term applied to prevention of significant deterioration (PSD) in classified airsheds and as such is not directly relatable to toxics. This change in control technology will address a small segment of carcinogenic emissions falling between the one in a million and one in a hundred thousand risk levels. It will have no effect on non-carcinogens. Emissions of carcinogens of greater

risk than one in a hundred thousand will not be allowed regardless of the control technology used. In real application, T-RACT as defined and implemented will closely approximate BACT

The assumptions that the IDHW uses when figuring these risk levels are conservative, that is, likely to err on the side of caution. These assumptions protect the maximally exposed individual as opposed to the average exposed individual. It is the position of the IDHW that given the combination of these very conservative assumptions and the limited segment of potential emissions that this change will cover, these changes represent a feasible compromise between the needs of industry and protection of public health.

Nonattainment for air quality pertains to a number of criteria pollutants (oxides of nitrogen and sulfur, particulates, etc.) and does not pertain to TAP. Therefor this concern is not directly relevant to the proposed TAP rules.

Comment #103: **Section 203.04 T-RACT Determination. A few commenters suggested that the economic feasibility aspects of the T-RACT determination are an unreasonable burden on industry and could be used arbitrarily. They asserted that old Section 203.04.e requires the applicant to determine the economic feasibility of every control technology approved by the Department and that this could be quite expensive and time consuming. If there are only one or two options worth considering, an economic analysis should only be done for them. Provisions to allow the applicant and the Department to agree on what control technology scenario will be evaluated should be included.**

IDHW Response: The rules have been changed in response to this comment. Without confirming the reasoning of the commenters, IDHW deleted old Section 203.04.e. The proposed rules and the rules that are submitted for adoption both provide that the applicant is to submit proposals that are technologically and economically feasible; not proposals that are technologically or economically feasible.

Comment #104: **Section 203.05.a. Emissions Screening. Since this requirement is only meant to address new sources, the language needs to be modified to reflect that.**

IDHW Response: The rules have been changed in response to this comment. This section has been rewritten to be more clear.

Comment #105: **Some commenters expressed concerns that the toxics provisions should apply only to new sources and that "the limiting factor is the additional quantity of a specific toxic in the atmosphere that results from operation of the proposed new source."**

Existing background should be taken into account when permitting new sources. Are the incremental increases to become part of background to be ignored if another addition was made in the future ad infinitum.

IDHW Response: The rules have been changed in response to this comment. On the issue of clarifying that the toxics policy applies to new sources and modifications, IDHW has rewritten and an reorganized sections to make this more clear. That the current toxics policy and the proposed rules deal with new sources and modifications only has been the IDHW position since the inception on the toxics policy in 1989.

The concern that the incremental increase will become part of the background is addressed the definition of Net Emissions Increase, §102.07 of the revised rules. This definition excludes this possibility and has been applied to Section 209.

IDHW acknowledges the tensions between the ability of industry to operate effectively and efficiently and the public's right to a safe and clean environment. It is IDHW's position that the rules changes noted above strikes a middle ground between these needs.

Comment #106: Air toxic impacts, both non-carcinogenic and carcinogenic, should only be evaluated at or beyond the facilities property boundary, even if the public has access to the property. The words "or the closest point of public access" should be deleted.

IDHW Response: The rules have been not changed in response to this comment. Section 209.b. (which replaces 203.05.c.) allows the use of the point of greatest impact located at or beyond the facility property boundary nearest the source or closest point of public access. Generally, people going to a source on business are not considered part of the "public" while on the property. Therefor, parking lots and the like will not generally be considered the closest point of public access.

Comment #107: Section 203.05.f. This section is redundant as the concept is already addressed in 203.05.h. and should be deleted.

IDHW Response: The rules have been changed in response to this comment. Section 203 has been reorganized to make it clearer and in so doing, subsection 203.05.f has been deleted.

Comment #108: Section 203.05.g. Unit Risk Factors are based on a 70-year exposure. This is not appropriate for an industrial park situation that will never be a residential application. The refined analysis should be liberalized to include a different model, actual meteorological data, more appropriate risk factors, actual hours of operation, more accurate emissions factors obtained

through source testing, more accurate annual potential to emit scenarios and any other justifiable refinements. New wording for this section has been suggested to reflect this.

IDHW Response: The rules have been changed in response to this comment. IDHW agrees that for industrial areas that will never be used for residential purposes, a 70 year risk base may be conservative. However, it is hard to predict future land use patterns. Examples of unforeseen new land uses with significant environmental and human health concerns have become quite common.

IDHW has based its emission numbers on the best available data. IDHW has strived to take a balanced approach taking into account the needs of industry to operate and the need to protect human health and the environment. Since it is not possible to account for such real life factors as lifetime exposures, additive or multiplicative effects of exposures to the large variety of industrial chemicals in use in Idaho, it is necessary to make our emissions standards generally applicable and reasonably conservative.

It is not possible for IDHW to carve out special exemptions or emissions factors for potential or hypothetical new or modified industrial sources or exposure scenarios. Our rules must take a balanced approach that is generally applicable and consistently applied. IDHW can not develop special emissions factors specifically for industry dominated areas. IDHW believes that the revised Section 210.02 Quantification of Emissions Rates and Ambient Concentrations, which allows site specific data gives adequate flexibility in compliance with toxic standards.

Comment #109: Section 203.05.j Screening Emissions Tables. Commenter recommends that ammonia be eliminated from the list of toxic pollutants or, alternatively, that emission levels for ammonia applicable to the danger caused by high concentrations and which also recognize the harmless effect of low concentrations be established. This request is based on a number of issues. First, ammonia was deleted from the EPA "189 list". Second, ammonia is generally considered relatively non or mildly toxic in very low concentrations. Third, ammonia is regulated under SARA Tile III for accidental release. Fourth, substantial releases of ammonia come from animal wastes and other organic materials. Fifth, the control of ammonia at the levels specified in the proposed rules would be severely burdensome for industry, particularly the fertilizer and sugar beet industries.

IDHW Response: The rules have not been changed in response to this comment. IDHW disagrees that Ammonia should be unregulated in Idaho. IDHW also declines to modify its screening emissions levels (EL) and acceptable ambient (AAC) concentration for ammonia.

In general, IDHW basis its non-carcinogenic standards on the work and occupational exposure limits developed by the American Conference of Government Industrial Hygienists. These standards

are set relative to the toxicity of the compound in question so the relatively low toxicity of ammonia is already reflected in the numbers.

In addition, IDHW has identified a specific procedure for developing ELs and AACs that is consistent for all sources and compounds. IDHW believes that deviating from this procedure would be unfair to other applicants and the public and introduce too much subjectivity into the process.

IDHW will address the specific areas of concern cited in the request to remove ammonia from the rules:

First, ammonia was deleted from the EPA "189 list". IDHW has reiterated its position on the "189 list" on numerous occasions. However, in brief the IDHW does not consider this to be a valid point because the "189 list" is a result of a political process on the national level. The "189 list" represents a list of pollutants that have significant national concern. The "189 list" was never meant to necessarily protect environments on a local level. Congress has made it clear the "189 list" and the Title III/ NESHAP program was not meant to replace state air toxics programs. Consequently, IDHW disagrees that the presences or absences of a compound on the EPA "189 list" is necessarily relevant to the Idaho TAP program.

Second, ammonia is generally considered relatively non or mildly toxic in very low concentrations. IDHW agrees that this is a valid point. However as mentioned above, the EL and AAC for this compound has taken the level of toxicity into account. In addition, 22 state and local air pollution control agencies have set standards for ammonia in air, some less stringent and some more stringent than Idaho. In addition, the Division of Health has been consulted and has recommended that ammonia continue to be regulated on the basis of its significant irritant effects.

Third, ammonia is regulated under SARA Title III for accidental release. SARA Title III is concerned with the catastrophic release of large quantities of dangerous chemicals and the communities right to know that these chemicals are being used and stored nearby. SARA Title III does not regulate these chemicals but only requires reporting of their presence. IDHW does not consider this to be excessive "double regulation". The intent of the IDHW TAP program and SARA Title III are very different so IDHW disagrees that this sort of "double regulation" is either unwarranted or unreasonable.

Fourth, substantial releases of ammonia come from animal wastes and other organic materials. While IDHW agrees that this is true, IDHW disagrees that this point is germane. The intent of the rules concerning toxic air pollutants is to control the emissions of toxics air pollutants from new and modified sources. Agricultural activities and services are generally exempted from the toxics rules.

Fifth, the control of ammonia at the levels specified in the proposed rules would be severely burdensome for industry, particularly the fertilizer and sugar beet industries. IDHW is very sensitive to the potential economic impacts of these proposed rules and economic impacts are always considered. However, these regulations apply to new and modified sources only. IDHW does not agree that economic effect on the regulated community will be so severe so as to out weigh their environmental benefit. Further, IDHW does not believe that it is appropriate carve out regulatory exemptions for the economic benefit of a particular industry or industries.

Comment #110: Section 203.05(j). Remove Phosphorous pentoxide from the Table in Section 203 .05(j).

IDHW Response: The rules have not been changed in response to this comment. The IDHW believes that our regulation of this chemical is both reasonable and responsible. Phosphorus pentoxide is an irritant and is being regulated on that basis.

Phosphorous pentoxide is listed on the EPA extremely hazardous substance list; It is listed in the Toxic Substances Control Act (TSCA) Substances Inventory; It is listed by the Department of Transportation (DOT) as a corrosive material; Sax's Dangerous Properties of Dangerous Materials. Vol. III. Eighth Ed. Richard J. Lewis, Sr. New York: Van Norstrand Reinhold 1992. 2795. notes that it is a "Poison by inhalation. A corrosive irritant to the eyes, skin and mucous membranes"; The Hazardous Substances Data Base (HSDB) produced by Micromedix, Inc. Vol. 16 notes that "Particles of solid Phosphorous pentoxide in contact with eye react vigorously, & even small amounts may cause burns of lids, conjunctivae, & corneas, producing blue-white opacities, which may be permanent."

Since phosphorous pentoxide in quite hydrophilic and rapidly forms phosphoric acid, the ACGIH Threshold Limit Value (TLV) of 1mg/m3 for phosphoric acid was used. In addition the HSDB reports that Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd Ed New York: John Wiley Sons, 1981-1982. recommends a Hygienic Std. of 1mg/m3.

Comment #111: Section 203.05.j. and 203.05.k. There should be short term ambient standards for non-carcinogens (8 and or 24 hr. standards). A formula for the development of such standards was submitted.

IDHW Response: The rules have been changed in response to this comment. An annual averaging period will be used for both screening and refined models for all toxic air pollutants. The issue is complex and important enough to deserve clarification.

The acceptable ambient concentrations (AAC) are not ambient air quality standards. Rather they are acceptable increments of

toxic air pollutants that are responsibly protective of human health and reasonably permissive of industrial expansion. Because the AAC are not ambient standards the air quality management techniques of averaging collective emissions to some total ambient build up do not apply.

In the design of this rule, the AAC relates to a stack emission rate. In the most prescribed sense, the AAC would be assured by a permitted emission limit. This emission limit then might be guaranteed by some ample control technology design or perhaps an operational limit prescribed in the permit.

Comment #112: Section 203.05.j. and 203.05.k. There is inadequate health based data for the ambient levels set. OSHA standards "were struck down in court" as a result of "OSHA's unlawful rule making" because OSHA's standards were not based the "significant risk" and "feasibility" requirements of the OSHA statutes" our ambient standards were on "...very shaky legal ground..."

IDHW Response: The rules have not been changed in response to this comment. The IDHW bases its non-carcinogenic levels on work done by the American Conference of Government Industrial Hygienists (ACGIH), not OSHA. The ACGIH is a respected health effects research body and the IDHW has every confidence in ACGIH data. For carcinogens, the IDHW used published unit risk factors from EPA and supporting data from the National Institutes of Health and the International Agency for Research on Cancer (IARC). It does not seem reasonable for IDHW to attempt to "reinvent the wheel" in the face of so much available data. To do so would be an astronomical undertaking, far beyond the capabilities of most if not all state governments.

Comment #113: Section 203.05.j. and 203.05.k. Standards derived from those of other states should be removed.

IDHW Response: The rules have not been changed in response to this comment. IDHW has included substances on our lists that we feel have valid health concerns. Some of these substances do not have Occupational Exposure Levels (OEL) published by an agency such as the ACGIH. However they do have substantial health data. On occasion, some states have looked at some of these chemicals and developed emissions and or ambient standards. We have no reason to believe that states such as Washington or New York are frivolous or capricious in their risk assessment actives. Quite the contrary, we consider other states to be responsible agencies subject to oversight by their respective legislatures, industry groups and the public, much like Idaho.

The IDHW then looks at these standards to see if we consider them reasonable, based on the available literature and other criteria. If we find that to be the case we may then adopt these standards or modify them as the data warrant. If, in the future,

the ACGIH develops standards differing from the standards we have adopted, we will seek to modify our rules accordingly.

Comment #114: **Section 203.05.j. and 203.05.k. Are some of the compounds on Appendix 1 are suspected carcinogens?**

IDHW Response: The rules have been changed in response to this comment. It is the policy the IDHW to regard any substance that is considered a B2 ranking by EPA (or equivalent ranking by IARC) a carcinogen for purposes of regulation. A B2 carcinogen is one that has sufficient animal evidence. C (or equivalent ranking by IARC) ranked compounds have limited animal evidence and inadequate or less human evidence. The IDHW does not believe that C ranked carcinogens have sufficient data available to support the regulatory scheme required by carcinogens. Therefore some compounds on Appendix 1 may be suspected carcinogens in other references. In addition, some carcinogens were mistakenly listed on both appendices. These errors have been corrected.

Comment #115: **Section 203.05.j. and 203.05.k. The range of allowable emissions of carcinogens is too narrow and the accuracy of the models used to calculate potential risks is inadequate.**

IDHW Response: The rules have not been changed in response to this comment. The narrow range of allowable carcinogenic risk reflects a upper limit of one in a hundred thousand, above which the IDHW considers risk to be unacceptable. The IDHW considers this to be reasonable and in line with risk acceptability of other states and the EPA.

The IDHW acknowledges that models used to calculate potential risk are not exact and that there are variations in the appropriateness of the models vis a vis specific applications. The IDHW has tried to allow maximum flexibility in model selection by requiring only that the model must be EPA approved and must be reviewed for appropriate application by the IDHW. The IDHW considers that EPA approval and IDHW review of all models used is a reasonable requirement.

Comment #116: **Section 203.05.j and 203.05.k Screening Emissions Tables. The publication in the rules of OEL and URF values that are based on continually changing OSHA, and EPA exposure criteria will contribute to confusion and errors in use of the most current (and appropriate) criteria.**

For modeling analyses, URFs should be taken from the EPA IRIS database, which is updated on a monthly basis. OELs should be taken from their source documents - either OSHA PELs, ACGIH TLVs, or NIOSH RELs, which are updated on an annual basis. The regulations should either reference these sources or include a statement to the effect that the OEL, URF, AAC, and AACC values may

change (based on the latest revision to the source) without requiring change to these regulations.

IDHW Response: The rules have not been changed in response to this comment. IDHW believes that annual updates through rulemaking and emergency rulemaking, if necessary, will provide an adequate and reasonable method to keep the appendices updated. Providing the appendices as part of the rules insures consistency. In addition, the Administrative Procedures Act of Idaho prohibits language that automatically incorporates by reference the latest edition of a reference. A specific document must be incorporated. IDHW would also note that this aspect of the rules was partially in response to industry's strongly stated desire to have the various references made part of the rules so that there would be regulatory consistency.

Comment #117: Section 205.06 - The cited Section 205.01.b. should be Section 205.01.b.ii.

IDHW Response: The Department did not modify this section in response to this comment. The cites are correct.

Comment #118: Section 209. PROCEDURE FOR ISSUING PERMITS. This section should perhaps be moved to after Section 400, et seq, since it applies to both permits to construct and tier II permits. In addition, the second reference to "major modification" in 209.01.c. must be changed to "modification." Finally, the last sentence in 209.05 must be deleted since permits to construct do not expire and are not "renewed" like operating permits.

IDHW Response: The Department has modified the rules in response to this comment. The sections in 209 that also apply to Tier II permits have been incorporated into Section 404.

Comment #119: Section 209 provides no time frame for conduction public comment periods or hearings after a proposed permit to construct is issued for major facilities or modifications. Language is suggested.

IDHW Response: The Department has not changed the rules in response to this comment. The Department makes every effort to conduct public comment periods and hearings in a timely manner.

Comment #120: Emissions Screening levels should take into account such realistic assumptions as reactivity of gaseous air toxics and deposition rates of dusts. It was suggested that the values be recalculated using these realistic assumptions.

IDHW Response: While IDHW agrees that gas reactivity and deposition rates of dusts are real world occurrences, it is impossible to use these assumptions in figuring emissions screening levels because of their site specific nature. Reactivity of gases varies considerably with different circumstances. For instance, the concentration of hydroxyl radicals in the atmosphere, the amount of sunlight present and various aspects of reaction kinetics are items that have a significant effect on atmospheric gas reactivity. Deposition rates of dusts and other particles can vary greatly with circumstances such as wind velocity and precipitation rates.

Comment #121: Section 209.01. This section should provide for language to a permit to be automatically deemed complete if the Department does not notify the applicant of incompleteness within 60 days, similar to Section 342.03

IDHW Response: The Department has not modified the rules in response to this comment. The rules provide for a completeness determination within 30 days. The Department has not had a permitting backlog for four years. Therefore, the Department believes that the suggested modification is unwarranted.

SECTION 300

Comment #122: Section 302.05. This provision must be expanded to include source categories designated by EPA.

IDHW Response: The Department has not modified this section (although it has been moved to section 101) in response to this comment. The Department is committed to updating the rules in accordance with future federal rule-making.

Comment #123: Section 313. Timely Application. We recommend that Section 342.02.a. be reworded to require one-third of Tier I facilities to submit their application before the end of the 12-month period, to enable the first third to be processed by the end of the 12-month period.

IDHW Response: The Department has modified the rules in response to this comment. Sections 313 and 367 have been modified to clarify how the Department will act on applications during the transition period.

Comment #124: Section 313.02. Preconstruction Permits. The Federal Program allows states to provide for concurrent processing of pre-construction permits and operating permits, provided that the procedural requirements of both programs are met. We recommend that applicants in Idaho be given this option.

IDHW Response: The Department has modified Section 209 in response to this comment. Subsection 209.05 describes the permit to construct procedures for Tier I sources.

Comment #125: Section 313.04. Renewal Applications. For purposes of permit renewal, redefine timely renewal application, a timely application is one that is submitted at least six months prior to the date of expiration, unless the applicant requests and the operating permit specifies a longer period (not to exceed 18 months).

IDHW Response: The Department has modified the rules in response to this comment. Sections 313 and 367 have been modified to clarify how the Department will act on applications during the transition period.

Comment #126: Section 313.04. In accordance with 40 CFR 70.5(a)(a)(iii), the State must require that applications for permit renewals be submitted between 6 and 18 months before expiration of the permit. Requiring renewal applications to be submitted more than 18 months before expiration is not approvable. This provision needs to be reworded to ensure that the application is submitted no earlier than 18 months prior to expiration and no later than (some time between 6 and 18) months prior to expiration.

The rules defining a timely application will be hard on commenter because of the need for very rapid turn around time needed in the semiconductor business.

IDHW Response: The Department has modified the rules in response to these comments. See Section 313.03.

Comment #127: Section 314.02. Standard Application Form and Required Information. Please clarify what type of description is required by this section. The Department should include in a Checklist or detailed Instructions on the level of detail and what criteria the Department will use to determine whether any response to this requirement is "complete."

The description of the source's products and processes must include information about the applicable SIC codes.

IDHW Response: The Department has modified the rules in response to these comments. Subsection 314.02.b clarifies that the description must include narrative and applicable SIC codes.

The Department has developed a completeness checklist and a draft Tier I operating permit guidance manual. These documents are available on request to the Department. The guidance manual will not be finalized until after the rules are final.

Comment #128: Section 314.04.a. Emissions Information. The application must also include information on all air pollutants, that are not also regulated air pollutants, for which the source is major. The Department must also have authority to require additional information to determine the applicability of applicable requirements for all air pollutants, not just regulated air pollutants and as necessary to collect any permit fees. In addition, the reference to exempted units must be more specific than simply "Section 314, et seq."

IDHW Response: The Department has modified this section in response to this comment.

Comment #129: 314.04.a. Emissions Information. This section requires specification of emissions of regulated air pollutants emitted from any non-exempt emissions unit. this requirement should be limited to information about "relevant emissions units," meaning only those emissions units that are subject to applicable requirements.

IDHW Response: The Department has not modified the rules in response to this comment. The Department must receive information as described in the preceding comment. Section 314 has been revised to clarify what information must be submitted in the Tier I operating permit application.

Comment #130: 314.04.a. Emissions Information. The second sentence of Section 314.04 states that the Department shall require additional information related to the emissions of regulated air pollutants sufficient to verify which requirements are applicable. This should be written in the form of a requirement for the applicant, rather than an instruction to the Department, to avoid having the Department requesting additional information after the application has been submitted. Suggested language is submitted.

IDHW Response: The Department has deleted this sentence.

Comment #131: Section 314.04.b. and 314.05.b. Emission Information. This section refers to requirements of the "Act." This should be a reference to the "Clean Air Act," since Title V permits are required to implement the applicable requirements of the Clean Air Act (which includes requirements under an approved SIP or preconstruction program). Requirements that applicable to the source pursuant to the (State) Act or these Rules only, are to be segregated from those requirements that are federally enforceable "applicable requirements" under the Federal Clean Air Act.

IDHW Response: The Department's modifications to the rules address this comment. See sections 314.04 and 322.17.j.

Comment #132: Section 314.04.c. Emission Information. We recommend using "applicable standard reference test method, if any" instead of "applicable test method."

IDHW Response: The Department has not modified this section in response to this comment. If there is no applicable test method, then the applicant will not have to identify terms necessary to establish compliance with the applicable test method.

Comment #133: Section 314.04.f. Emission Information. Since Title V operating permits address "regulated air pollutants," this requirement should be so limited.

IDHW Response: The Department has not modified the rules in response to this comment. The applicant is required to submit information regarding all air pollutants that are regulated by the Clean Air Act. In addition, any applicant that has a permit to construct that addresses Toxic Air Pollutants will be required to submit information regarding those emission.

Comment #134: Section 314.08. Additional Information. This section should include, in addition to "alternate operating scenarios," other provisions, such as emissions trading and emissions caps, allowed by the Clean Air Act. These alternate provisions, if incorporated into the permit, may be implemented without a permit revision.

Alternative Operating Scenarios. This section should clearly provide intent of alternative operating scenarios and include permit allowances for emissions trading, emissions caps, or other optional requirements pertinent to maintaining operational flexibility.

The last phrase needs to be revised to clarify that the additional information relates to permit terms and conditions allowing for emissions trading and cross reference the appropriate Idaho bubble rules.

IDHW Response: The Department has modified Section 314 to include a section relating to alternative operating scenarios (314.09) and a section relating to trading scenarios (314.12).

Comment #135: Section 314.09. Pursuant to 40 CFR 70.5(c)(8)(iv), the compliance plan must also include a schedule for submission of certified progress reports no less frequently than every 6 months for every source required to have a compliance schedule to remedy a violation.

Section 314.11.c. Certification of Compliance. Compliance certifications will require an enormous commitment of resources because of the certifications as to accuracy and completeness required of a senior official. Requiring certification more frequently than annually will be costly and will serve little purpose. We recommend that the Idaho Program be consistent with the Federal Program, except where the applicant and the Department have agreed to a more frequent certification in a compliance schedule.

Section 314.11.d. This paragraph must be revised to require a statement indicating "whether" the source is in compliance, not "that the source is in compliance."

IDHW Response: The Department has rewritten the sections covering Compliance Certifications and Compliance Plans (now Sections 314.10 and 314.11). These sections were rewritten to improve the organization and to clarify what information is required. The modifications to these sections address these comments.

Comment #136: **Section 314.13. The phrase "activities which are exempted from permitting requirements of Sections 200 et seq." must be changed to "insignificant activities." The requirements of Title V (operating permits) of the Clean Air Act are completely different from the requirements of Title I (new source review) and the exemptions for construction permits are not approvable as exemptions from operating permits. Also, in the case of insignificant activities, the source must also submit such information as is necessary to demonstrate that the exemption applies.**

IDHW Response: The Department has deleted this section. New Section 314.04.b has been added to clarify that Insignificant Activities need only be listed in the Tier I operating permit application. The Department believes that the list of Insignificant Activities is specific enough that sources do not need to demonstrate that the definition applies.

Comment #137: **Section 315. Duty to Supplement or Correct Application. One commenter notes that Section 315 provides that the Department may request additional information deemed to be necessary to evaluate or take final action on the application and recommends adding language to allow the applicant to file a contested case, if the applicant believes the information is not authorized by law or the rules, or is not reasonably necessary to evaluate or take final action on the application.**

IDHW Response: The rules have not been changed in response to this comment. Completeness determinations are based on a limited review of the application so IDHW often needs to request additional information from applicants in order to conduct the full review of

the application and issue a permit action. The request is not a final action, and thus, it is not appealable as a contested case. Applicants may respond to the request from IDHW by explaining why the applicant believes the information has already been provided or why the information is unnecessary. If IDHW agrees with the applicants explanation, IDHW continues with the review. If IDHW disagrees, it notifies the applicant and the applicant may provide the information or IDHW will deny the permit application. A denial of the permit application is an appealable action.

Comment #138: Section 317. Permit Continuance. For additional clarity, this paragraph should cross reference the provision which gives sources the ability to operate without a permit if the source submitted a timely application.

IDHW Response: The Department has deleted this section and has modified Section 301 (see 301.02.a) to clarify that sources may continue to operate if the source is in compliance with Sections 311 through 315.

Comment #139: Section 322. Standard Permit Requirements. The permit must also require the reporting of deviations from permit requirements and must define promptness in relation to the degree and type of deviation likely to occur and the applicable requirements in accordance with 40 CFR 70.6(a)(3)(iii)(B).

IDHW Response: The Department has not modified this section in response to this comment. Section 326 covers deviations from permit requirements and provides time frames for reporting for each type of excess emission event.

Comment #140: Section 322.01. Standard Permit Requirements. The permit must include emission limitations that assure compliance with all applicable requirements even if such requirements are identified after submission of the application.

IDHW Response: The Department has not modified this section in response to this comment. However, Section 315 requires the applicant to promptly provide information regarding requirements that become applicable after the date a complete application was file by prior to the release of a proposed action.

Comment #141: Section 322.03. Standard Permit Requirements. This provision needs to be revised to clarify that there must be at least one permit term for each requirement.

IDHW Response: The Department has incorporated the suggested modification into the rules.

Comment #142: **Section 322.04. Alternative Operating Scenarios. Commenter commends IDHW for incorporating the alternative operating scenario provisions, and is recommending that two phrases be added to clarify that the source must outline reasonably foreseeable operating scenarios in its permit application for IDHW to approve them as a part of the operating permit.**

IDHW Response: The Department has not modified the rules in response to this comment. The Department does not want to be put in the position of deciding whether or not an applicant could reasonably foresee operating under a proposed operating scenario. Maximum flexibility requires that the Department to base approval of alternative operating scenarios based on their compliance with underlying requirements not on whether or not a facility would ever operate under the requested scenario.

Comment #143: **Section 322.04. Alternative Operating Scenarios. The reference to operating scenarios approved in accordance with Section 314.08 is confusing because Section 314.08 does not address the approval of such scenarios, only the information to include in an application. The permit must also include provisions that assure compliance with all applicable requirements for each such scenario.**

IDHW Response: The Department has modified this section in response to this comment.

Comment #144: **Section 322.10.e. Compliance Certifications. The state is the only regulatory agency, so the reference for sending certifications to EPA could be deleted.**

IDHW Response: The Department has not modified the rules in response to this comment. This section is required by 40 CFR 70.6(c)(5)iv.

Comment #145: **Section 322.13. Tier II Applicable Requirements. This provision must be deleted since no Tier II requirements can be applicable to Tier I sources. A source is either subject to Title V of the Clean Air Act or it is not.**

IDHW Response: The Department has deleted this section.

Comment #146: **Section 322.14. Provisions Stating the Following. This section lists provisions that are included in the permit. A subsection needs to be added that allows PTC/PSD permits to be automatically included into the operating permit. Without this, a PTC/PSD permit could be obtained but the modification could not take place until the operating permit was also changed. Rather**

than have the delay and duplication of two separate permitting activities there should be one activity.

IDHW Response: The Department did not modify the rules in response to this comment. Sections 209.05 and 385 cover the relationship between these two programs.

Comment #147: Section 322.14(f). Provisions Stating the Following. It is unclear whether requiring all information requested under Section 122 is as broad as 40 CFR 70.6(a)(6)(v). This could perhaps be clarified by the Attorney General opinion.

IDHW Response: The Department has not modified the rules in response to this comment. The Attorney General opinion on the final rules will cover this issue.

Comment #148: Section 322.14(h). Provisions Stating the Following. This provision is contrary to 40 CFR 70.6(f) and Section 325 of the Idaho regulations in that it doesn't provide that the permit is a shield only as to applicable requirements listed in the application and expressly determined in writing by the permitting authority not to be applicable.

IDHW Response: The Department has deleted this section. The Department has rewritten Section 325 to clarify the shield provisions and to replace instructional language with actual language.

Comment #149: Section 322.15. Provisions Prohibiting. The last clause should be revised to clarify that it refers to a "modification under any provision of 42 U.S.C. Section 7401 to 7515."

IDHW Response: The Department has modified this section to prohibit facility alterations without complying with Sections 380 through 387.

Comment #150: Section 322.17. TIER I Limits. This section seems to render everything federally enforceable. This section should be modified to differentiate between State enforceable regulations and Federally enforceable regulations. Suggested language is included.

IDHW Response: The Department has modified this section (now 322.17.j) in response to this comment.

Comment #151: Section 322.20. Provisions Requiring Registration Fees. As discussed below, Idaho must demonstrate that all Tier I sources are subject to Sections 525 through 538. For example, it

is not clear that Tier I sources which are major only for hazardous air pollutants would be subject to registration fees.

IDHW Response: The Department has not modified this section in response to this comment.

Comment #152: **Section 322.22. Permit Duration. The phrasing is awkward and could possibly be revised to state: "...a permit term of five years; except...." Also, the provision allowing for permits of shorter duration during the first four years after EPA approval cannot be applicable to acid rain sources.**

IDHW Response: The Department has modified this section (now 322.15) in response to this comment.

Comment #153: **Section 326. Excess Emissions. One commenter has suggested substantial additions, deletions and modifications to Section 326.**

Section 326.01. This provision is not approvable and will preclude EPA from approving Idaho's Title V operating permit program. An upset must still be considered a violation. A state may, however, provide reasonable procedures for the exercise of enforcement discretion for upsets. Also, exercise of enforcement discretion for scheduled maintenance, start up and shut down is strictly limited. Idaho's provision is far too broad.

Section 326.03(a). By linking reporting to detection, the rule is much more permissive than Idaho's existing upset rule, which links reporting to occurrence. By linking reporting to detection, they can always say they didn't know about the upset. This provision must be revised to be consistent with the current requirements.

Section 326.03.d. This section allows the Division to shut down an entire facility if one emissions unit is the cause of excess emissions. The conditions under which an entire facility will be shut down should be well defined. Prior to the last sentence before i., add: "The decision regarding whether to shut down a facility will be based on the amount the rest of the facility contributes to excess emissions. Under no circumstances will an entire facility be shut down, if the shut down of the emissions unit resolves the problem."

IDHW Response: The Department has modified Section 326 in response to these comments. Most of the suggested modifications have been incorporated into this section. For suggested changes to sections 329.03 e-g, the Department has responded by editing these sections and deleting the "avoidable" and "absolve" clauses. The Department has retained the ability to revoke or modify the procedures because the approval will be issued with 48 hours to allow continued operations so there will be very limited review. The ability to revoke or modify will allow the Department to more liberally grant approvals initially because the Department can revoke or modify the

approval if new information becomes available, the permittee abuses the approval, or if the public objects.

Comment #154: Section 326.04. Excess Emissions. Allowing sources to send written notice within 15 days is more liberal than their current upset provision, which requires written notice by the end of business on the next working day. This provision must be revised to be consistent with the current requirement.

IDHW Response: The Department has not modified this section in response to this comment. For startup, shutdown and scheduled maintenance, the permittee is required to notify the Department no later than 2 hours prior to the start of the excess emissions event. For upset and breakdown, the permittee must notify the Department of the event no later than 24 hours after occurrence. The permittee is then required to submit a written report for each excess emissions event no later than 15 days after the beginning of the event.

Comment #155: Section 326. Excess Emissions. The section on permit content must include a provision meeting 40 CFR 70.6(b) regarding designation of state only requirements in the Tier I permit.

IDHW Response: The Department has modified the rules in response to this comment. See Section 322.17.k.

Comment #156: Section 342.03. Action on Applications. Section 342.03 provides that the Department shall promptly provide notice to the applicant of whether the application is complete and that, unless it is within the one year after EPA approves Idaho's Tier I Operating Permit Program or the Department requests additional information, or otherwise notifies the applicant of incompleteness within 60 days of receipt of an application, the application shall be deemed complete. Commenter recommends that the completeness determination be made with 60 days of submission of the application, regardless of when the application is submitted and that the permit shield be extended, and an application check list be provided.

This provision is contrary to 40 CFR 70.7(a)(4) in that it suspends the 60 day automatic completeness for applications submitted within one year after EPA approval of the program.

IDHW Response: The Department has modified the rules in response to this comment. See Section 361.

Comment #157: Section 342.01. Action on Applications. Clauses (b) and (c) appear to apply to the same actions, but use different

language. Making them consistent would avoid any possible ambiguity.

IDHW Response: The Department has modified these sections in response to this comment.

Comment #158: Section 342.01(f). Action on Applications. This provision does not appear to relate to any other subparagraphs in Section 342.01. It seems awkwardly placed. In addition, it is unclear whether this provision also includes increases in emissions of acid rain authorized by allowances, which, pursuant to 40 CFR 70.6(a)(4), must also be allowed without permit revision.

IDHW Response: The Department has deleted this section.

Comment #159: Section 342.02(a). Action on Applications. This provision also appears awkwardly placed, since it does not relate to the lead in provision of 342.02. Perhaps 342.02(a) should be renumbered 324.02, and the rest of what is now Section 342.02 should be renumbered 342.03.

IDHW Response: The Department has modified the rules in response to this comment.

Comment #160: Section 342.02.c and 342.06. Action on Applications. The definition of complete application allows open time limit if the Department determines application is not complete within 60 days. This section should require the Department to take final action on any complete Tier I operating permit application within six months of the permit application submittal.

IDHW Response: The Department has not modified the rules in response to this comment. Assuming that a complete application has been submitted, the Department must make a completeness determination within 60 days. Once the completeness determination has been made the Department must produce a draft Tier I operating permit within 60 days. The Department must provide a 30 day public comment period. The Department must then respond to comment and prepare a proposed permit within 30 days. The proposed permit will be sent to EPA for review period not to exceed 45 days. Therefore the expected time from submittal of a complete application to issuance of a final permit is seven and a half months barring any appeals.

The Department will reexamine the time required to take final action on a permit in the third year of the transition period. If warranted, the Department will shorten the 18 month deadline for final action on complete applications.

Comment #161: Section 342.02(d). Action on Applications. For clarification, this sentence should be revised: "Submittal of Tier I operating applications for and the permitting of...."

IDHW Response: The Department has modified this section in response to this comment.

Comment #162: Section 342.04. Action on Applications. This provision should be revised to clarify that the memorandum must set forth the "legal and factual basis" for the proposed permit.

IDHW Response: The Department has modified the rules in response to this comment. See Section 362.

Comment #163: Section 342.05. Action on Applications. For further clarity, this provision should be revised to make clear it refers to a complete Tier I application.

IDHW Response: The Department has modified the rules in response to this comment. See Section 361.03.

Comment #164: Section 342.06. This provision does not include the requirement that a responsible official must certify the submitted information.

IDHW Response: The Department has modified the rules in response to this comment. See Section 314.01.

Comment #165: Section 343.03.a. Permit Renewal & Expiration. While 343.03.a includes Tier II operating permits, 343.03.b. does not. Suggested language is included.

Section 343.03. and (b). This provision must be revised to clarify that the application must be both timely and complete. Furthermore, the references to "permit to construct" and "Tier II operating permit" must be deleted as Sections 300 et seq. do not apply to those permits.

IDHW Response: The Department has modified this section (now 368) in response to this comment.

Comment #166: Section 344. Off Permit Changes. The Department has included provisions incorporating this requirement in its draft regulations. Commenter is asking that additional language be added to specifically authorize trading of emission increases and decreases, and to otherwise accommodate SIP-authorized emissions trading. Additional language is included.

IDHW Response: The Department has modified the rules in response to this comment. See Sections 314.12 and 322.05.

Comment #167: Section 344. Off Permit Changes. Entitling this provision "off permit" changes is confusing, because Part 70 refers to changes of the type referred to in Section 322.16 as "off permit" changes. Changes of the type referred to in this paragraph are authorized under 40 CFR 70.4(b)(12). It may help to clarify Idaho's Title V program if all provisions allowing for operational changes outside the permit revision process were in the same place, such as off-permit changes, 502(b)(10) changes, and other operational flexibility provisions. Currently, some such provisions are here and some are either also or only in the permit content provision. This paragraph must also be revised to expressly exclude acid rain sources from making changes of the type permitted under this Section 344. In addition, this paragraph uses the term "emissions allowable under the permit," but that terms is not defined in Idaho's regulations. The term "emergencies" should also be defined.

IDHW Response: The Department has made modifications to the rules that address this comment. The Department has created a new section entitled "Alterations". The purpose of this section is to clarify what changes are allowed, the procedures that must be followed for each alteration, and the permit shield applicability of each type of alteration.

The Department has added or expanded the definitions mentioned in the comment. See Section 103.

Comment #168: Section 345. Administrative Permit Amendments. This provision can not apply for the acid rain portion of the permit. Instead, such amendments shall be governed by acid rain regulations.

IDHW Response: The Department has modified the rules in response to this comment. See Section 384.01.b.

Comment #169: Section 346. Minor Permit Modification Procedures. This provision can not apply for the acid rain portion of the permit. Instead, such modification shall be governed by acid rain regulations.

IDHW Response: The Department has modified this section (now 385) in response to this comment.

Comment #170: Section 346. Minor Permit Modification Procedures. IDHW has adopted minor permit modifications procedures. Commenter concurs with this approach, and has suggested some additional

language to make the purpose of the minor permit modification procedures more apparent. Commenter has also suggested a provision to allow group processing of minor modifications.

IDHW Response: The Department has modified this section (now 385) in response to this comment. The Department has added provisions allowing group processing of minor modifications (Section 385.07).

Comment #171: Section 346.01(d)(i). Minor Permit Modification Procedures. This provision must be clarified to provide that the emissions cap must be federally enforceable. Also, is the reference to "act" to Idaho law or to the Clean Air Act. The reference should include Title I modifications.

IDHW Response: The Department has not modified the rules in response to this comment.

Comment #172: Section 346.03. Minor Permit Modification Procedures. This provision must also require the State promptly to send any notice required under 40 CFR 70.8(b)(2).

IDHW Response: The Department has added this provision to the rules. See Section 385.04.

Comment #173: Section 346.04. Minor Permit Modification Procedures. This provision must be revised to provide: "Within 90 days of the Department's receipt of a complete application under the minor permit modification procedures or within 15 days after the end of EPA's 45 day review period, which ever is later,..."

IDHW Response: The Department has modified the rules in response to this comment. See Section 385.04.

Comment #174: Section 346.05. Minor Permit Modification Procedures. Based on the idea that the source also needs to comply with both the applicable requirements governing the change and the proposed permit terms and conditions until the Department takes action on 364.04.d. Commenter submitted new language.

IDHW Response: The Department has modified this section in response to this comment and to use terms consistent with the new Section 380.

Comment #175: Section 346.06. Minor Permit Modification Procedures. The permit shield does not apply to minor permit modifications at any time per 40 CFR 70.7(2)(vi).

IDHW Response: The Department has modified this section (now 385.06) in response to this comment.

Comment #176: Section 346. Minor Permit Modification Procedures. This section does not contain the requirements set forth in 40 CFR 70.7(e)(2)(iv) on the prohibition on issuance until after EPA review.

IDHW Response: The Department has modified the rules in response to this comment. See Section 385.04.

Comment #177: Section 348.01. Reopening For Cause. Subparagraphs (c) and (g) appear redundant. Also, the program must allow for reopenings for new requirements for acid rain sources in accordance with 40 CFR 70.7(f)(ii).

IDHW Response: The Department has modified this section (now 387) in response to this comment.

Comment #178: Section 348.02. Reopening For Cause. This provision must provide that reopenings shall be as expeditiously as possible. In the alternative, this assurance could be made elsewhere in the program submittal.

IDHW Response: The Department has modified this section (now 387.03) in response to this comment.

Comment #179: Section 349.03. Reopening For Cause by EPA. This provision should be revised to provide that the 90 days runs from receipt of an EPA objection.

IDHW Response: The Department has modified this section (now 387.05) in response to this comment.

Comment #180: Section 350.05. Public Participation. The language "...unless the director deems that additional time is required..." should be changed to provide for a 90 day maximum.

IDHW Response: The Department has not modified the rules in response to this comment. The Department makes every effort to respond to public comment expeditiously.

SECTION 400

Comment #181: Section 401. TIER II OPERATING PERMIT. Section 401.01. must be revised so that it applies to sources that are

subject to Section 300 et seq. not just Section 525. Tier II operating permits must be available to all sources which are not subject to Tier I operating permits and the applicability provisions of Section 525 are not the same as for Tier I operating permits. Furthermore, the parenthetical phrase must be revised because a source doesn't "net out" of applicability but rather limits its potential to emit to levels below the applicability provisions.

IDHW Response: The Department has modified this section in partial response to this comment. The Department has not changed the "net out" language.

Comment #182: Section 401.02. TIER II Operating Permit. Section 02. requires "that anyone with a permit to construct which establishes any emission standard different from those in these rules" to acquire a Tier II permit. If the Permit to Construct is valid for the life of the source then the emissions limitations included in the permit are also enforceable for the life of the source and nothing is really gained by the process of applying for additional permits. Section 03. is sufficiently broad to cover nearly any other circumstances. Delete section 02. and renumber the subsequent sections.

IDHW Response: The Department has not modified this section. This requirement is in the currently effective rules. Permits to construct do not have expiration dates but are superseded by operating permits issued after the permit to construct was issued.

Comment #183: Section 408.03. Conditions for TIER II Operating Permits. This section requires that all tier II operating permits be reissued every 5 years. The director, under section 401.03, has a great deal of discretion to modify or revise a Tier II permit. A permit to construct is issued for the life of the source. Delete Section 03. and renumber section 04.

IDHW Response: The Department has not modified this section. This requirement is in the currently effective rules.

Comment #184: Section 402. APPLICATION PROCEDURES. The phrase "by the owner or operator" should be replaced with "in accordance with Section 123" now that section 123 sets out who must be the certifying official for permits to operate. Furthermore, the reference to Section 300 must be replaced with Section 400.

IDHW Response: The Department has modified this section in response to this comment.

Comment #185: Section 402. APPLICATION PROCEDURES. The structure of this provision is confusing. Since all of section 402 applies to Tier II permits, the lead in to Section 402.01 should perhaps be revised to state: "An application for a Tier II permit must contain the following:" Also, the reference to Section 200 in 402.03 should be changed to Section 400 et seq.

IDHW Response: The Department has modified Section 402 to incorporate all applicable requirements from Sections 200 through 299.

Comment #186: Section 403. REQUIREMENTS FOR ALTERNATIVE EMISSION LIMITS (BUBBLES), Section 404. REQUIREMENT FOR BANKING EMISSION REDUCTION CREDITS (ERC'S), Section 405. REQUIREMENTS FOR EMISSION REDUCTION CREDIT and Section 406. DEMONSTRATION OF AMBIENT EQUIVALENCE. The structure of this part of the state's regulation is strained since Sections 400 et seq. apply to Tier II operating permits yet these Sections cover both Tier I and Tier II operating permits. These Sections should be relocated after Sections 400 - 499, since they apply to all sources, not just sources subject to Tier I operating permits.

IDHW Response: The Department has relocated these sections in response to this comment. See Sections 440, 441, 460 and 461.

Comment #187: Section 403.04. REQUIREMENTS FOR ALTERNATIVE EMISSION LIMITS (BUBBLES). This section needs to refer to all of the National Emission Standards for Hazardous Air Pollutants, not just those in 40 CFR Part 61 but those in Part 63 as well.

IDHW Response: The Department has modified this section in response to this comment.

Comment #188: Section 407.03. Procedures for Issuing Permits. Idaho may wish to consider using the term "permit revision" rather than "permit modification"

IDHW Response: The Department has modified this section in response to this comment.

Comment #189: Section 408.02. Conditions for Tier II Operating Permits. To ensure enforceability, this provision should specify a time period within which the source must provide the Department with a copy of the test results.

IDHW Response: The Department has not modified the rules in response to this comment. The Department can specify time periods for submission of test results in the Tier II operating permit.

Comment #190: Section 997. CONFIDENTIALITY OF RECORDS. One commenter noted that the Idaho rules which are incorporated by reference into these rules in Section 997 do not meet the requirements of 40 CFR Part 70 and Section 114 of the Clean Air Act. The rules must be revised in order for Idaho's Tier I operating permit program to receive full federal approval. In addition, another commenter noted that under Section 316 Tier I operating permit applicants may claim confidentiality for application information.

IDHW Response: The rules have been changed in response to this comment and to more accurately reflect the language and intent of current Idaho statutes. Old Sections 316 and 997 have been deleted and replaced with new Section 126. Section 126 provides procedures for a person to request IDHW to treat information as confidential information, requires Tier I operating permit applicants and permittees to submit copies of confidential information directly to EPA and clarifies that all information is subject to disclosure in accordance with Idaho Code §§ 39-111 and 9-301 et seq.

Guideline for Performing Air Quality Impact Analyses

Stationary Source Program
AQ Division

State of Idaho
Department of Environmental Quality
July 2021

REC 4431

TR 1116

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Abbreviations, Acronyms, and Symbols

DEQ	Idaho Department of Environmental Quality
EPA	US Environmental Protection Agency
Acfm	actual cubic feet per minute
AERMIC	American Meteorological Society/Environmental Protection Agency Regulatory Model Improvement
AQCR	air quality control region
AQRV	air quality related value
BPIP	Building Profile Input Program
Btu	British thermal unit
CO	carbon monoxide
DEM	digital elevation model
DEQ	Department of Environmental Quality
EL	screening emission level
EPA	Environmental Protection Agency
FEC	facility emission cap
ft	feet
GEP	good engineering practice
H_2S	hydrogen sulfide
IBR	incorporate by reference
IDAPA	A numbering designation for all administrative rules in Idaho promulgated in accordance with the Idaho Administrative Procedures Act.
ISCST3	Industrial Source Complex, Short Term Ver. 3; a refined air pollution model
K	Kelvin
lb/hr	pounds per hour
m	meter
m/sec	meters pèr second
mg/m^3	milligrams per cubic meter
mrem/yr	millirem per year
NAA	nonattainment area
NAAQS	National Ambient Air Quality Standards
NO_2	nitrogen dioxide
NO_x	oxides of nitrogen

NWS	National Weather Service
Pb	lead
$PM_{2.5}$	Particulate matter with an aerodynamic diameter less than or equal to 2.5 micrometers
PM_{10}	Particulate matter with an aerodynamic diameter less than or equal to 10 micrometers
PSD	prevention of significant deterioration
PTC	permit to construct
SCREEN3	An air pollution model used to establish the general distance to the maximum concentration from the facility
SIL	significant impact level
SIP	state implementation plan
SO_2	sulfur dioxide
TAP	toxic air pollutant
T/yr	tons per year
URF	unit risk factor
USGS	U.S. Geological Survey
UTM	Universal Transverse Mercator
VOC	volatile organic compounds
F	Degrees Fahrenheit
$\mu g/m^3$	micrograms per cubic meter

1 Introduction

1.1 Overview

This guideline is intended to assist air permit applicants, air quality specialists, and others who are reasonably proficient at performing atmospheric dispersion modeling analyses, in understanding the Idaho Department of Environmental Quality's (DEQ's) expectations for performing ambient air quality impact analyses associated with air quality permitting. This guideline does not have the force and effect of a rule and is not intended to supersede statutory or regulatory requirements or recommendations of the state of Idaho or the Environmental Protection Agency (EPA). It is provided as general guidance and does not alter the discretionary authority of DEQ to protect public health.

A working-level knowledge of air pollutant dispersion and air quality assessment is needed to understand and use this guideline. Applicants not proficient in atmospheric dispersion modeling are encouraged to use environmental consultants specializing in air quality modeling or other sufficiently experienced professionals having such modeling capabilities. DEQ does not have available resources to educate applicants or consultants in the fundamentals of performing atmospheric pollutant dispersion modeling analyses.

DEQ staff will not recommend a specific consultant; however, DEQ may provide a list of consultants used by applicants for recent permit applications for which dispersion modeling was required. Recent permit applications, DEQ-issued permits, and the Statement of Basis for issued permits are available on DEQ's website, and consultants used by specific applicants are often identified in application materials and the DEQ modeling memorandum (the modeling review memorandum is typically included as an appendix to the Statement of Basis). DEQ may perform the atmospheric dispersion modeling analyses for applicants in some circumstances. Section 1.2 of this guideline describes cases in which DEQ may perform the analyses.

Table 1 provides a basic step-by-step description of an air quality impact analysis, with specific sections of this guideline referenced for each step.

The purpose of an air quality impact analysis, performed in support of an air quality permit application, is to demonstrate that all applicable ambient air quality standards will be met if a proposed project is implemented or to demonstrate an existing facility's compliance with the standards.

Demonstration of compliance with the National Ambient Air Quality Standards (NAAQS), toxic air pollutant (TAP) increments, and prevention of significant deterioration (PSD) increments is required by the state of Idaho for permit issuance and certain exemptions. DEQ has determined this demonstration generally requires the applicant to perform air quality impact analyses using an atmospheric dispersion model, referred to as modeling analyses in this guideline.

The extent of the required modeling analyses will vary from one project to another depending on the type and magnitude of emissions and applicability of specific permitting requirements. For simple facilities (e.g., few sources and buildings), compliance may be shown by using screening- level techniques, including a screening-level model. No further analyses will be required if compliance can be adequately demonstrated with the use of an appropriate screening technique. Projects for which compliance cannot be demonstrated using screening techniques must use more refined methods. Complex multi-point emitting sources or sources with unusual pollutant dispersion environments, for

which screening techniques are not appropriate, are also required to use more refined modeling techniques. Facilities submitting applications for which the PSD requirements are applicable are required to perform more extensive analyses than when submitting a minor source application. This guideline focuses on the requirements for non-PSD applications. Facilities submitting a PSD application should refer to the New Source Review Workshop Manual (EPA 1990) and other available materials from EPA for additional guidance and should consult with DEQ before performing the required analyses.

This guideline follows the Rules for the Control of Air Pollution in Idaho (IDAPA 58.01.01 {Idaho Air Rules}), EPA guidance in the New Source Review Workshop Manual (EPA 1990), and the Guideline on Air Quality Models (EPA 2005). The 2005 version of the Guideline on Air Quality Models was used to develop this version of the guideline. However, the most current version of the Guideline on Air Quality Models should always be used when evaluating appropriate methods and data for a specific project.

The Guideline on Air Quality Models specifies:

"...air quality modeling techniques that should be applied to State Implementation Plan (SIP) revisions for existing sources and to new source reviews (NSR), including prevention of significant deterioration (PSD). Applicable only to criteria pollutants, it is intended for use by EPA Regional Offices, in judging the adequacy of modeling analyses performed by EPA, State and local agencies and by industry. The guidance is appropriate for use by other Federal agencies and by State agencies with air quality and land management responsibilities."

DEQ highly recommends that a modeling protocol be developed and submitted to DEQ for approval before performing any modeling analyses. A DEQ-approved protocol will help assure that methods and data used in the modeling analyses are appropriate and will be acceptable to DEQ reviewers. Guidance on the contents of a protocol is provided in Section 6.1.

Table 1. Sections of the Guideline Used in Performing an Air Impact Analysis

Step in Air Impact Analysis	Section
1) Determine whether professional assistance is needed for performance of the air impact analyses?	1.1, 1.2, 2.0
2) Review general modeling requirements and develop a methodology.	5.0, 6.0
3) Calculate the emissions increase for modeling applicability purposes.	3.3, 6.3
4) Determine whether dispersion modeling is required – compare applicability inventory to modeling thresholds.	3.1, 3.2
5) Select the appropriate model.	6.2, 5.0
6) Set up the modeling analysis, including facility layout, buildings, ambient air boundary, receptors, and elevation data.	6.4.3, 6.4.4, 6.4.5, 6.5, 6.6, 6.7, 6.9
7) Select meteorological data.	6.8
8) Determine background concentrations.	6.10
9) Prepare and submit protocol, and obtain DEQ approval.	6.1
10) Calculate emissions for significant impact analyses and TAPs analyses.	5.1.1, 6.3, 6.3.1, 6.3.2, 6.3.3, 6.4.1
11) Calculate/obtain emissions release parameters and document.	6.4.2
12) Evaluate model results for significant impact analyses and TAPs analyses.	4.1, 4.2, 4.3, 6.11
13) Calculate emissions for cumulative NAAQS analyses and document.	5.1.2, 6.3.1, 6.3.2, 6.3.3, 6.4.1
14) Evaluate model results for cumulative NAAQS analyses.	4.1, 6.11.1
15) Perform comprehensive quality assurance/control of the analyses and evaluation of results.	2.0, 6.11.2
16) Prepare permit application and modeling report.	6.12, 7.0

1.2 Responsibility for Modeling Analyses

The accuracy and representativeness of methods and data used in the modeling analyses is the responsibility of the applicant. DEQ may provide applicants with appropriate meteorological data (not always preprocessed and ready for model input) and default background pollutant concentration values, as described later in this guideline.

DEQ modeling staff may assist applicants or may perform the required modeling analyses in some instances. The following are cases in which DEQ may perform the modeling analyses for permit applicants:

- Renewal of a Tier II operating permit. If a facility has not been modified since issuance of a previous Tier II operating permit, DEQ may use the previously performed modeling results to demonstrate compliance with NAAQS. Previously conducted modeling analyses will not be acceptable if DEQ identifies errors in methods or data used, or if the model used is substantially outdated, such that compliance with NAAQS may be questionable. Changes in applicable standards would also trigger the need to remodel the facility.
- DEQ has current modeling files for the facility. In instances where DEQ has a current model for the facility, slight changes to account for a new source or modification can sometimes be easily made by DEQ modeling staff. The applicant will be responsible for providing, justifying, and

documenting all input parameters needed to adequately address the proposed changes. Modeling analyses performed by DEQ staff will be done outside of the regulatory time limit for permit application review and will be dependent on DEQ staff workload. The applicant must include justification and documentation of all parameters, even those provided in previously submitted analyses. DEQ's permitting process requires that each application be a complete package in itself and not merely reference previously submitted applications.
If compliance with standards cannot be easily demonstrated by DEQ's analyses it will be the applicant's responsibility to conduct more refined analyses.

- Simplistic modeling analyses for small businesses. DEQ may conduct the modeling analyses for small business in situations where there are a small number of sources and a simple facility layout. These decisions will be made on a case- by-case basis and will depend on current DEQ workload.

Modeling analyses performed by DEQ for permit applicants will typically be done outside of the regulatory review process and any review timelines. Data and results will typically be forwarded to the applicant for their review when the analyses are completed by DEQ staff. The applicant will then combine those analyses with other components of the application and submit the complete application to DEQ to initiate the agency review process.

Permit applicants will be responsible for submitting the following information/data to enable DEQ to perform modeling analyses:

- Detailed description of operations and equipment used.
- Requested allowable emissions rates for all criteria pollutants and TAPs for all applicable averaging periods.
- Maximum operational and material processing rates.
- Site description and scaled site plot plan, including a detailed description of any structures. Universal Transverse Mercator (UTM) coordinates, with the applicable datum listed, must be provided for all building corners, and heights of all building tiers must be provided.
- Emissions point information (stack location in UTM coordinates with the applicable datum listed, stack height, stack diameter, stack gas temperature, and flow rate) with thorough justification and documentation of such information.

If DEQ's analyses do not initially demonstrate compliance with applicable standards, it will be the applicant's responsibility to refine the analyses to achieve an adequate compliance demonstration.

DEQ has developed, or is in the process of developing, specific modeling approaches for several industrial types. For example, DEQ has conducted non-site-specific modeling for truck-mix concrete batch plants and portable hot-mix asphalt plants; and no source- specific modeling is require for these plants if they meet the production rate limits, minimum stack parameter specifications, and setback distances from specific receptors. DEQ air dispersion modeling staff should be consulted regarding availability and details of industry-specific modeling approaches.

2 Use of the Modeling Guideline

2.1 This Guideline Most Useful in Common Instances

This modeling guideline is presented as suggestions and instructions for performing a modeling analysis in the most common instances. The methods and data presented are not appropriate for all sources,

locations, and/or situations, and use of a method presented in the guideline does not necessarily assure DEQ approval of the method. DEQ may approve or require methods and/or data differing from those presented in this guideline, depending on the characteristics of the specific situation.

2.2 Level of Knowledge Required to Use This Guideline

This guideline is not intended to educate permit applicants or consultants in the basic principles of atmospheric dispersion or in the operation of various dispersion models, as stated in Section 1.1. A wide variety of commercially available courses are available for applicants to develop the level of knowledge needed to correctly perform pollutant dispersion modeling analyses.

If your specialist (your staff) or consultant and cannot easily answer the following questions, they may not be adequately skilled to properly perform an air impact analysis involving dispersion modeling for air permitting purposes:

1. Have you performed an atmospheric dispersion modeling analysis within the last five years?
2. Do you understand why a stack with a horizontal or rain-capped release is sometimes modeled using a stack flow velocity of 0.001 meters per second?
3. Do you know what a significant impact is, and its implications for modeled impacts?
4. Do you know when background concentrations are used in a modeling analysis and when they are not?
5. Do you understand the difference between a significant impact analysis and a cumulative NAAQS impact analysis?
6. Do you know what surface roughness, Bowen ratio, and surface albedo are and how they are used in the model programs and preprocessor programs?
7. Do you understand the difference in how point sources, area sources, and volume sources are treated in AERMOD, SCREEN3, and/or AERSCREEN?
8. Do you know whether AERMOD uses daily or hourly meteorological data?

Permitting regulations require the applicant to demonstrate that emissions will not cause or significantly contribute to a violation of a standard. The regulations do not require that the analyses estimate actual impacts to the greatest degree possible. Therefore, it is advised that applicants use reasonably conservative data and methods to demonstrate compliance – data and methods that both DEQ and the applicant agree will generate impacts greater than those that would be reasonably expected. However, overly conservative estimates of input parameters, especially emission quantities, may substantially overstate impacts. This could result in the inappropriate applicability of certain requirements and/or the imposition of unnecessary permit provisions and restrictions.

Use of unrealistic release parameters, such as stack flow rates or stack gas temperatures, could shift the location of maximum impacts. In situations where the modeling analyses involve numerous sources, this could result in either under-estimation or over-estimation of combined impacts. Therefore, it is recommended that reasonably accurate release parameters be used when modeling multiple sources, rather than overly conservative parameters. In some instances, where reasonably expected parameters are highly variable, it may be more appropriate to use multiple operational scenarios to evaluate the effects of varying parameters.

3 Requirements to Perform Air Impact Analyses

This section outlines the permitting requirement to demonstrate compliance with NAAQS and TAP increments, and it describes when project-specific air impact modeling analyses are needed for issuance of a PTC or Tier II Operating Permit. It discusses pollutant-specific regulatory applicability, regulatory requirements for permit issuance, and calculation of emission increases for project modeling applicability.

3.1 Air Impact Analysis Regulatory Requirements for Permit Issuance

3.1.1 NAAQS and TAP Compliance Demonstration Requirements

Idaho Air Rules Section 203.02 states that "no permit to construct shall be granted for a new or modified stationary source or modified stationary source unless the applicant shows to the satisfaction of the Department" that the source or modification "would not cause or significantly contribute to a violation of any ambient air quality standard." Section 203.03 similarly requires that no permit be issued unless it is demonstrated through the use of methods in Section 210 that the source or modification would not "injure or unreasonably affect human or animal life or vegetation as required by Section 161."

Air impact analyses are also required for the issuance of Tier II Operating Permits, with requirements of Idaho Air Rules Section 403.02 mirroring Section 203.02 for PTCs. There are no TAP impact analysis requirements for Tier II Operating Permits.

3.1.2 Below Regulatory Concern Exemption from Demonstration Requirement

Certain projects may be exempt from the requirement to demonstrate compliance with NAAQS or TAP increments. If a project would qualify for a Below Regulatory Concern (BRC) permit exemption as per Idaho Air Rules Section 221 if it were not for potential annual emissions of one or more pollutants exceeding the BRC threshold of 10 percent of emissions defined by Idaho Air Rules as "significant," then a NAAQS compliance demonstration may not be required for those pollutants with emissions below BRC levels. DEQ's regulatory interpretation policy of exemption provisions of Idaho Air Rules Section 221.01 is that: "A DEQ NAAQS compliance assertion will not be made by the DEQ modeling group for specific criteria pollutants having a project emissions increase below BRC levels, provided the proposed project would have qualified for a Category I Exemption for BRC emissions quantities except for the emissions of another criteria pollutant.[1]" The interpretation policy also states that the exemption criteria of uncontrolled potential to emit (PTE) not to exceed 100 ton/year (Idaho Air Rules Section 220.01.a.i) is not applicable when evaluating whether a NAAQS impact analysis is required. A permit will be issued limiting PTE below 100 ton/year, thereby negating the need to maintain calculated uncontrolled PTE under 100 ton/year.

The BRC exemption cannot generally be used to exempt a project from a pollutant-specific NAAQS compliance demonstration where a PTC is required for the action regardless of emission quantities, such as the modification of an existing emission or throughput limit.

However, in this instance, if post-project facility-wide annual emissions of the criteria pollutant are also below BRC thresholds, then a NAAQS compliance demonstration is not required.

3.1.3 Regulatory Requirements of the Air Impact Analyses

Once a permit is required for a proposed project, an air impact analysis is required for permit issuance unless the pollutant can be exempt from the requirement to demonstrate compliance with NAAQS and TAP increments, as described above in Section 3.1.2. Idaho Air Rules Section 203 for PTCs and Section 403 for Tier II Operating Permits require that air impact analyses demonstrate compliance with NAAQS and TAP increments "to the satisfaction of the Department." A key consideration is what constitutes DEQ satisfaction of compliance.

Use of unquestionably-conservative methods and data for all components of the analyses will generate predicted impacts that demonstrate compliance at near complete certainty. As analyses move back from methods and data that are highly conservative, then the certainty of NAAQS and TAP increment compliance decreases. Determining the point at which analyses no longer satisfactorily demonstrate compliance then becomes an important concern. This point is not defined in the regulations. DEQ asserts that a satisfactory compliance demonstration is an analysis where NAAQS and TAPs increment compliance is "highly confident," considering all variability and uncertainty in analytical methods and data.

The confidence level of compliance with air quality standards will be affected by the following:

- Magnitude and spatial extent of modeled impacts in comparison to applicable thresholds or standards.
- Potential for public exposure to impacts exceeding standards.
- Representativeness of meteorological data used, and the accuracy/conservatism of meteorological data processing methods used.
- Uncertainty and variability of estimated emissions. Emissions that will be verified by source testing will be considered as near certainty, while emissions based on low-ranked AP-42 factors (which usually represent an average across the industry) will be considered as low confidence.
- Method used to account for atmospheric chemistry (NO/NOx chemistry primarily).
- Representativeness and conservatism of background concentrations (note that using design value background levels with design value modeled results is more conservative for short-averaging periods than for annual averaging periods).
- Level of conservatism in modeling expected operational scenarios (handling variable load conditions, multiple intermittent sources, etc.).
- Representativeness/conservatism of methods used to handle complex emission points such as fugitive releases.
- Handling of building downwash.
- Handling of complex terrain.
- Methods use to hand co-contributing sources in a cumulative impact analysis.

3.2 Emission Thresholds Triggering Site-Specific Impact Analyses

Emission quantities from a source directly affect pollutant impacts to ambient air, and therefore affect the likelihood of a source to cause or contribute to a violation of an ambient air quality standard. Where emission rates are minimal, DEQ can be highly confident that the source will not cause or contribute to a standard violation without performing an impact analysis using pollutant dispersion modeling. Screening Emission Levels (ELs) are specified in the Idaho Air Rules as a de *minimis* TAP emission quantity, below which compliance with the TAP increment is assured. De *minimis* levels for criteria pollutants are not specified in Idaho Air Rules. However, this section presents criteria pollutant de *minimis* levels that DEQ

asserts will reasonably assure NAAQS compliance for various circumstances. These levels were established using the professional judgement of DEQ scientists and engineers, combined with results from computerized pollutant dispersion models for various generic configurations.

DEQ established emission de *minimis* levels as a function of the Significant Emission Rates (SERs) defined in Idaho Air Rules Section 005.108. The SERs are expressed as annual emission rates. To use SERs for NAAQS with short-term averaging periods, the SER is divided by 8,760 hours/year and compared to maximum hourly emissions for 1-hour standards or maximum daily emissions divided by 24 for 24-hour standards. DEQ also developed Significant Impact Level (SIL) thresholds for modification projects; emissions less than these rates are reasonably assured to have impacts less than the applicable SIL. SIL thresholds were developed by DEQ using dispersion modeling analyses of a generic facility with one point source.

Whether a specific emission quantity can cause or contribute to a violation greatly depends on whether those emissions occur from a new facility or are added to those of an existing facility, and whether the existing facility has recently demonstrated NAAQS compliance on a facility- wide basis through dispersion modeling. The confidence of NAAQS compliance is high where project emissions occur from a proposed new facility in an attainment area and predicted emission quantities are low. NAAQS compliance confidence is also high for projects at existing facilities where facility-wide air impact analyses were recently performed and emissions associated with the modification are minimal. Even if the increase in emissions at a previously modeled existing facility could cause impacts exceeding the SIL, it is unlikely that impacts could exceed the NAAQS when combined with co-contributing sources and background concentrations. This is because any high impacts from new sources are not likely to coincide in time and space with high impacts from the existing facility. In the unlikely event that such minimal emissions combine with a high background concentration and impacts from nearby sources to produce an impact exceeding the NAAQS, it is likely that such impacts would only occur in a small area, would only occur for limited periods, and would not affect areas where sensitive individuals could be present.

A modeling applicability threshold assuring project impacts less than the SIL is used for modification projects to facilities where facility-wide NAAQS compliance demonstrations have not been recently performed. This threshold assures with high confidence that the project will not significantly contribute to any potentially existing NAAQS violation. These threshold values were based on modeling of a generic DEQ-generated facility, using the AERMOD regulatory model with Idaho meteorological data. The analyses used the following parameters: stack height = 10 meters; stack diameter = 0.5 meters; velocity at stack exit = 10 meters/second; stack gas temperature at exit = 200 °F; ambient air is at a distance of 100 meters from the stack; the stack is centered on a 10 meter square building, 5 meters high. The SIL thresholds are emission rates that, when modeled using the generic DEQ-generated facility, result in impacts just below the applicable SIL.

Figures 1 and 2 show the project-specific air impact analysis applicability determination process for new facilities and modifications to existing facilities, respectively. This process should only be used for projects proposed in attainment or unclassifiable areas. DEQ should be consulted if a proposed project is located in a non-attainment area. Also, if DEQ observes project-specific conditions that suggest a threshold is not appropriate or protective of NAAQS, then DEQ may require project-specific air impact modeling even though emissions are below the listed threshold.

Table 2 lists the modeling applicability threshold values referenced in Figures 1 and 2.

Table 2. Modeling Applicability Thresholds (values in pounds/hour[(a)])

Pollutant and Averaging Period	SIL Threshold	BRC	1/8 SER	1/4 SER	SER
CO 1-hr	84	2.3[b,c]	2.9[b]	5.7[b]	100 ton/yr
CO 8-hr	26	2.3[b,c]	2.9[b]	5.7[b]	100 ton/yr
NO_2 1-hr	0.38	0.91[c]	1.14	2.3	40 ton/yr
NO_2 ann	0.43 (1.9 ton/yr)	4.0 ton/yr	5.0 ton/yr	10.0 ton/yr	40 ton/yr
SO_2 1-hr	0.40	0.91[c]	1.14	2.3	40 ton/yr
PM_{10} 24-hr	0.32	0.34[c]	0.43	0.86	15 ton/yr
$PM_{2.5}$ 24-hr	0.092	0.23[c]	0.29	0.57	10 ton/yr
$PM_{2.5}$ ann	0.085 (0.37ton/yr)	1.00 ton/yr	1.25 ton/yr	2.5 ton/yr	10 ton/yr
Pb 3-month	0.00102 (0.73 lb/mon)	9.9 lb/mon	12.3 lb/mon	24.7 lb/mon	0.6 ton/yr

a) Values in pounds/hour as averaged over the averaging period of the NAAQS, unless noted otherwise. Pound/hour values listed as a function of the SER were calculated by dividing the annual SER value by 8,760.

b) These values are more restrictive than the SIL Threshold. Therefore, the SIL Threshold may be used in place of these values.

c) BRC is based only on annual emissions. The pounds/hour values listed as BRC for short term standards are the annual BRC rate divided by 8,760 hours/year. Annual emissions from the project should be divided by 8,760 hours/year and then compared to the listed pounds/hour BRC threshold to evaluate whether the project can be exempt from NAAQS compliance demonstration requirements for the applicable pollutant.

d) These values are more restrictive than the SIL Threshold. Therefore, the SIL Threshold may be used in place of these values.

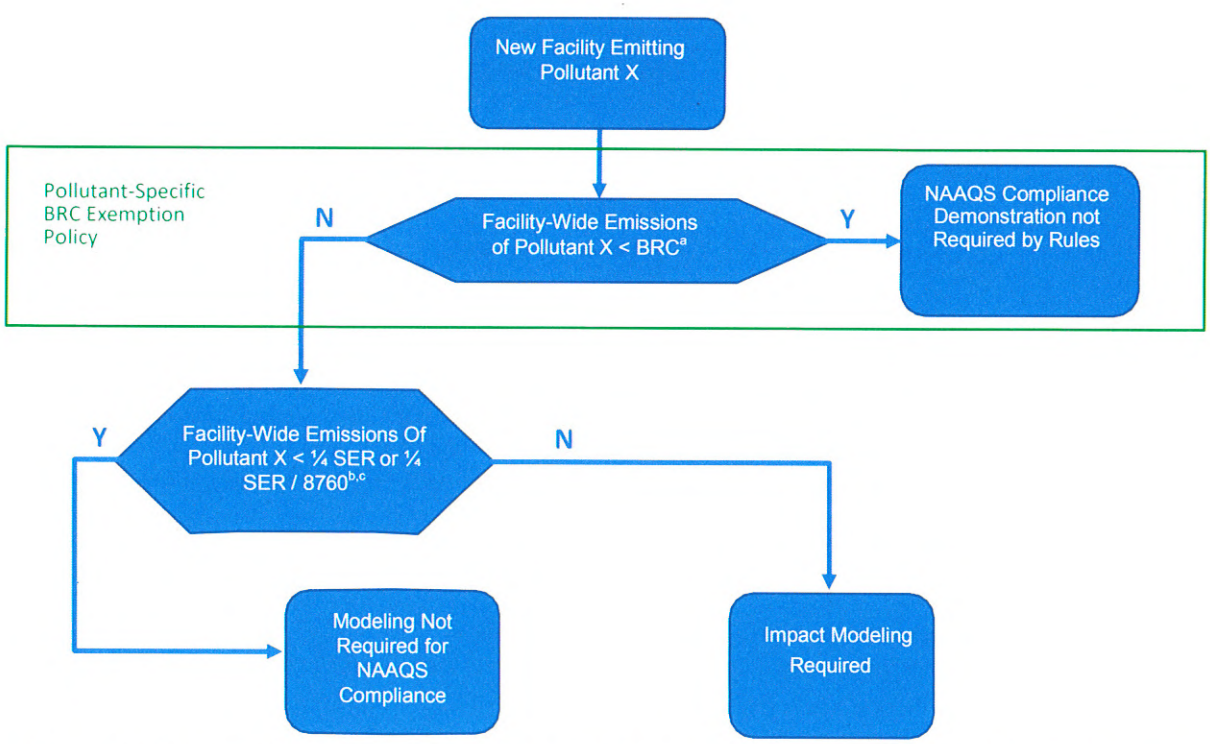

Figure 1. Pollutant-Specific Modeling Applicability Flow Chart for New Facilities in Attainment or Unclassifiable Areas

a) This evaluation is DEQ's regulatory interpretation of permit exemption rules, as described in: *Policy on NAAQS Compliance Demonstration Requirements*. Idaho Department of Environmental Quality Policy Memorandum. July 11, 2014. The evaluation is based only on annual emissions, and emissions qualifying as "fugitive" as defined by Idaho Air Rules for permit applicability are not included in the evaluation. Example: A company proposes to construct a widget maker facility. The project would qualify for a BRC permitting exemption under Idaho Air Rules Section 221.01, with emissions of Pollutant X below the BRC threshold, except that emissions of Pollutant Y exceed the BRC threshold and trigger the requirement to obtain a PTC. By DEQ regulatory interpretation, a NAAQS compliance demonstration for Pollutant X is not required by Idaho Air Rules for permit issuance.

b) Emissions calculated according to DEQ-specified methods. Fugitive emissions associated with the project are included in this evaluation. The threshold of 1/4 SER is applicable to NAAQS regulated on an annual average; and 1/4 SER/8760 is applicable to NAAQS on a short-term average, with the pound/hour threshold value compared to the maximum potential/allowable emission for the averaging period divided by the hours in the averaging period.

c) If DEQ observes project-specific conditions that suggest these thresholds are not appropriate or protective of NAAQS, then DEQ may require project-specific air impact modeling even though emissions are below listed thresholds.

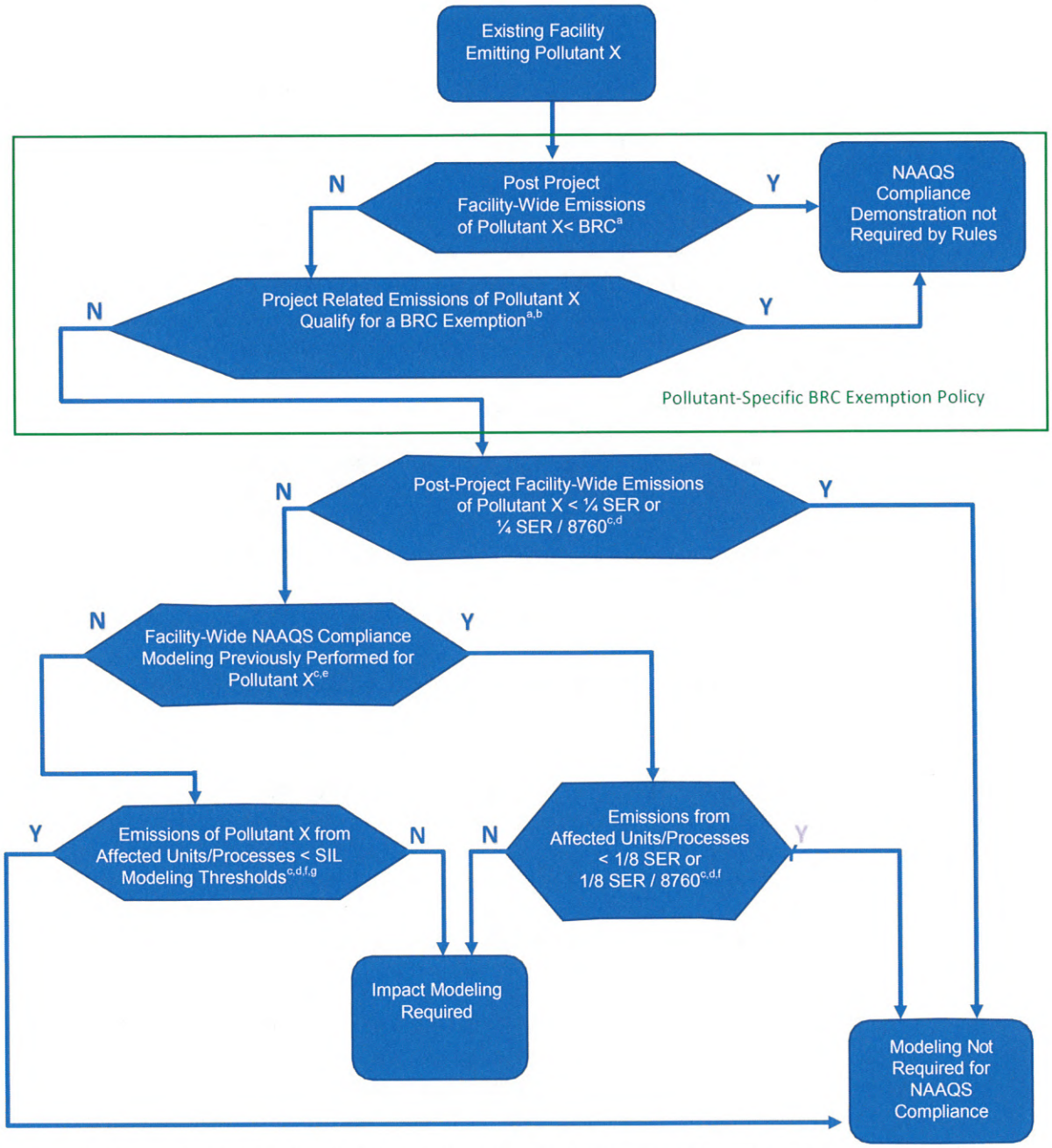

Figure 2 Pollutant-Specific Modeling Applicability Flow Chart for Modifications to Existing Facilities in Attainment or Unclassifiable Areas

a) This evaluation is DEQ's regulatory interpretation of permit exemption rules, as described in: Policy on NAAQS Compliance Demonstration Requirements. Idaho Department of Environmental Quality Policy Memorandum. July 11, 2014. The evaluation is based only on annual emissions, and emissions qualifying as "fugitive" as defined by Idaho Air Rules for permit applicability are not included in the evaluation.

b) Examples:

1. A company proposes to construct a widget maker at their existing facility. The project would qualify for a BRC permitting exemption under Idaho Air Rules Section 221.01, with emissions of Pollutant X below the BRC threshold, except emissions of Pollutant Y exceed the BRC threshold and trigger the

requirement to obtain a PTC. By DEQ regulatory interpretation, a NAAQS compliance demonstration for Pollutant X is not required by Idaho Air Rules for permit issuance.

2. A facility proposes to increase production at their existing, permitted widget maker. The existing permit limits widget production at 50 widgets per hour. The project proposes to increase production to 100 widgets per hour. The increase in emissions of Pollutant X is below the BRC threshold, but total emissions of Pollutant X from the unit are above the BRC threshold. A NAAQS compliance demonstration for Pollutant X is required because the project could not qualify for a permitting exemption, regardless of the emissions from other pollutants. The modification requires changing an existing permit condition, and therefore, could not qualify for a BRC exemption.

c) Fugitive emissions associated with the project are included in this evaluation.

d) If DEQ observes project-specific conditions that suggest these thresholds are not appropriate or protective of NAAQS, then DEQ may require project-specific air impact modeling even though emissions are below listed thresholds.

e) This applies if facility-wide modeling of the specific pollutant was performed for the averaging period of the NAAQS. Facility-wide modeling may be associated with a past permitting project or performed independently, and it may conservatively use allowable emissions or a more-refined reflection of actual emissions. Modeling must have been approved by DEQ, performed within the previous five years, be representative of the existing facility and operations, and include the pollutant of interest.

f) Emissions increase calculated according to DEQ-specified methods, including methods to handle projects involving relaxation of an emission-affecting permit limit.

g) SIL Modeling Threshold based on modeling of a generic hypothetical source.

3.3 Emission Increase Calculation for Project-Specific Modeling Applicability

Whether project-specific air impact modeling is required for a project depends on the increase in emissions resulting from implementation of the project. The emission increase for a new facility is simply the sum of potential or permit-allowable emissions from all emission sources associated with the project. The emission increase for a modification is defined in Idaho Air Rules as "the amount by which projected actual emissions exceed baseline actual emissions of an emissions unit." Section 3.3.2 provides more details on calculating the emission increase associated with modifications for modeling applicability.

The following types of emissions sources should be included in the modeling applicability calculation:

- All emissions sources that may be included in the permitting analyses or the issued permit, regardless of whether those sources may have (or will be issued) emissions or operating limits. Sources that are exempt from permitting as per Idaho Air Rules Section 220-223 must normally be included in the modeling applicability calculation. DEQ's modeling group should be consulted if there are questions regarding the inclusion or exclusion of emission sources in the modeling applicability determination.
- Process fugitive emissions from material handling, processing, etc. Fugitive emissions from vehicle traffic on facility roadways and wind erosion emissions from storage piles will not typically be considered for minor source permitting applicability unless DEQ determines such sources may have a substantial contribution to ambient concentrations. Mining facilities are typically in this category where such fugitive sources must be included.
- Intermittent sources such as batch processes, flaring, bin dumping, engine testing, etc. Emissions of NOx from intermittent testing of engines powering emergency generators and fire suppression water pumps can typically be excluded from the modeling applicability

determination for 1-hour NO2 NAAQS compliance demonstrations. Appendix A provides DEQ's final guidance on the modeling of NOx from intermittent testing and maintenance operations of engines powering emergency generators and fire suppression water pumps.

Sections 3.3.1 and 3.3.2 describe how emission quantities should be calculated for various scenarios to evaluate the need to conduct project-specific impact modeling. The modeling applicability emission inventory (used to determine whether modeling is needed) may be different than the modeling analysis emission inventory (used to conduct a significant impact analysis), as explained in Section 6.3.1.

3.3.1 Determining Whether Modeling is Needed for a New Source or Facility

Proposed allowable emissions, as specified in a permit application or calculated as potential to emit, of all new emissions sources will be used to evaluate the need for modeling a proposed new emissions source or new facility. No emission sources are typically exempt from the evaluation of whether modeling is needed. Also, any reductions in emissions at a different source cannot be considered at the modeling applicability stage.

3.3.2 Determining Whether Modeling is Needed for Modifications

Air impact modeling requirements for a modification hinge on the quantity of increased emissions that could occur as a result of the modification. For the purpose of project-specific applicability for performing an air impact analysis, any emission decreases are not typically considered. Creditable decreases may be considered in air impact modeling performed once the requirement to perform impact modeling has been established. If removal of an existing source or installation of control equipment on a source occurs concurrently with a modification, the emission reduction associated with such activities will not typically be considered in the evaluation of whether emissions exceed modeling applicability thresholds.

Emission increases for a modification must be carefully calculated to obtain an accurate or conservative assessment. From a regulatory standpoint, "Emissions Increase" is defined in Idaho Air Rules Section 007.04 as, "The amount by which projected actual emissions exceed baseline actual emissions of an emissions unit." Baseline actual emissions are a best-estimate of emissions that could realistically occur by operation of the source before modification. If the source is permitted, such emissions may be those allowed under the restrictions of the existing permit (using best available emission estimation methods and considering the permit limits that are the most restrictive to emission-causing operations). The following should be considered when calculating baseline actual emissions to evaluate the need for project-specific modeling:

- For a given process, the same emission calculation method and emission-affecting assumptions should be used for baseline actuals as is used for calculating future permit allowables, unless there are changes in the process that necessitate using different methods and assumptions. A change in emission factors or methods used to estimate emissions from a given process cannot be used to reduce the change in emissions associated with a proposed modification.
- Emissions considered as a conservative estimate for post-project allowable emissions (over-estimation of emissions), will result in an overestimate of baseline actual emissions for future projects. This may then result in an underestimation of the future project emission increase. DEQ approval of a conservatively high emission estimate of a source for initial permitting may not be appropriate for calculating baseline emissions for a future modification. However, the same emission factor or estimation method should be used for a given process, as noted in the previous bullet. For example, if a project involves increasing allowable throughput and the

emission generating mechanism does not change, the same emission factor should be used for both baseline actual emissions and post-project allowable emissions. Also, the applicant should use a factor they are confident does not underestimate post-project allowable emissions, even if it is suspected use of the factor overstates baseline actual emissions.

- Permit applicants should not simply use emission factors and other emission-affecting parameters from previous air impact analyses as a representation of baseline actual conditions. Many previous analyses were only required to demonstrate that the project will not cause a violation, and this was often accomplished by using simplistic estimates that substantially overestimate emissions. More accurate and updated emission rate data and release parameter information are frequently available for a source after initial permit issuance. This results from performance tests or from changes in emission factors. Baseline actual emissions should generally be calculated using the most accurate methods available. Overestimating baseline emissions will result in underestimation of the change in emissions resulting from a modification.
- Full operational levels (as allowed by the existing permit) can be considered in the calculation of baseline actual emissions, provided the facility/equipment could have accommodated such a level of operation. For example, a certain unit has a throughput limit of 1,000 units per day, and operational records indicate that only a maximum of 900 units per day has been processed. Baseline emissions can be calculated by assuming 1,000 units per day if it can be demonstrated that the facility could effectively attain those levels without a facility modification.
- Many permits contain both specific emission limits and limits on production. Baseline emissions must be based on the most restrictive limitation in the permit. As an example, consider a case where source testing has demonstrated that emissions per unit of production are lower than anticipated during initial permitting. As part of a proposed modification, the facility would like to raise the allowable production rate but not change the permitted emission rate. In this case, there will be an increase in allowable emissions because there is an increase in throughput. However, the applicant may calculate the increase in emissions using an updated emission factor that is based on recent source testing.

Future projected actual emissions will simply be permit-allowable emissions. Conservative emission estimates that overstate these emissions are acceptable and encouraged to facilitate expeditious DEQ approval of the modeling-applicability calculation.

Relaxation of Existing Permit Restrictions

Some modification projects involve the relaxation of an existing emission-affecting permit restriction, such as throughput limit, limit on hours of operation, material restriction on the type of material processed, or a direct emissions limit. In these cases, especially where the existing limit was needed to assure compliance with a NAAQS or a TAP increment, DEQ may require that the entirety of emissions from the unit be considered for modeling applicability rather than the increase alone. This approach is used because of the following:

- An increase in emissions at an existing emission point is more likely to cause or contribute to a NAAQS or TAP increment violation than if those emissions occurred at a new point. This is because emissions at two separate points must have overlapping plumes for their impacts to be additive.
- If a limit was needed on an emission point to assure NAAQS or TAP increment compliance, then increasing emissions at such a point would likely cause a violation.

This approach is intended to address potential "sham" permitting. A sham permit occurs when a facility originally intends to operate at a certain level, and equipment permitted is fully capable of operating at such levels, but NAAQS or TAP increment compliance cannot be demonstrated. As a result, the facility is issued a permit limit on the source(s) to assure compliance. Sometime after permit issuance, the facility then submits a permit application to relax the limit, addressing only the increase from the previous limit for impact analyses. This approach effectively circumvents the requirement to comply with NAAQS and/or TAP increments. To address this concern, the emission increase is calculated using a baseline associated with the facility prior to issuance of the permit establishing the limit that the facility now proposes to relax.

Generally, DEQ will use a 5-year period during which a project that involves relaxation of a limit (without a physical change at the facility) will be considered an adjustment/correction of previous permitting project rather than a new project. The emission increase will be calculated using the base emissions allowable prior to the previous permitting project (the project that established the limit to be relaxed) and the new proposed limit.

Replacement Projects

The need for modeling replacement projects that do not qualify as routine replacement is based on total allowable emissions from the proposed new source. The decrease in emissions associated with the removal of the old equipment is not generally considered for modeling applicability.

For example, if a sawmill proposes replacing an existing kiln with a new kiln (not routine replacement), modeling applicability would be based on the proposed allowable emissions of the new kiln without any consideration of the decrease in emissions associated with removal of the older kiln. The creditable emissions decrease associated with the kiln removed can be used in the air impact modeling to offset the emissions from the new kiln, modeled as negative values to evaluate the net impact of the project.

Modification of a Permitted Source

This scenario involves alteration of an existing and permitted emissions source. The need for modeling is normally based on the emission increase as determined by the difference between baseline actual emissions and future projected emissions (permit allowables). However, if the modification alters the release characteristics of the source (temperature, stack gas flow rate, stack height, etc.), then the entire allowable emissions from the modified source must be included for the purpose of modeling applicability. If the emission release characteristics do not change, then the applicable emissions will be considered as the increase resulting from the modification. An example of this is increased emissions-generating activities (that do not affect the temperature or volume of air exhausted) in a room where air is exhausted to the atmosphere through an existing stack. The emissions increase would be calculated as the difference between the current emissions rate and the new proposed allowable emissions rate. Determining the need for project-specific air impact modeling based on only the increase in emissions is approved by DEQ on a case-by-case basis, considering whether the point of release and release characteristics are very similar between the existing and modified emissions points.

A permit is not specifically required for instances where physical changes made at a facility affect dispersion but do not meet the definition of a "modification." Although such changes do not typically require a permit, they do effectively invalidate any dispersion modeling analyses performed prior to those changes and could alter the NAAQS compliance status of the facility. In some cases, DEQ may request facilities to perform air quality dispersion modeling analyses to affirm compliance with applicable standards.

4 Applicable Standards

This section discusses the applicable standards for assessing impacts on ambient air.

4.1 Criteria Pollutants

Table 3 lists the significant impact levels (SILs) used to determine whether or not the proposed project would have a significant impact on the air quality in the area. The proposed project has a significant impact on the ambient air quality if the resulting ambient concentrations exceed these levels due to an emissions increase.

Table 4 presents the NAAQS which are incorporated by reference (IBR) into Idaho Air Rules Section 107.03.b. Typically, there is about a year of lag time between when a new NAAQS is promulgated by EPA and the time when it is IBR into Idaho Air Rules. A NAAQS compliance demonstration involving modeling analyses for a specific standard is only required for permits issued after the date the standard is IBR into Idaho Air Rules. In cases where a NAAQS has been promulgated by EPA but not yet IBR to Idaho Air Rules, DEQ should be consulted for a determination on what specific analyses may be required for permit issuance.

Table 3. Significant Impact Levels (IDAPA 58.01.01.006)

Pollutant	Averaging Time	Significant Impact Levels ($\mu g/m^3$)[a]
CO	1-hour	2000
CO	8-hour	500
NO2	1-hour	4 ppb[b,c] (7.5 $\mu g/m^3$)[d]
NO2	Annual	1.0
SO2	1-hour	3 ppb[e] (7.9 $\mu g/m^3$)[d]
SO2	3-hour	25
SO2	24-hour	5
SO2	Annual	1.0
PM_{10}	24-hour	5.0
PM_{10}	Annual	1.0
$PM_{2.5}$	24-hour	1.2
$PM_{2.5}$	Annual	0.3[f]

a) Micrograms per cubic meter

b) ppb - parts per billion

c) Interim SIL (EPA 2010a)

d) µg/m3 value calculated for standard conditions

e) Interim SIL (EPA 2010b)

f) This value is the upper limit as listed in 40 CFR 51.165(b)(2). Without monitoring data supporting this value, DEQ will use the 0.2 $\mu g/m^3$ value recommended by EPA (EPA 2018)

Table 4. National Ambient Air Quality Standards

Pollutant	Averaging Time	Standard (µg/m^3)[a]
CO	1-hour	40,000[b]
CO	8-hour	10,000[b]
NO2	1-hour	100 ppb[c] (188 µg/m3)
NO2	Annual	100[d]
SO2	1-hour	75 ppb[e] (196 µg/m3)
SO2	3-hour	1,300[b]
SO2	24-hour	365[b]
SO2	Annual	80[c]
PM_{10}	24-hour	150[f]
PM_{10}	Annual	50[g]
$PM_{2.5}$	24-hour	35[h]
$PM_{2.5}$	Annual	12[i]
Pb	Quarterly	1.5[j]
Pb	3-month	0.15[k]

a) Micrograms per cubic meter.
b) Not to be exceeded more than once per year.
c) Three-year average of the 98th percentile of the annual distribution of 1-hour average daily maximum concentrations not to exceed standard.
d) Not to be exceeded in any calendar year.
e) Three-year average of the 99th percentile of the annual distribution of 1-hour average daily maximum concentrations not to exceed standard.
f) Never expected to be exceeded more than once in any calendar year.
g) Standard has been revoked.
h) Three-year average of the 98th percentile of the annual distribution of 24-hour average concentrations not to exceed standard,
i) Three-year average of the annual mean concentrations not to exceed standard.
j) Not to be exceeded in any quarter of any calendar year.
k) Not to be exceeded in any 3-month rolling average of any calendar year.

4.2 TAPs Increments

Applicable TAPs increments are listed in Idaho Air Rules Section 585 for non-carcinogens (AACs) and 586 for carcinogens (AACCs). The tables found in these sections of Idaho Air Rules list the ELs in pounds per hour (lb/hr) as well as the AACs for non-carcinogens and AACCs for carcinogens. Note that the concentrations for the non-carcinogens are in units of milligrams per cubic meter (mg/m3) and the concentrations for carcinogens are in units of micrograms per cubic meter (µg/m3).

4.3 Toxics

Idaho Air Rules Section 161 states, "Any contaminant which is by its nature toxic to human or animal life or vegetation shall not be emitted in such quantities or concentrations as to alone, or in combination with other contaminants, injure or unreasonably affect human or animal life or vegetation." DEQ may

require toxics analyses as a case-by-case basis in instances where DEQ suspects impacts of toxics may have an unacceptable impact.

5 Modeling Methodology

The required level of analysis will generally depend on the complexity of the proposed construction or modification, surrounding emissions sources and terrain features, current air quality levels, and classification (attainment vs non-attainment) in the impact area. Screening techniques may be adequate for simplistic or isolated sources. Screening techniques are not appropriate in complex situations such as a large number of buildings in the immediate area that create downwash for a point source or the presence of complex terrain within the modeling domain. More refined modeling will be necessary when screening modeling is inappropriate or cannot demonstrate compliance with applicable air quality impact limits.

5.1 Requirements for Permit Applications

As recommended by EPA (EPA 1990), dispersion modeling analysis generally involves two distinct phases. The first phase is the preliminary analysis, also known as the significant impact analysis; the second phase is the full impact analysis, also known as the cumulative NAAQS analysis. These analyses may be performed with either a simple "screening model" or with a more complex "refined model." A flowchart showing the general modeling methodology for permit modeling is presented in Figure 3.

5.1.1 Significant Impact Analysis

In the significant impact level (SIL) analysis, the highest estimated concentration in ambient air is compared to the SILs in Table 3. A five-year mean of the highest estimated concentration from each year can be used in the SIL analysis for pollutants with probabilistic standards. These pollutants include 24-hour PM2.5, annual PM2.5, 1-hour NO2, and 1-hour SO2. Only the changes in emissions associated with the proposed project are modeled in the significant impact analysis for new sources or modifications. Impacts from nearby and other background sources, including background concentrations, are not considered in the significant impact analysis. Section 6.3 provides guidance on sources and emissions to include in the significant impact analysis. No further analysis is generally required for the NAAQS or PSD increments if the estimated concentration is below applicable SILs. The source or modification is determined to have a significant impact on ambient air if the estimated impact exceeds the SILs. In this case, a cumulative NAAQS analysis will be necessary to demonstrate to the satisfaction of DEQ that the stationary source or modification would not cause or significantly contribute to a violation of any ambient air quality standard. Also, if DEQ has information that indicates existing facility emissions may not meet NAAQS, then DEQ may require the facility to demonstrate full NAAQS compliance at the time of the current permitting action or a later date.

The ambient concentration due to any proposed construction or modification cannot exceed the SILs listed in Table 3 for minor stationary sources in non-attainment areas (NAAs). Offsets are required even if the ambient impacts are below the SILs for major stationary sources or major modifications at major stationary sources in NAAs. The DEQ air modeling coordinator should be contacted for locations of NAAs in Idaho.

5.1.2 Cumulative NAAQS Analysis

In a cumulative NAAQS analysis, the scope of the analysis is expanded from the significant impact analysis to include impacts from all other sources at the facility and background concentrations. Assessing impacts from potential co-contributing sources may also be required in the cumulative NAAQS analyses. It is the applicant's responsibility to identify potential co- contributing sources. The factors to be reviewed include the type of source, distance between the facilities, location of potential impact, pollutants emitted, and emission rates of pollutants of interest. If impacts of neighboring sources, on receptors showing a significant impact from the sources subject to the permitting action, are not adequately accounted for by the background concentration used, then emissions from those sources must be modeled.

When conducting cumulative NAAQS modeling, the sources not explicitly included in the model (e.g., mobile sources; small, stationary sources; some fugitive sources; and large, distant sources) are accounted for by adding a background concentration representative of the air quality in the area. Background concentrations are based on ambient air monitoring data collected in the area or from similar areas determined to be reasonably representative. Section 6.10 provides a more detailed discussion of appropriate background concentrations. Background concentrations must account for all impacts not accounted for by sources specifically modeled. Current default background concentrations must be obtained from a DEQ air quality modeler.

Modeling assessments for major new source/modifications subject to the PSD program, and where project emissions cause an impact exceeding SILs, must include emissions from all point sources within the radius of significant impact and all sources outside the radius of significant impact that cause a significant impact within the radius of significant impact.

5.2 Additional Requirements for PSD Applications

Major facilities subject to PSD rules have many more responsibilities in the permitting process. DEQ engineers and analysts make the final determination of PSD applicability. If the proposed project is subject to PSD, the applicant should consult with DEQ during the early phases of the project development. If the proposed project is subject to PSD, the applicant should consult with DEQ during the early phases of the project development. This guideline only provides a brief summary of the PSD permitting program.

A PSD review is required if a proposed new facility is defined as a designated facility (Table 5) and emits or has projected actual emissions, after controls, of 100 tons per year (T/yr) or more of any regulated air pollutant. If the new facility is not one of the types listed in Table 5, then a PSD review is required if the facility emits or has projected actual emissions, after controls, of 250 T/yr or more of any regulated air pollutant. For PSD review, the potential to emit is defined as the maximum capacity of a stationary source to emit a pollutant under its physical and operational design (defined in Idaho Air Rules Section 006). A PSD review is also required if proposed emissions from a modification to an existing PSD major source are greater than the significant emissions rates listed in Table 6.

The location of the facility is important, as it determines the applicable increment of allowable air quality deterioration. Other factors, such as the topography and meteorology of the area and the proximity to a Class I area (specified areas of pristine air quality such as certain national parks, wilderness areas, etc.) or NAA, also determine the control requirements. The allowable increments, as of the publication of this document, for Class I, II, and III areas are listed in Table 7. Additional increment

limits can be promulgated by the EPA or DEQ, so it remains the applicant's responsibility to verify applicable PSD increment limits. The Class I areas in Idaho and surrounding states are shown in Appendix B. The remainder of the state is currently designated as Class II. There are no Class III areas in Idaho.

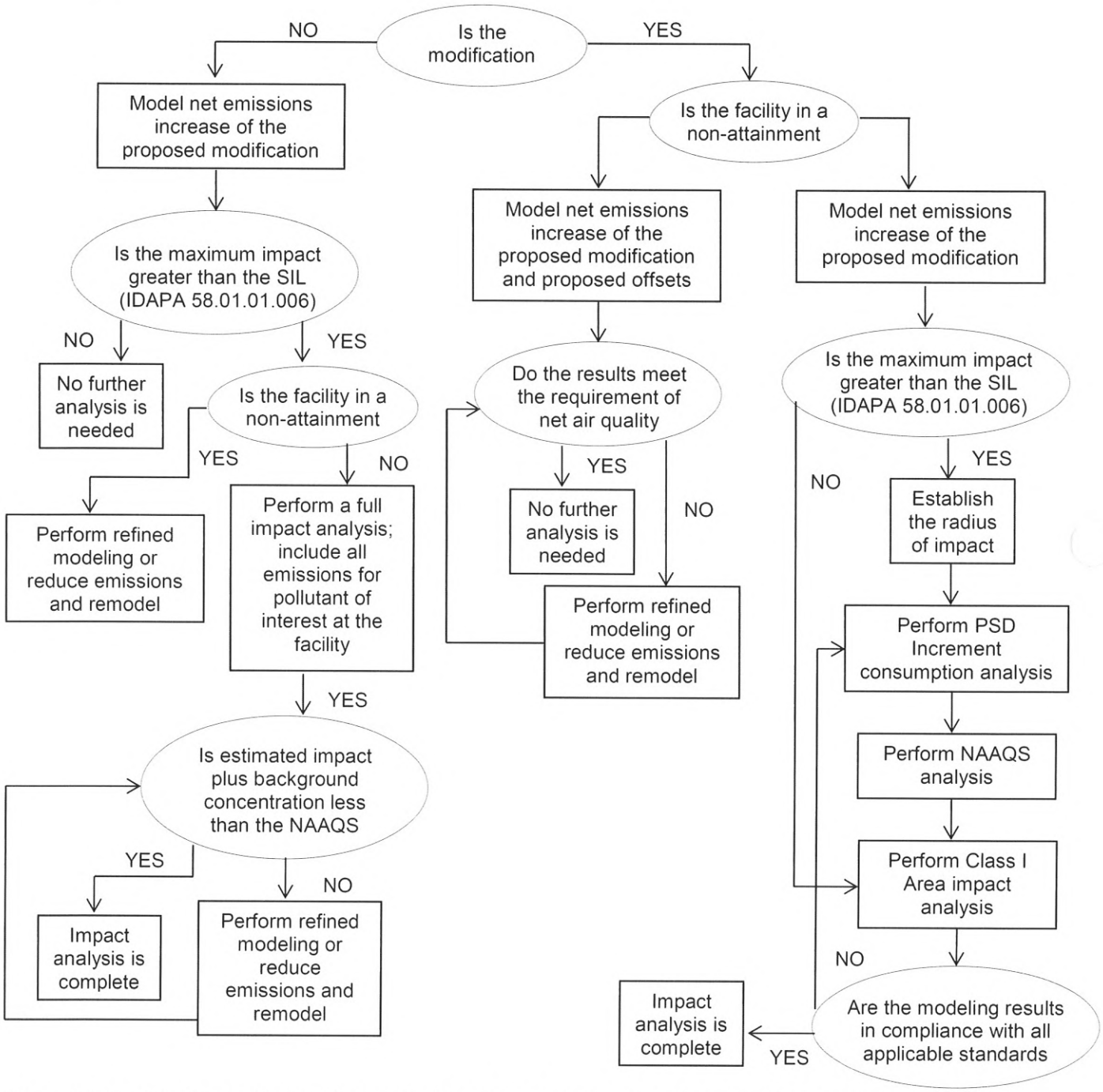

Figure 3. Flow Chart for Criteria Pollutant Ambient Impact Analysis for Permit to Construct Application

Pre-construction air quality is determined through ambient air monitoring. In some cases, there may already be enough data to establish the baseline. However, the applicant may be required to conduct up to one year of ambient monitoring at strategic locations if monitoring data are not available for the source area of the proposed construction site. Pre-construction monitoring will automatically be required if the model-predicted impact of the proposed source exceeds the levels in Table 8 and there are no current ambient air monitoring data available. DEQ may require pre-construction monitoring in other situations.

The following additional analyses are required in PSD applications:

- PSD increment consumption
- Class I area visibility and Air Quality Related Values (AQRVs) analysis
- Growth analysis
- Ambient air quality impact analysis (during construction)
- Soils and vegetation impacts
- Visibility impairment (in impact area, separate from the Class I area visibility analysis)

Refer to the *New Source Review Workshop Manual* (EPA 1990) for additional guidance.

Designated Facility Types as found in IDAPA.58.01.01.006:

1. Fossil fuel-fired, steam electric plants of more than 250 million British thermal units (Btu)per hour heat input
2. Coal cleaning plants (with thermal dryers)
3. Kraft pulp mills
4. Portland cement plants
5. Primary zinc smelters
6. Iron and steel mill plants
7. Primary aluminum ore reduction plants
8. Primary copper smelters
9. Municipal incinerators capable of charging more than 250 tons of refuse per day
10. Hydrofluoric acid plants
11. Sulfuric acid plants
12. Nitric acid plants
13. Petroleum refineries
14. Lime plants
15. Phosphate rock processing plants
16. Coke oven batteries
17. Sulfur recovery plants
18. Carbon black plants (furnace process)
19. Primary lead smelters
20. Fuel conversion plants
21. Sintering plants
22. Secondary metal production plants
23. Chemical process plants
24. Fossil fuel boilers (or combination thereof) totaling more than 250 million Btu/hour heat input
25. Petroleum storage and transfer units with a total storage capacity exceeding 300,000 barrels
26. Taconite ore processing plants
27. Glass fiber processing plants
28. Charcoal production plants

Table 5. Significant Emissions Rates (40 CFR 52.21 (b)(23); IDAPA 58.01.01.006)[a]

Pollutant	Emission Rate (T/yr)
CO	100
NOX	40
SO2	40
PM_{10}	15
$PM_{2.5}$	10 (40)[b]
Particulate matter	25
Ozone (VOC)	40 (of VOCs)
Pb	0.6
Asbestos	0.007
Beryllium	0.0004
Mercury	0.1
Vinyl chloride	1
Fluorides	3
Sulfuric Acid Mist	7
Hydrogen Sulfide (H_2S)	10
Total Reduced Sulfur (including H_2S)	10
Radionuclides from facilities regulated under40 CFR Par 61, Subpart H	0.1 mrem/yr
Reduced sulfur compounds (Including H_2S)	10
Any other pollutant regulated under the Clean Air Act including radionuclides	Any emission rate
Each regulated pollutant (from a major facility or major modification)	Emission rate that causes air quality impact of 1 µg/m3 or greater (24-hour basis) in any Class I area located within 10

a) A PSD review is required if the operation is modified and actual emissions of a pollutant will be greater than shown above

b) SO_2, NOx, and VOCs as precursors

Table 6. Prevention of Significant Deterioration Increment Limits

Pollutant	Averaging Period	Class I (µg/m^3)	Class II(µg/m^3)	Class III (µg/m^3)
NO_2	Annual[c]	2.5	25	50
SO_2	Annual[b]	2	20	40
SO_2	24-hour[c]	5	91	182
SO_2	3-hour[c]	25	512	700
PM_{10}	Annual[b]	4	17	34
PM_{10}	24-hour[c]	8	30	60
$PM_{2.5}$	Annual[b]	1	4	8
$PM_{2.5}$	24-hour[c]	2	9	18

a) The Class I, II, and III areas are defined and shown in Appendix A.

b) Never to be exceeded.
c) Not to be exceeded more than once a year.

Table 7. Modeled Impacts Above which Preconstruction Monitoring cannot be Exempted for PSD-Applicable Projects

Pollutant	Ambient Concentration ($\mu g/m^3$)	Averaging Period
CO	575	8-hour
NO2	14	Annual
SO2	13	24-hour
PM10	10	24-hour
PM2.5	4	24-hour
Ozone	100 T/yr increase of VOCs	N/A
Pb	0.1	Quarterly
Mercury	0.25	24-hour
Beryllium	0.0001	24-hour
Fluorides	0.25	24-hour
Vinyl chloride	15	24-hour
Hydrogen sulfide	0.2	1-hour

5.3 Facility Emission Cap (FEC) Permit Modeling

Contact DEQ for guidance on modeling requirements for FEC permits. In general, the modeling submitted must support all possible future emissions rates sources, and facility configuration.

6 Performing a Modeling Analysis

An application will be considered incomplete if it lacks sufficient information and/or a valid modeling analysis, supported by adequate documentation and justification of methods and data. Appendix C includes a copy of the DEQ modeling checklist, which is designed to help the applicant prepare the information necessary for a complete modeling package.

The procedures in this document, as well as the EPA documents *Guideline on Air Quality Models* (EPA 2005), *New Source Review Workshop Manual* (EPA 1990), and other more issue- specific guidance should typically be followed when conducting the modeling analysis. These documents provide guidance on appropriate model applications. DEQ will work with the applicant to determine acceptable impact assessment procedures where EPA or state policies are not clear cut or involve case-by-case review.

6.1 Modeling Protocol

Applicants are highly advised to contact the DEQ stationary source air quality modeling supervisor at (208) 373-0502 and submit a modeling protocol, as suggested in the modeling checklist (Appendix C), to ensure appropriate models, meteorological data, background concentrations, and procedures are applied. Use of a modeling protocol is a key component of DEQ's permit streamlining program, which

focuses on establishing mutually agreed upon methods and data prior to permit application submittal. This approach substantially reduces DEQ review time and the potential for the application to be determined incomplete or the permit denied because of problems with the modeling analyses.

The content of the modeling protocol is dependent on the type of permit application. A modeling protocol for a new, major source or a major modification at a major facility will be more detailed than one for a new, minor source or a minor modification. A modeling protocol checklist is presented in Appendix D. A description of the general methodology, as well as justification for assumptions and data used, should be included in the modeling protocol.

A modeling protocol, in written form and agreed upon by DEQ, provides the applicant the assurance that their approach and methodology as described will be accepted. However, the approval of a modeling protocol is not meant to imply approval of a completed modeling analysis. The facility should submit as much detailed information as possible in the modeling protocol to increase the likelihood of having the modeling analysis approved. The applicant should prepare the application with the understanding that DEQ will require a higher degree of documentation/justification of data and methods in cases where modeled concentrations are very near regulatory thresholds/standards.

A modeling protocol may be submitted in hard-copy format or may be emailed to the DEQ stationary source modeling coordinator. DEQ will typically provide comments on or approval of the protocol within two weeks from the date the protocol was received.

The following are key issues that should be addressed in the protocol:

- Ambient air boundary. It is the applicant's responsibility to accurately evaluate the ambient air boundary and identify any unique situations affecting the ambient air boundary that may exist at the facility. Such unique situations may include rivers bisecting the facility, easements or public roadways bisecting the facility, railways, lease agreements, and operating a business where the general public is allowed on site. See Section 6.5.
- Justification/documentation of stack parameters. The protocol should thoroughly describe how emissions release parameters (flow rates and stack temperatures) were measured or estimated, if such data are available at that time. A simple indication that parameters were checked will not be accepted as documentation and justification. Calculations of initial dispersion coefficients for volume sources should be provided such that DEQ reviewers can easily and quickly verify the values. See Section 6.4.2.
- Design concentrations. The protocol should clearly state what modeled concentrations will be used to evaluate compliance. For example, the maximum of 6th highest modeled concentrations at each receptor is typically used as the PM10 24-hour design value when modeling a five-year data set. See Section 6.11.1.
- Meteorological data. If meteorological data are not provided by DEQ, the applicant should thoroughly justify selection of the data, demonstrating how the data used are representative for the application site. The protocol should also describe the quality of the data, clearly demonstrating the data are adequate for use in an air impact analysis. See Section 6.8.
- Receptor grid. The receptor grid spacing proposed for the analyses should be thoroughly described. See Section 6.6.
- Background concentrations. Within the protocol, the applicant may either propose appropriate background concentrations or request that DEQ provide reasonably conservative background concentrations. See Section 6.10.
- Unique circumstances or scenarios used in the analyses. Any atypical conditions associated with the site or the project that could affect the results of the air impact analyses, or DEQ's approval

of the project, should be described in the protocol. Protocol approval only assures acceptability that those conditions or issues accurately described in the protocol are acceptable.

6.2 Choosing the Appropriate Models

Air quality models approved by the EPA for regulatory use are required (Idaho Air Rules Section 202.02 and 402.03). The DEQ modeling coordinator should be consulted to discuss or verify the model most appropriate for the release being simulated. Factors to consider when determining the appropriate model include, but are not limited to, type of release (e.g., elevated point or area), downwash, location of ambient air, meteorological conditions (e.g., stagnation), and availability of meteorological data. All modeling must use the current versions of models recommended in the EPA's *Guideline on Air Quality Models* (EPA 2005). Many of these models can be found on the EPA's Support Center for Regulatory Air Models (SCRAM) website (http://www.epa.gov/ttn/scram). Modeling performed with older versions may be rejected. Any modification or alteration of a guideline model must be approved by DEQ and, in most instances, the EPA. Approval of the use of other models is completely at the discretion of DEQ. When alternative models are used, DEQ may require the submittal of additional data (e.g., sensitivity analysis) for verification. The use of proprietary models (those models that are not available free of charge to the public) is generally not allowed for the demonstration of compliance with NAAQS, PSD increment, or TAPs increments. Proprietary graphical user interfaces (GUIs) that use unaltered publicly available regulatory models are not considered proprietary models. Results generated by such GUIs will be accepted provided input and output files are submitted and such files can be readily used as input for the publicly available model without the proprietary GUI.

6.2.1 Readily Available Models

The following is a summary of the most commonly used air quality models:

AERMOD – AERMIC (American Meteorological Society/Environmental Protection Agency Regulatory Model Improvement Committee) was formed to introduce state-of-the-art modeling concepts into EPA's air quality models. AERMIC's focus is on a new platform for regulatory steady-state plume modeling. This platform includes: 1) air turbulence structure, scaling, and concepts; 2) treatment of both surface and elevated sources; and 3) simple and complex terrain. The modeling system has three components: AERMOD - the air dispersion model; AERMET - the meteorological data preprocessor; and AERMAP - the terrain data preprocessor. AERMOD is the replacement model for ISCST3.

AERSCREEN – AERSCREEN is the screening-level model for applications where AERMOD would be appropriate.

SCREEN3 – SCREEN3 is a screening version of the ISCST3 model.

SCREEN3 is not considered an acceptable screening model for AERMOD, which is the model replacing ISCST3. *Analyses performed with SCREEN3 will no longer be accepted by DEQ for permitting purposes in most instances.*

CTSCREEN – (Complex Terrain Screening model) –A screening technique when complex terrain is important. CTSCREEN is a screening version of the CTDMPLUS model. CTSCREEN and CTDMPLUS are the same basic model. The primary difference is that CTSCREEN uses

an extensive array of predetermined meteorological conditions where site-specific meteorological data are not available.

AERMOD is considered a more refined model for complex terrain. AERSCREEN incorporates the same terrain algorithms as AERMOD, and may yield more favorable results than CTSCREEN.

ISCST3 – (Industrial Source Complex Model) – Historically, the most commonly used refined Gaussian plume model.

ISCST3 has been replaced as an EPA guideline model by AERMOD. *DEQ will generally no longer accept air quality analyses conducted with ISCST3 for permitting purposes.*

CTDMPLUS – (Complex Terrain Dispersion Model Plus Algorithms for Unstable Situations) – A refined air quality model for use in all atmospheric stabilities with sources located in or near complex topography. Since the model accounts for the three-dimensional nature of plume and terrain interaction, it requires detailed terrain and meteorological data that are representative of the modeling domain.

CALPUFF – A multi-layer, multi-species, non-steady-state, puff dispersion model that simulates the effects of time- and space-varying meteorological conditions on pollutant transport, transformation, and removal. CALPUFF is most commonly used to assess impacts on Class I areas and is applied at distances over 50 kilometers. It includes algorithms for subgrid scale effects (such as terrain impingement), as well as longer range effects (such as pollutant removal due to wet scavenging and dry deposition, chemical transformation, and visibility effects of particulate matter concentrations).

CALPUFF is not an EPA-approved model for near-field impact assessment (within 50 kilometers of a source). Any use of CALPUFF in the near-field must be thoroughly justified and approved specifically by DEQ and often by EPA.

VISCREEN – A screening model to assess visibility impacts on Class I areas. Calculates the potential impact of a plume of specified emissions for specific transport and dispersion conditions.

Screening models, such as SCREEN3 and AERSCREEN, are used to simulate the probable worst-case condition under normal, maximum operating conditions. They are generally simplistic representations, typically taking less computer time and yielding conservative impact predictions. A screening analysis must follow EPA guidance in *Screening Procedures for Estimating the Air Quality Impact of Stationary Sources, Revised* (EPA 1992) or any current EPA guidance for AERSCREEN. If a properly conducted screening analysis does not indicate an exceedance of the ambient standards from a proposed construction or modification, then a more refined analysis is not necessary to adequately demonstrate compliance.

6.2.2 Replacement of ISC by AERMOD

AERMOD was promulgated as the replacement model for ISC. During the one-year transitional period, between November 2005 and November 2006, applicants could use either ISCST3 or AERMOD to demonstrate compliance. After that, ISCST3 was no longer a guideline model and analyses conducted with ISCST3 were not typically accepted by DEQ.

There are several modeling scenarios that are problematic when using AERMOD:

1. Hot, buoyant plumes released horizontally or with a rain cap. With ISCST3 the typical approach is to set the exit velocity to 0.01 or 0.001 meters per second (m/sec) to effectively eliminate the plume vertical momentum flux, then increase the exit diameter to a point where the modeled volumetric flow is equal to that of the source. This approach cannot be used for AERMOD if plume downwash is considered because downwash behavior is a function of stack diameter in the PRIME downwash algorithm within AERMOD.

   Modeling with the actual stack diameter and a 0.001 m/sec exit velocity is recommended as a conservative measure. This method effectively eliminates vertical momentum of the plume; however, it also eliminates thermal buoyancy effects. In some instances, hand calculations of plume rise, using those equations in the AERMOD algorithms, may show that thermal buoyancy is overwhelmingly the dominant plume rise mechanism. In such cases, the source may be modeled as an uninterrupted vertical release. Use of this method or other methods should be discussed with DEQ prior to use.

   Methods to accurately model hot horizontal releases and capped vertical releases within AERMOD have been developed for Beta versions of AERMOD. Applicants should contact DEQ as to the availability of AERMOD versions to handle hot horizontal and capped releases.

2. Representative meteorological data are rather limited for many areas within Idaho. More site-specific meteorological and land surface characteristics are needed to run AERMOD than what is used for ISC. Therefore, using meteorological data from a distant station is more of a concern when using AERMOD.

   It is the applicant's responsibility to demonstrate the meteorological data used are representative of meteorological conditions at the application site. Applicants may be required to use specialized methods to demonstrate compliance in cases where available meteorological data are of questionable representativeness. Such methods could involve running additional modeling analyses using multiple meteorological data sets or otherwise providing a demonstration that use of on-site data could not reasonably be expected to give results that exceed applicable regulatory thresholds or standards.

6.3 Pollutants and Sources to be Included in the Impact Analyses

This section discusses what pollutants and sources should be included in modeling analyses submitted in support of applications for permits to construct (PTCs), Tier II operating permits, and FEC permits. Specific emissions sources that are exempt from permitting requirements are not necessarily exempt from a modeling analysis when a PTC or Tier II Operating Permit is required for other sources/reasons. DEQ modeling staff should be consulted before any emissions sources eliminated from the modeling analyses.

DEQ does have a list of activities that may be treated as "trivial" and are not required to be addressed in the permit application. In addition to the trivial activities listed below, Idaho Air Rules Section 317 list activities that are "presumptively insignificant emission units." DEQ has determined that these activities must generally be included in Tier II and PTC applications when facility-wide modeling is required. The list below was generated from an EPA white paper entitled Streamlined Development of Part 70 Permit Applications (EPA 1995).

Activities That May be Treated as "Trivial" (EPA 1995):

1. Combustion emissions from propulsion of mobile sources, except for vessel emissions from outer continental shelf sources.
2. Air-conditioning units used for human comfort that do not have applicable requirements under Title VI of the Clean Air Act.
3. Ventilating units used for human comfort that do not exhaust air pollutants into the ambient air from any manufacturing/industrial or commercial process.
4. Noncommercial food preparation.
5. Consumer use of office equipment and products, not including printers or businesses primarily involved in photographic reproduction.
6. Janitorial services and consumer use of janitorial products.
7. Internal combustion engines used for landscaping purposes.
8. Laundry activities, except for dry cleaning and steam boilers.
9. Bathroom/toilet vent emissions.
10. Emergency (backup) electrical generators at residential locations.
11. Tobacco smoking rooms and areas.
12. Blacksmith forges.
13. Plant maintenance and upkeep activities (e.g., grounds keeping, general repairs, cleaning, painting, welding, plumbing, re-tarring roofs, installing insulation, and paving parking lots) provided these activities are not conducted as part of a manufacturing process, are not related to the source's primary business activity, and do not otherwise trigger a permit modification.[(a)]
14. Repair or maintenance shop activities not related to the source's primary business activity, not including emissions from surface-coating or degreasing (solvent metal cleaning) activities, and not otherwise triggering a permit modification.
15. Portable electrical generators that can be moved by hand from one location to another.[(b)]
16. Hand-held equipment for buffing, polishing, cutting, drilling, sawing, grinding, turning or machining wood, metal or plastic.
17. Brazing, soldering and welding equipment, and cutting torches related to manufacturing and construction activities that do not result in emission of hazardous air pollutant metals.[(c)]
18. Air compressors and pneumatically operated equipment, including hand tools.
19. Batteries and battery charging stations, except at battery manufacturing plants.
20. Storage tanks, vessels, and containers holding or storing liquid substances that will not emit any volatile organic compound or hazardous air pollutant.[(d)]
21. Storage tanks, reservoirs, and pumping and handling equipment of any size containing soaps, vegetable oil, grease, animal fat, and nonvolatile aqueous salt solutions, provided appropriate lids and covers are utilized.
22. Equipment used to mix package soaps, vegetable oil, grease, animal fat, and nonvolatile aqueous salt solutions, provided appropriate lids and covers are utilized.
23. Drop hammers or hydraulic presses for forging or metalworking.
24. Equipment used exclusively to slaughter animals, but not including other equipment at slaughterhouses, such as rendering cookers, boilers, heating plants, incinerators, and electrical power generating equipment.
25. Vents from continuous emissions monitors and other analyzers.
26. Natural gas pressure-regulator vents, excluding venting at oil and gas production facilities.
27. Hand-held applicator equipment for hot-melt adhesives with no volatile organic compounds in the adhesive formulation.

28. Equipment used for surface coating, painting, dipping, or spraying operations, except those that will emit any volatile organic compound or hazardous air pollutant.
29. Carbon dioxide lasers, used only on metals and other materials that do not emit hazardous air pollutants in the process.
30. Consumer use of paper trimmers/binders.
31. Electric- or steam-heated drying ovens and autoclaves, but not the emissions from the articles or substances being processed in the ovens or autoclaves, or the boilers delivering the steam.
32. Salt baths using nonvolatile salts that do not result in emissions of any regulated air pollutant.
33. Laser trimmers using dust collection to prevent fugitive emissions.
34. Bench-scale, laboratory equipment used for physical or chemical analysis, but not for lab fume hoods or vents.[e]
35. Routine calibration and maintenance of laboratory equipment or other analytical instruments.
36. Equipment used for quality control/assurance or inspection purposes, including sampling equipment used to withdraw materials for analysis.
37. Hydraulic and hydrostatic testing equipment.
38. Environmental chambers not using hazardous air pollutant gasses.
39. Shock chambers.
40. Humidity chambers.
41. Solar simulators.
42. Fugitive emissions related to movement of passenger vehicles, provided the emissions are not counted for applicability purposes and any required fugitive-dust-control plan or its equivalent is submitted.
43. Process-water filtration systems and demineralizers.
44. Demineralized-water tanks and demineralizer vents.
45. Boiler-water treatment operations, not including cooling towers.
46. Oxygen scavenging (de-aeration) of water.
47. Ozone generators.
48. Fire suppression systems.
49. Emergency road flares.
50. Steam vents and safety relief valves.
51. Steam leaks.
52. Steam cleaning operations.
53. Steam sterilizers.

a) Cleaning and painting activities qualify as trivial they are not subject to volatile organic compound or hazardous air pollutant control requirements. Asphalt batch plant owners/operators must still get a permit if otherwise required.

b) "Moved by hand" means the generator can be moved without the assistance of any motorized or non-motorized vehicle, conveyance, or device.

c) Brazing, soldering and welding equipment, and cutting torches that emit hazardous air pollutant metals and are related to manufacturing and construction activities are more appropriate for treatment as insignificant activities instead of trivial activities based on size or production-level thresholds. Brazing, soldering, welding, and cutting torches that emit hazardous air pollutant metals and are directly related to plant maintenance, upkeep, and repair, or maintenance shop activities, are appropriately treated as trivial.

d) Consideration of storage tanks containing petroleum liquids or other volatile organic liquids as a trivial source should be based on size limits such as storage tank capacity and vapor pressure of liquids stored are not appropriate for this list.

e) Many lab fume hoods or vents might qualify for treatment as insignificant (depending on the applicable State Implementation Plan) or can be grouped together for purposes of description.

6.3.1 Permits to Construct

Criteria Pollutants

All increases in emissions of criteria pollutants are generally required to be accounted for in the significant impact analyses for PTC applications. However, the emissions sources and inventory used to evaluate the need for modeling, described in Section 3 of this guideline, may differ from the sources and inventory used for the significant impact analyses. All emissions changes associated with a proposed project are generally used in the significant impact analyses, including emissions reductions associated with sources removed from operation. Also, sources included in the significant impact analyses for minor source permitting may differ from sources included for PSD permitting. For minor source permitting, the significant impact analyses for criteria pollutants generally includes: all emissions increases and decreases associated with the proposed project. For PSD permitting, the net emissions increase, as defined in Idaho Air Rules Section 007, is modeled. The net emissions increase includes all increases and decreases that occurred within the previous five years or since the issuance of any PSD permit to the facility, whichever is a shorter period.

Cumulative impact analyses are required if impacts associated with the significant impact analyses exceed SILs, as described in Sections 5.1.1 and 5.1.2. A cumulative impact analysis involves modeling facility-wide emissions, modeling any co-contributing sources, and adding an appropriate background value to results.

DEQ highly suggests that applicants specify in a modeling protocol those sources to be included and/or excluded in the significant impact analyses with thorough justification and documentation. The following provides general guidance for the significant impact analyses performed for specific minor source scenarios:

- Modification to an existing emissions unit where the release parameters (flow rate, stack gas temperature, etc.) do not change. The emissions increase associated with the modification is modeled. If the existing source is currently permitted, the emissions increase will be calculated as the differences between the current permit limit (or whatever emissions rate was used in previous modeling analyses) and the future proposed limit. If the source is not currently regulated by a permit emissions limit, then current emissions should be based on actual emissions as defined by Idaho Air Rules.
- Modification to an existing emissions unit where the release parameters change as a result of the modification. Existing emissions for permitted and non-permitted sources should be calculated as described for scenario "a;" however, current emissions should be modeled as negative emissions (using the existing release parameters) and future allowable emissions modeled as positive emissions (using the new release parameters).
- Removal of, or emissions reductions from, an existing emissions unit. Emissions reductions from such units should be modeled as negative emissions to account for the net project impacts. Existing permit-allowable emissions rates may be used, or actual emissions (based on two years of operations within the previous ten years) for units not regulated by an existing emissions limit.

- Replacement or relocation of an existing emissions unit. Replaced units should be treated in the same manner as removed units, described in scenario "c."
- Addition or removal of units exempt from permitting. Units that are exempt from permitting should be included in the significant impact analyses in most instances, unless such units are considered as trivial per Table 9 in Section 6.3 of this guideline. Existing and future emissions should be based on maximum potential emissions unless otherwise directed or approved by DEQ.

TAPs

All TAPs, except those exempted under Idaho Air Rules Section 210.20, with project-total emissions increases above the DEQ TAP ELs (discussed in Section 4.0) must be included in the modeling analysis. The DEQ TAPs checklist, available on the DEQ website, should be used to demonstrate compliance with TAPs.

Fugitive Sources

Fugitive emissions are defined in Idaho Air Rules Section 006 as, "those emissions which could not reasonably pass through a stack, chimney, vent, or other functionally equivalent opening." This definition includes windblown dust from a stockpile. Generally, modeling is required for all fugitive emissions sources determined not to be unquantifiable. Fugitive emissions from vehicle traffic on roads and wind erosion from material storage piles are normally not included in the modeling analyses for minor source applications. However, DEQ may require modeling of these sources in instances where these emissions could substantially contribute to ambient concentrations and a potential exceedance of air quality standards. Process fugitive emissions such as those from material handling operations and equipment leaks should be included in the modeling analyses.

Intermittent Sources

Emissions sources that operate intermittently may be excluded from the SIL analysis and/or cumulative NAAQS analysis, approved by DEQ on a case-by-case basis, to the extent that it can be reasonably concluded that such sources could not measurably affect the compliance determination. If the intermittent sources are engines powering emergency generators or fire suppression water pumps, and operations are less than 100 hours/year for operational testing and maintenance, the sources can be excluded from compliance demonstrations for the 1-hour NO2 NAAQS, unless specifically required at the discretion of the DEQ Director. This guidance is explained in more detail in Appendix A.

Inconsequential Sources

The applicant may determine that some sources are "inconsequential" when estimating the design concentration (i.e., only contribute to a small percentage of the total, maximum, ambient impact for that project) and exclude them from the modeling analysis. If this is the case, the applicant must justify the exclusion of these sources. This justification, which is pollutant and averaging-period specific, must be based on emissions rates and a qualitative discussion of impacts. For example, if an emissions unit operates 24 hours per day but only 500 hours per year, the source may be "inconsequential" for the annual emissions, but not for the 24-hour emissions. The justification should include the following two phases:

1. Compare the emissions and operating conditions of each emissions source to the total emissions that would be modeled. If the uncontrolled emissions are "negligible" compared to the total emissions and are not expected to impact the maximum ambient concentration, the individual

emissions source may be deemed as "inconsequential" and may be excluded from the modeling analysis.

Unless there are a large number of negligible sources that will substantially slow the model run time, it may be easier to include such sources in the analyses rather than provide justification for their exclusion.

2. If more than one emissions source is excluded from the modeling analysis, the total emissions of those sources excluded and the total estimated ambient concentration must be compared to the total modeled emissions and qualitatively evaluated for impacts. This will ensure that all of the excluded sources are still "inconsequential" as a whole.

Non-Attainment Areas

Facilities located in an a non-attainment area for a specified pollutant may be required to model all the emissions for that specified pollutant, even those emissions that are deemed to be inconsequential. This process will be treated on a case-by-case basis. It is recommended that the applicant meet with DEQ staff prior to beginning the modeling analysis to discuss what sources will be included.

6.3.2 Facility-Wide Tier II Operating Permits

All emissions for the entire facility, excluding those listed in Table 9, are required to be included in a facility-wide Tier II application. All criteria pollutant emissions are generally required to be included in the modeling analysis submitted with the Tier II operating permit application. Facility-wide TAPs emissions are not typically required to be included in the modeling analysis for the Tier II application. DEQ reserves the right to request additional information or analysis, including the modeling of other pollutants, under Idaho Air Rules Section 402.04, if there is a concern relative to compliance with Idaho Air Rules Section 161. Modeling of all fugitive emissions may be required if DEQ determines it necessary to protect ambient air quality standards.

As with the PTC application, the applicant may determine that some criteria pollutant sources are "inconsequential" when estimating the design concentration (i.e., only contribute to a small percentage of the total, maximum, ambient impact for that project) and exclude them from the modeling analysis. The applicant should use the process presented above in Section 6.3.1. Facilities located in non-attainment areas for a specified pollutant must contact the DEQ modeling coordinator at (208) 373-0112 prior to submitting the Tier II application. DEQ modeling staff will review the current SIP for the area to determine the appropriate level of analysis. This process will be treated on a case-by-case basis. It is recommended that the applicant meet with DEQ staff prior to beginning the modeling analysis to discuss what sources will be included.

6.3.3 FEC Permits

Permit applications utilizing a facility emissions cap (FEC) must provide sufficient modeling scenarios to reasonably assess maximum impacts of potential source configurations. The modeling requirements for these permits are facility-specific and will vary greatly depending on the operational flexibility desired by the permit applicant.

6.4 Source Information Required

This section discusses the source information that is required for a modeling analysis.

6.4.1 Emission Rates

Tables 8.1 and 8.2 in the *Guideline on Air Quality Models* (EPA 2005) present the emissions information required for air dispersion modeling. The emissions rate used in the modeling analysis must be that associated with maximum design capacity or a federally enforceable permit condition (40 CFR 51, Appendix W, Table 9-2). For a major modification, the emissions rate to be modeled in the significant impact analysis for criteria pollutants is the net emission rate increase, as defined in Idaho Air Rules Section 007. To demonstrate compliance with applicable standards, potential emissions must be used in the modeling analyses rather than future projected actual emissions. For minor modifications, the emissions modeled are the emissions changes associated with the proposed project, as described in Section 6.3.1 of this guideline. Emissions decreases are modeled as negative values in the significant impact analyses. However, in instances where NAAQS compliance may be questionable, DEQ may require facility-wide modeling even though results of the significant impact analysis indicate impacts are below SILs. When a cumulative NAAQS analysis is required, the potential emissions for all sources and, if requested, any co-contributing sources are used in the modeling analyses.

For PTCs, the project-wide emissions rate increase of TAPs is compared to the EL in Idaho Air Rules Section 585 and 586. Any TAP that has a total project emissions increase that exceeds the EL must be modeled.

The maximum emissions rate for each averaging period must be identified. For example, PM2.5 has both a 24-hour and an annual standard. If a source will only operate 7,000 hours per year but can operate for 24 hours in a single 24-hour period, then different emissions rates would be modeled for the 24-hour standard and annual standard.

If any pounds per hour emissions rate used in a modeling analysis differs from that used in the emissions inventory, the application should clearly show how the modeled rate was calculated. For example, a source has a maximum hourly emissions rate of 2.0 pounds per hour and a maximum daily operations rate of 12 hours per day (not restricted to any specific daily schedule). The modeled emissions rate for demonstrating compliance with a 24-hour standard would be 1.0 pounds per hour ((2.0 lb/hr x 12 hr/day) / 24 hr = 1.0 lb/hr).

Modeling intermittent sources in a representative and worst-case manner can present a challenge to the modeler. These sources can be modeled in two ways:

1. The allowable emissions can be modeled for a time period equal to that of the actual source. The emissions event is then selected to reasonably represent worst-case impacts or a series of potential operational scenarios are modeled.
2. The allowable emissions for the event are evenly divided over the pollutant averaging period of interest.

As an example, a mill may have fugitive PM2.5 emissions from periodic loadout of a waste bin. The emissions may occur for one hour, three times per week. Modeling must demonstrate compliance with both the 24-hour and annual standards. It is determined that only one loadout can occur during any 24-hour period. Since there is no specific time when the loadout is likely to occur, 24-hour modeling was conducted by evenly dividing the emissions from one loadout throughout the entire 24-hour period. Annual impacts were modeled by calculating annual allowable emissions, and evenly dividing those emissions among each hour of the year.

If it is known that emissions are most likely to occur during a certain time of the day, it may be appropriate to distribute emissions only over those hours of the day. The applicant should consult with DEQ modeling staff to obtain approval of such methods prior to modeling intermittent sources.

DEQ may allow exclusion of some very infrequent periodic emissions from the modeling analyses. Monthly testing of an emergency generator for 35 minutes could be an example of an infrequent periodic emissions source. Approval of excluding such sources from the modeling analyses will be made by DEQ on a case-by-case basis considering:

- The pollutant of interest and the averaging period of the standard
- Quantity of emissions from the source
- Frequency of the emissions
- Averaging period of standards associated with pollutants emitted
- Number of sources to be excluded
- Distance from source to ambient air receptors
- Nearby sensitive receptors (hospitals, schools, residences)
- Modeled impact of other sources in relation to applicable standards

As indicated in Section 6.3.1. Intermittent Sources, DEQ allows the exclusion of NOx emissions from intermittent testing and maintenance of engines powering emergency generators and fire suppression water pumps for demonstrating compliance with the 1-hour NO2 NAAQS.

6.4.2 Source Parameters

Stack parameters for each point source that are required to be modeled are as follows:

- Stack base elevation (feet or meters)
- Stack height (feet or meters)
- Stack inside diameter (feet or meters) (If the stack is not circular, use equivalent dimensions determined by Area = d2/4, where d is the stack's inner diameter)
- Stack exit velocity (meters/second) or exit flow rate (actual cubic feet per minute (acfm))
- Stack exit temperature (F or K)

Source parameters for area sources include the following:

- Source height (meters)
- Easterly dimension (meters)
- Northerly dimension (meters)
- Initial vertical dimension (meters)
- Angle from North (degrees)

Source parameters for volume sources include the following:

- Source height (meters)
- Initial horizontal dimension (meters)
- Initial vertical dimension (meters)

The application must provide detailed documentation and justification of all source parameters used in the analyses, including calculations where appropriate. Applications not providing sufficient documentation/justification of source parameters will be declared incomplete or denied. Stating that parameters were provided by the manufacturer or design engineer is not considered as adequate documentation/justification.

Flow Rates and Stack Gas Temperatures

Maximum flow rates and maximum stack gas temperatures should not typically be used in the modeling analyses unless the source predominantly operates at such a rate. Although maximum emissions are typically associated with maximum flow rates and stack gas temperatures, maximum impacts are often associated with lower emissions rates and lower stack gas flow rates and temperatures. Applicants should either use multiple scenarios of emissions, flow rates, and temperatures, or conservatively use maximum emissions with more typical stack gas flow rates and temperatures.

Submitted modeling analyses should provide detailed documentation and justification of all release parameters used in the analyses. Stack gas temperatures and flow rates substantially affect dispersion, and the application should clearly show how these parameters were calculated or measured. If gas temperatures are based on measurements made at locations other than near the stack exit, the temperature used in the model should be adjusted to derive a temperature appropriate for the stack exit. Stack gas exit velocities exceeding 50 m/sec will generally be viewed as suspect by DEQ reviewers, and greater documentation of values used will be required.

Unrealistic stack parameters submitted in applications are most commonly associated with internal combustion engines, and typically involve overly high exit velocities and stack temperatures. Applicants often use temperature and flow data obtained for the exhaust manifold rather than for the point of release to the atmosphere. Actual flows and temperatures at the release point will be substantially lower after heat loss through the walls of an exhaust pipe and through an exhaust muffler.

Stack Orientation

DEQ also requires the following be included in the application and modeling analysis:

- Orientation of the stack (horizontal or vertical)
- Indication of the presence or absence of a rain cap or other obstruction in the released flow from a stack

Stack orientation information is important because it affects the dispersion characteristics of the pollutants. If either a horizontal stack or rain cap (or other obstruction) is present, it must be accounted for in the modeling analysis, since upward plume momentum is zero because of either the obstruction or the orientation of the stack.

The method recommended by DEQ for modeling horizontal or rain-capped sources, when using the model AERMOD where downwash is not considered, is based on a procedure recommended by EPA (July 9, 1993, memorandum from Joseph A. Tikvart, Source Receptor Analysis Branch, to Ken Eng, Chief, Air Compliance Branch, Region II). The method involves setting the stack velocity to 0.001 meters per second to effectively turn off momentum plume rise. The memo also recommends turning stack tip downwash off for horizontal releases.

The recommended method for modeling point sources of non-buoyant emissions with horizontal release or vertical release with the presence of a rain cap is as follows:

1. Define the emissions source as a point source, entering in the model the actual height of release, stack gas temperature, and the Universal Transverse Mercator (UTM) coordinates.
2. Plumes from horizontal emissions releases or vertical stacks with rain caps experience no momentum induced plume rise. Set the stack gas exit velocity to 0.001 meters per second to effectively prevent the model from accounting for momentum plume rise.

3. Stack tip downwash is not appropriate for horizontally released emissions. If the emissions vent in the horizontal direction, the stack diameter can be set to 0.001 meters to prevent stack tip downwash effects. This step should not be used for sources that vent vertically with a rain cap over the stack, since the rain cap will not prevent stack tip downwash effects. The actual inside stack diameter should be used for rain-capped stacks.
4. Run the model as otherwise required.

By setting the flow velocity and/or stack diameter to 0.001, plume rise from hot, buoyant plumes is inappropriately eliminated. Since the PRIME downwash algorithm within AERMOD is affected by stack diameter, it is not acceptable to artificially increase the diameter by a substantial degree to generate a more accurate mass of hot stack gas emitted.

Non-regulatory versions of AERMOD allow the modeler to identify sources as a horizontal release or rain-capped source, and the model will consider the thermal buoyancy flux in the plume rise calculation while not considering a vertical momentum flux. To use the non- regulatory version, the actual temperature, stack diameter, and flow rate are entered into the model, then the source is identified in the AERMOD input file as a capped or horizontal release. DEQ must approve the use of any non-regulatory options in AERMOD.

Alternate methods may be approved by DEQ on a case-by-case basis if there are unique circumstances. In such cases, DEQ strongly advises that the permit applicant or consultant contact DEQ prior to modeling to discuss the issue, prepare a modeling protocol, and obtain prior approval from DEQ to use the proposed method.

Initial Plume Dimensions for Volume Sources

Initial horizontal plume dimensions for volume sources should be calculated as follows:

- Single volume source:
  $\sigma y0$ = side length of source divided by 4.3
- Line source represented as a series of volume sources (separated or adjacent):
  $\sigma y0$ = side length of source divided by 2.15

Initial vertical plume dimensions for volume sources should be calculated as follows:

- Surface based source:
  $\sigma z0$ = height of source divided by 2.15
- Elevated source on or adjacent to a building:
  $\sigma z0$ = building height divided by 2.15
- Elevated source not on or adjacent to a building:
  $\sigma z0$ = building height divided by 4.3

6.4.3 Scaled Plot Plan

A scaled plot plan showing emissions release locations, nearby buildings, property lines, fence lines, and roads is required (Section 8.1.2(b), *Guideline on Air Quality Models* (EPA 2005). The dimensions of the buildings (height, width, and length) should be noted either on the plot plan or in a table in the report. If building dimensions are listed in a table format, then it should be easy to cross-reference between the plot plan, model input file, and table.

The use of site plot plans generated directly from the modeling files does not meet the scaled plot plan submittal requirement. The submittal should include those scaled plot plans used to generate the modeling files.

6.4.4 Building Downwash Parameters

According to Section 6.2.2 in the *Guideline on Air Quality Models* (EPA 2005), the air quality impacts associated with cavity and wake effects due to the nearby building structures should be determined for any stacks with stack heights less than good engineering practice (GEP). If AERSCREEN is used with the option of entering dimensions of a single building, the building with the greatest corresponding GEP stack height should be analyzed. This may not necessarily be the building closest to the stack. When the EPA's AERMOD model is used and stacks are less than GEP stack height, building profile information is required for use in the modeling. The recommended building profile software is the EPA's *Building Profile Input Program* (BPIP). This program can also be used to determine which building should be used in the screening analysis. BPIP is available on EPA's SCRAM website.

6.4.5 Source, Building, and Receptor Coordinates and Elevations

UTM coordinates are typically used to define locations of emissions points, building corners, and receptor locations. The datum (e.g., NAD27, NAD83, WGS84) must be specified for the coordinates used, and the same datum must be used for all locations specified in the modeling analysis to assure consistency. The same coordinate system should also be used to evaluate elevations for emissions points, buildings, and receptors.

6.5 Ambient Air Boundary

The ambient air boundary must be determined before an ambient air assessment can be completed. The definition of ambient air in Idaho Air Rules Section 006 is, "that portion of the atmosphere, external to buildings, to which the general public has access." The EPA has further stated that "the exemption from ambient air is available only for the atmosphere over land owned or controlled by the source and to which public access is precluded by a fence or other physical barriers" (Costle 1980). Based on these definitions, DEQ has developed the following guidance to be used when determining the ambient air boundary for a facility.

It shall be assumed that the air within the facility boundaries is ambient air unless the facility can demonstrate that public access is precluded. The facility-proposed ambient air boundary must include justification that demonstrates the facility has reasonable control of the area and effectively precludes public access on a routine basis. The following criteria must be satisfied when developing a facility-proposed, ambient-air boundary justification. A justification must accompany the answers.

For the purpose of defining ambient air, the "general public" is considered anyone not directly associated with the facility. In general, if someone present at the site would not be subject to OSHA or other worker exposure regulations, then they are considered as the general public.

1. Facility Control
    - Is general public access precluded by a physical barrier (e.g., fence with a gate)? If "yes," the facility is assumed to be controlled and public access effectively precluded, and the ambient air boundary can be set at the fence line. Proceed to No. 2. If "no," then proceed to No. 1b. Rugged terrain or a water body is not typically considered as a physical barrier.

- Is general public access discouraged by the type of area (e.g., industrial park site away from residential or recreational areas), size of the facility (e.g., the facility is surrounded by a buffer zone that is controlled by the facility), or a remote location away from the proximity of human habitation or activities? Is the facility controlled by reasonable posting of the property with "no trespassing" signs, or reasonable patrol of the property by a security person who routinely asks trespassers to leave? If "yes" to BOTH questions, the facility is assumed to be controlled, with public access effectively precluded, and the ambient air boundary is determined to be at the property boundary. Proceed to No. 2. If "no," to EITHER question, proceed to No. 1c.
- If the facility is not controlled by a physical barrier AND/OR general public access is not discouraged by the type of area, size of the facility, or the remoteness of the facility location, then the ambient air boundary is determined to be inside the property boundary. The actual point at which the ambient air boundary occurs is dependent on several factors, such as the type of operation at the facility (e.g., are employees outside on a regular basis?) and whether employees have a clear view, from the location where the employees normally work, of the entire property (e.g., are trees blocking the sight?). The ambient air boundary is determined to be at a point where employees are not regularly present and where they do not have a clear view of the property. To meet this criteria, a very detailed description of the facility and property must be provided. If a justification cannot be provided, the ambient air boundary is determined to be all air that is external to the buildings. Proceed to No. 2.

2. Facility Business
   Is the general public invited as part of the normal business conducted on the facility site (e.g., the facility includes a commercial establishment or service provider)? If "yes," then the area into which the public is invited is determined to be ambient air. Adjust the ambient air boundary determined in No. 1. If "no," the ambient air boundary determined in No. 1 is not changed. Proceed to No. 3.
3. Right-of-Way Access
   Is the general public allowed on site as a part of a right-of-way easement or a common service road? If "yes," then the right-of-way is determined to be ambient air. Adjust the ambient air boundary determined in No. 1. If "no," the ambient air boundary determined in No. 1 is not changed. Any streams or rivers transecting a facility will be considered as ambient air at all locations between high water levels unless the applicant adequately demonstrates and documents that public access can be legally precluded. Idaho Department of Lands and Fish and Game rules governing public access should be used for such a demonstration.
4. Leased Property
   Does the facility lease a portion of their site to another industry, business, or individual OR does the facility lease property from another entity? For example, if a facility leases part of its property to a farmer for growing crops, that portion leased may be considered as ambient air. These situations are frequently complicated, and DEQ should be consulted regarding any specific case involving leased property as it affects the ambient air boundary.

Any area outside the facility's (or facilities' if they are under common ownership) control will be considered ambient air. This includes other industrial facilities. The employees of other facilities are considered to be general public for the facility in question. Evaluation of the ambient air quality must include all sources within facility control if the source or source modification exceeds the SILs defined in IDAPA 58.01.01.006 (definition of significant contribution).

6.6 Receptor Network

A receptor network establishes locations where the air dispersion model calculates a pollutant concentration. Each location is called a receptor, to represent a receptor that might be exposed to that concentration at that location. Receptors are required to be placed in all areas considered to be ambient air.

Modeling must be conducted using a sufficiently dense receptor grid to reasonably resolve the maximum modeled concentration and confidently demonstrate compliance with standards.

DEQ may determine an application incomplete or may deny a permit if DEQ is not confident the receptor grid spacing used is adequate to confidently demonstrate NAAQS compliance. DEQ may also include additional receptors during verification modeling if it is questionable whether the maximum concentrations have been resolved, and approval will not be granted if results do not comply with applicable standards. Adequacy of the receptor grid can be evaluated by reviewing a plot of modeled design value concentrations and considering the following:

- Maximum modeled concentrations in relation to a trigger value (SILs, NAAQS, or AACs/AACCs)
- Concentrations at receptors immediately adjacent to the maximum modeled concentration
- Terrain features within the modeling domain and areas beyond the domain if maximum modeled concentrations are near the boundary of the domain

6.7 Elevation Data

Terrain elevations for sources and receptors should be used when appropriate (EPA 2005). Where AERMOD is the model used to demonstrate compliance, the applicant should generally use the latest established procedures and guidance provided by EPA (see the SCRAM website on EPA's TTNWeb-Technology Transfer Network (*http://www.epa.gov/ttn/scram*). Prior to 2009, elevations of receptors, sources, and buildings used in the modeling analyses were determined from U.S. Geological Survey (USGS) Digital Elevation Model (DEM) files. AERMAP now supports processing terrain elevations from the National Elevation Dataset (NED) developed by the USGS. Since the DEM files will no longer be updated, NED represents more up-to-date and accurate data, and these should be used in preference to DEM files. These data can be downloaded in a seamless data set in GeoTiff format for use in AERMAP.

A single, consistent source of terrain data should be used to establish elevations for receptors, emissions sources, and site structures. Using different datums within a single modeling analysis can result in critical problems such as sources located beneath ground-level, buildings suspended above ground-level, or facilities located on hillsides rather than valley floors.

6.8 Meteorological Data

The meteorological data used in the modeling analysis should be representative of the meteorological conditions at the particular site of the proposed construction or modification. Section 8.3 in the *Guideline on Air Quality Models* (EPA 2005) states that representativeness of the meteorological data is dependent on the following: (1) the distance from the meteorological monitoring site to the area under consideration; (2) the complexity of the terrain surrounding both the meteorological monitoring site and the area under consideration; (3) the exposure of the meteorological monitoring site; and (4) the period of time during which data are collected.

When using AERMOD, representativeness will also depend on the similarity between the monitoring site and the application site for: 1) surface roughness; 2) land type characteristics that influence parameters such as albedo and Bowen Ratio (vegetative cover and moisture content). Consult with the DEQ air quality modeling coordinator to determine if representative meteorological data are available for the area under consideration. If the only available meteorological data are of questionable representativeness, DEQ may require applicants to perform modeling analyses using multiple meteorological data sets. Alternatively, site-specific data could be acquired by the facility. Site-specific meteorological data are typically only required for PSD applications or when DEQ has concern regarding NAAQS compliance.

The collection of site-specific meteorological data should follow the recommendations provided in *Meteorological Monitoring Guidance for Regulatory Modeling Applications* (EPA 2000), as well as Section 8.3.3 in the *Guideline on Air Quality Models* (EPA 2005). Site-specific meteorological data must be approved prior to use in a modeling analysis. Generally, following EPA recommendations and procedures is determined to be adequate for DEQ approval. To receive approval, the facility must provide DEQ staff with standard operating procedures, the quality assurance plan for operating the meteorological tower, and quality control audit reports that cover the entire year of data. DEQ will review this information and respond with either an approval or denial letter. The facility should either reference or include a copy of the approval letter when meteorological data are used in a modeling analysis. This will help to expedite the review process of the permit application. If DEQ does not approve the data for air modeling purposes, the analyses will not be approved and alternate approaches must be developed.

There are several sources of meteorological data besides on-site collected data. The National Weather Service (NWS) collects data throughout the country. Much of these data are collected at airports. These and other data are available through the National Climatic Data Center (*http://www.ncdc.noaa.gov/oa/ncdc.html*), through EPA's SCRAM website, or possibly through DEQ's modeling coordinator.

As stated in Section 8.3.1.1 in the *Guideline on Air Quality Models* (EPA 2005), the model user should "acquire enough meteorological data to ensure that worst-case meteorological conditions are adequately represented in the model results." Section 8.3.1.2 recommends using five years of NWS data or at least one year of site-specific data. If more than one year of site-specific data are available, then all years, up to five years, should be used (see Section 8.3.1.2(b) in EPA 2005). Site-specific meteorological data must be subjected to DEQ-approved quality assurance procedures.

The following should be considered when generating meteorological data with AERMET:

- Surface characteristics specified for landuse types in AERMET are based on the meteorological measurement site, not the facility application site.
- The EPA program AERSURFACE should be used, following recommendations specified in the user's guide, to define season- and sector-specific surface parameters (albedo, Bowen Ratio, and surface roughness).
- A current aerial photograph of the meteorological measurement site, or a detailed land- use map, should be used to check the accuracy of land-use files used in AERSURFACE.
- Sector-specific values of surface characteristics should be calculated for each season.
- Documentation of the surface characteristics analyses should be submitted with the application. Sufficient detail must be provided such that DEQ staff can regenerate the AERMET output meteorological files.

6.9 Land-Use Classification

Determining if the area surrounding the facility is urban or rural is necessary before a dispersion modeling analysis can be conducted correctly. Two methods of classifying an area as urban or rural are described in Section 7.2.3.c in the *Guideline on Air Quality Models* (EPA 2005). The first is the land-use method. The area is classified according to the current land usage (according to the meteorological land-use typing scheme proposed by Auer [1978]) of its surroundings in a three-kilometer (approximately 1.8-mile) radius centered at the source. If 50 percent or more of the surrounding area is classified as I1, I2, C1, R2, or R3 (using classifications listed in Auer 1978), the source would be considered an urban source. Otherwise, the source would be considered rural. Appendix E provides a summary of the meteorological land-use typing scheme proposed by Auer (1978).

A second method relies on population density. If the population density within a three-kilometer (approximately 1.8-mile) radius, centered at the facility, is greater than 750 people per square kilometer, the urban modeling option for the area can be used. However, the population density method of source classification should not be applied to highly industrialized areas. This is because highly industrialized areas typically have low population densities, but the presence of buildings and areas of asphalt and concrete make the source more urban in nature. The *Guideline on Air Quality Models*, Section 7.2.3.e, states that, of the two methods, the land-use procedure is more definitive (EPA 2005).

6.10 Background Concentrations

Section 8.2 in the *Guideline on Air Quality Models* (EPA 2005) discusses the use of background concentrations in a cumulative NAAQS analysis. Background concentrations of regulated criteria pollutants must be included in cumulative NAAQS analyses for both PSD and non-PSD applications. The modeler is required to contact DEQ prior to performing the modeling analysis to obtain the appropriate, reasonably conservative background concentration(s) for the area and time intervals of concern. A different pollutant-specific concentration is needed for each applicable averaging period.

Background concentrations are developed based on air quality monitoring data collected from the area of the proposed project or from similar areas determined to be reasonably representative. DEQ has developed applicable background concentrations for specific areas and default concentrations for areas where monitoring data are not available. Facilities may propose alternate/refined background concentrations based on their own analyses. Use of an alternate background concentration should be proposed within a modeling protocol submitted to DEQ. An alternate background concentration proposal analysis should include the following:

- Description of monitoring data proposed as representative of the proposed project area. The description should include the statistics of the data set and the quality control/assurance measures conducted for the data if data were not provided by DEQ.
- Description of all emissions sources in the area of the proposed project and sources in the area(s) where claimed representative monitoring data were obtained. This should include both point sources and area/mobile sources, and should also address emissions source density. A discussion should be provided that compares the two areas and supports the use of the monitoring data for the project site.
- A detailed assessment of the meteorology of the project area and the area where monitoring data were obtained. Differences between the areas should be assessed for the effects they may have on pollutant dispersion and concentrations in ambient air.

Air monitoring data for Idaho can be obtained at the following EPA website address: *http://www.epa.gov/air/data/index.html*. In most instances, background concentrations calculated in the following manner will be accepted by DEQ:

- 24-hour PM2.5: The maximum 3-year mean of 98th percentile of 24-hour average concentrations over 1-year periods.
- Annual PM2.5: The maximum 3-year mean of annual averages, using 5 consecutive years of data.
- Short term standards of PM10, SO2, and CO: The maximum 2nd highest monitored value over each year of applicable data.
- 1-hour NO2: The maximum 3-year mean of the 98th percentile of the daily maximum 1-hour average concentrations over 1-year periods.
- 1-hour SO2: The maximum 3-year mean of the 99th percentile of the daily maximum 1-hour average concentrations over 1-year periods.
- Annual Standards of SO2 and NO2: The maximum annual average for the applicable data. The most recent 5-year data set should be used.

Existing emissions from a facility may have a measurable impact to monitored concentrations in some instances. It is the facility's responsibility to assess their contribution to the background concentration. Prior to this assessment, a protocol must be submitted to, and approved by, DEQ. The assessment must then be done in accordance with the DEQ-approved protocol. In such cases, the facility's impact may be subtracted from the monitored value to establish an appropriate background concentration value. The following should be considered in such analyses:

- To evaluate a facility's impact on background monitored values, modeling must be performed using meteorological data collected during the same period when monitoring data were collected.
- Site-specific meteorological data must be used. These data must be highly representative for both the facility site and the monitoring site.
- Actual emissions for the period modeled must be used in the analyses.
- Monitored and modeled values must be paired in time and space; i.e. modeled values subtracted from monitoring results must be those values modeled at the site of the monitor for the averaging period associated with the monitored value.
- One suggested approach would be to start with the highest monitored value and model the facility's impact on that value. If the result is lower than the next-highest monitored value, this process should be repeated for that monitored value. This process is repeated until the highest adjusted value is greater than the next unadjusted value. The highest adjusted value is used for the background concentration.

Use of other methods to calculate a background concentration will be evaluated on a case-by- case basis. Proposals for such methods should be thoroughly described in the protocol.

6.11 Evaluation of Compliance with Standards

6.11.1 Approval Criteria

The applicant must demonstrate compliance with all other applicable impact limits in addition to demonstrating compliance with NAAQS. For PSD applications, these include impact limits for Class I areas within 300 kilometers, non-attainment area impact limits (when in or potentially significantly impacting a non-attainment area), and TAPs increment standards in Idaho Air Rules Sections 585 and

586 (when emitting TAPs above DEQ ELs). Federal land managers have the responsibility to protect the natural and cultural resources of Class I areas from adverse impacts of air pollution. Refer to the Federal Land Managers Air Quality Related Values Workgroup (FLAG) Phase I Report- Revised (USFS et al 2010). In some cases, deposition of airborne pollutants (e.g., radionuclides or fluorides, for example) or human risk pathways associated with deposition of airborne emissions may be subject to regulatory impact limits.

The highest modeled ambient concentration must be used for comparison against the SILs for all applicable criteria pollutants. A multi-year average, consistent with the years of meteorological data modeled, of the maximum modeled concentration of each year modeled can be used for the probabilistic standards, including 24-hour PM2.5, annual PM2.5, 1-hour NO2, and 1-hour SO2.

The following design concentrations must be used when demonstrating compliance with the cumulative NAAQS:

- CO
  - 1-hour averaging period – maximum of second highest ambient concentrations at each receptor
  - 8-hour averaging period – maximum of second highest ambient concentrations at each receptor
- NO2
  - 1-hour averaging period – maximum of 5-year averages (at each modeled receptor) of the 98th percentile of the annual distribution (equal to the 8th high) of maximum daily 1-hour ambient concentrations
  - Annual averaging period – maximum of ambient concentrations at each receptor
- SO2
  - 1-hour averaging period – maximum of 5-year averages (at each modeled receptor) of the 99th percentile of the annual distribution (equal to the 4th high) of maximum daily 1-hour ambient concentrations
  - 3-hour averaging period – maximum of second highest ambient concentrations at each receptor
  - 24-hour averaging period – maximum of second highest ambient concentrations at each receptor
  - Annual averaging period – maximum of ambient concentrations at each receptor
- PM10
  - 24-hour averaging period – "the projected 24-hour average concentrations will not exceed the 24-hour NAAQS more than once per year on average" (EPA 2005). The design concentration is dependent on the number of meteorological data years used in the analysis. For example, if five years of NWS data were used, then the design concentration would be the sixth highest 24-hour ambient concentration that occurred at each receptor over that five-year period.
- PM2.5
  - 24-hour averaging period – maximum of multi-year average of annual maximum 24- hour ambient concentrations at each receptor. Using the multi-year average of the 98th percentile of the annual distribution (equal to the 8th high) of 24-hour concentrations for both the modeled design value and background is not adequately conservative because background concentrations are frequently the controlling factor for PM2.5.
  - Annual Averaging Period - maximum of multi-year average of annual ambient concentrations at each receptor.

- Pb
  - Quarterly averaging period – maximum of ambient concentrations at each receptor
  - 3-month rolling average – maximum of ambient concentrations at each receptor

If meteorological data used in the analyses are of questionable representativeness, DEQ may require a more stringent design value. DEQ may also require analyses using multiple meteorological data sets to compensate somewhat for increased uncertainty.

The following design concentrations must be used when demonstrating compliance with TAPs requirements:

- Noncarcinogens – 24-hour averaging period – maximum of ambient concentrations at each receptor
- Carcinogens – total averaging period (1-5 years depending on meteorological data availability) – maximum of ambient concentrations at each receptor

6.11.2 Adequacy of Analyses Results

The submitted analyses must demonstrate to the satisfaction of DEQ that applicable emissions do not cause or significantly contribute to a violation of any air quality standard, as per Idaho Air Rules Section 203 for PTCs and Idaho Air Rules Section 403 for Tier II operating permits. Approvability of the submitted analyses will depend on the results of the analyses as well as the representativeness and quality of input data and parameters used. DEQ recognizes the uncertainty in typical dispersion modeling analyses and the variability and uncertainty associated with input parameters such as background concentrations, emission quantities, operational characteristics, etc. These uncertainties will be considered in DEQ's evaluation and determination of acceptability.

DEQ will evaluate model inputs and parameters more carefully as modeling results more closely approach applicable standards. Modeled concentrations within about 90 percent of the standard will be more closely reviewed by DEQ. At these concentrations, approval will be based on a "weight of evidence" type approach, considering the model results, input data/parameters, potentially exposed public, any monitoring requirements specified in the proposed permit, and operational variability. DEQ will not approve any modeling results that do not show compliance with applicable standards. The following provides discussion on how DEQ will evaluate compliance in situations where modeled concentrations are very near applicable standards:

- Modeled Concentrations: Results within about 90 percent of the air quality standard will generally trigger DEQ to more carefully evaluate the analyses. In some instances, the analysis may not adequately demonstrate compliance even though modeled concentrations are below a standard.
- Emissions Estimates: Estimates of emissions can be a substantial source of uncertainty and/or variability. It is important to evaluate both uncertainty in the estimate and variability, and to distinguish between them. Where estimates of maximum emissions are highly uncertain and the estimate is not necessarily conservative, DEQ may consider modeling results slightly below the standard as not adequately demonstrating compliance. Alternatively, if emissions are highly variable and the allowable emission rate is set at the maximum, DEQ will consider the likelihood of high emissions occurring concurrently with conditions of poor dispersion.
- Representativeness of Meteorological Data: Using meteorological data from a distant location where the representativeness is questionable will add to the uncertainty of the modeling analyses. Applicants may be requested by DEQ to provide a more detailed assessment of the area's meteorology and qualitative comparisons to data used in the analyses. Such assessments

should be performed by meteorologists or those having considerable knowledge in surface meteorology. In some instances, DEQ may request an applicant to install and operate a meteorological station to resolve concerns with data representativeness. In cases where meteorological data used in the analyses are of questionable representativeness, DEQ may require the use of multiple meteorological data sets in the analyses.

- Background Concentrations: Background concentrations are often a very large source of uncertainty and variability, especially for 1-hour NO2, PM10, and PM2.5, where background concentrations can be a considerable fraction of the standard. When modeled 1-hour NO2, PM10 and PM2.5 concentrations are very near the standard, applicants should review and compare the meteorological conditions associated with the modeled result and the background concentration.
- Modeled Emissions Release Parameters: Parameters characterizing the release of emissions (stack temperature, flow rate, initial plume dimensions for volume sources, etc.) greatly impact the modeling results. The conservatism of these parameters will be considered by DEQ during the review.
- Permit Requirements: As modeled concentrations approach applicable standards, DEQ may require more extensive emissions monitoring, source testing, and possibly ambient air monitoring.
- Areas with High Concentration Impacts: DEQ will consider the land use of areas where models project high concentrations. DEQ will require a higher degree of certainty for areas where there is a high potential for exposures to the public, such as actual residences, businesses, parks, etc. However, it is important to consider that dispersion models are reasonably accurate at predicting the magnitude of maximum concentrations but often perform poorly at predicting the location or time of maximum concentrations.

6.12 Air Quality Modeling Report

The applicant must supply an air quality modeling report that presents the case as to how the modeling results demonstrate compliance with all applicable air quality standards. The level of detail of the report will depend on the complexity of the proposed facility and the permitting project.

Each submitted application must be a complete package in itself. Referencing previously submitted materials, such as those submitted in an earlier application, will not generally be considered as meeting the stated requirements to provide documentation/justification of air quality analyses and data used as inputs for those analyses.

Below is an example annotated outline of an air quality modeling report. The report should thoroughly describe all aspects of the air impact analyses performed. Specific sections of this guideline should be consulted to evaluate the details needed for the modeling report regarding certain aspects of the analyses.

I Purpose

- State the purpose of the air quality modeling analyses (i.e., demonstrating compliance for a permit to construct or a Tier II operating permit).
- Provide a detailed description of regulatory requirements as they relate to modeling, citing specific applicable regulations.

II Model Description/Justification

- Discuss what model was chosen and justify why it is the appropriate model for the situation. This discussion may be very brief if the applicant is proposing to use AERMOD for near-field impacts.

III Emissions and Source Data

- Present tables showing the current (either actual or permit allowable) emission rates, future allowable emissions rates (maximum for each applicable averaging period), and the requested emission increase (future allowable minus actual or current allowable).
- If cumulative NAAQS impact analyses are required, the applicant must thoroughly document all emissions used in the model, even when such sources are not affected by the particular proposed project. Emissions calculations, source test data, and/or other information justifying the value used should be provided for all sources unless those emissions are based on a specific emissions limit presented in an issued permit.
- Provide justification for those sources and/or pollutants determined to be "inconsequential" (if applicable).
- Provide stack parameters (emissions rates, stack height, stack elevation, stack diameter, stack gas exit velocity, and stack gas exit temperature) for each modeled emissions point. Values for stack parameters should be justified and well documented, indicating whether values are estimated or measured.
- Provide a facility plot plan to scale showing the fence line, ambient air boundary, emission sources at the facility, and buildings. Include the height, width, and base elevation of each building at the facility.
- Provide UTM coordinates of all emissions points, and list the datum used.

IV Ambient air boundary

- Thoroughly describe how the public are precluded from accessing all areas excluded from the receptor network, describing any complicating ambient air issues such as rivers bisecting the facility, leasing agreements, retail sales operations at the site, right of ways, etc.

V Receptor Network

- Describe the receptor network used. Include the distance between receptors for the fine and coarse grids. Justify any deviation from minimum recommendations in EPA or state guidelines, and provide a demonstration that the receptor grid allows for resolution of the maximum modeled concentration.

VI Elevation Data

- Describe any elevation data used and the source of the information, including the datum for the coordinates used. If necessary, include a USGS 7.5-minute map showing the location of the facility. A justification must be provided if elevation data are not used.

VII Meteorological Data

- Describe the source of the meteorological data and present a representative analysis according to Section 6.8. Electronic copies of the files must be included with the modeling report if meteorological data were not provided in model-ready format to the applicant from DEQ. If site-specific data are used, provide documentation that DEQ has reviewed and approved the data.
- If the applicant has generated AERMOD input meteorological files by running AERMET, rather than using AERMOD input files provided by DEQ, supporting AERMET documentation must be submitted with the application. A detailed report on the processing of meteorological data

should be submitted, including a report on running AERSURFACE to evaluate surface characteristics and a detailed report on data collection and quality for any on-site data processed. Copies of the raw meteorological data must also be submitted to DEQ.

VIII Land-Use Classification

- State the land-use classification for the area surrounding the source and provide the justification.

IX Background Concentrations

- State whether background concentrations were used and identify the source of the information.
- If DEQ default background concentrations were not used, the report must thoroughly describe and document how background concentrations were determined.

X Evaluation of Compliance with Standards

- Include tables summarizing the air quality model output (example tables are shown in Appendix F).

XI Electronic Copies of the Modeling Files

- Provide modeling input/output files (including BPIP and meteorological data, and intermediate files generated by AERMET, AERMAP, and AERMOD) on compact disk or other means.

7 DEQ Review of Modeling Analyses

DEQ dispersion modeling staff will review the submitted air quality analyses prior to approval and issuance of the permit. Review of the analyses will occur in two phases: 1) completeness review; 2) technical review of submitted analyses. The completeness review will focus on evaluating whether the required analyses were performed and the primary components of the air quality analyses were submitted with the application. The technical review will evaluate whether the data and methods used in the analyses are accurate and appropriate for the project.

Several methods and approaches can be used by the applicant to ensure the submitted modeling analyses are approved by DEQ or, if there are problems with the analyses, such problems are identified early in the completeness review and will minimize delays to the project:

1. Submit a modeling analyses protocol prior to conducting the analyses. The protocol, as described in Section 6.1, should provide details on the proposed methods and data to the greatest degree possible.
2. Provide a detailed and well-organized modeling analyses report, as described in Section 6.12. This will allow DEQ staff to quickly assess the appropriateness and technical accuracy of the analyses. If a modeling protocol was submitted to DEQ prior to the application, a copy of the protocol and DEQ's protocol approval notification should be included with the application.
3. Provide clear justification for methods and data used, and provide supporting documentation. Calculations should be provided such that the DEQ reviewer can easily verify the calculated values.
4. Ensure that emissions sources are named consistently between the emissions inventory used for the permit application forms and the modeling analyses.

Conduct quality assurance/control measures to minimize error in the submitted analyses. The following are some measures that will help minimize or identify errors in the analyses:

- Print or view a three-dimensional representation of the sources, building, receptors, and the ambient air boundary. This will identify any errors in UTM coordinates and elevations.
- Check that all sources included in the application are included in the modeling analyses. If some sources are not included, a detailed justification should be provided. If facility-wide modeling is needed for a cumulative impact analysis, the emissions inventory of other sources, not directly addressed by the current permitting action, should be thoroughly documented.
- Emissions rates used in the modeling analyses should be identical to those listed in the permit application forms and the emissions calculation section of the application. Any differences between emissions rates should be thoroughly documented and all calculation steps should be shown. This will allow DEQ reviewers to quickly evaluate how emissions rates were calculated.

8 Summary

This document provides guidance for performing an ambient air assessment, for permitting purposes, in the state of Idaho. This document should be used in conjunction with the EPA's *Guideline on Air Quality Models* (EPA 2005) and *New Source Review Workshop Manual* (EPA 1990), and other applicable guidance materials. Following the guidance in this document, as well as EPA guidance, will help expedite DEQ's review of the application.

References

40 CFR 52.21, *Prevention of Significant Deterioration of Air Quality.*

Auer, A.H., Jr., 1978. *Correlation of Land Use and Cover with Meteorological Anomalies*. Journal of Applied Meteorology, 17(5): 636-643.

Costle, Douglas, M., 1980. *Correspondence to Senator Jennings Randolph*. December 19, 1980.

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EPA, 1992. *Screening Procedures for Estimating the Air Quality Impact of Stationary Sources, Revised*. EPA Publication No. EPA-454/R-92-019. U.S. Environmental Protection Agency, Research Triangle Park, NC.

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EPA, 2005. *Guideline on Air Quality Models*. 40 CFR Part 51, Appendix W, Federal Register Vol 70, No. 216, Wednesday, November 9, 2005.

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EPA 2009b. *AERMOD Implementation Guide*. AERMOD Implementation Workgroup. U.S. Environmental Protection Agency, Research Triangle Park, NC.

EPA 2010a. *General Guidance for Implementing the 1-hour NO2 National Ambient Air Quality Standard in Prevention of Significant Deterioration Permits, Including an Interim 1-hour NO2 Significant Impact Level*. EPA Memorandum from Anna Marie Wood, Acting Director, Air Quality Policy Division, to Regional Air Division Directors. U.S. Environmental Protection Agency, Research Triangle Park, NC. June 28, 2010.

EPA 2010b. *General Guidance for Implementing the 1-hour SO2 National Ambient Air Quality Standard in Prevention of Significant Deterioration Permits, Including an Interim 1-hour SO2 Significant Impact Level.* EPA Memorandum from Anna Marie Wood, Acting Director, Air Quality Policy Division. U.S. Environmental Protection Agency, Research Triangle Park, NC. August 23, 2010.

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EPA's SCRAM website: http://www.epa.gov/scram001/index.htm

IDAPA 58.01.01, et seq. *Rules for the Control of Air Pollution in Idaho*

Idaho Department of Environmental Quality Policy Memorandum, *Policy on NAAQS Compliance Demonstration Requirements*, July 11, 2014.

Appendix A. Guidance for 1-Hour NO_2 Modeling of Intermittent Sources

DEQ Guidance for Minor New Source Review Modeling of 1-Hour NO_2 from Intermittent Testing of Emergency Engines



State of Idaho
Department of Environmental Quality

September 2013

TR 1172

Certain industrial facilities have internal combustion (IC) engines that are used only to power emergency generators or fire-suppression pumps. These engines only operate for periodic testing and during an actual emergency. As such, these sources with intermittent emissions are difficult to model in a way that accounts for impacts in a reasonably accurate but conservative manner. As a result, Tyler Fox, leader of Environmental Protection Agency's (EPA) Air Quality Modeling Group, developed a memorandum entitled "Additional Clarification Regarding Application of Appendix W Modeling Guideline for the 1-hour NO2 National Ambient Air Quality Standard, dated March 1, 2011. The memo provides states with the flexibility to exclude certain types of sources with intermittent emissions from Appendix W modeling.

Upon a review of other states' application of the Tyler Fox memo, comments from the public and Idaho industry, an internal review of Idaho sources, NO2 background levels, and various sample model runs; DEQ has determined that Nitrogen Oxides (NOx) emissions from the intermittent operational testing of engines powering emergency generators or fire-suppression water pumps may be excluded from the project-specific significant impact level (SIL) analysis and the cumulative NAAQS analysis for 1-hour NO2, providing the annual hours of operation from testing and maintenance are less than or equal to 100 hours per engine.

This determination is applicable to minor source air permitting projects and is not limited to any specific number of engines present at a facility. The Director may require deviation from this guidance if deemed appropriate to assure compliance with 1-hour NO2 NAAQS and IDAPA 58.01.01.203 or 01.403. DEQ will determine how emergency engines are included in permits for major sources, specifically those applicable to the Prevention of Significant Deterioration (PSD) program, on a case-by-case basis.

This guidance does not have the force and effect of a rule and is not intended to supersede statutory or regulatory requirements or recommendations of the state of Idaho or EPA. This guidance may be altered upon new or revised guidance from EPA, development of new methods to appropriately handle such emissions, or new information gained from technical analyses.

Contact the DEQ stationary source air modeling coordinator at (208) 373-0112 for any questions or additional information regarding data and methods for assessing air quality impacts from intermittently operated sources.

Appendix B. Class I Areas

Class I Areas

This appendix shows Class I areas in and near Idaho. The areas represent situations where air quality impact limits are stricter than the NAAQS. The information in this appendix is current as of the date of this document. Please check with DEQ to verify if it is still current.

Area Classifications

The Class I, II, and III areas are defined below (shown in Figure 1).

1. Class I - National park, recreation, and wilderness areas that were already established when the 1977 Clean Air Act was passed, and other designated parts of the country that now benefit from high quality air and where a high priority has been established for the maintenance of pristine conditions. Additional degradation of the air is severely restricted.
2. Class II - Areas that need reasonably or moderately good air quality protection. This is presently the class designation of most areas in the United States. Increments of deterioration have been stipulated that will generally accommodate most proposed development projects.
3. Class III - Areas that can, at the discretion of the states, be designated as allowing for larger increments of air quality degradation and therefore greater growth and development potential. No Class III areas have been designated in Idaho.

The Class I areas in Idaho include the following: Hells Canyon, Sawtooth, and Selway- Bitterroot wilderness areas, Craters of the Moon National Monument, and Yellowstone National Park.

Class I areas near Idaho's borders include the following: Spokane Indian Reservation, Washington; Hells Canyon and Eagle Cap Wilderness areas, Oregon; Cabinet Mountain and Anaconda-Pintler Wilderness areas, Red Rock Lakes, and Flathead Indian Reservation, Montana; Yellowstone National Park, Montana and Wyoming; Teton National Park, Wyoming; and Jarbidge Wilderness, Nevada.

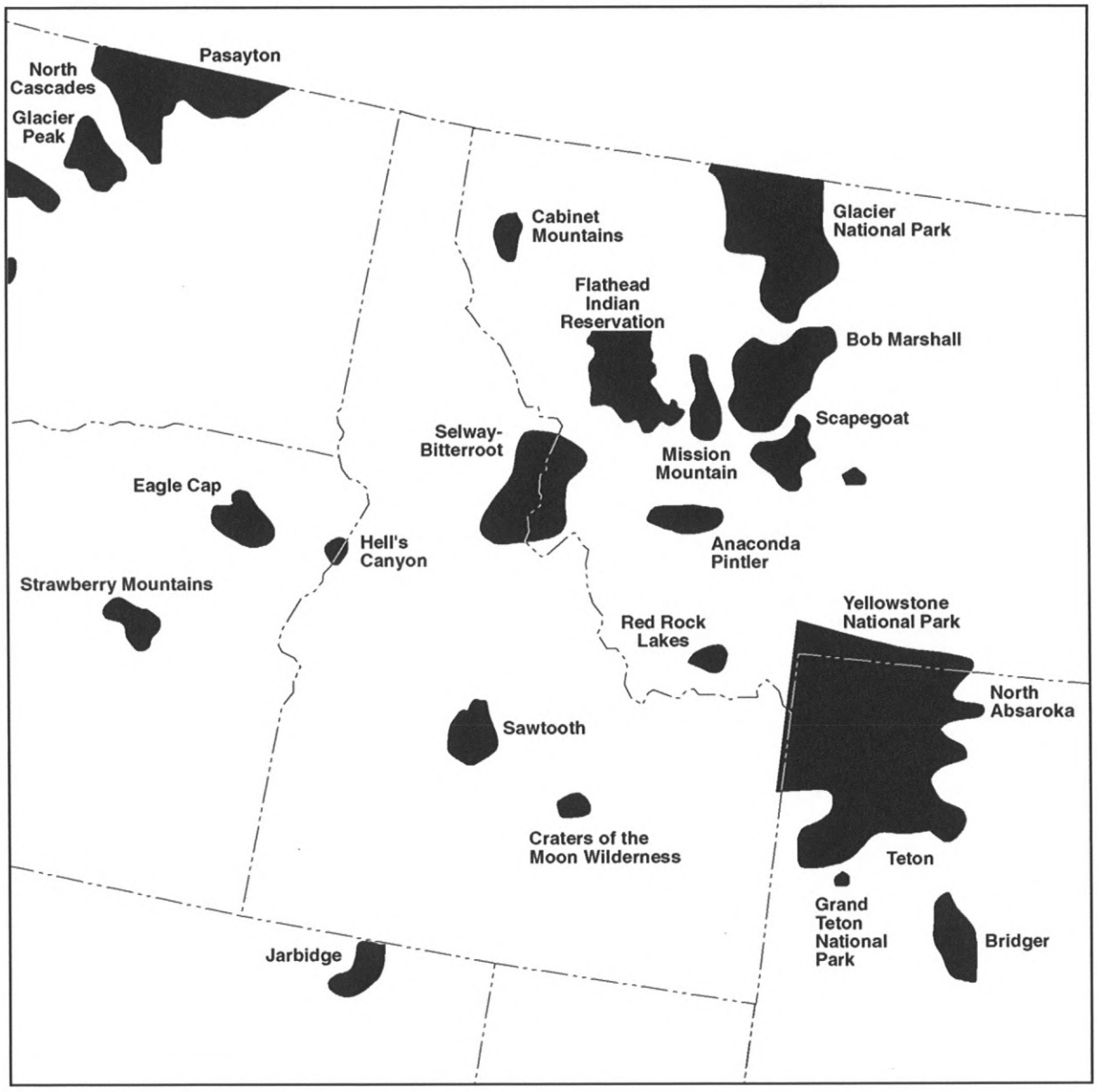

Figure A-1. Class I areas in and near Idaho.

Appendix C. Idaho DEQ Air Dispersion Modeling Checklist

Idaho DEQ Stationary Source Air Dispersion Modeling Checklist

- ☐ Reviewed the Idaho Air Quality Modeling Guideline and have determined the appropriate methods and data for use in this permitting action, contacting DEQ as needed to provide clarification.
- ☐ A modeling applicability analysis was performed for all criteria pollutants emitted by the new facility or modification, and modeling was performed for those pollutants having a total increase in emissions exceeding DEQ modeling thresholds.
- ☐ A TAPs modeling applicability analysis was performed for all TAPs emissions increases associated with the project, and TAPs modeling was performed for those TAPs having a project total emissions rate exceeding the emissions screening levels.
- ☐ Provided a description of the ambient air boundary and demonstrated how public access will be precluded from all areas excluded from ambient air.
- ☐ The receptor grid used meets minimal requirements specified by DEQ AND is adequate to reasonably resolve the maximum modeled concentration and confidently demonstrate compliance with applicable standards.
- ☐ The modeling domain used is sufficiently large to resolve the maximum impacts, accounting for impacts on distant elevated terrain.
- ☐ A scaled site plot plan was included in the application, showing emissions sources, buildings, and the ambient air boundary.
- ☐ Thoroughly documented all release parameters used in the model and provided justification for their use.
- ☐ Emissions rates provided in the emissions inventory section of the application are identical to those used in the modeling analyses or, if emissions rates are not identical, thorough justification of modeled rates has been provided.
- ☐ A cumulative NAAQS impact analysis was performed for all criteria pollutants for which modeled impacts from the significant impact analysis exceeded SILs. The cumulative NAAQS impact analysis included facility-wide emissions, emissions from any co-contributing sources, and a DEQ approved background concentration. Documentation of all emissions rates and release parameters used in the cumulative NAAQS impact analyses are provided in the application.
- ☐ Included all input and output modeling files for all pollutants and averaging periods.
- ☐ If a modeling protocol was prepared and submitted to DEQ prior to performing the air impact analyses, the protocol and DEQ's protocol approval notice is included with the application.

Appendix D. Modeling Protocol Checklists

Modeling Protocol Checklist for New Minor Sources or Minor Modifications

The following should be thoroughly addressed in a modeling protocol submitted to DEQ:
Introduction and Purpose

- General overview, facility description, description of area where facility is located.
- Project overview.
- Goals of the air quality impact analysis (i.e., demonstrate compliance for a PTC for a modification, PTC for a new facility, or a Tier II operating permit).
- Applicable regulations and requirements.
- Pollutants of concern.

Emissions and Source Data

- Description of facility processes and emissions controls affected by the permitting action.
- List of emissions points that will be included in the modeling analyses. Present a table showing current actual/allowable and future allowable emission rates (using pounds per hour rates for all applicable averaging periods) and the requested emissions increase (future allowable minus current actual or allowable).
- Good engineering practice (GEP) stack-height analysis for any stacks approaching GEP height.
- Graphic showing the facility layout: location of sources, buildings, emissions points, and fence lines.
- Description of methods used to calculate or otherwise determine source parameters (emissions rates, UTM coordinates, stack height, stack elevation, stack diameter, stack- gas exit velocity, and stack-gas exit temperature) for each source included in the modeling analyses.
- Methodology for including area and volume sources in the modeling analysis, including justification and calculations of initial dispersion coefficients and release heights.
- Methodology for including/excluding sources from the modeling analyses.

Air Quality Modeling Methodology

- Description of model selection and justification. This may be minimal in cases where the regulatory guideline model is used (AERMOD in most cases).
- Description of model setup and application
  - Model options (i.e., regulatory default). Describe and provide justification for any non-default settings.
  - Averaging periods used in the analyses and how emissions rates were calculated for specific averaging periods.
  - Land-use analysis in all cases where "urban" is used and in cases where land use is not obviously "rural."
  - Methods used to account for building downwash in the analyses.
  - Treatment of any chemical transformations (e.g., NO to NO2) accounted for in the analyses.
  - Any other unique methods or data used.Description of how elevations of sources, buildings, and receptors were determined.
- Receptor network
  - Description of receptor grids – include methodology for ensuring the maximum concentration will be estimated
  - Discussion/justification of ambient air boundary, including a description of how the general public will be excluded from areas not considered ambient air.

- Meteorological data
  - Selection of meteorological databases – justification of appropriateness of meteorological data to area of interest
  - Meteorological data processing
  - Meteorological data analysis (e.g., wind rose)
- Background concentrations

Applicable Regulatory Limits

- Methodology for evaluation of compliance with standards (i.e., determination of design concentration)
- Significant Impact analysis
  - Comparison to SILs
  - TAPs analysis
- Cumulative NAAQS impact analysis
  - NAAQS analysis
- Presentation of results – state how the results of the modeling analysis will be displayed (i.e., list what information will be included)

Appendix E. Land-Use Classification Procedure

Land-Use Classification Procedure

See Section 8.2.8.b of *Guideline on Air Quality Models* (EPA 2001) for additional information.

1. Determine a circular area centered on the source with a radius of three kilometers.
2. Classify the land use within this area using the meteorological land-use typing scheme presented in Table D-1.
3. If land-use types I1, I2, C1, R2, and R3 account for 50 percent or more of the area, use urban dispersion coefficients; otherwise, use rural dispersion coefficients.

Table D-1. Identification and Classification of Land-Use Types (Auer 1978)

Type	Use	Structures	Vegetation
I1	Heavy Industrial	Major chemical, steel, and fabrication industries; generally 3-5 story buildings, flat roofs	Grass and tree growth extremely rare; <5% vegetation
I2	Light-moderate Industrial	Rail yards, truck depots, warehouses, industrial parks, minor fabrications; generally 1-3 story buildings, flat roofs	Very limited grass, trees almost totally absent; <5% vegetation
C1	Commercial	Office and apartment buildings, hotels; >10 story heights, flat roofs	Limited grass and trees; <15% vegetation
R1	Common residential	Single family dwellings with normal easements; generally one story, pitched roof structures; frequent driveways	Abundant grass lawns and light-moderately wooded; >70% vegetation
R2	Compact residential	Single, some multiple, family dwellings with close spacing; generally <2 story, pitched roof structures; garages (via alley), no driveways	Limited lawn size and shade trees; <30% vegetation
R3	Compact residential	Old multi-family dwellings with close (<2m) lateral separation; generally 2 story, flat roof structures; garages (via alley) and ash pits, no driveways	Limited lawn size, old established shade trees; <35% vegetation
R4	Estate residential	Expansive family dwellings on multi-acre tracts	Abundant grass lawns and lightly wooded; >80% vegetation
A1	Metropolitan natural	Major municipal, state, or federal parks, golf courses, cemeteries, campuses; occasionally single story structures	Nearly total grass and lightly wooded; >95% vegetation
A2	Agricultural natural		Local crops (e.g., corn, soybeans); >95% vegetation
A3	Undeveloped	Uncultivated; wasteland	Mostly wild grasses and weeds, lightly wooded; >90% vegetation
A4	Undeveloped rural		Heavily wooded; >95% vegetation
A5	Water surfaces	Rivers, Lakes	Not applicable

Appendix F. Example Tables for Air Quality Modeling Report

Example Tables for Air Quality Modeling Reports

This appendix contains examples of tables that are useful in presenting information in modeling reports.

Table E-1. Example Stack Parameters Table

Parameter[a]	Generator Stack	Boiler Stack
Computer Model Identifier (Alias)		
Emissions Rate (lb/hr)		
Stack Height (ft)		
Stack Diameter (ft)		
Exit Temperature (°F)		
Exit Flow Rate (acfm)		

a) Provide thorough justification/documentation of values used in the model, including calculations used to generate values.

Table E-2. Example Significant Impacts Summary ($PM_{2.5}$)

Year	5-Year Mean of Highest Annual Concentration ($\mu g/m^3$)	Radius of Significant Annual Impact (m)	5-Year Mean of Highest 24-hour Concentration ($\mu g/m^3$)	Radius of Significant 24-hour Impact (m)
1987-1991				
Significant Impact Level	0.3	Not applicable	1.2	Not applicable

Table E-3. Example Maximum Impacts for Cumulative NAAQS Analysis (NO_2 impacts, 1-hour averaging period)

Years Modeled	Multi-Year Mean of 8th Highest Daily Maximum 1-Hour Concentration ($\mu g/m^3$)	Receptor Location		
		East (m)	North (m)	Elevation (m)

Table E-4. Example Maximum Impacts for Toxic Air Pollutants Analysis (Carcinogens)

TAPs	Period Average (5-year) Concentration ($\mu g/m^3$)	Receptor Location		
		East (m)	North (m)	Elevation (m)

Table E-5. Example Maximum Impacts for Toxic Air Pollutants Analysis (Noncarcinogens)

TAPs	Highest 24-hour Concentration ($\mu g/m^3$)	Receptor Location		
		East (m)	North (m)	Elevation (m)

Table E-6. Example NAAQS and Toxic Air Pollutants Impact Analysis Summary

Pollutant	Averaging Period	Total Ambient Impact (Baseline Plus Modification and Co-Contributing Sources) ($\mu g/m^3$)	Background Conc. ($\mu g/m^3$)	Total NAAQS Conc. ($\mu g/m^3$)	NAAQS ($\mu g/m^3$)
CO	1-hour				40,000
CO	8-hour				10,000
NO_2	1-hour				188
NO_2	Annual				100
SO_2	1-hour				196
SO_2	3-hour				1,300
SO_2	24-hour				365
SO_2	Annual				80
$PM_{2.5}$	24-hour				35
$PM_{2.5}$	Annual				12
PM_{10}	24-hour				150

Idaho
Risk Evaluation Manual for Petroleum Releases

Idaho Department of Environmental Quality
1410 North Hilton
Boise, Idaho 83706

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Idaho
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Acronyms and Abbreviations

µg	Microgram
AST	Above Ground Storage Tank
ASTM	American Society for Testing and Materials
AUL	Activity and Use Limitation
BTEX	Benzene, Toluene, Ethyl Benzene, and Xylene
CAL-EPA	California Environmental Protection Agency
CAP	Corrective Action Plan
CAS	Chemical Abstract Service
cm^3	Cubic Centimeter
CLP	Contract Laboratory Program
COI	Chemical(s) of Interest
C_{cw}	Concentration in Groundwater (Between Source and Surface Water) at Alternate Point of Compliance
cm^2	Square Centimeter
CSF	Cancer Slope Factor
C_{soil}	Source Area Concentration in Soil
C_{swpoe}	Point of Exposure Concentration in Surface Water
DAF	Dilution Attenuation Factor
DEQ	State of Idaho, Department of Environmental Quality
DOE	U.S. Department of Energy
DQO	Data Quality Objective
Eh	Redox Potential
EPA	U.S. Environmental Protection Agency
EU	Exposure Unit
ft	Foot
gm	Gram
GW	Groundwater
GWP	Groundwater Protection
HI	Hazard Index
HQ	Hazard Quotient
IDAPA	Idaho Administrative Procedures Act
IDWR	Idaho Department of Water Resources
IELCR	Individual Excess Lifetime Cancer Risk
IRIS	Integrated Risk Information System
ISCE	Initial Site Characterization and Evaluation
IUPAC	International Union of Pure and Applied Chemists
IUR	Inhalation Unit Risk
kg	Kilogram

L	Liter
LNAPL	Light Non-Aqueous Phase Liquid
m	Meter
MCL	Maximum Contaminant Level
mg	Milligram
MTBE	Methyl Tertiary Butyl Ether
NA	Natural Attenuation
NAPL	Non-Aqueous Phase Liquid
NCEA	National Center for Environmental Assessment
NFA	No Further Action
NPDES	National Pollutant Discharge Elimination System
PAH	Polycyclic Aromatic Hydrocarbons
POC	Point of Compliance
POE	Point of Exposure
PSC	Petition for Site Closure
PST	Petroleum Storage Tank
QA	Quality Assurance
QAPP	Quality Assurance Project Plan
QC	Quality Control
RA	Relative Absorption
RATL	Remedial Action Target Level
RBCA	Risk-Based Corrective Action
RCRA	Resource Conservation and Recovery Act
REDOX	Reduction-Oxidization
REM	Risk Evaluation Manual
RE	Risk Evaluation
RF	Reduction Factor
RfD	Reference Dose
RfC	Reference Concentration
RMP	Risk Management Plan
RNA	Remediation by Natural Attenuation
ROE	Route(s) of Exposure
RSL	EPA Regional Screening Level
RUSL	Residential Use Screening Level
SAB	EPA's Science Advisory Board
SCM	Site Conceptual Model
SF	Slope Factor
SVOC	Semi-Volatile Organic Chemical
STATECOMM	State Communications Center
SW	Surface Water
TEQ	Total Toxic Equivalency

TEF	Toxic Equivalency Factors
UCL	Upper Confidence Limit
UECA	Uniform Environmental Covenants Act
USACE	United States Army Corps of Engineers
VOC	Volatile Organic Compound

Introduction

In April 2009, the Idaho Legislature approved the Department of Environmental Quality (DEQ) Rules IDAPA 58.01.24, Standards and Procedures for Application of Risk Based Corrective Action at Petroleum Release Sites (the Rule). This rule required that DEQ prepare a risk evaluation manual for petroleum releases which would be used as guidance for implementation of the Rule. This document represents that implementation guidance. The Rule may be obtained at: *http://adminrules.idaho.gov/rules/2012/58/0124.pdf*

Organization of This Document

The document begins with a general description of the steps in the risk evaluation (RE) process, which is then followed by detailed implementation information for each step. DEQ has developed software that complements the process described and is provided at no charge. Contact DEQ regarding its availability.

Information in the body of this manual is supported by 12 appendices. Appendices A–D address default exposure factors, fate and transport parameter values, physical and chemical properties, and toxicity values. Appendix E presents models and equations. Appendix F provides the methodology and calculations for remedial action target levels (RATLs). Appendix G discusses the vapor intrusion pathway, and Appendix H addresses the application of natural attenuation. Appendix I describes the estimation of exposure point concentrations. A sample table of contents from a risk evaluation report is provided in Appendix J. Appendix K addresses practical quantitation limits, and Appendix L contains a quality assurance project plan (QAPP) template.

Section 1. Overview of the Risk Evaluation Process

1.1 Steps in the Risk Evaluation Process

The overall evaluation process for a site where a petroleum release is discovered and reported to DEQ is illustrated in Figure 1. The process consists of multiple steps, each of which is briefly described in the pages following Figure 1. In some cases, when adequate data are available concerning a release, the owner or operator (as defined IDAPA 58.01.24.010) of the release site may skip the screening level evaluation and proceed directly to the site-specific RE, a more detailed level of evaluation, without formally completing the intermediate steps. DEQ should be notified in these instances. A comparison of the two RE options, with the types of values, models, and other factors used in each option, is presented in Table 1.

1.1.1 Site Discovery

The risk-based site management process begins with the discovery of a petroleum release site. A petroleum release site may be discovered and reported to DEQ under a variety of circumstances. These include, but are not limited to, citizen complaints, investigations conducted as a part of real estate transactions, environmental impacts observed in surface water bodies, and notification of accidents and spills. It is the owner/operator's responsibility to ensure that DEQ is notified.

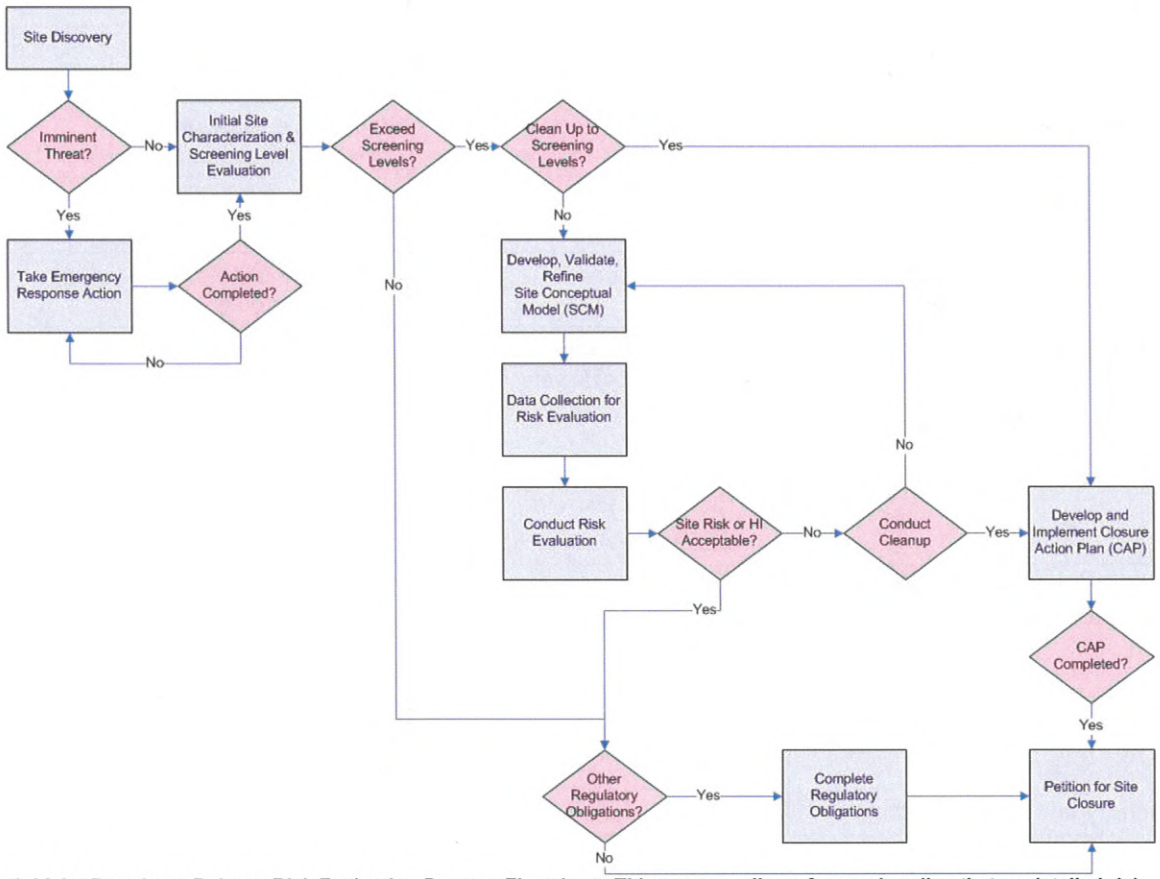


Figure 1. Idaho Petroleum Release Risk Evaluation Process Flowchart. This process allows for moving directly to a detailed risk evaluation without first completing a general screening level evaluation.

Table 1. Comparison of Risk Evaluation Options

Factors	Screening Level Evaluation	Site-Specific Risk Evaluation
Exposure Factors	Default	Site-specific/default
Toxicity Factors	Rule-specified values	Rule-specified values
Physical and Chemical Properties	Default	Default or DEQ accepted values
Fate and Transport Parameters	Default	Default/Site-specific
Unsaturated Zone Attenuation	None	None/Site-specific
Fate and Transport Models	Default	Default or other models acceptable to DEQ
Exposure Point Concentrations	Maximum	Statistical evaluation: Conservative Estimate of Mean:
Acceptable Target Risk	1×10^{-6}	Cumulative effects considered; target of 1×10^{-5}
Acceptable Target Hazard Quotient/Hazard Index	Hazard Quotient = 1	Cumulative effects considered; Hazard Index Target of 1
Groundwater Protection	Maximum contaminant level or risk based target levels	Maximum contaminant level or risk based target levels
Outcome of Evaluation	Either: • Petition for Site Closure, or • Risk Evaluation, or • Corrective Action Plan	• Petition for Site Closure, or • Refine RE, or • Corrective Action Plan
Soil Concentration Protective of Groundwater	Default model with point of exposure at source	Default model with point of exposure determined as per Section 4. Flexibility in model may be used subject to DEQ approval
Surface Water Classification	See Section 4	See Section 4
Point of Exposure	Source	See Section 4
Activity and Use Limitations	None	See Section 6

1.1.2 Determination of Imminent Threat

Upon site discovery, the owner/operator should carefully evaluate the available information to determine whether the site poses any imminent threat to human health or safety, or to the environment. Threats include, but are not limited to, impacts to water wells; vapors or odors in residential and commercial structures; concentrations approaching explosive levels; impacts to a surface waterbody; and impacts to human health and the environment. If any imminent threats are identified, the owner/operator should notify DEQ or State Communications Center (STATECOMM) immediately (see Section 2) and take immediate steps to abate the threat. Documentation of abatement activities and confirmation that imminent threats have been removed should be provided to DEQ. Further details of this step are provided in Section 2.

1.1.3 Initial Site Characterization and Evaluation

Upon completion of the emergency response action, if any, it is necessary to perform an initial site characterization and evaluation (ISCE). As a part of the ISCE, media-specific data (for soil, soil vapor, and groundwater media) should be collected to characterize the source. This step is intended to identify the maximum contaminant concentrations for the identified petroleum products in soil and groundwater. Since a site may be a candidate for closure after the completion of the screening level evaluation (see ☐), it is very important that the data collected at this time identify the maximum media-specific concentrations. Further details of this step are provided in Section 2.

1.1.4 Comparison with Screening Levels

This step involves the comparison of the maximum media-specific concentration of each contaminant, identified in the ISCE, with the screening levels developed by DEQ and presented in Table 2. There is a screening level for each contaminant in each media. The screening level is the lowest of the media-specific (soil, soil vapor, and groundwater) risk-based concentrations for the applicable exposure pathways. Screening levels are considered criteria that, if met (that is, maximum contaminant concentrations are below the screening levels), will allow unrestricted (residential) use of the property. Since exposure to these low concentrations (below the screening levels) of contaminants does not pose a threat to human health, if the owner/operator chooses to meet these criteria, they will not be required to evaluate site-specific exposure pathways and develop a site conceptual model (SCM), and no land use restrictions will be needed on the property.

When DEQ and the owner/operator agree that a petroleum release has been adequately characterized, DEQ will not require any further action of the owner/operator related to the release if the maximum contaminant concentrations in soil, surface water, and groundwater do not exceed the screening levels, subject to other applicable requirements, if any, as referenced in IDAPA 58.01.24.001.02. If any of the maximum soil, groundwater, or soil vapor concentrations exceed the screening levels, the owner/operator may either:

- adopt the screening levels as cleanup criteria and develop a corrective action plan (CAP) to achieve these levels, or
- perform a site-specific RE. Further details of this step are provided in Sections 3 and 4.

1.1.5 Development and Validation of a Site Conceptual Model

If the screening levels are exceeded, and the owner/operator chooses to conduct a more detailed (site-specific) RE, it is first necessary to develop and validate an SCM. An SCM provides the framework for the overall management of the site and should help guide data collection and risk management activities while the RE is being performed. The key elements of the SCM are:

- release scenario(s),
- source description,
- petroleum chemicals of interest (COI),
- an exposure model that incorporates the appropriate receptors,
- exposure pathways and routes of exposure (ROE),
- the site stratigraphy and hydrogeology, and
- the spatial and temporal distribution of the petroleum COI.

An important part of this step is to validate the SCM based on site-specific data. Further details of this step are provided in section 4.1.

1.1.6 Identify and Collect Data for Risk Evaluation

Depending on the site-specific conditions, the RE may require the collection of additional site-specific data. To prepare for conducting an RE, the owner/operator should review the SCM, identify requirements for filling data gaps, and collect additional data if necessary. This data will be used to calculate estimates of site-specific exposure point concentrations (see section 4.3.4 and Appendix I) and an estimate of the site-specific cumulative risk (see section 4.5) and, potentially, to develop RATL concentrations using the guidance provided in this document. Further details of this step are provided in section 4.2.

1.1.7 Site Specific Risk Evaluation

Conducting the RE requires developing site-specific estimates of exposure point concentrations for soil and groundwater, estimating site-specific cumulative risk, comparing these with acceptable target risk levels and, if necessary, developing media-specific RATL concentrations. RATLs are target concentrations developed by the owner/operator using a combination of conservative default and site-specific parameters. These concentrations depend on the receptor, media, pathway, and ROE and are developed for each petroleum COI and each media identified in the SCM. Using RATL concentrations instead of the defaults (the screening level criteria) may require that limitations be placed on activities and land uses that are allowed on the property. This step is discussed in section 4.6 and Appendix F.

1.1.8 Comparison with Acceptable Target Risk Levels and Decision Making

Once the site-specific cumulative risk has been estimated, it is compared to acceptable target risk levels, as specified in the Rule. If acceptable target risk levels are not exceeded, the site is eligible for closure, subject to other applicable requirements, if any, as referenced in IDAPA 58.01.24.001.02. If the site-specific cumulative risk exceeds the acceptable target risk levels, two options are available:

- Calculate and adopt media-specific RATL concentrations for each petroleum COI and develop and implement a CAP to achieve these concentrations.
- Refine the SCM and RE. It is possible that the site-specific cumulative risk is lower than initially estimated and may not pose an unacceptable risk, but this can only be determined with a more refined SCM and RE. This may involve the collection of additional data or the use of other models. Before collecting these additional data, it is optional to develop a work plan that outlines additional data needs and the overall approach for the refined evaluation. The plan may be submitted to DEQ for review and approval before proceeding with data collection and the evaluation. Although optional, the work plan and suggestions from DEQ may help with completing the required work more efficiently than might be the case without a DEQ-reviewed work plan. Details of this step, including the basic contents of a work plan, are included in section 4.7.

Upon completion of the RE, the owner/operator should provide recommendations to DEQ. In most cases, it is anticipated that DEQ and the owner/operator will work together to identify the best alternative. Note that it is not necessary to complete a screening level evaluation before conducting an RE, however, it is recommended that the owner/operator inform DEQ whether they will do a screening level evaluation or not. Often, DEQ can make suggestions to improve efficiency in the overall process.

1.1.9 Development and Implementation of a Corrective Action Plan

Based on the results of the RE process, the owner/operator proposes a set of remediation standards and prepares a CAP describing the measures that will be used to achieve the standards. The CAP is submitted to DEQ for approval. The CAP may include a combination of options for active remediation and passive remediation along with limitations on activities and land uses that were assumed in the RE step. Details of this step are included in Section 5.

1.1.10 Evaluation of Progress Toward Remedial Goals and Modification of the Corrective Action Plan if Necessary

The data collected during implementation of the CAP must be evaluated by the owner/operator and submitted to DEQ so that DEQ can determine whether the CAP is progressing as anticipated. Modifications to the CAP may be necessary in some circumstances. Circumstances that might require modifying the CAP include identification of significant deviations from the remedial strategy or unacceptable risk levels to receptors, by either DEQ or the owner/operator. Modification of the CAP also might be required if the data indicate that site cleanup is not progressing at the rate anticipated. In these cases, appropriate modifications to the CAP should be considered and an amended CAP should be submitted to DEQ for approval The specific modifications to the CAP that are needed will vary from site to site.

1.1.11 Site Closure with a Corrective Action Plan

The primary objective of the CAP at any site is to ensure the long-term protection of human health and the environment, taking into consideration the current conditions at the site and conditions that are reasonable to expect in the future. When the regulatory obligations specified in the DEQ-approved CAP have been achieved, the site is eligible for closure. Closure typically involves the owner/operator submitting documentation that all the work specified in the CAP has been completed and all remedial action goals have been achieved accompanied with a request for site closure.

1.1.12 Certification by a Registered Professional

If work is performed that the State of Idaho requires a professional geologist or professional engineer (Idaho Code, Title 54, Chapters 12 and 28) to perform, the owner/operator shall employ the use of, and obtain certification from, a professional geologist or professional engineer registered in Idaho for that work.

Section 2. Site Discovery and Initial Steps

2.1 Determining Imminent Threats

The first step, once an impacted site has been identified or a release is known to have happened, is to determine whether contamination poses any imminent threat to human health or the environment. If so, abatement measures must be completed before any other activities. Examples of abatement measures include taking action to prevent further release into the environment, providing an alternate water supply if drinking water supplies are impacted, evacuating residents/commercial workers if they are or could be exposed to vapors at high concentrations, installing booms on surface waterbodies that have a sheen, or ventilating utility facilities where vapors are present. If there is an imminent threat, or uncertainty regarding potential threats, associated with a release, call DEQ or STATECOMM at 1-800-632-8000 or (208) 846-7610. Releases that do not pose an imminent threat do not have to be reported to STATECOMM, but do have to be reported to DEQ. Owner/operators shall follow the Petroleum Release Reporting, Release Response and Initial Abatement Measures as provided in IDAPA 58.01.02.851 and 852.

2.2 Initial Site Characterization

2.2.1 Site Characterization Introduction

Within the RE process, initial site characterization is performed after any necessary emergency response actions are completed. The overall objective of the initial site characterization is, at a minimum, to identify the maximum chemical concentrations on the site in each of the affected media. These maximum concentrations are then compared with screening level criteria to determine the need for any further action.

A brief description of the initial site characterization process is presented below.

2.2.2 Site Description and Adjacent Land Use

The owner/operator should conduct a thorough site reconnaissance and a historical review of site operations to identify source(s) of contamination on site. Sources may be identified based on knowledge of a known or documented release; location of certain structures that typically represent a contamination source such as underground storage tanks (USTs), pipes, pumps, etc.; interviews with current and former site employees who may have knowledge of source areas.

In addition to identifying sources, the owner/operator should collect data related to historic, current, and future land use on and adjacent to the site. A chronology of relevant site activities is often useful in understanding the site.

Based on this information, the owner/operator should identify the type of petroleum that may have been released at the site. Data collected during initial site characterization should, at a minimum, satisfy the following requirements:

- Quality Assurance/Quality Control (QA/QC) measures recommended by the United States Environmental Protection Agency (EPA) have been met,
- Analyte quantitation limits (the minimum amount that can be detected by the laboratory), where feasible, do not exceed screening levels,

- Appropriate petroleum COI have been identified and included for analysis,
- Source areas have been adequately characterized to identify the maximum concentration, and
- Analytical methods used are appropriate for petroleum COI at the site.

2.2.3 Soil Source Characterization

The owner/operator should collect soil data representative of the release's maximum concentration of petroleum COI. The exact number of samples, the analytical methods used, and the specific technology used to collect data will vary among sites. It is recommended, but not required, that the owner/operator develop a work plan and have it reviewed and approved by DEQ before beginning the work. At a minimum, the owner/operator should verbally confer with DEQ before collecting any data.

The overall intent of initial site characterization is to identify maximum concentrations of petroleum COI. However, for sites that will likely require further characterization, it may be efficient and cost-effective to collect additional data at this stage of the evaluation. Additional data may be used to identify the nature and extent of contamination and potential for exposure. For example, if contamination is suspected to exist in both surficial and subsurface soil zones, samples representing maximum concentrations in both zones should be collected.

2.2.4 Groundwater Source Characterization

In the initial site characterization, if there is evidence of possible groundwater impact from the site release, the owner/operator should collect groundwater samples below or immediately adjacent to the source. For sites with a very localized source, it may be sufficient to collect only one groundwater sample using a temporary well. Sites with multiple sources may require multiple wells and samples. For sites that will require further characterization, it may be more efficient and cost-effective to install at least three monitoring wells so the magnitude and the direction of groundwater flow can also be established.

2.2.5 Documentation of Initial Site Characterization

The owner/operator should document the initial site characterization results in a brief report that is submitted to DEQ. The chemical data collected should initially be evaluated using the screening levels as discussed in Section 3, all of which should be described in this report. The report should discuss:

- Site history,
- Site description,
- Current site use,
- Sources and petroleum COI identified at the site,
- Methods used to collect and analyze soil samples,
- Locations of all samples (identified on a site map), including sample depths,
- Results from soil chemical data analyses,
- Methods used to collect and analyze groundwater samples,
- Location, construction, and lithology of all wells,
- Results of groundwater chemical data analyses,
- Other site hydrogeological test data results, and
- QA/QC information.

Section 3. Screening Level Evaluation

Data collected during the initial site characterization is typically initially evaluated using screening levels. This evaluation is intended to achieve the following objectives of the screening level evaluation:

- Demonstrate that the site or portions of the site do not pose a threat to human health and hence does not require any further evaluation, and
- Identify areas of the site that need further evaluation.

These objectives are achieved by comparing the maximum site concentrations with the screening level values.

3.1 Screening Levels

The screening levels for the petroleum COI in the Rule have been developed by DEQ and are included in Table 2. The screening levels are risk-based target concentrations developed with the following:

- the assumption that receptors will be residential,
- conservative input parameter values,
- an acceptable target risk of 10^{-6}, and
- a hazard quotient (HQ) of 1.

Specific exposure factors and models used to develop screening levels are presented in Appendices A and E. Screening levels are the lowest target concentrations for the following exposure pathways and ROE for soil, soil vapor, and groundwater.

Specifically, screening levels for soil are the lowest of the following concentrations:

- Surficial and subsurface soil concentrations protective of exposure via groundwater ingestion at maximum contaminant levels (MCLs) or risk-based concentrations at the downgradient edge of the source or
- Subsurface soil concentrations protective of exposure via indoor inhalation of vapors emanating from soil for a residential scenario, or
- Surficial soil concentrations protective of combined ingestion, dermal contact, and outdoor inhalation exposures for a residential scenario.

Screening levels for groundwater are the lowest of the following concentrations:

- MCLs for chemicals that have them or calculated values for ingestion of water in a residential scenario, or
- Groundwater concentrations protective of exposure via indoor inhalation of vapors emanating from groundwater for a residential scenario.

Screening levels for soil vapor are protective of exposure via indoor inhalation of vapors emitted from contaminated soil or groundwater. Screening levels in sub-slab and near-source soil gas are derived by applying attenuation factors of 0.03, to the EPA Regional Screening Levels (RSLs) for both residential and industrial ambient air.

Table 2 lists the screening levels for unrestricted use. For comparison, Table 2 provides the risk-based concentrations in soil and groundwater for all the pathways and ROE listed above. The screening level values incorporated in the Rule are indicated in bold.

Because of the methods and assumptions used in the development of the screening levels and the current limitations of laboratory analytical methods, the calculated screening levels may be lower than the practical quantitation limit reported by a laboratory for selected chemicals. In these situations, site-specific review by DEQ will be required based on the criteria provided in Section 500 of the Rule and Appendix K.

Table 2. Screening Level Concentrations for Soil, Groundwater, and Soil Vapor

	SOIL (mg/kg)			GROUNDWATER (mg/L)		TARGET SUB-SLAB AND NEAR-SOURCE SOIL GAS CONCENTRATIONS (ug/m3)	
						Unrestricted Use	Commercial/ Industrial
CHEMICAL	Vapor Intrusion	Direct Contact	Groundwater Protection	Vapor Intrusion	Ingestion	Vapor Intrusion	Vapor Intrusion
Benzene	0.08	8.3	**0.025**	0.044	**0.005**	**12**	53
Toluene	1300	7930	**6.6**	340	**1**	**170000**	733333
Ethylbenzene	**0.25**	39	7.4	**0.05**	0.700	**37**	163
Xylenes	**27**	6100	93	**8.7**	10	**3500**	14667
Naphthalene	**0.12**	44	21	**0.07**	0.73	**2.8**	12
MTBE	2.4	340	**0.08**	6.8	**0.04**	**360**	1567
1,2-Dichloroethane	0.02	3.7	**0.013**	0.03	**0.005**	**3.6**	16
Ethylene Dibromide	0.001	0.27	**0.00014**	0.004	**0.00005**	**0.16**	0.67
Acenaphthene	NA	4470	**200**	NA	**2.2**	NA	NA
Anthracene	NA	22300	**3200**	NA	**11**	NA	NA
Benzo(a)anthracene	106	1.4	**0.68**	0.60	**0.00022**	**0.56**	6.67
Benzo(a)pyrene	NA	**0.14**	2.1	NA	**0.0002**	NA	NA
Benzo(b)fluoranthene	NA	**1.4**	2.29	NA	**0.00022**	NA	NA
Benzo(k)fluoranthene	NA	**14**	22.5	NA	**0.0022**	NA	NA
Chrysene	NA	139	**69**	NA	**0.022**	NA	NA
Fluoranthene	NA	2970	**1400**	NA	**1.5**	NA	NA
Fluorene	NA	2970	**240**	NA	**1.5**	NA	NA
Pyrene	NA	2230	**1000**	NA	**1.1**	NA	NA

Values in bold are current screening level values. Screening level values for sub-slab and near-soil gas concentration are equivalent to EPA Regional Screening Levels (EPA, 2018) for residential and industrial ambient air divided by an attenuation factor of 0.03.

NA: not applicable because the chemical does not meet EPA volatility criteria or does not have a Regional Screening Level for ambient air.

3.2 Comparison of Site Concentrations with Screening Levels

Based on the initial site characterization (discussed in Section 2), the owner/operator should identify the maximum soil and ground water petroleum COI concentrations at the site. These maximum concentrations are then compared with screening levels, obtained from Table 2.

If the maximum site concentration does not exceed the screening level for any petroleum COI in any media, the site is eligible for closure subject to other regulatory obligations (IDAPA 58.01.24.200) The owner/operator may request DEQ approval for site closure. If the maximum site concentration for any petroleum COI exceeds the screening level, the owner/operator must select one of the following options:

- Option 1: Adopt screening levels as cleanup remediation standards and develop a CAP (see Section 1).
- Option 2: Perform a more detailed, site-specific RE.

The owner/operator should clearly indicate to DEQ which option has been chosen.

3.3 Screening Level Evaluation Report

The owner/operator must submit a screening level evaluation report to DEQ if they have chosen option 1 above. The report should include, at a minimum:

- Site maps indicating land use, structures on site, locations and depths of samples, and locations of contaminant sources,
- A description of site history and activities leading to the release,
- A description of current land use adjacent to the site,
- A summary of initial site characterization results for soil and, as appropriate, groundwater,
- A discussion of data quality,
- A comparison of maximum soil and, as appropriate, groundwater concentrations with screening levels,
- A list of recommendations, and
- Laboratory reporting sheets, including QA/QC data.

Section 4. Site-Specific Risk Evaluation

Site-specific RE is needed only if the owner/operator chooses not to conduct a screening level evaluation or to use the default screening levels as the remediation standards.

Conducting a site-specific RE requires the completion of several important steps. These include developing an SCM, identifying the chemicals present in environmental media, assessing exposure and exposure pathways, assessing the toxicity of the chemicals present, characterizing human risks, and characterizing the impacts on or risks to the environment. This section describes each of these steps and also provides the suggested format for some of the deliverables (most of which are reports) that assist in developing and documenting the evaluation.

4.1 Site Conceptual Model

An SCM provides an overall understanding of the site and an SCM report can be a convenient format for compiling all the relevant data associated with a release. The SCM provides a framework for the entire project and can help identify specific data needs (the correct quality and quantity of data that will be needed). An SCM is necessary in the development of any data collection work plan and is also an important communication tool for regulators, owner/operators, and stakeholders.

In addition to basic site information (discussed in section 4.1.1), there are three key elements that should be included in the SCM. Each element will require certain types of data in order to validate the SCM. The amount of data required is typically based on site-specific considerations. The SCM is a dynamic entity that should be revisited and potentially refined any time additional data is collected for a site. The resulting SCM refinements should be incorporated, if necessary, into the RE.

The three key elements are:

- **Sources**: Contaminant source areas (nature, magnitude, and extent of release) and COI (see section 4.1.2).
- **Pathways**: Release fate and transport mechanisms, exposure pathways, and ROE (see section 4.1.3).
- **Receptors**: Characteristics of land use and likely receptors (see section 4.1.4).

More detailed information on these elements is provided below and in the sections on data requirements (section 4.2) and exposure assessment (section 4.3).

4.1.1 Site Characteristics

The following basic site characteristics should be included in the RE; each is described in the following sections:

- Site history and map,
- Ground surface conditions,

- Location of utilities on and adjacent to the site, and
- Location and description of site structures.

4.1.1.1 Site History and Map

The SCM should include a comprehensive chronology of events including remediation projects, tank removal activity, reported releases, etc. The chronology of events must be clearly and accurately documented.

All maps should be made to scale, with a bar scale and a north arrow. As appropriate, multiple site maps should be prepared to show sample collection points and locations of various site structures. A detailed facility map showing the layout of USTs, above ground storage tanks (ASTs), pipes, loading and unloading areas, sumps, paved and unpaved areas, canopy buildings, etc. should be prepared. A second facility map should be prepared to show locations of all on-site monitoring wells, water use wells, soil borings, soil vapor extraction wells, and soil excavation areas. All on-site structures should be clearly identified.

4.1.1.2 Ground Surface Conditions

Before conducting an RE, DEQ highly recommends the owner/operator and any other parties that will be involved make a site visit and walk through. It is important to document areas of the site that are paved, unpaved, landscaped, or covered with buildings. It is also highly useful to note the type, extent, slope, and general condition of the ground surface, and current land uses.

4.1.1.3 Location of Utilities on and Adjacent to the Site

Due to potential for preferential flow of contaminated groundwater and vapors into underground utility lines and conduits, a thorough documentation of the location of and potential impacts to underground utilities should be performed. Utilities may include phone lines, water lines, sanitary sewers, storm sewers, and natural gas lines. A combination of site observations, knowledge of buried utilities, and discussions with utility representatives and the site owner should reveal the utility locations.

At a minimum the following activities should be performed:

- Locate all underground utility lines and conduits within the area of known or potential soil and groundwater impact, both on site and off site, where the release may have migrated, or may migrate in the future.
- Determine the direction of flow in the utilities (water, storm water, and sewage).
- Identify utility lines/conduits on a base map that illustrates the extent of soil and groundwater impacts.
- Determine depth of utility lines/conduits relative to the depth of groundwater. Seasonal fluctuations of groundwater levels should be carefully evaluated. As appropriate, a cross-sectional diagram should be provided illustrating the depth to groundwater and the locations and depths of the lines/conduits.
- Determine any past impacts to utilities and any pertinent complaints that may have been previously filed with DEQ.

4.1.1.4 Existing Structures

The location, condition, and construction characteristics of each structure on and adjacent to the site should be described.

4.1.2 Contaminant Source Areas

This element of the SCM should include a discussion of the nature, location, timing, and magnitude of petroleum products spilled at the site. The petroleum COI should be determined. Any actions performed as a part of emergency response should be delineated and their impact on the source evaluated. The residual size of the source after any emergency or interim actions should be determined.

Knowledge about the nature, magnitude, and extent of the release is necessary to identify the petroleum source in soil and/or the groundwater at the site as well as to identify the petroleum COIs. The following information regarding a release, if available, is critical:

- Release location,
- Release quantity,
- Petroleum product released, and
- Interim corrective action measures performed.

Release-related information can be obtained by reviewing inventory records, interviewing current and past employees, and checking any spill incident reports filed with DEQ. Information related to site activities can also help identify source location and petroleum COIs.

4.1.2.1 Location of Release

The location of the release defines the source of the petroleum that is in the soil and potentially the groundwater. Likely release locations include, but are not limited to, corroded or damaged tanks, pipe bends and joints, and loading and unloading areas.

The owner/operator should review operational history to determine the likely location of the source. The assessment should focus on the identified release area; however, the exact location and timing of the spill source area may not be known. In these cases, soil and groundwater sampling should be used to identify the extent (vertical and horizontal) of residual soil and/or groundwater source. The exact number and location of necessary samples shall be determined on a site-specific basis using professional judgment. It will be important to understand the location and timing of past spills and releases in making decisions regarding assessment needs related to current releases. It is recommended, but not required, that the owner/operator consult with DEQ before conducting sampling. DEQ may be able to provide information at this point that can help the owner/operator improve the overall efficiency of sample collection or the entire RE.

4.1.2.2 Quantity of Release

The RE process does not necessarily require knowledge of the exact release quantity. However, an estimate of the amount released may help evaluate the severity of the impact and extent of contamination, and may help in planning site characterization measures. Estimation of release quantities is typically based on inventory records.

4.1.2.3 Chemicals of Interest and Spatial and Temporal Trends

This section should include a discussion of chemicals detected in each media and their spatial and temporal distribution. As appropriate, contour maps indicating concentrations of individual petroleum COIs may be useful. Graphs of petroleum COI groundwater concentrations in individual wells and concentration along the flow line (concentration vs. distance plots) may be useful as well. Based on data collected over time, it should be determined whether the chemical concentrations are stable, declining, or expanding.

Identification of specific petroleum product(s) spilled or released is important to identify the petroleum COIs. Evaluation of non-petroleum chemicals in addition to those in Subsection 800.01 (Table 1) may be required by DEQ when there is a reasonable basis based on site-specific information. A reasonable basis shall be demonstrated by DEQ when it can show documentation of releases or suspected releases of other non-petroleum chemicals. The environmental behavior (mobility, persistence, bio-degradation, and inter-media transport) of the petroleum product and its adverse environmental and human health effects depend on chemical properties and their concentrations in the petroleum product.

If a release can be identified as a single petroleum product based on a documented release, free product analysis, or location of impact (e.g., tank bottom of a particular product tank), only the COIs for that petroleum product need to be analyzed. If the product released cannot be conclusively identified, it is recommended that monitoring samples be analyzed for all petroleum COIs associated with the products suspected to have been stored at the site. Additional assessment may be required to identify the source of the release.

If previously collected data did not include all suspected site petroleum COIs, additional sampling may be necessary for petroleum COIs before an RE can be performed.

4.1.3 Pathways and Transport Mechanisms

The objective for this portion of the SCM is to describe site characteristics and mechanisms which have influenced or will influence the release, fate, and transport of chemicals of interest and to determine which exposure pathways and ROE will be most likely to occur.

4.1.3.1 Site Stratigraphy and Hydrogeology

The owner/operator should conduct a review of published literature and any investigations conducted on adjacent sites to determine regional hydrogeology, soil types, and aquifer characteristics. This evaluation should be used to determine the type and depth of aquifers in the area and whether they are confined, semi-confined, or unconfined. Regional information will help the owner/operator in efficiently collecting site-specific soil and groundwater information. The SCM should include a detailed discussion of site-specific stratigraphy and hydrogeology. Site stratigraphy should be determined based on boring logs and an adequate number of geologic cross sections.

The hydrogeologic discussion should include estimates of horizontal and vertical hydraulic gradients, seasonal variations in groundwater elevations and flow direction, and hydraulic conductivity of relevant water-bearing zones. How these characteristics may influence the fate and transport of chemicals to potential receptors should be discussed.

The survey should also locate potentially impacted surface waterbodies located within one-half (1/2) mile of the site. If a surface water body is identified, information including the type (perennial or intermittent), water flow rate, flow direction, depth of water, width or surface area of the water body, and water use should be provided. The location of the water body must be indicated on an area map.

4.1.3.2 Complete Exposure Pathways and Routes of Exposure

A complete exposure pathway involves a source of petroleum products, release and transport mechanisms, ROE, and potential receptors. The definition of complete exposure pathways starts with knowledge of the release, petroleum COIs, and site physical conditions (described above), then combines these with assumptions about land use and likely receptors. Exposure pathways and ROE are described and discussed in more detail in section 4.3.3.

The SCM should identify each of these components in its descriptions of exposure pathways. One example of a common exposure pathway would be leaching of petroleum chemicals from a gasoline release in soils (release) to the groundwater with subsequent transport (fate and transport) to a residential well where water is extracted for drinking water and ingested by residents (land use and likely receptors). Another would be volatilization of petroleum chemical vapors from a soil source with subsequent transport through the soil and into the air in an occupied structure where they are inhaled.

Another part of defining the complete or potentially complete exposure pathways and ROE in an SCM is identifying the locations where exposure to petroleum chemicals can occur and the media of concern at those locations. These known or potential exposure locations are commonly called exposure units. The exposure unit for each complete pathway and receptor should be described. The exposure unit may consist of a specific location such as a well or it may be an area, such as a parcel, over which receptors move. For large sites, it may be useful or necessary to subdivide the site into multiple exposure units. This may also be true at sites where impacts of the release have moved offsite.

Exposure pathways defined in the SCM are subsequently used in the exposure assessment phase of the RE, which is described in detail in section 4.3.

4.1.3.3 Protection of Groundwater

During the development of the SCM, it should be assumed groundwater may be used for drinking water. Consequently, if groundwater is not remediated to levels suitable for ingestion, the CAP must also include provisions in the final remedy for implementing limitations on activities and land uses. Such limitations are achieved through environmental covenants (activity and use limitations [AULs]) to prevent exposure via groundwater ingestion throughout the horizontal and vertical extent of the plume that has concentrations exceeding the criteria for groundwater ingestion presented in Table 2.

The SCM, as it relates to the use of groundwater, should include characterization and evaluation of the following groundwater aspects.

- The current and historical use of the groundwater for drinking water or irrigation.

- The location and approved use of existing groundwater wells within a one-half (1/2) mile radius from the release point at the contaminated site.
- The potential for communication between the impacted groundwater and other groundwater-bearing zones or surface water.
- The location of delineated source water protection areas for public drinking water systems.

This information, along with other data collected for the evaluation, will be used to determine if groundwater ingestion is a complete exposure pathway in the SCM, and will guide the selection and use of appropriate remedial target concentrations, measures, timeframes, and compliance conditions.

A water well survey should be conducted to identify all water use wells within a one-half (1/2) mile radius. Information sources include the U.S. Geological Survey, the Idaho Department of Water Resources (IDWR), water system operators, and local residents. If available, well characteristics including depth, water use, and screened interval should be documented. It is necessary to identify any dewatering wells located within a 1,000-foot radius of the site (or greater if the groundwater plume is extensive).

Land use considerations include, but are not limited to:

- Current zoning and land use. Consultation with local planning and zoning officials regarding future land use planning direction and interpretation of planning and zoning policies.
- Land use development trends. Conversion of agricultural land to residential land uses requires development of drinking water sources. The proximity of these conversions to urban centers and available public drinking water supplies should be taken into account.
- Local ordinances that include agreements with IDWR governing well drilling or state-designated restrictions or specifications for constructing wells into groundwater in a locality for drinking water purposes.
- The existence of source water assessment delineations and source water protection plans and ordinances associated with public drinking water supplies.
- The availability of alternative water supplies.

4.1.4 Land Use and Receptors

This portion of the SCM describes the current and future assumptions about land use as they relate to identifying potential receptors. The identification of land uses includes both the site of the release as well as adjacent properties which may be impacted by the release.

4.1.4.1 Land Use

Evaluating current and reasonably likely future land uses at and adjacent to the release site is a critical component when determining potential exposure points, exposure pathways, receptors, and exposure factors during the RE process and when determining cleanup concentrations.

Residential land use generally requires lower target concentrations. Cleanup to residential standards will usually allow unrestricted land use. Whenever assumed land use is other than

residential and cleanup is not to residential standards, DEQ may require that an AUL be imposed on the property through the use of an environmental covenant.

Residential land uses include use by sensitive subpopulations. Examples of land uses with sensitive subpopulations include but are not limited to hospitals, nursing homes, schools, childcare centers, farms with houses, and any other areas/structures with sensitive human activity.

The owner/operator should submit to DEQ illustrated land use maps clearly identifying current land uses at the site and the adjacent properties. One map should clearly show the area within one-half (1/2) mile of the known or likely extent of contamination. At sites where there is likelihood that the extent of impacts may be greater, due to the magnitude of the spill or other site-specific conditions, a land use map covering the entire impacted and potentially impacted area is necessary. A walking land use survey should be conducted for the area within a 500-foot radius of the source, with an emphasis on the down-gradient direction and potential offsite impacts. The survey should clearly identify the following: schools, hospitals, residences (apartments, single-family homes, and others), day care centers, nursing homes, and types of businesses. In addition to this survey, efforts should be made to identify structures with basements (which may enhance the transport of contamination) in areas in closer proximity to the source and where site conditions warrant it, such as where shallow groundwater or non-aqueous phase liquid (NAPL) is present. The map should also identify surface water bodies, parks, recreational areas, wildlife sanctuaries, wetlands, and agricultural areas.

Current land use refers to land use as it exists today and that can be readily determined by a site visit. A site visit should identify homes, playgrounds, parks, businesses, industries, or other land uses at, and in close proximity of, the release site. As appropriate, state or local zoning boards; the U.S. Census Bureau; zoning, topographic, land use, housing and other types of maps; and aerial photographs can provide information for determining land use.

Undeveloped land should be characterized by the most likely future use of that property, considering current zoning restrictions. If the undeveloped parcel is located in a predominantly nonresidential area, nonresidential classification may be appropriate. However, if the setting is more rural or land-use is mixed, the undeveloped land should be considered residential unless the owner/operator develops and implements an AUL as a part of a DEQ-approved CAP.

The exposures to be evaluated in an RE depend upon the activities that could occur under likely future uses of land and groundwater at the site. The future groundwater use should be consistent with the most likely future land use.

For example, consider property that is currently used as farmland. If the impacted farmland includes a residence, the current land use is residential. However, if the owner/operator provides information establishing clear plans to develop the residence into a nonresidential building in the near future, the likely future use may be evaluated as nonresidential.

While evaluating likely future land use(s) presents uncertainties, DEQ has identified certain factors that assist in this evaluation. These factors include, but are not limited to, local zoning ordinances; knowledge of current land use and changing land use patterns; zoning decisions; community master plans; interviews with current property owners; nonresidential appraisal

reports; proximity to wetlands, critical habitat, and other environmentally sensitive areas, such as source water protection areas; and the use of remedial action institutional controls at a site.

Assumed future land use designations other than residential must be justified and there should be a high likelihood that the land will be used for those purposes. Absent such a justification, DEQ will consider the residential land use scenario as the default future land use.

Site characterization will include a determination of the on-site and off-site areas of impact. These areas are considered in determining the pathway-specific exposure units for each type of receptor. Exposure units are discussed in more detail in section 4.3 and Appendix I.

4.1.4.2 Receptors

The objective of the RE is to quantify the adverse health effects to current and potential future receptors both onsite and offsite. For simplification, the following definitions should be used:

- On-Site –The area located within the legal property boundaries within which the source of the release is located. This includes soil, groundwater, surface water, and air within those boundaries. Adjacent property purchased subsequent to the release will be considered off-site.
- Off-Site –The areas of concern located outside the boundaries of the property where the release source is located. This includes soil, groundwater, surface water, and air located outside the property boundaries.

In a residential exposure scenario, risk is evaluated for either a child receptor or a composite receptor, depending on the specific exposure route, and whether the petroleum COI is noncarcinogenic, carcinogenic, or carcinogenic with a mutagenic mode of action. The composite receptor is based on an exposure duration of 30 years, and for some chemicals and exposure routes risk calculations incorporate modifications based on exposure occurring at different life stages.

For land uses other than residential, a typical receptor might be a commercial or industrial worker where the risk to adults is considered. Finally, under a construction scenario adult construction workers are considered. If warranted by site-specific conditions, other types of receptors may need to be defined and evaluated.

4.1.4.3 Ecological Risk Considerations

In addition to identifying potential impacts to human receptors the SCM should also attempt to identify potential pathways by which sensitive habitats, such as wetlands, surface water bodies, or other ecologically significant environments near the site, may be impacted by the release where wildlife may be the potential receptors.

Threatened and endangered species that may be exposed to site-specific chemicals should be identified. Note that within the RE process, protection of surface waters and streams is independent of ecological RE. As appropriate, a walking survey in the vicinity of the site may be necessary to identify ecological receptors.

Contact DEQ to obtain additional guidance on these issues.

4.2 Data Requirements and Evaluation

Once the SCM has been developed, an evaluation of data collection needs, data quality needs, and data collection methodology should be conducted. Depending on the amount and complexity of the proposed data collection effort, a work plan may be needed to guide the data collection process. The suggested contents of this work plan are discussed in section 4.7.

This section describes general data collection objectives and requirements for the RE process. This includes the general QA/QC considerations to help ensure the data collected is of sufficient quality and quantity to meet desired objectives, the categories of data necessary to meet these objectives, and data collection techniques.

Data collection objectives for RE include, but are not limited to:

- Accurately characterize the magnitude, nature, and extent of contamination, including the characterization of petroleum chemical concentrations for all impacted media, as appropriate,
- Allow the development and/or validation of an accurate SCM, and
- Develop sound estimates of risks posed by the release.

4.2.1 Data Collection Planning

Sound data collection planning involves a careful review of all available site information and data for its suitability in the RE. This process, in the context of the SCM, should identify any data gaps with the goal of determining the types, locations, quality, and numbers of samples or measurements needed.

Depending on what stage of the RE process is in for a given site, the relative importance of each objective described above will vary and specific data requirements will also vary. The goal of data collection for RE is to efficiently reduce uncertainty in those areas that contribute the most to potential or actual risk and for which the greatest uncertainty exists.

For example, it may be determined through the SCM that vapor intrusion represents the largest potential source of risk at a site, but little is known about subsurface conditions which may impact exposure point concentrations and only soil or groundwater data are available. In order to more realistically model this pathway, it may be most effective to better characterize subsurface stratigraphy and properties, document the conditions supporting biodegradation, and collect soil vapor data.

At many impacted sites, data collection efforts may have been conducted multiple times over an extended period of time. For example, interim corrective action measures may have been undertaken prior to planning for the RE. Soil and groundwater data collected prior to such activities may not be representative of current conditions and generally should not be used in RE. At such sites, collection of additional soil and groundwater concentration data may be needed after completion of interim corrective measures.

The exact number of samples required is a site-specific decision based on the balance between cost and representativeness and requires professional judgment and expertise. Numerous tools are available to assist in estimating the number of samples required for statistical analysis, but

none provide a definitive number and statistical analysis may not be practical in many cases. These tools include, but are not limited to, data quality objectives (DQO) and statistical and geo-statistical evaluation. Selected references to assist in developing and completing sound data collection efforts are listed in section 7.2.

4.2.2 Quality Assurance/Quality Control Considerations

The RE process relies on site-specific data to make decisions related to the magnitude of site risk, nature and extent of remedial activity, and site-closure. Thus it is very important that data be reliable, representative, complete, and of known quality.

In order to assure the data will be of appropriate quality, QA/QC activities must be applied to all environmental data collection activities throughout the RE process (site characterization, risk evaluation, remediation implementation, and monitoring).

Elements of QA/QC include:

- Using approved methodologies to collect data,
- Decontaminating field equipment as appropriate,
- Using EPA approved methods for laboratory analysis, and
- Including QA/QC samples, such as duplicates, equipment blanks, trip blanks, etc.

While the level of QA/QC applied to data collection efforts will vary (depending on factors such as site complexity, size of the release, and the immediacy of the response) all the elements of QA/QC described above that were used during a given data collection effort should be provided to DEQ when reporting the results of environmental sampling. This will allow an adequate review of the quality of the data used in the analysis.

If a work plan is submitted to DEQ for approval, it should include a QAPP. The QAPP integrates the appropriate technical and quality aspects of a project, including planning, implementation, and assessment. The purpose of the QAPP is to document planning for the collection of environmental data and to provide a project-specific "blueprint" for obtaining the type and quality of data needed for a specific decision or use. The QAPP documents the QA/QC procedures applied to various aspects of the project to assure that the data obtained are of the type and quality required.

The EPA has developed guidance for the development of QAPPs which can be obtained at: *http://www.epa.gov/quality/qs-docs/g5-final.pdf.*

To further assist in the development of a QAPP, DEQ has also developed an abbreviated QAPP template. The purpose of the template is to provide the user with an annotated outline format of a QAPP with all the required elements. From there, it is a simple matter to fill in appropriate site-specific information applicable to each element. The QAPP template is reproduced in Appendix L. This template is periodically updated. Contact DEQ for the latest version.

Documentation of all QA/QC efforts implemented during data collection, analysis, and reporting phases is important to data users, who can then consider the impact of these control efforts on data quality.

The QAPP is implemented during the data collection process. Problems can be identified and corrected at this stage. The impact of field and laboratory techniques and sampling and analysis conditions on data quality are determined using field and laboratory QC samples and periodic audits. Oversight and corrective action can prevent improper procedures or techniques from continuing.

Data verification, validation, and assessment should be performed to validate data quality and assess data quality and usability. Data verification and validation is particularly dependent on compliance with field and laboratory procedures for sample collection, identification, handling, preservation, chain of custody management, shipping, analysis, and reporting.

EPA provides several guidance documents to assist in performing data verification and validation (EPA, 1999; EPA, 2002a). The EPA Contract Laboratory Program National Functional Guidelines for Organic Data Review (EPA, 1999) provides guidance on data verification and validation of contract laboratory program (CLP) data, but may also be used as guidance for non-CLP data. EPA 2002a provides more generic guidance on conducting these tasks.

4.2.3 Documentation of the Data Collected

Once data have been collected, a field investigation report should be prepared and include:

- Dates when data were collected and names of individuals who collected the data.
- A list of data collected and reference to any work plan that may have been followed.
- All data collected, clearly tabulated, and contoured (if necessary),
- All boring logs and relevant cross-sections, where appropriate, to depict site stratigraphy,
- All QA/QC data, laboratory results, data validation and verification, assessment of data usability, and chain of custody forms,
- Contour maps of groundwater potentiometric surface indicating the predominant direction of groundwater flow, and
- A discussion of the SCM.

4.2.4 Data Collection Methods

The common categories of data that are the focus of data collection efforts for RE include:

- Vadose zone soil characteristics,
- Saturated zone characteristics, and
- Distribution of petroleum COIs in soil, soil vapor, groundwater, and surface water bodies.

DEQ has developed default values for many of the vadose and saturated zone characteristics that affect the fate and transport of petroleum COIs. These values are presented in Appendix B. For site-specific REs, these default values can be used or site-specific values can be established. This appendix describes typical collection methods for those properties of the vadose zone and saturated zone important for RE. It also addresses the collection of chemical concentration data from these media.

4.2.5 Vadose Zone Soil Characteristics

The vadose zone or unsaturated zone soil is the media through which petroleum COIs can migrate to the groundwater and vapors can move upward to the surface and into an enclosed space. Thus, characteristics of vadose zone soils have considerable impact on risk estimates and target concentration calculations. Relevant vadose zone characteristics include:

- Vadose zone thickness and depth to groundwater,
- Bulk density,
- Porosity,
- Water and air content, and
- Fractional organic carbon content.

In addition to parameters mentioned above, additional site-specific, pathway-specific parameters that may be valuable to measure include:

- Vapor permeability, effective diffusion coefficient, and building characteristics where indoor inhalation is a potentially complete pathway, and
- Infiltration rates for developing a detailed evaluation of the potential for leaching to groundwater.

4.2.5.1 Thickness of Vadose Zone and Depth to Groundwater

Vadose zone thickness is determined from boring logs. This thickness is the distance from the ground surface to the depth at which the water table is encountered, less capillary fringe thickness.

Depth to groundwater is used in estimating vapor emissions from groundwater. For indoor inhalation, depth to groundwater below the "floor" of an existing structure of concern or the most likely location of a future structure should be used.

For sites with considerable seasonal fluctuation in water table level, depending on the data available and the nature of the fluctuations, a yearly average depth or a time-weighted depth may be used. The vadose zone depth that is estimated should also form the basis for the selection of soil samples to be used in evaluation of subsurface soil vapor emissions to indoor air. Shallower water table depths often result in groundwater target levels set at lower concentrations to be protective of inhalation pathways.

4.2.5.2 Porosity

Porosity is the ratio of the volume of voids to the total undisturbed field volume of soil. Many laboratories use dry bulk density and specific gravity data to determine porosity using the following equation:

$$n = 1 - \rho_b / \rho_s \qquad (4\text{-}1)$$

where,

n = porosity (cubic centimeter per cubic centimeter [cc/cc])

ρ_b = dry bulk density (grams per cubic centimeter [gm/cc])

ρ_s = specific gravity or particle density (gm/cc)

Dry bulk density is the dry weight of a soil sample divided by the field volume of the soil sample. An accurate measurement of bulk density requires determining the dry weight and volume of an undisturbed sample. This method involves collecting a core of known volume, using a thin-walled sampler, such as a Shelby tube or similar coring device, to minimize disturbance of the sample, and transporting the core to a laboratory for analysis. This method is described in American Society for Testing and Materials (ASTM) Method D2937-00, Standard Test Method for Density of Soil in Place by the Drive-Cylinder Method (ASTM, 2000a).

The Standard Test Method for Specific Gravity of Soil, ASTM Method D854-00 (ASTM, 2002), may be used to determine specific gravity. If specific gravity is not assessed, then 2.65 gm/cc can be assumed as the particle density.

Consideration should be given to collecting multiple samples if multiple lithologies are present that might affect COI transport.

If site-specific values of porosity are not available, it should be estimated based on values provided in an appropriate literature source.

4.2.5.3 Volumetric Water Content/Moisture Content

Volumetric water content is the ratio of water volume to the total soil volume. The ASTM Method D2216-98, Standard Test Method for Laboratory Determination of Water [Moisture] Content of Soil and Rock by Mass (ASTM, 1998) is a gravimetric oven-drying method; however, the water content value used in most models is the volumetric water content.

Hence, it may be necessary to use the following equation to convert gravimetric water content to a volumetric basis:

$$\theta_{wv} = \theta_{wg} * \frac{\rho_b}{\rho_l} \qquad (4\text{-}2)$$

where,

θ_{wv} = volumetric water content (cc water/cc soil)

θ_{wg} = gravimetric water content, typically reported by the laboratory (gm of water/gm of soil)

ρ_b = dry bulk density (gm of dry soil/cc of soil)

ρ_l = density of water (gm/cc)

Volumetric water content can also be measured in the field through the use of a variety of instruments such as a neutron probe, time domain reflectometer, or gypsum block sensors. For more information on these methods, see Part VII of Wilson et al. (2000).

4.2.5.4 Fractional Organic Carbon Content in Soil

Fractional organic carbon content is the organic carbon weight in the soil divided by soil weight and is expressed either as a ratio or as a percent. The Walkley Black Method (Page et al., 1982)

is a chemical oxidation method (rapid dichromatic oxidation) while ASTM Method 2974-00 is a furnace method (ASTM, 2000b) for determining fractional organic carbon content in soil. Results are usually reported as percent organic carbon content. The reported value can be converted to a fraction by dividing by 100.

If measurements of total organic matter content are available, they should be divided by 1.724 to estimate the fractional organic carbon content. This adjusts for the portion of soil organic matter that is actually carbon. Typically, total organic carbon content is estimated using ASTM Method 2974-00. Organic carbon content should be determined using soil samples not impacted by the release.

4.2.6 Saturated Zone Characteristics

Petroleum COIs that reach the water table typically travel horizontally through the saturated zone. However, if a vertical gradient is present, chemicals may also move vertically in the direction of the gradient. Saturated zone characteristics that determine the travel time and direction for the petroleum COIs include:

- Horizontal hydraulic conductivity,
- Horizontal and vertical hydraulic gradients (magnitude and direction), and
- Saturated zone soil characteristics (fractional organic carbon content and porosity).

4.2.6.1 Hydraulic Conductivity

Hydraulic conductivity is the discharge of water per unit area per unit hydraulic gradient in a subsurface formation. Estimates of site-specific hydraulic conductivity can be obtained by conducting aquifer tests such as slug or pump tests. Data gathered during the tests are then analyzed using appropriate methods. Slug tests are easier to conduct than pump tests, generate no wastewater for treatment, and may be more appropriate for low-permeability formations. The primary disadvantages are the small aquifer volume that is explored, resulting in the need to conduct multiple tests across the site. Properly conducted pump tests will often provide better estimates of hydraulic conductivity. The simplest pump tests are single-well short-duration (2 to 4 hours) tests. The best pump tests employ a pumping well and multiple observation wells and are of longer duration (12 hours or more). These tests will identify boundary effects. Regardless of the type of test conducted, different methods of data analysis will often yield different estimates of hydraulic conductivity. ASTM Method D4043 provides guidance on the selection of aquifer test methods (ASTM, 1996).

In the absence of these tests, estimates of hydraulic conductivity may be obtained from literature, with values corresponding to the type of soil in the saturated zone, using empirical equations based on the grain size distribution of the porous formation, or they may use specific capacity data from well logs of wells in the vicinity of the site that are representative of the aquifer being investigated. In either case, adequate references and justification for the value chosen should be provided.

4.2.6.2 Hydraulic Gradient

The magnitude and direction of the hydraulic gradient is estimated by comparing water levels measured in the monitoring wells. Typically, water level contour maps are prepared based on

measured data using a computer program or manual calculations along with professional judgment. Calculations done using automated procedures should be spot-checked with hand calculations. Three wells or more are needed to adequately estimate the direction of flow and magnitude of the gradient. When drawing the contour maps, care should be taken to ensure that the measurements used are from monitoring wells that are screened in the same interval or hydrologic unit.

For sites that have seasonal variation in hydraulic gradient, estimate the average hydraulic gradient for each season. Consideration should also be given to determining any vertical gradients. This requires a comparison of adjacent water levels in wells screened in different intervals.

In areas where the shallow aquifer has been impacted and a deeper aquifer is used for drinking water, the vertical gradient should be determined. When drilling deep wells, care should be taken to avoid cross contamination.

4.2.6.3 Saturated Zone Soil Characteristics

In addition to hydraulic conductivity, other important saturated zone soil characteristics include fractional organic carbon content, porosity, and bulk density. These parameters are required to quantify the movement of chemicals within the saturated zone. The laboratory methods to measure these parameters were discussed in section 4.2.5.

4.2.7 Indicators of Biodegradation

Biodegradation of petroleum chemicals occurs in all media (soil, soil vapor, groundwater). Depending on the media, different indicators (chemical concentrations, geochemical indicators, microorganisms, oxygen, and carbon dioxide) can be measured at a site to demonstrate the occurrence of biodegradation of these organic substances.

When evaluating the potential for biodegradation in groundwater, these indicators are commonly classified into three groups: primary, secondary, and tertiary lines of evidence. Data collected under each line of evidence can be evaluated qualitatively or quantitatively to determine the occurrence of biodegradation.

The primary line of evidence demonstrates spatial stability or a reduction in chemical concentrations at a site by evaluating measured concentrations within monitoring wells, groundwater velocity, rates of contaminant transport, and time of the release.

The secondary line of evidence refers to measurement of geochemical indicators including reduction-oxidization (REDOX) potential, dissolved oxygen, dissolved nitrates, manganese, ferrous iron, sulfate, and methane. These indicators should be measured in at least three wells located along the flow line, one of which should be located at a background or up-gradient location, one within the plume near the source, and one within the plume down-gradient from the source.

The tertiary line of evidence involves microbiological studies such as identification of types of subsurface microbial populations and microbe cell counts.

Commonly used methods to estimate biodegradation rates include mass balance analysis for expanding, stable, or shrinking plumes and plots of plume concentration vs. distance. Additional details on biodegradation for petroleum COIs in groundwater are provided in Appendix H.

When evaluating the potential for, or presence of, biodegradation in soil or soil vapor, the most common indicators used are soil vapor concentrations, oxygen, and carbon dioxide. These are commonly measured at multiple depths in the subsurface and related to a potential source. More information on evaluation of biodegradation of petroleum vapors in relation to the vapor intrusion pathway is provided in Appendix G.

4.2.8 Distribution of Petroleum Chemicals of Interest

Petroleum COI may be distributed between soil, soil vapor, groundwater, surface water, and sediments present at a release location. Knowledge of contaminant distribution entails a determination of the spatial extent and magnitude of concentrations in each of these media, where they are present.

4.2.8.1 Distribution of Petroleum Chemicals of Interest in Soil

Adequate soil concentration data are necessary to estimate risk to receptors, compare representative concentrations for each complete pathway to target levels, and define the soil source dimensions. Sufficient data should be collected to define horizontal and vertical extent of impacts. The vadose zone investigation(s) should be organized to:

- Identify the horizontal and vertical extent of soil impacts. Unless otherwise directed by DEQ, the extent of impact should be defined as those areas where petroleum COI concentrations exceed screening level concentrations.
- Identify areas of maximum concentration of petroleum COIs.
- Collect samples adequate to estimate exposure point concentrations for the potentially complete exposure pathways that have been defined based on the SCM.

To determine the spatial extent of contamination, soil borings should be drilled starting from the known or suspected source area and drilling outwards until borings with sample concentrations at or below screening levels are reached in all directions. To determine the vertical extent of contamination, soil borings should be extended to the base of petroleum impact and samples collected from surface and subsurface soil zones as explained in the following sections.

The soil analytical data should help identify the soil source area. If more than one source area is identified at a site, each source area should be evaluated separately. Once the soil source(s) is identified, source dimensions can be estimated. These dimensions are used in the computational software which accompanies the guidance and rule, along with other input parameters, to estimate risk and RATL concentrations protective of indoor inhalation and to evaluate the soil to groundwater leaching pathway. Depth to subsurface soil source (used to estimate the target concentrations) should be the depth, in the source area, from the surface to the zone where concentrations are above quantification limits. Professional judgment should be used in choosing the representative depth.

4.2.8.1.1 Surficial Soil Sampling

The RE process distinguishes between surficial soil and subsurface soil zones. Surficial soil is defined as the soil zone from the ground surface to 1 foot below ground surface. Pathways that may apply to the surficial soil zone include direct contact exposure via incidental ingestion, inhalation of vapors and particulates, dermal contact, and leaching of petroleum COIs to groundwater and surface water.

Evaluation of soil exposure pathways within the surficial soil zone requires collection of an adequate number of soil samples to estimate both maximum and representative concentrations of all potential petroleum COIs. Given the small vertical depth interval of this soil zone, close attention should be given to vertical variations in contamination. The acceptability of vertical depth-composite samples versus samples from discrete depth intervals is a site-specific decision. Criteria that influence this decision include the type of petroleum COIs, vertical extent of contamination, and areal extent of the contaminated zone. Sampling within the surficial soil zone is typically done from test pits using hand samplers such as trowels or corers.

The presence of impervious (paved) surfaces poses difficulties for sampling. In some cases, very permeable material may be located 2 inches below the pavement. Residues from the paved surface may also be present. When sampling beneath impervious surfaces, sampling should begin 2 inches or deeper below concrete or asphalt pavement. Cracked areas in impervious surfaces may represent conduits for chemical migration or leaching and should be evaluated during the selection of sampling locations.

4.2.8.1.2 Subsurface Soil Sampling

Soil below the surficial soil zone (more than one foot below ground surface) and extending to the water table is termed the subsurface soil zone. Pathways evaluated for this zone include volatilization from soil to indoor air and leaching to groundwater and surface water. Most receptors will not have direct exposure to this soil. However, some construction workers may be involved in excavation activities below the surficial soil zone and subsurface soil removed during excavation may be deposited at the surface allowing greater exposure. This possibility should be considered during the development of the SCM.

To test for indoor inhalation of vapors from subsurface soils, it is preferable to collect soil vapor data however soil data can also be used. Soil samples should be collected to characterize the complete horizontal and vertical extent of contamination. Soil moisture conditions and soil vapor permeability are also important parameters affecting soil vapor transport. If petroleum contamination exists adjacent to existing structures, additional sampling should be focused in these areas. More information on evaluation of the vapor intrusion pathway is provided in Appendix G.

To test for exposure to a construction or utility worker during excavation activities, soil samples should be collected from both surface and subsurface soil zones to depths where construction-related activities are likely to occur.

To test for leaching of petroleum COIs in soil to groundwater, it is critical to determine the thickness of the contaminated soil zone, the distance from the bottom of the contaminated zone to the water table, if any, and representative concentrations of petroleum COIs within the contaminated zone.

Soil sampling must be done in accordance with the following guidelines and procedures:

- Samples must be collected from the source area(s). Samples must be collected to determine the full horizontal and vertical extent of soil contamination. Sampling should strive to characterize any horizontal or vertical stratigraphic variation at the site that could impact petroleum COI fate and transport. Where required to fully characterize the vertical extent of contamination, borings should be extended to the water table and features such as the capillary fringe and any smear zone, if encountered, should be characterized. Vertical sampling intervals generally should not be greater than 5 feet.
- Soil borings should be logged and samples for laboratory analyses collected in accordance with current industry practice.
- All samples must be adequately preserved according to requirements of the laboratory analyses and analyzed within holding times required by each method. Sample analyses must be conducted in accordance with current, EPA Office of Solid Waste and Emergency Response SW-846 Methods, or other accepted methods.
- Adequate QA/QC procedures must be used to ensure sample quality and integrity. Section 4.2.2 contains additional information on QA/QC considerations.
- All sampling equipment must be decontaminated using current state of industry practice such as described in ASTM D-5088-90, Practice for Decontamination of Field Equipment Used At Nonradioactive Waste Sites (ASTM, 1990).
- Abandonment of boreholes that extend to the water table, which are considered wells by IDWR, should follow IDWR abandonment procedures (IDAPA 37.03.09.16). Appropriate methodology for abandoning other boreholes is described in detail in the Standard Guide for Decommissioning Ground Water Wells, Vadose Zone Monitoring Devices, Boreholes, and Other Devices for Environmental Activities, Standard Guide D5299-99 (ASTM, 1999a).

4.2.8.1.3 Subsurface Soil vapor Data

At sites where petroleum COIs in soil or groundwater are volatile and there is concern about potential indoor inhalation of vapors, it may be useful to assess soil vapor concentrations. For details about these samples, refer to Appendix G (Evaluation of the Vapor Intrusion Pathway).

4.2.8.1.4 Logging of Soil Boreholes

Each soil boring must be logged to record depths correlating with changes in lithology (with lithologic descriptions), soil vapor (e.g., photo-ionization detector) analyses, occurrence of groundwater, total depth, visual and olfactory observations, and any other pertinent data.

When a monitoring well is installed, as-built diagrams with depth to groundwater and construction details must be submitted for each well. A continuous soil profile from at least one boring with detailed lithologic descriptions may be useful. Particular emphasis should be placed on characteristics that control chemical migration and distribution, such as zones of greater or lesser permeability, changes in lithology, correlation between soil vapor concentrations and different lithologic zones, obvious areas of soil discoloration, organic content, fractures, and other lithologic characteristics.

4.2.8.2 *Distribution of Petroleum Chemicals of Interest in Groundwater*

Adequate groundwater samples should be collected to delineate the extent of free product, dissolved contaminant plumes in all directions, maximum petroleum COI concentrations, and representative concentrations based on the SCM. This sampling should take into account knowledge of the soil source and the direction of groundwater flow.

4.2.8.2.1 Groundwater Sampling

If groundwater has been impacted, temporary sampling points may be used to screen levels of groundwater impacts and to assist in determining optimal locations of permanent monitoring wells. A sufficient number of monitoring wells should be installed to identify source areas and to document petroleum COI migration and groundwater flow. The monitoring wells should be installed in accordance with current IDWR rules (IDAPA 37.03.09) and industry standards such as ASTM D 5092-95, Standard Practice for Design and Installation of Ground Water Monitoring Wells in Aquifers (ASTM, 1995b). EPA documents such as the Resource Conservation and Recovery Act (RCRA) technical guidance for groundwater monitoring (EPA, 1986, 1992a) are also useful references.

Adequate numbers of monitoring wells must be installed to sufficiently delineate the horizontal and the vertical extent of the groundwater plume. The number and location of wells should also allow a site-specific estimate of the direction of groundwater flow. Well placement and design must consider the concentration of petroleum COIs in the source area, and the occurrence of NAPL at the site.

Well casing and screen materials must be properly selected. The screen interval length should be minimized to the extent possible but should be set at least 2 to 3 feet above the expected high water table and encompass the range of expected variation in water table depth. EPA (1992) recommends screen interval lengths of 10 to 15 feet except where specific monitoring objectives or site knowledge result in other requirements. Wells must be properly developed and gauged after installation. A site survey must be conducted to establish well casing elevations. Based on the groundwater elevations, groundwater flow direction and gradient should be determined and plotted on a map.

Groundwater samples must be collected in accordance with the following guidelines and procedures:

- Monitoring wells must be purged of an adequate number of well volumes prior to collecting a sample (usually 3 to 5 volumes). Low-flow purging and sampling techniques (EPA, 2002b) may also be acceptable when included in a DEQ-approved QAPP.
- Samples must be collected using EPA approved methods and equipment.
- All samples must be adequately preserved according to the requirements of the laboratory analyses and analyzed within holding times required by each method.
- Sample analyses must be conducted in accordance with EPA Office of Solid Waste and Emergency Response SW846 Methods, or other accepted methods.
- Adequate QA/QC procedures must be used to ensure sample quality and integrity. See section 4.2.2 for additional information on QA/QC considerations. All sampling equipment must be decontaminated using current state of industry practice such as

described in ASTM D-5088-90, Practice for Decontamination of Field Equipment Used At Nonradioactive Waste Sites (ASTM, 1990).

- If the plume is not delineated in all directions, locations of new monitoring wells must be chosen based on groundwater flow direction and location of the soil source area.

4.2.8.3 Surface Water and Sediment Sampling

Appropriate samples should be collected when petroleum COI migration is known or suspected to have impacted surface water. Water samples should be collected from upstream and downstream of a groundwater discharge point. Sediment samples should be collected if the SCM indicates a potential for releases to surface water.

In places where a groundwater plume may discharge into a stream, it is necessary to estimate the discharge concentration into the stream. This can be achieved by installing one or more monitoring wells or temporary wells within the plume adjacent to the stream.

4.3 Exposure Assessment

The goals of the exposure assessment portion of the RE are to:

- Characterize the physical setting,
- Identify potentially exposed populations,
- Identify complete or potentially complete exposure pathways,
- Estimate exposure concentrations, and
- Estimate petroleum chemical intakes.

The exposure assessment uses much of the data collected in support of and assumptions contained in the SCM (described earlier in section 4.1). A graphical display of the SCM like the sample shown in Figure 2 is helpful for assessing exposure.

4.3.1 Physical Setting

Characterization of the physical setting for exposure assessment identifies those site factors which may influence the fate and transport of chemicals from the source to a receptor. These factors include climate, meteorology, geologic and hydrogeologic setting, soil types, biodegradation potential, and surface water hydrology. When these factors are considered in the context of the media from which petroleum COIs are released (surficial soils, subsurface soils, groundwater, surface water, etc.), the transport mechanisms for the petroleum COIs from each media (leaching, groundwater transport, volatilization, etc.), and the chemical concentrations and distribution of the petroleum COIs in each media, the potential for a chemical to reach a receptor can be assessed. A more thorough discussion of the data needs related to description of the physical setting can be found in section 4.1 (Site Conceptual Model).

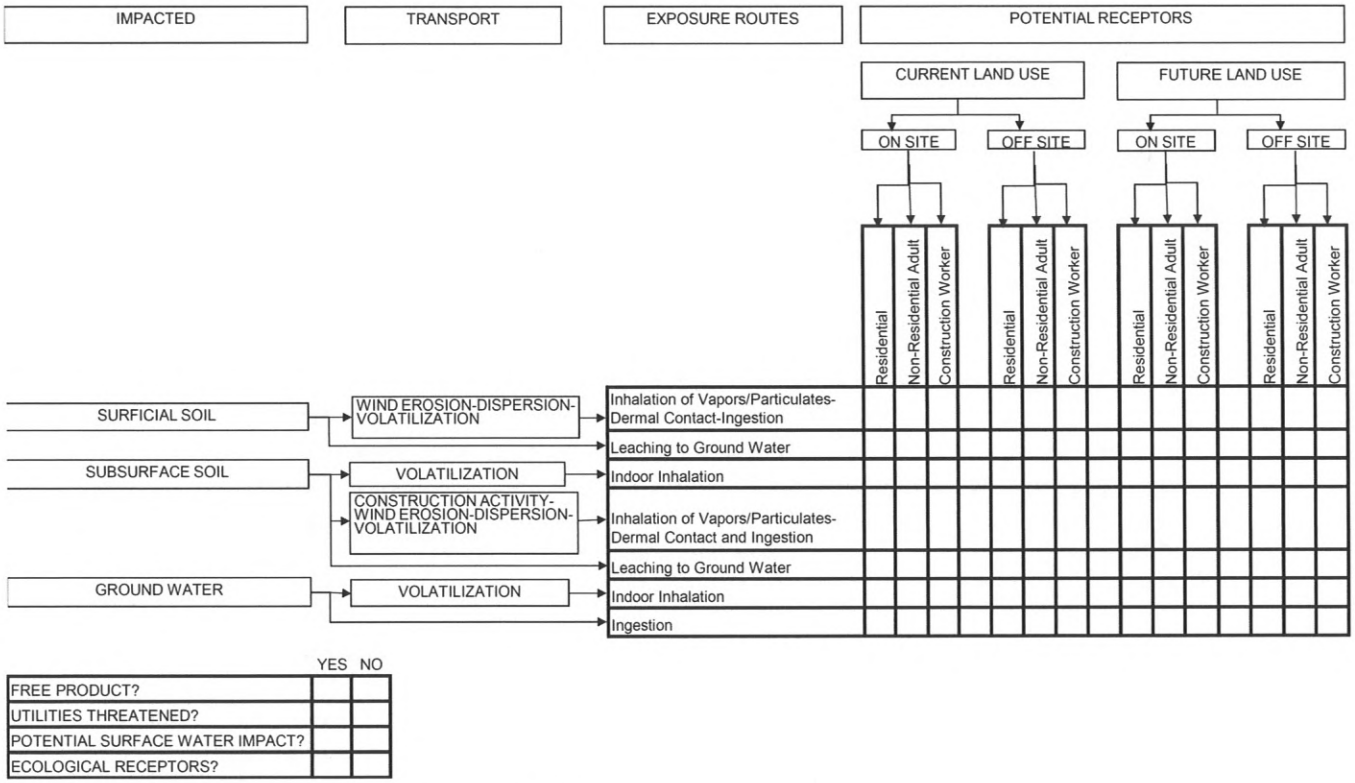


Figure 2. Sample Graphical Display of a Site Conceptual Model

4.3.2 Potentially Exposed Populations/Receptors

Potential exposure populations/receptors should be identified from the information contained in section 4.1 (Site Conceptual Model).

4.3.3 Exposure Pathways

A receptor comes in contact with petroleum COIs through a complete exposure pathway. If some but not all of the following elements are present, the pathway is incomplete. For a pathway to be complete, all of the following must be present:

1. a source of petroleum,
2. a mechanism by which the petroleum is released,
3. a transport medium through which petroleum travels from the point of release to the receptor location,
4. an ROE by which the petroleum chemical enters the receptor's body (ingestion, inhalation, or dermal contact) and
5. a potential receptor.

If the migration of petroleum chemicals to a receptor or contact by a receptor is not possible (e.g., due to formal engineering controls such as a paved site that will prevent human contact with petroleum-contaminated soil) under current and most likely future land use conditions, the site-specific petroleum COI concentrations may not pose a risk.

DEQ has identified the most commonly encountered exposure pathways for various environmental media for which an evaluation must be conducted. These pathways are discussed below. At sites where receptors, exposure pathways, or ROE other than those discussed below are important, the owner/operator must identify them and discuss their quantitative evaluation with DEQ. In some cases it may be determined that one or more of the pathways are incomplete and therefore do not need to be quantitatively evaluated. Adequate justification for exclusion of these pathways must be provided to and approved by DEQ.

4.3.3.1 Pathways for Surficial Soils (0–1 foot below ground surface)

Surficial soils are defined as soils extending from the surface to 1 foot below ground surface. For construction worker exposure, however, the applicable depth is the depth of excavation. The exposure pathways associated with impacted surficial soils include:

- Groundwater protection (leaching of petroleum chemicals from soil to groundwater with subsequent potential ingestion of groundwater),
- Surface water protection (leaching of petroleum chemicals from soil to groundwater with subsequent migration to a surface waterbody), and
- Ingestion of soil, outdoor inhalation of vapors and particulate emissions from soil, and dermal contact with soil.

4.3.3.2 Pathways for Subsurface Soils (1 foot below ground surface to the water table)

Subsurface soils are defined as soils extending from 1 foot below the ground surface to the water table. The exposure pathways associated with subsurface soils include:

- Indoor inhalation of vapor emissions from soil,
- Groundwater protection (leaching of petroleum chemicals from soil to groundwater with subsequent potential ingestion of groundwater), and
- Surface water protection (leaching of petroleum chemicals from soil to groundwater with subsequent migration to a surface waterbody).

4.3.3.3 Pathways for Groundwater

Potentially complete exposure pathways for impacted groundwater include:

- Indoor inhalation of vapor emissions from groundwater, and
- Current and/or future ingestion of water on or off site.

Appendix G describes in detail the process used to evaluate potential exposure via indoor inhalation of vapors from soil and groundwater.

4.3.3.4 Pathways for Surface Water and Sediments

Depending on the beneficial use designation of impacted surface waters, complete pathways for surface water include:

- Intentional ingestion of surface water and ingestion of fish when surface water is used as a drinking water supply, and
- Ingestion of fish from surface waters designated for recreational use.

4.3.3.5 Other Exposure Pathways

Other complete or potentially complete exposure pathways, such as ingestion of produce grown in impacted soils, ingestion of fish, contact with contaminated sediments, or use of groundwater for irrigation purposes, should be evaluated on a case-by-case basis. The owner/operator should contact DEQ for further guidance.

4.3.4 Exposure Point Concentrations

Exposure point concentrations are the average petroleum chemical concentrations to which receptors could be exposed over a specified duration within a specified geographical area. The geographical area about which a receptor moves and within which a receptor contacts contaminated media during the specified exposure duration is termed an exposure unit (EPA, 2001). The exposure unit of all receptors must be considered and described. The exposure unit, or spatial area over which a given receptor is likely to be exposed, must be established for on-site receptors as well as any off-site impacted or potentially impacted receptors and for each exposure pathway or ROE. The same site may have different exposure units for current and future use scenarios.

A detailed discussion of the estimation of exposure point concentrations and the use of exposure units for RE is provided in Appendix I. This appendix describes the sources of uncertainty which affect the estimation of exposure point concentrations, strategies to reduce this uncertainty, and methodologies to evaluate data quality. It also provides guidance on the selection of appropriate data for various ROE and appropriate statistical methods for analysis of available data.

The RE report should clearly identify specific data and methods used to estimate the exposure point concentrations, and provide a rationale for the method and data used. The following information should be provided in a table:

- Media
- ROE/pathway
- Receptor
- Data used
- Method of estimation

Table 3 shows how such a table might be constructed with examples of the type of information that would be supplied.

Table 3. Example Table Describing Derivation of Exposure Point Concentrations

Media	Route of Exposure	Receptor	Data Obtained From	Method
Surficial Soil	Direct Contact	Construction Worker	Unpaved Area	Average
Subsurface Soil	Indoor Inhalation	Commercial Worker	Building Footprint	Maximum
Groundwater	Ingestion	Residential	Source Area	Upper Confidence Limit
Soil Vapor	Indoor Inhalation	Commercial Worker	Sub-slab and near soil gas samples	Maximum

As presented in Table 3, an exposure point concentration is estimated for each complete ROE. Various methods available to estimate the exposure point concentrations are discussed in Appendix I. Use of the maximum concentration as the exposure point concentration is most conservative and also the easiest to calculate when compared with other ways of calculating exposure point concentration (average, area-weighted average, upper limit of the confidence interval around the mean). Thus, if the risk that is calculated using the maximum concentration is acceptable, considerable computational effort can be avoided.

4.3.4.1 Soil

Exposure point soil concentrations used to evaluate protection of the groundwater pathway should be calculated based on soil data collected within the source area only.

Soil data from the most recent investigation (assuming it was a comprehensive investigation) should be used. The use of older soil data (more than 4 years old), while discouraged, may be

acceptable if site conditions that would result in an increase in petroleum COI concentrations (such as a new release) have not changed. If a new release has or may have occurred, additional soil assessment activities that adequately characterize current conditions should be performed. New data collection efforts may be documented in a work plan and submitted for approval by DEQ.

4.3.4.2 Groundwater

Based on the SCM, several exposure point groundwater concentrations at a site may have to be estimated. These could include exposure point concentrations for the source area, at compliance locations, for protection of indoor inhalation on-site and off-site, and for off-site areas. Estimation of these concentrations will often require the use of fate and transport models, discussed in section 4.3.5.

In order to account for site-specific conditions such as source characteristics in relation to the depth to groundwater and the age of the release, it is typically necessary to perform multiple sampling events over time to ensure that the potential for the release to impact groundwater has been accounted for and that groundwater concentrations are representative. However, if these factors can be accounted for, it may be possible to perform an RE using data from one sampling event. If temporal data indicate significant variability, additional sampling events may be required prior to conducting the RE. Subsequent to RE, DEQ may require additional monitoring data to be collected. If recent groundwater data (less than one year old) is unavailable, current data may be necessary for the RE. The owner/operator may elect to document data collection objectives in a work plan submitted to DEQ for review and approval.

4.3.4.3 Point of Exposure and Point of Compliance

The point of exposure (POE) is the location where a receptor has or could come in contact with petroleum COIs under current and likely future conditions. A separate POE is associated with each complete exposure pathway-receptor combination identified in the SCM. For direct exposure pathways, the POE is located at the source of the petroleum COIs. For example, for the ingestion of surface soil, the POE is at the same location as the soil source. For indirect exposure pathways, the POE and the source of petroleum COIs are physically separate. For example, for the case of indoor inhalation of vapors from soil, the POE is inside the building (the breathing space) whereas the source is the soil below and adjacent to the building. The POE location for the protection of the groundwater for groundwater ingestion is discussed in section 4.3.3.3.

A point of compliance (POC) is a location where concentrations are measured to determine if compliance with remedial goals has been achieved. Concentration measurements at the POC may be in any media (e.g., soil, groundwater, soil vapor, etc.). The location of a POC may be identical to the POE or may be located between the source and the POE. In the latter case, the target concentrations at the POC are back-calculated to ensure that the concentrations at the POE do not exceed the target concentration at the POE. For example, for the protection of the groundwater pathway, the POC well may serve as a sentry well for protection of the POE. The calculated target levels for the POC are then compared to measured concentrations. POC locations may be predetermined based on program-specific requirements. Most sites, particularly those involving groundwater impacts, will have multiple POC locations.

4.3.4.4 Estimating Point of Compliance Well Concentrations

As a part of the RE process, it is necessary to designate and monitor appropriate POCs. The POCs, located onsite and/or offsite, are used to provide additional assurance that approved concentrations at a selected POE are not exceeded. Monitoring of POC locations is required, and data obtained are compared with approved RATL concentrations. Monitoring of POC locations must be continued until the concentrations stabilize below approved levels. Concentrations at the POC may also be used to determine the need for additional remedial activities.

4.3.5 Fate and Transport and Exposure Models

Different types of models or equations, uptake equations, risk equations, and fate and transport models, are required to calculate chemical intake, risk, exposure point concentrations, and target concentrations. Fate and transport models simulate the transfer of chemicals from one media (such as soil) to another (air). They also are used to simulate the movement of chemicals within a given media, such as the transport of chemicals in groundwater from a source area to a POE. They allow the estimation of concentrations at points distant from the source. A schematic and the equations for each of these models are presented in Appendix E. DEQ has selected the following default fate and transport models:

Indoor Inhalation of Volatile Emissions from Soil and Water: This pathway requires an emissions model and an indoor air-mixing model. These models are combined together and included in the Johnson and Ettinger Model (Johnson and Ettinger, 1991; EPA, 2003). The Johnson and Ettinger Model does not include the effects of attenuation by biodegradation, which may be significant for petroleum COI.

Surficial Soil Outdoor Inhalation: This pathway requires an emissions model for vapors, an emissions model for particulates, and an outdoor air-mixing model. The vapor emissions model used is based on the volatilization model developed by Jury et al. (1983) for an infinite source, the particulate emissions model is the Cowherd model (Cowherd, et al., 1985), and the outdoor air-mixing model is based on a simplified form of the Gaussian Dispersion model. These models are presented in Soil Screening Guidance: Technical Background Document (EPA, 1996a).

Leaching to Groundwater: This pathway uses a three-phase equilibrium partitioning equation to convert soil concentrations to leachate concentrations. These leachate concentrations are then used with a dilution attenuation model to simulate mixing of leachate with regional groundwater. Models used are described in Soil Screening Guidance: Technical Background Document (EPA, 1996).

Horizontal Migration in Groundwater: The Domenico steady-state analytical infinite-source model is used to quantify down-gradient migration of chemicals (Domenico, 1982, 1990). This model incorporates the processes of advection, sorption, three-dimensional dispersion, and degradation.

Alternative models may be used with prior DEQ approval.

4.3.5.1 Fate and Transport Parameters

Fate and transport parameters are necessary in the models used to estimate exposure point concentrations and compliance point concentrations for indirect pathways such as vapor intrusion and protection of groundwater. These parameters characterize the physical site properties such as depth to groundwater, soil porosity, and infiltration rate. DEQ has selected the conservative default values listed in Appendix B. Justification for these parameters is included in Appendix B. For RE, a combination of site-specific and default values for these parameters is typically used. However, the value of each parameter used, whether site-specific or default, must be justified based on site-specific conditions. Where fate and transport models other than those selected by DEQ are used, the specific fate and transport parameters required to calculate exposure point concentrations and risk may vary and have specific data collection requirements.

4.3.5.2 Physical and Chemical Properties of the Petroleum Chemicals of Interest

The development of target levels requires the selection of values for the physical and chemical properties of petroleum COIs. Values of these parameters are listed in Appendix C. To use different values, the owner/operator must provide sufficient justification to DEQ. The use of different values will be allowed only with prior DEQ approval. DEQ will update the data in Appendix C as new information becomes available.

4.3.6 Estimation of Chemical Intake

Risk evaluation requires quantifying the magnitude, frequency, and duration of exposure for the receptor populations and exposure pathways selected for analysis. Oral exposures are quantified on a dose per unit body weight basis while inhalation exposure is based on concentration in air.

4.3.6.1 Exposure Factors

In order to determine receptor and pathway-specific intake estimates, it is necessary to select values for a number of exposure parameters in the equations used to calculate intake. The selection of values for the following parameters is based on an assessment of recommendations in various guidance documents, as well as the open scientific literature. When determining these values, it is often necessary to make assumptions. Details and rationale regarding these assumptions are provided in Appendix A. Exposure assumptions for surface water related pathways are incorporated into the toxics criteria for surface water discussed in section 4.6.

Exposure factors describe the physiological and behavioral characteristics of the receptor. These factors include the following:

- Water ingestion rate,
- Body weight,
- Exposure duration for each ROE,
- Exposure frequency,
- Soil ingestion rate,
- Exposure times for indoor/outdoor inhalation,
- Dermal relative absorption factor,

- Skin surface area for dermal contact with soil,
- Soil-skin adherence factor, and
- Oral relative absorption factor.

A list of default exposure factors values selected by DEQ and justification for their choice is presented in Appendix A. Site-specific values of exposure factors, other than default values, may be used. However, the owner/operator must submit a proposal for the use of alternative values to DEQ for approval, and approval must be obtained before using alternative values for exposure factors.

4.4 Toxicity Assessment

4.4.1 Chemical-Specific Toxicological Factors

The toxicity of chemicals with carcinogenic adverse health effects is quantified using cancer slope factors (CSF) for oral and dermal ROE, or inhalation unit risk (IUR) for the inhalation route. A CSF is an upper-bound estimate of the probability of a response (developing cancer) per unit intake of a chemical over a lifetime. The IUR is the upper-bound excess cancer risk estimated to result from continuous exposure to a chemical at a concentration of 1 $\mu g/m^3$ in air.

For chemicals that cause noncarcinogenic health effects, toxicity is typically quantified by reference doses (RfD) for oral and dermal ROE, and reference concentrations (RfC) for the inhalation ROE. The RfD is an estimate of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without risk of adverse health effects during a lifetime. Since RfDs are based on oral exposure, they are modified for use in dermal exposure assessment to take account of differences between gastrointestinal and dermal absorption. The RfC is an estimate of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of adverse health effects over a lifetime.

The primary source of information for toxicity factors for the petroleum COI is the EPA RSL tables (RSL) (EPA, 2018) found at:
http://www.epa.gov/reg3hwmd/risk/human/rb-concentration_table/index.htm

Toxicity factors selected by DEQ for the petroleum COIs are presented in Appendix D.

Table 4. Default Toxicity Values for Risk Evaluation.

DEFAULT TOXICITY VALUES FOR RISK EVALUATION							
CHEMICALS	**CAS Number[a]**	**Oral Slope Factor (SF_o) (kg-day/mg)**	**Inhalation Unit Risk (IUR) (ug/m^3)**	**Oral Reference Dose (RfD_o) (mg/kg-day)**	**Inhalation Reference Concentration (RfC) (mg/m^3)**	**Oral RA[b] Factor (RAF_o)**	**Dermal RA Factor (RAF_d)**
Benzene	71-43-2	0.055	7.8E-06	0.004	0.03	1	0
Toluene	108-88-3	NA	NA	0.08	5.0	1	0
Ethylbenzene	100-41-4	0.011	2.5E-06	0.1	1.0	1	0
Total Xylenes	1330-20-7	NA	NA	0.2	0.1	1	0
Naphthalene	91-20-3	NA	3.4E-05	0.02	0.003	1	0.13
MTBE[c]	1634-04-4	0.0018	2.6E-07	NA	3.0	1	0
1,2-Dichloroethane	107-06-2	0.091	2.6E-05	0.006	0.007	1	0
Ethylene Dibromide	106-93-4	2	6.0E-04	0.009	0.009	1	0
Acenaphthene	83-32-9	NA	NA	0.06	NA	1	0.13
Anthracene	120-12-7	NA	NA	0.3	NA	1	0.13
Benz(a)anthracene	56-55-3	0.1	1.1E-04	NA	NA	1	0.13
Benzo(a)pyrene	50-32-8	1	1.1E-03	3.0E-04	NA	1	0.13
Benzo(b)fluoranthene	205-99-2	0.1	1.1E-04	NA	NA	1	0.13
Benzo(k)fluoranthene	207-08-9	0.01	1.1E-04	NA	NA	1	0.13
Chrysene	218-01-9	0.001	1.1E-05	NA	NA	1	0.13
Fluoranthene	206-44-0	NA	NA	0.04	NA	1	0.13
Fluorene	86-73-7	NA	NA	0.04	NA	1	0.13

Pyrene	129-00-0	NA	NA	0.03	NA	1	0.13
Notes:							
a Chemical Abstract Service							
b Relative Absorption							
c Methyl tert-butyl ether							
NA: No data available							
Source of toxicity values is the Regional Screening Level Summary Table (May 2018) found at the U.S. EPA Regional Screening Table website. The website is located at http://www.epa.gov/reg3hwmd/risk/human/rb-concentration_table/index.htm.							

4.4.2 Carcinogens with a Mutagenic Mode of Action

Current EPA guidance for risk assessment of carcinogens addresses the potential for increased susceptibility to cancer from exposure to carcinogens that occurs early in life (EPA, 2005a; EPA, 2005b). When information is available to establish the mode of action of a chemical for early-life and adult exposures, it may be appropriate to develop separate risk estimates for childhood exposure and exposure occurring later in life. When the mode of action cannot be established, risk estimates are based on a lifetime daily average exposure without adjustment. Currently, there is sufficient information to develop separate risk estimates only for chemicals having a mutagenic mode of action.

Specifically, when data indicate a mutagenic mode of action for a chemical, meaning that the chemical interacts directly with DNA, available studies indicate higher cancer risk for a given exposure when it occurs early in life compared to a similar exposure in adulthood. Among the petroleum chemicals of interest, the following carcinogenic chemicals are considered mutagens:

- Benzo(a)anthracene
- Benzo(a)pyrene
- Benzo(b)fluoranthene
- Benzo(k)fluoranthene
- Chrysene

For these chemicals, the following adjustments are made to risk estimates:

- For exposures between birth and two years of age, a ten-fold adjustment (multiplication factor) is applied. Toxicokinetic and toxicodynamic differences between children and adults are greatest for this age group.
- For exposures occurring to those in the age categories of two to six years of age and between six and sixteen years of age, a three-fold adjustment is applied.
- For exposures occurring after 16 years of age, no adjustment is applied.

These adjustments are combined with corresponding age-specific exposure parameters to assess cancer risk. For a standard residential exposure scenario of 30 years, a ten-fold adjustment is made for the first two years, a three-fold adjustment is made for the next fourteen years, and no adjustment is made for the final fourteen years of the exposure period.

The screening levels are based on unrestricted (residential) exposure; therefore they incorporate the adjustments described here. The effect of the adjustments will be a somewhat higher estimate of risk for a given exposure (and thus somewhat lower screening levels) compared to risk estimates without age-specific adjustment. Calculated risk estimates for residential exposure will incorporate these adjustments, but nonresidential risk estimates will not, as they are based on adult exposure.

4.5 Risk Characterization

The process of risk characterization consists of combining the intake estimates developed through the exposure assessment and toxicity information for the petroleum COIs and calculating carcinogenic risk and noncarcinogenic hazard. Calculations are made for each pathway-receptor combination and are summed to calculate a cumulative risk and a hazard index (HI) for each receptor. These risk results are then presented and discussed in a risk summary and are compared to acceptable target risk levels.

Risk and hazard calculations are completed using a standard set of risk equations provided by the EPA in their User's Guide for RSLs (EPA, 2012) and presented in Appendix E. Estimates made using these equations should be presented using one significant figure, although an additional significant digit should be carried through the supporting calculations, such as when summing risks from multiple petroleum chemicals or pathways, in order to minimize rounding errors. For example, calculated cancer risks would be presented as $1 \times 10^{-4}$and HQs or HIs would be expressed as 2, 0.7, or 0.03.

This risk-based decision-making process specifies the acceptable risk levels for both carcinogenic and noncarcinogenic health effects. For carcinogenic effects, risk is quantified using the individual excess lifetime cancer risk (IELCR) that represents an increase over background in the probability of an individual developing cancer due to exposure to specific petroleum COI through a specific exposure pathway. Since a receptor may be exposed to multiple petroleum chemicals through multiple ROEs, the acceptable risk level should account for the effect of simultaneous exposure to multiple petroleum chemicals and multiple ROEs. Overall site carcinogenic risk is calculated as the sum of the individual chemical risk estimates. The probability of a receptor getting cancer is thus the sum of the probabilities of getting cancer from exposure to each petroleum chemical through each exposure route. In this calculation there is an assumption of independence of action of the individual chemicals. If the carcinogenic actions of different petroleum chemicals are not independent there is the possibility of synergistic interaction in which case risk may be underestimated. However, information is generally not available to address this possibility.

For noncarcinogenic effects, risk is quantified using an HQ that represents the ratio of the estimated dose of a petroleum chemical for a ROE to the reference or allowable dose. When a

receptor is exposed to multiple chemicals and multiple ROEs, individual HQs are added together to estimate the HI.

For site-specific REs, the following target risk criteria must be satisfied at the POE:

Acceptable Target Risk Level: For combined exposure to all carcinogens and ROE, IELCR must be less than or equal to $1x10^{-5}$ for a receptor at a reasonable maximum exposure.

Acceptable HI: The summation of HQs for all petroleum chemicals that have noncarcinogenic health effects and ROE must be less than or equal to 1.

The target risk level and HI must be met for each current and potential future receptor at the site. If the initial calculated HI exceeds 1 further evaluation, including analysis of mode of action and target organ for each petroleum chemical, can be completed. If this analysis indicates sufficient independence of target organs and mode of action for different chemicals, it may be acceptable to present separate HQs, and/or one or more HI for subsets of the chemicals. This kind of analysis should be performed by a toxicologist.

In addition to the target risk levels, DEQ requires that MCLs, or comparable risk-based values for groundwater ingestion, be met at the POE when there is a high probability of groundwater use. When there is a low probability of groundwater use for drinking water, alternate risk-based groundwater target concentrations, based on the other potentially complete exposure pathways identified for the site, must be met at the POE. Similarly, for impacts to surface water bodies, calculated target concentrations must be met.

The risk summary should include an analysis and discussion of the sources of uncertainty so that the risk estimates can be placed in perspective. The uncertainty analysis can be qualitative or quantitative in nature. It is more important during the analysis to identify the key site-related parameters and assumptions in the SCM that contribute the most to the uncertainty than to precisely quantify the degree of uncertainty (EPA, 1989). It is typically the case that there is insufficient information available at a given site to be able to reliably quantify the uncertainty in a given risk estimate, such as through conducting a probabilistic risk assessment or sensitivity analysis. The typical sources of uncertainty that are included in the analysis include the petroleum COIs selected and their estimated site concentrations, the toxicity values used, the fate and transport models used to estimate exposure point concentrations, the exposure parameter values used in the exposure assessment, and the summing of risks from multiple pathways or petroleum chemicals.

4.6 Risk-Based Target Levels

As described in the Risk Characterization section 4.5, if the calculated risk or hazard for all petroleum COIs and complete ROE for identified potential receptors exceeds the Acceptable Target Risk or Hazard Levels and corrective action is required, then risk-based target concentrations (RATLs) to achieve these targets should be calculated. Ingestion of water is not included in this calculation. The procedure used to calculate RATLs requires chemical-specific toxicological factors, receptor-specific exposure factors, fate and transport parameters, physical and chemical properties of the petroleum COIs, and mathematical models. In calculating risk-

based target concentrations, all of these factors, properties, and models are typically the same as used for calculations of other risk-based levels.

Target concentrations should be estimated using an allocated risk process that apportions the acceptable target cumulative risk and HI among the different chemical-pathway combinations. The primary goal is to develop target concentrations in all media such that the acceptable target risk levels and hazard levels are met. There is no standard way to apportion the cumulative risk. To develop RATL concentrations, the default option selected by DEQ apportions cumulative risk and HI equally among all contributing petroleum chemical-pathway combinations such that those petroleum chemicals which contribute the greatest proportion of the total risk have the most stringent remediation standards. This methodology is described in detail, with examples, in Appendix D and is implemented in the computational software provided by DEQ to complement this guidance.

If a petroleum COI has toxicity that is based on both carcinogenic and noncarcinogenic effects, the applicable RATL for that chemical should be the lower of the two calculated allowable concentrations.

Site-specific considerations may result in an owner/operator choosing to utilize a different method for calculating target concentrations. For example, at a site having volatile and semi-volatile petroleum COIs contributing to the cumulative risk, the owner/operator may choose a technology that specifically reduces the volatile chemical's concentrations but marginally reduces the concentration of the semi-volatile chemical. A different owner/operator may choose to significantly reduce the concentration of the semi-volatile chemical and marginally reduce the concentration of the volatile chemical. The two strategies will result in different cleanup levels for each chemical; however, both will be acceptable provided cumulative risk meets the acceptable target risk criteria.

4.6.1 Developing RATL Concentrations for Groundwater and Surface Water Protection

For groundwater and surface water protection, target concentrations are calculated using somewhat different procedures, described below.

4.6.1.1 Groundwater Protection

The RATL concentrations for groundwater ingestion are equivalent to the federal MCLs or a risk-based calculated equivalent. MCLs are health-protective target concentrations promulgated by the EPA and adopted by the state of Idaho for the protection of drinking water and specified groundwater resources. For any petroleum COI that has an MCL, the RATL concentration for groundwater ingestion is equal to the MCL. For any petroleum COI that does not have an MCL, the risk-based equivalent level is calculated using the following input values and equations:

- A target risk level of $1x10^{-6}$ for carcinogenic effects and an HQ of 1 for noncarcinogenic effects,
- The residential exposure factors in Appendix A,
- The toxicity values in Appendix D, and
- Risk equations for the direct ingestion of water.

Calculations are made for residential receptors.

The RATL concentrations will apply at the POE. The POE will be the down-gradient property boundary, as it existed when the release occurred, or the nearest down-gradient location where a well exists or could be reasonably placed. Depending on site-specific conditions it is also possible to have multiple points of exposure.

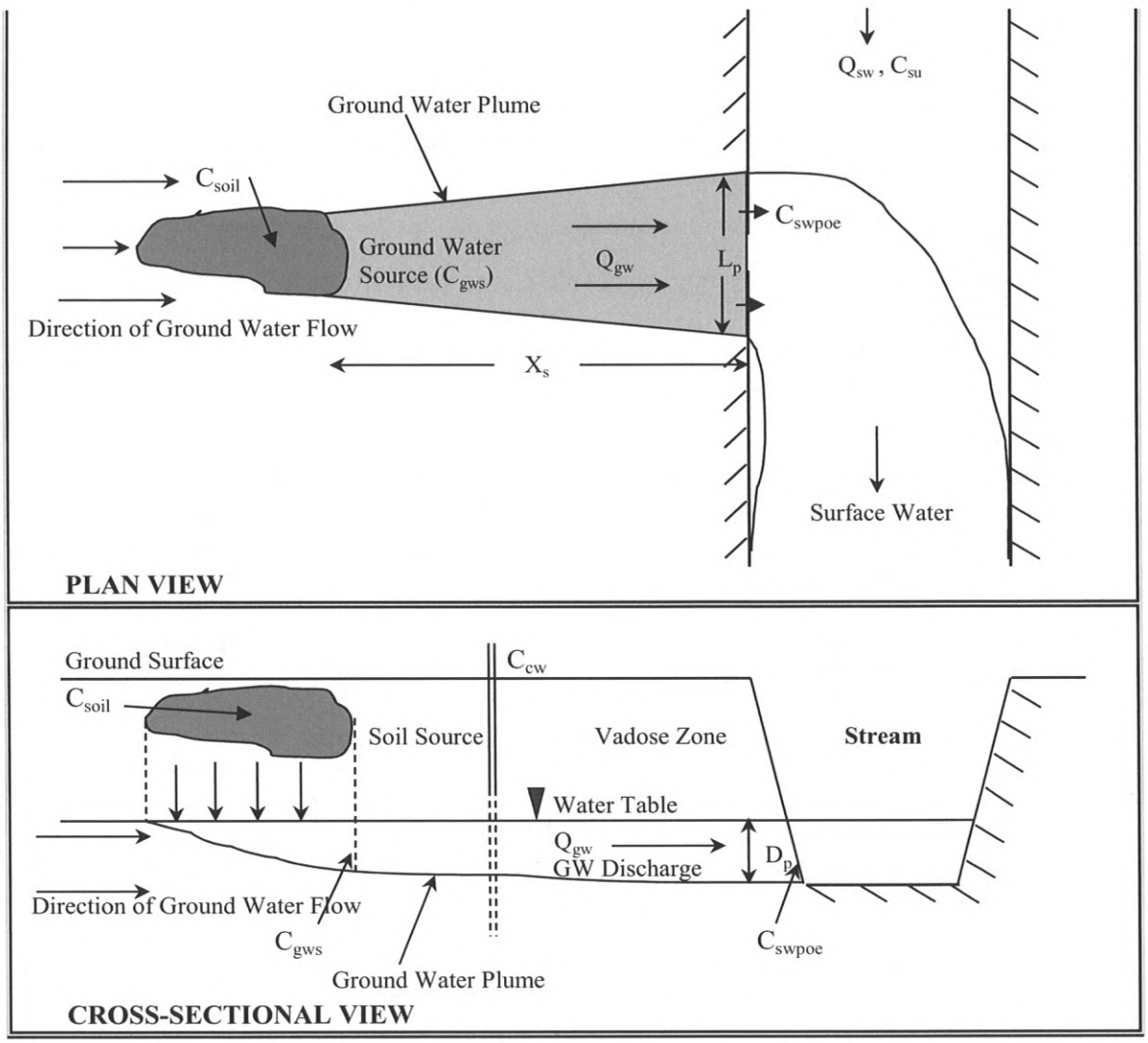
4.6.1.2 Surface Water Protection

Potential impacts to streams and other surface waterbodies from a petroleum release must be evaluated and surface water quality must be protected as per IDAPA 58.01.02 (Water Quality Standards and Wastewater Treatment Requirements). The primary receptors and ROE for potentially impacted surface waters evaluated in the RE process are described in section 4.6.1.2.1. Other ROE, such as contact with contaminated sediments or overland flow discharge, are evaluated on a case-by-case basis.

This section describes the evaluation of potential impacts to surface water via discharge of impacted groundwater to a surface waterbody. A schematic illustrating this exposure pathway is shown in Figure 3. This figure shows the relevant compliance and exposure locations and associated concentrations. Within the RE process, protection of surface waterbodies requires the owner/operator to determine or calculate the applicable surface water standards at the point where groundwater discharges into a surface waterbody (C_{swpoe}). Once the appropriate surface water standard is determined, compliance with the standard may be achieved in a number of ways. These include measuring surface water concentrations at the point of groundwater discharge, measuring groundwater concentrations at the point of discharge into the surface waterbody, or determining appropriate alternate concentrations in other media and at POC locations. Selection of alternate locations may be most appropriate for those sites where contamination has not yet reached a surface waterbody. Alternate concentrations (or RATLs) and POC locations can include:

- Source area soils (C_{soil}), or
- Compliance points in groundwater at different distances between the surface water and the source (C_{cw}) other than the point where groundwater discharges into the surface waterbody.

The owner/operator can back-calculate allowable soil (C_{soil}) and compliance well concentrations (C_{cw}) using dilution attenuation factors (DAFs). Specific equations, combining the Summer's mixing model and the Domenico analytical groundwater transport model, are presented in Appendix E. If measured concentration(s) at the soil source or the compliance well exceeds corresponding allowable concentrations, cleanup to RATL concentrations or performance of a more detailed, site-specific evaluation to refine DAFs are options.



Explanation of Symbols

Q_{sw} = Stream flow upstream of the point of ground water discharge
C_{su} = Concentration upstream of the ground water discharge
Q_{gw} = Impacted ground water discharge into the stream
C_{sw} = Allowable downstream concentration after uniform mixing
C_{swpoe} = Allowable concentration at the point of ground water discharge to the stream
C_{gws} = Allowable concentration in the ground water at the edge of the soil source
C_{soil} = Allowable soil concentration at the source protective of the stream
C_{cw} = Allowable soil concentration in ground water at different distances between the stream and the source
L_p = Width of ground water plume discharging to the stream
D_p = Thickness of ground water plume discharging to the stream
X_s = Distance from the downgradient edge of the ground water source to the stream

Figure 3. Schematic of Leachate Migration from the Soil Source to the Stream

4.6.1.2.1 Surface Water Quality Standards

The allowable concentration at the point of groundwater discharge into the surface water (C_{swpoe}), or the surface water quality standard, depends on the beneficial use designations of the surface waterbody as per IDAPA 58.01.02.100 and criteria assigned to protect those beneficial uses (IDAPA 58.01.02.200-250).

Beneficial uses include:

- Aquatic life: Cold water, salmonid spawning, seasonal cold water, warm water, or modified.
- Recreation: Primary contact or secondary contact.
- Water supply: Domestic, agricultural, or industrial.

Each beneficial use has associated numerical and narrative criteria. Numerical criteria are specified values that are not to be exceeded. For narrative criteria involving toxic substances, concentrations are not specified, but must be low enough to ensure that designated beneficial uses are not impaired. When necessary, development of numeric criteria for toxic substances is governed by IDAPA 58.01.02.210.05.

The allowable concentrations for certain toxic substances associated with these beneficial uses are tabulated in IDAPA 58.01.02.210.01.b .

4.6.2 Determination of Applicable Risk Based Levels

The calculated allowable RATL concentrations for protection of groundwater and/or surface water and those calculated for other potentially complete exposure pathways are compared to determine which media-specific concentrations will guide the cleanup. Typically, the lower of these concentrations will be selected.

Using groundwater as an example, target POE concentrations will be based on the most limiting concentrations determined from evaluation of the complete or potentially complete pathways in addition to the groundwater ingestion pathway. These pathways may include indoor inhalation of vapors volatilized from groundwater, groundwater impacts to surface water, impacts to deeper groundwater systems with the potential for use as drinking water supplies, and also incidental ingestion of and dermal exposure from irrigation water. Also included is potential impairment of other beneficial uses of groundwater such as for agricultural or industrial water supplies.

The applicable POE will be based on the location of the plume (on-site vs. off-site) and which pathway(s) and receptors are limiting with respect to risk and allowable groundwater concentration. In many cases, particularly if a plume has migrated off-site, there may be multiple POE and pathways that will need to be considered.

For example, a petroleum-sourced volatile organic compound (VOC) plume may have migrated off-site into a residential area and have the potential to discharge to a down-gradient stream. Source area groundwater concentrations on-site must be controlled such that concentrations at the POE where groundwater discharges to the stream meet applicable criteria. In addition, unless vapor intrusion has been separately addressed, such as through the use of soil vapor, residential

vapor intrusion criteria in groundwater would need to be met at the down-gradient boundary of the source property and commercial criteria for on-site POE.

4.7 Deliverables

The primary deliverables associated with conducting a site-specific RE typically include an optional work plan for the collection and evaluation of data, an optional data collection report, and the required RE report. In many cases, the results of a data collection effort are combined with the RE report. If the results of the RE report indicate the need for corrective action, a CAP must also be developed and submitted. The contents of CAPs are discussed in Section 5. This section describes the contents of a work plan.

4.7.1 Work Plan

A work plan may be desirable where extensive data collection activities or significant departures from default exposure assumptions or modeling are being proposed.

As appropriate, a work plan to fill identified data gaps may be prepared and submitted to DEQ for review. The amount of detail to be included in the work plan will vary among sites. At sites where a considerable amount of data has already been collected, the work plan may be a brief letter indicating activities to be performed to fill in the data gaps. For a complex or large site, a very detailed work plan, including the SCM, data collection methodology, analysis methods, a data QAPP, and a health and safety plan may need to be developed.

An RE work plan should address each item discussed in sections 4.7.1.1 through 4.7.1.11 as appropriate to the purpose and goals of the RE.

4.7.1.1 Purpose and Goals

The purpose and goals of the work plan should be clearly stated. If the purpose is to fill data gaps, then a listing and description of the data gaps should be provided along with an explanation as to why they constitute data gaps and how the work proposed will fill those gaps.

If the purpose of the work plan is to propose use of alternative models, exposure factors, physical and chemical properties, toxicity factors, or methods of calculating remedial target concentrations, then a rationale should be provided as to why the alternatives proposed are needed. A short description of the scope and nature of the work proposed should be provided.

4.7.1.2 Site Background

This portion of the work plan may refer to documents previously submitted to DEQ; it is not necessary to repeat the entire site background description. Reference should be made to document(s) that contain a comprehensive chronology of site investigations.

4.7.1.3 Site Conceptual Model

A concise summary of the existing SCM should be provided. In those cases where the goal of the work plan is to revise a previously completed RE, then an SCM already exists that can be referenced rather than repeated. If validation or revision of a previous SCM is necessary, those

aspects of the current SCM that are the target of the work plan should be described. Refer to section 4.1 for the suggested content of the SCM.

4.7.1.4 Exposure Factors

If alternate exposure factors values are proposed in the work plan these factors must be justified and acceptable to DEQ. The default exposure factor values are listed in Appendix A.

4.7.1.5 Physical and Chemical Properties

Owner/operators should use the default physical and chemical properties for the petroleum COIs as listed in Appendix C.

4.7.1.6 Toxicity

The Rule specifies that toxicity values for petroleum chemicals listed in Appendix D must be used in the RE.

If additional chemicals need to be included in the RE, as provided for in Section 100.02 of the Rule, their physical chemical properties and toxicity values should be obtained from the EPA RSL website (EPA, 2018).

4.7.1.7 Fate and Transport Models

If alternative models are being proposed, the work plan should include reasons for using alternative models; it should demonstrate that the proposed models will better simulate site-specific conditions, and that the sufficient site-specific data are available or will be collected to justify the use of the proposed model. Alternative models must be approved by DEQ before they are used.

4.7.1.8 Fate and Transport Parameters

Data collection may be proposed to collect site-specific values in lieu of using DEQ default values for fate and transport parameters (listed in Appendix B) used in models for the RE. The parameters for which values are to be obtained should be specified and the methodology used to obtain those values described.

DEQ accepts the use of chemical-specific biological decay rates or attenuation factors in the fate and transport models. Use of decay rates in a RE must use values supported by site-specific information. Refer to Appendices G and H for data necessary to demonstrate occurrence of natural attenuation and methods to calculate decay rates. Examples of this type of information include, but are not limited to:

- Consistent stable or decreasing concentration (above the Residential Use Screening Levels [RUSLs]) trends in properly located and constructed monitoring wells, and
- Measurements of natural attenuation parameters that provide evidence of biodegradation.

4.7.1.9 Calculating RATL Concentrations

The process of calculating target concentrations (RATLs) is described in section 4.6 and Appendix F. If a method of apportioning risk and calculating RATLs different than the DEQ

default method is desired, the proposed methodology and rationale for the choice should be described.

4.7.1.10 Methodology and Quality Control

Work plans in support of data collection efforts should describe the methodology that will be used to obtain the data and provide a clear description of the level of data quality required to meet the stated objectives, and how this data quality will be achieved and ensured.

4.7.1.11 Schedule and Deliverables

The optional work plan should include an overall project schedule and deliverables that will be submitted to DEQ. The schedule should include any agency meetings necessary during work plan implementation.

4.7.2 Implementing the Work Plan

Upon receipt of a work plan approval, the owner/operator should implement the work plan according to the schedule in the work plan. In case there are delays, it is the owner/operator's duty to inform DEQ of the delay and revised schedule. If there were deviations in the work performed from that specified in the approved work plan, DEQ should be notified of the deviations and their impact on the goals and purposes of the work plan.

Upon completion of work specified in the work plan, the owner/operator should document the results and submit them to DEQ. If the purpose of the work plan included data collection, the data collection results can be summarized in a separate data collection report or incorporated into a revised RE report.

4.7.3 Risk Evaluation Report

The RE for a site must be clearly and concisely documented and submitted to DEQ for review. An example outline of an RE report is presented in Appendix J.

Section 5. Developing and Implementing Corrective Action Plans

Development and implementation of a CAP may be necessary if, after the screening level evaluation or site-specific RE, concentrations exceed screening levels or an unacceptable risk is identified and the owner/operator has chosen not to perform additional evaluation. The owner/operator must then develop cleanup criteria (also referred to as remediation standards) and create a CAP to achieve those standards or to ensure that the remaining risk is acceptable. The risk management strategy described in the CAP depends on the results of the RE (which pathways, petroleum chemicals, and media are responsible for the unacceptable risk) and other circumstances unique to the site.

5.1 Contents of a Corrective Action Plan

As required in the Rule, the CAP must include:

- A description of remediation standards selected, points of exposure, and points of compliance,
- A description of the remedial strategy and actions to be taken to achieve the remediation standards,
- Current and future land use and use of groundwater and surface water both onsite and offsite,
- AULs that will be required as part of the remedial strategy and the associated environmental covenants,
- Estimated timeline for completion of remedial actions,
- The monitoring plan to gauge effectiveness of the remedial strategy, and
- A description of practical quantitation limits and background concentrations as they apply to the remediation.

Additional elements that should also be a part of the plan include:

- A brief site description,
- A brief description of the RE approved by DEQ, including assumptions used for receptors and land use, and a list of approved cleanup levels for specific pathways, media, chemicals, and specific areas of the site (if applicable),
- A clear description of reasons a CAP is needed,
- An identification of the area(s) to be managed under the CAP,
- A description of the strategy selected to achieve cleanup goals, including a comparison and evaluation of remedial alternatives considered in development of the overall strategy. A rationale for the strategy selected should be presented; any data collected in support of or to determine the feasibility of a particular remedial measure such as pilot testing, should be presented,
- A description of what QA/QC measures will be implemented to ensure that data collected in support of remedial decision making is of adequate quality,
- A description of project closure requirements, and
- A reporting schedule to document progress of the corrective action.

5.2 Implementing a Corrective Action Plan

The CAP should not be implemented until approved by DEQ. Within 30 days of receiving a CAP, DEQ must provide an approval, an approval with modifications, or a rejection (specifying reasons for the rejection) in writing. Provisions are made in the Rule (Section 200.04) for extending this timeframe.

While DEQ is reviewing the CAP, implementation of interim corrective action measures may take place. However, as provided in IDAPA 58.01.02.852.06.c, owner/operators may, in the interest of minimizing environmental contamination and promoting more effective cleanup, begin cleanup of soil, surface water, and groundwater before the CAP is approved provided that they fulfill certain conditions including:

- Notifying DEQ of their intention to begin cleanup;
- Compliance with any conditions imposed by DEQ, including halting cleanup or mitigating adverse consequences from cleanup activities; and

- Incorporation of these self-initiated cleanup measures in the CAP that is submitted to DEQ for approval.

Typical interim corrective actions include excavating and disposing contaminated soil, removing free product, extracting soil vapor, and pumping and treating groundwater.

Upon approval of the CAP, the owner/operator must implement the plan according to the proposed schedule. All performance data should be submitted to DEQ in a timely manner. This data should be carefully evaluated by both the owner/operator and DEQ to determine if the CAP is progressing as anticipated. Major deviations in schedule or plan implementation should be communicated to DEQ for review and approval well in advance of proposed implementation, along with recommended modifications if necessary. The specific modifications that may be needed will vary from site to site.

When the CAP has been successfully implemented, the owner/operator should document these conditions in a completion report along with a petition to DEQ for site closure.

Section 6. Activity and Use Limitations

An AUL is a restriction or obligation, with respect to real property, that is created by an Environmental Covenant pursuant to the Uniform Environmental Covenants Act (UECA), Chapter 30, Title 55, Idaho Code. It is available at: *http://legislature.idaho.gov/idstat/Title55/T55CH30.htm*

The purpose of AULs is to reduce the potential for exposure to contaminants at a release site. AULs are also commonly referred to as "institutional controls." AULs are typically proposed to DEQ for approval through the RE process. Non-remedial land use restrictions (e.g., local zoning ordinances) may reinforce the sustainability of AULs; however, they are not considered sufficient by themselves. These types of non-remedial land use restrictions, such as zoning ordinances, may change or be removed without DEQ approval and therefore are not approved by DEQ as part of a CAP. However, non-remedial land use restrictions may be relevant to evaluating current and reasonably likely future use and exposure scenarios at a site.

6.1 Environmental Covenants

Owner/operators may propose an Environmental Covenant as part of the CAP which will include the AUL language. Any proposed Environmental Covenant must be consistent with UECA. Each proposed Environmental Covenant is reviewed and evaluated on a site specific basis.

Following is a *non-exclusive* list of the types of activity and use limitations that may be included in an Environmental Covenant:

- Restrictions on Water Use:
  - Prohibit use
  - Limit use
  - Monitor use
  - Report use
  - Operation and maintenance procedures for physical controls and devices
  - Prohibit well installation and operation
  - Abandon an existing well.
- Restrictions on Land Use:
  - Prohibit, or require DEQ approval for, disturbance of soil, cap, or vegetation
  - Limit activities and land use
  - Limit structures and buildings.
- Actions Regarding Access:
  - Right of Access necessary to implement the activity and use limitation
  - Limit or deny public access.
- Obligations to perform certain actions in order to maintain the effectiveness of an approved corrective action. For example, this may involve the need to do periodic inspections and maintenance in order to ensure that a cover or barrier retains its primary

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function. In this case there might be a specific reference in the Environmental Covenant to an Operations and Maintenance Plan, developed as part of the corrective action.

DEQ has an Environmental Covenant template that owner/operators can use when proposing activity and use limitations as part of a CAP. The DEQ website includes a copy of the latest Environmental Covenant template at *http://www.deq.idaho.gov/environmental-covenants*. The owner/operator can propose an environmental covenant consistent with UECA for consideration and approval by DEQ.

6.2 Specific Application of Activity and Use Limitations at Petroleum Release Sites

Section 600.01 of the Rule outlines the circumstances under which AULs will be included as part of a CAP. These include:

- Where the assumed onsite land use for the purpose of the RE is not residential and either the maximum media concentrations exceed the screening levels or the calculated risk for a residential receptor is unacceptable
- Where off-site groundwater concentrations exceed RUSLs or risk-based concentrations, and
- Where DEQ determines, based on the proposed CAP, that such AULs are required to assure the continued protection of human health and the environment or the integrity of the cleanup action.

6.3 Use of Activity and Use Limitations at Impacted Neighboring Properties

Implementability and enforceability issues become more complicated when an owner/operator proposes use of AULs on impacted neighboring properties. It is the owner/operators's obligation to negotiate language and reach agreement with both the impacted property owner and DEQ.

6.4 Non-Remedial Land Use Restrictions

Non-remedial land use restrictions (e.g., local zoning ordinances) may reinforce the sustainability of AULs; however, they are not considered sufficient by themselves. These types of non-remedial land use restrictions, typically implemented by other governmental agencies, may change or be removed without DEQ approval and therefore are not approved by DEQ as part of a CAP. The presence of such non-remedial restrictions may be relevant when determining the current and likely future uses of impacted properties.

REC 4565

TR 1250

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Appendix A: Default Exposure Factors

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Exposure Factors

Risk assessment requires quantifying the magnitude, frequency, and duration of exposure for the receptor populations and exposure pathways selected for analysis. To determine pathway-specific intake estimates, it is necessary to select values for a number of variables in the equations used to calculate intake. The following variables were selected based on an assessment of recommendations in various guidance documents and scientific literature. When determining these values, it is often necessary to make assumptions, and in these cases, the rationale for the assumption is provided. These exposure factors are summarized in Table 1.

Averaging Time

The period over which exposure to chemicals is averaged depends on the type of toxic effect being assessed. For chronic exposure to noncarcinogenic toxicants, intakes are averaged over the period of exposure, so the averaging time is equal to the exposure duration. Intakes of carcinogens are calculated by prorating the total cumulative dose over a lifetime. The different approach is based on the idea that for carcinogens, a higher dose received over a shorter period is equivalent to a corresponding lower dose spread over a lifetime. The averaging time selected for carcinogens, 70 years, is based on the U.S. Environmental Protection Agency's (EPA) *Risk Assessment Guidance for Superfund* (EPA 1989).

Body Weight

It is appropriate to use an average value for this parameter. The default body weight for adult receptors is 70 kilograms (kg) and represents the EPA standard default exposure factor (EPA 1991a). There is evidence presented in the *Exposure Factors Handbook* (EPA 2011) that Americans are getting heavier, and currently the actual average adult body weight is 80 kg. However, the derivation of cancer slope factors assumes a body weight of 70 kg, so it is more appropriate to also use this value for average body weight. The child body weight value is 15 kg, which is the mean value for children aged 6 months to 6 years (EPA 2011). It is also a standard default value in EPA's 1991 *Risk Assessment Guidance for Superfund* (EPA 1991a).

Exposure Duration

The residential exposure duration is the EPA standard default of 30 years (EPA 1991a). This period is divided into 6 years of exposure as a child and 24 years as an adult. These time periods are used in combination with other age group–specific exposure parameters to assess exposure to carcinogenic chemicals. Noncarcinogenic chemical exposure is conservatively assessed using the child receptor and an exposure duration of 6 years. For the nonresidential adult receptor, the exposure duration is 25 years, which is an EPA standard default exposure factor (EPA 1991a) and is also used in *Risk Assessment Guidance for Superfund, Part B* (EPA 1991b). This value was a 95th-percentile value for men in the manufacturing sector, based on an analysis of U. S. Bureau of Labor Statistics data (EPA 2002). An exposure duration of 25 years is considered protective across a wide spectrum of industrial and commercial sectors (EPA 2002) and so is an appropriate default for nonresidential receptors. The exposure duration for the construction

worker is 30 days (0.08 year); this is assumed to be a conservative estimate of exposure for most construction projects.

Exposure Frequency

The exposure frequency for residential receptors is 350 days per year for all exposure routes that do not involve direct contact with soil. This exposure frequency is the EPA standard default exposure factor (EPA 1991a). The nonresidential scenario assumes an exposure frequency of 250 days per year. This value is the EPA standard default for commercial or industrial scenarios (EPA 1991a) and so was considered appropriate for all nonresidential receptors except for construction workers. For the construction worker scenario, the exposure frequency is 30 days per year.

Exposure Frequency for Direct Contact with Soil

For exposure routes involving direct contact with soil—including soil ingestion, dermal exposure, and vapor and particulate inhalation—it is assumed that receptors have contact with soil primarily in warmer months when the ground is not frozen or snow covered. For this reason, an exposure frequency of 270 days per year is used for these exposure routes for the residential scenario; 180 days per year is used for the nonresidential scenario. The direct contact exposure frequency for construction workers is 30 days per year.

Soil Ingestion Rate

The soil ingestion rate for residential child and adult receptors is 200 milligrams per day (mg/day) and 100 mg/day, respectively. These values are EPA standard default exposure factors (1991a). Although both EPA (1991a) and the *Exposure Factors Handbook* (EPA 1997) recommend a soil ingestion rate of 50 mg/day for workers other than construction workers, it was decided to use a value of 100 mg/day to adequately address the potential soil exposures encountered by all nonresidential adult receptors.

For example, a value of 50 mg/day might be appropriate for office workers, but it would not adequately address exposure of outdoor workers, for whom a value of 100 mg/day is more appropriate (EPA 2002). The construction worker soil ingestion rate is 330 mg/day. This value is based on the 95th percentile for adult soil intake rates reported in a soil ingestion mass-balance study (Stanek et al. 1997, cited in EPA 2002).

Water Ingestion Rate

The water ingestion rate for children is 1 liter per day (L/day). Currently EPA uses 1 L/day as a default drinking water ingestion rate for infants and children, and it is considered to be an appropriate upper percentile tap water ingestion rate for children less than 10 years of age (EPA 2008). The residential adult receptor ingestion rate is 2 L/day. This value is an EPA standard default exposure factor (EPA 1991a). According to EPA (1997), the intake rate of 2 L/day corresponds to the 84th percentile of the intake rate distribution among adults in a study by Ershow and Cantor (1989). EPA (1997) lists an average tap water intake for adults of 1.41 L/day. The nonresidential adult ingestion rate is 1 L/day; this value is an EPA standard default exposure factor (EPA 1991a).

Exposure Time for Outdoor Inhalation

Residential receptors are assumed to spend 2 hours outdoors at their residence. This is an EPA-recommended value (1997). Nonresidential receptors are assumed to spend 6 hours outside; this value overestimates exposure of indoor workers, but it is appropriate for outdoor workers. Construction workers are assumed to spend 10 hours per day outdoors, as construction workers often work 10-hour days. These exposure times are used in the inhalation portion of the direct contact equations used to derive screening levels and risk.

Dermal Relative Absorption Factor

The dermal relative absorption factor values are based on recommendations contained in the EPA's *Risk Assessment Guidance for Superfund, Part E, Supplemental Guidance for Dermal Risk Assessment* (EPA 2004). The EPA recommends an absorption factor of 0.13 for benzo(a)pyrene and other polynuclear aromatic hydrocarbons (PAHs) and 0 for volatile organic compounds (VOCs).

Soil-to-Skin Adherence Factor

The soil-to-skin adherence factor values are derived from recommendations from an analysis of soil adherence study data by the EPA (EPA 2004). This analysis calculated body-part-weighted adherence factor values using studies involving upper-end activities for soil-skin adherence and median values of body surface area. The recommended adult residential value, based on a central-tendency-weighted adherence factor of a high-end soil contact activity (e.g., gardening), is consistent with a reasonable maximum exposure (RME) for contact rates in a variety of activities. The same approach of using the high end of a mean is used for the recommended child value, which is the 50th percentile weighted adherence factor for children playing in wet soil. Similarly, the commercial/industrial worker recommended adherence factor is based on the 50th percentile weighted adherence factor for utility workers, a high-end contact activity. For the construction worker, a 95th percentile weighted adherence factor is used to represent RME.

Skin Surface Area for Dermal Contact with Soil

Skin surface areas for dermal soil contact are based on residential and industrial RME recommended values contained in EPA's *Risk Assessment Guidance for Superfund, Part E, Supplemental Guidance for Dermal Risk Assessment* (EPA 2004).

Table 1. Default Exposure Factors

Exposure Parameter	Symbol	Units	Default Value	Reference
Averaging Time (AT)				
Averaging Time—Carcinogen	ATc	years	70	EPA 1989 (p. 6-23)
Averaging Time—Noncarcinogen	ATnc	years	Equivalent to exposure duration	EPA 1989 (p. 6-23)
Body Weight (BW)				
Child	BWc	kg	15	EPA 1991a (p. 15)
Adult	BWa	kg	70	EPA 1991a (p. 15)
Exposure Duration (ED)				
Resident (child)	EDc	years	6	EPA 1991a (p. 15)
Resident (adult)	EDa	years	24	EPA 1991a (p. 15)
Nonresidential Worker	ED	years	25	EPA 1991a (p. 15)
Construction Worker	ED	years	1	EPA 2002 (Exhibit 5-1)
Exposure Frequency (EF)				
Resident	EFr	days/yr	350	EPA,1991a (p.15)
Nonresidential Worker	EF	days/yr	250	EPA 1991a (p.15)
Construction Worker	EF	days/yr	30	Professional judgment
Exposure Frequency for Direct Contact Pathways (EF)				
Resident	EFres	days/yr	270	Professional judgment
Nonresidential Worker	EFd	days/yr	180	Professional judgment
Construction Worker	EFd	days/yr	30	Professional judgment
Soil Ingestion Rate (IR)				
Resident (child)	IRs-c	mg/day	200	EPA 1991a (p. 15)
Resident (adult)	IRs-a	mg/day	100	EPA 1991a (p. 15)
Nonresidential Worker	IRs	mg/day	100	EPA 2002 (Exhibit 1-2)
Construction Worker	IRs	mg/day	330	EPA 2002 (Exhibit 1-2)
Daily Water Ingestion Rate (IRw)				
Resident (child)	IRw-c	L/day	1	EPA 2008
Resident (adult)	IRw-a	L/day	2	EPA 1991a (p. 15)
Nonresidential Worker	IRw	L/day	1	EPA 1991a (p. 15)
Exposure Time for Inhalation (ET)				
Resident (child)	ETo-c	hr/day	Outdoor: 2 Indoor: 24	EPA 1997 (p. 15-17)

Exposure Parameter	Symbol	Units	Default Value	Reference
Resident (adult)	ETo-a	hr/day	Outdoor: 2 Indoor: 24	EPA 1997 (p. 15-17)
Nonresidential Worker	ETo	hr/day	Outdoor: 6 Indoor: 8	Professional judgment
Construction Worker (outdoor only)	ETo	hr/day	10	Professional judgment
Oral Relative Absorption Factor (RAF)				
Oral Relative Absorption Factor	RAFo	—	Assume 100%	EPA 2004 (p. 4-2)
Dermal Relative Absorption Factor (RAFd)				
Volatile organic compounds	RAFd	—	0	EPA 2004 (pg. 3-18)
Benzo(a)pyrene and other polynuclear aromatic hydrocarbons	RAFd	—	0.13	EPA 2004 (Exhibit 3-4)
Soil-to-Skin Adherence Factor (M)				
Residential (child)	Mc	mg/cm^2	0.2	EPA 2004 (p.3-14)
Residential (adult)	Ma	mg/cm2	0.07	EPA 2004 (p. 3-14)
Nonresidential Worker	M	mg/cm^2	0.2	EPA 2004 (p. 3-17)
Construction Worker	M	mg/cm^2	0.3	EPA 2004 (Exhibit 3-3)
Skin Surface Area for Dermal Contact with Soil (SA)				
Child Receptors	SAc	cm^2/day	2800	EPA 2004 (Exhibit 3-5)
Adult Receptors	SAa	cm^2/day	5700	EPA 2004 (Exhibit 3-5)
Nonresidential Worker Receptors	SA	cm^2/day	3300	EPA 2004 (Exhibit 3-5)
Construction Worker Receptors	SA	cm^2/day	3300	EPA 2004 (Exhibit 3-5)

Note: Exposure factors for the age-adjusted resident are calculated from the values listed for child and adult receptors using the equations in Appendix E.

Exposure to Mutagenic Carcinogens

Exposure to these chemicals carries greater risk when it occurs early in life. Therefore, the age at which exposure occurs must be considered for residential receptors. For these receptors, the 30-year exposure duration is divided into four periods: exposures occurring between the ages of 0–2 years, 2–6 years, 6–16 years, and 16–30 years (EPA 2005).

Different multipliers are incorporated for these time periods so that early-life exposure is weighted more heavily. The 0–2 year and 2–6 year exposure periods use the child-specific values for several exposure parameters: body weight, soil ingestion rate, soil-to-skin adherence factor, and skin surface area for dermal contact. The corresponding adult-specific values are used for the 6–16 year and 16–30 year exposure periods.

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Appendix B: Default Fate and Transport Parameter Values

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Introduction

Several routes of exposure evaluated in the *Idaho Risk Evaluation Manual for Petroleum Releases* (REM) involve pathways where chemicals transfer across media. These pathways include inhalation of vapors originating from the volatilization of chemicals of interest (COI) from petroleum-impacted soil or ground water in indoor air, ingestion of ground water containing chemicals leached from soil, and inhalation of volatiles and particulates from surficial soil. Models are used to simulate these cross-media transfer processes, estimate exposure point concentrations, and calculate target levels. This appendix describes the models and selection criteria for the default fate and transport parameter values used to develop the Idaho default screening levels and to some degree the remedial action target levels. A summary of the parameters and sources used to develop them is provided in Table 1 at the end of this appendix.

Soil Properties

Unsaturated Zone

Generic unsaturated zone soil properties were based on an assumed sandy loam soil textural class. Nielson and Rogers (1990) and Hers (2002) present data on average soil physical and hydraulic properties for 12 Natural Resources Conservation Service soil textural classes. Data obtained from these compilations include mean particle diameter, total porosity, saturated moisture content, residual moisture content, van Genuchten parameters describing the shape of the moisture characteristic curve, and saturated hydraulic conductivity. Bulk density was calculated from total porosity. Soil vapor permeability was calculated using van Genuchten equations described in the U.S. Environmental Protection Agency's (EPA) *User's Guide for Evaluating Subsurface Vapor Intrusion into Buildings* (EPA 2003), the hydraulic properties of the sandy loam soil noted above, and average moisture content conditions. Derivation of the average moisture contents is described below.

Infiltration rates for high- and low-precipitation areas of Idaho were developed, and the value for high-precipitation areas is used as the Idaho default target level value. The high-precipitation area annual infiltration rate of 25 centimeters is based on field studies and water balance calculations done in northern Idaho on the Rathdrum Prairie (Hammel et al. 1995). This value represents about 40% of the total annual precipitation. The annual infiltration rate for low-precipitation areas (1.4 centimeters) is based on investigations by Cecil et al. (1992). This latter work was conducted in areas of native vegetation at the Idaho National Laboratory in eastern Idaho. Using stable isotopes and other tracers, a long-term estimate of 1 centimeter per year infiltration was calculated.

This infiltration rate represents approximately 5% of total annual precipitation. This percentage was applied to the total annual precipitation in Boise (11.7 inches/year), with the assumption that Boise conditions represent average low-precipitation conditions.

Average soil moisture content values for low- and high-precipitation conditions were derived by simulating infiltration into a homogeneous soil profile with the sandy loam hydraulic properties discussed above. The variably saturated flow and transport code HYDRUS-1D (Kool and van Genuchten 1991) was used to conduct the simulations. The simulations were run until steady-state conditions were achieved, and the moisture content at that time was noted. These values (0.17 cm^3/cm^3, low precipitation, and 0.20 cm^3/cm^3, high precipitation) are consistent with field capacity (0.33 bar) moisture content values for sandy loam texture class soils presented by Rawls et al. (1982).

The moisture content in the capillary fringe and the capillary fringe thickness were derived using methods and equations described in the EPA *User's Guide for Evaluating Subsurface Vapor Intrusion into Buildings* (2003). The mean particle diameter of 0.03 centimeters used in these calculations is typical of a sandy loam soil type.

The default value for fractional organic carbon content in the vadose zone (0.001) was selected from the statistical analysis of national soil survey data by Carsel et al. (1988). It represents the median value for subsoils with sandy loam textures.

Saturated Zone

The default scenario selected to represent the saturated zone is a sandy, alluvial aquifer of moderate hydraulic conductivity. Selected saturated zone properties and ground water mixing zone thickness were taken from those developed for the soils protective of ground water pathway in Appendix A of the *Risk Based Corrective Action Guidance Document for Petroleum Releases* (DEQ 1996). Total porosity, bulk density, and fraction organic carbon are similar to that of the unsaturated zone soil.

Enclosed Space Parameters

The enclosed space parameters are used in combination with soil and ground water properties to define the conditions controlling the volatilization of COI vapors from petroleum-impacted soil, ground water, and soil vapor into indoor spaces and to predict exposure point concentrations of chemicals in indoor air. Scenarios were developed for residential and nonresidential settings. Both the residential and nonresidential scenarios selected consist of one-story, slab-on-grade structures lying directly over the source of contamination. For structures with finished basements, reasonable values for basement depth below grade of 200 cm and height of enclosed space of 366 cm (EPA 2003) can be assumed. Structures with crawl spaces are not as readily characterized because of the common occurrence of earthen floors and variable size and ventilation. The primary differences between the two scenarios are the size of the structure and the number of air exchanges per time period. The nonresidential structure is larger and exchanges more air than the residential structure.

The size of structure for each scenario was based on residential and commercial building survey data collected by the U.S. Department of Energy (DOE 1995, 2001). Data from the western census region of the 1993 housing survey (DOE 1995) were used to further describe residential structures. In this region, 33% of all homes had heated floor space square footage between 1,000

and 1,599 square feet, constituting the largest proportion of all size classes. Approximately 50% of all homes were one-story, single-family homes. The next largest category was multistory apartment buildings, accounting for 29% of all residential structures. Homes with concrete slabs or crawl spaces each constituted about 33% of all homes, while 15% had basements. A sensitivity analysis evaluating the impact of concrete slabs versus crawl spaces on target levels showed little difference.

For nonresidential structures, data from the mountain division of the western region of the 1999 Commercial Building Energy Consumption Survey was used (DOE 2001). The median square footage per commercial building in this area was 5,000 square feet, and 66% of all buildings in this area were one story. A slab-on-grade foundation and indoor building height of 8 feet were assumed. These values can be modified during the development of a site-specific evaluation to accommodate actual structure conditions.

The default value chosen for air exchange rates in commercial buildings is based on expected values for buildings built to meet ventilation standards of the American Society of Heating, Refrigeration, and Air Conditioning Engineers (ASHRAE 2004). The default value for residential structures is based on an analysis by the Michigan Department of Environmental Quality (MDEQ 1998). Values for other structural parameters—specifically the dimensions of foundation cracks, wall/foundation thickness, and pressure differentials between the space and the outdoors—are based on data presented in the *User's Guide for Evaluating Subsurface Vapor Intrusion into Buildings* (EPA 2003).

In the Johnson-Ettinger model equations, there is a dependent relationship between the width of foundation cracks (equivalent crack radius) and the fraction of the total floor space below grade occupied by cracks. It was decided to fix the equivalent crack width at 0.1 centimeters and allow the fraction of cracks to vary, with a minimum value of 0.0005 specified, during the calculation of the total area of cracks in the default structure. This minimum value is what is suggested as a reasonable lower end of the range for this parameter by Johnson (2005).

Source characteristics for calculation of indoor air pathways assumed a 1-foot separation distance between the top of the soil or ground water source and the building foundation. This distance is the minimum that can be considered by the model and was considered extremely conservative with respect to maximizing vapor migration into a structure.

For ground water sources, this soil separation distance includes the capillary fringe thickness of 25 centimeters. In making finite mass calculations, the soil source was assumed to be 5 feet (153 centimeters) thick.

Particulate Emission Factor Parameters

All parameter values used in the calculation of the particulate emission factor are taken directly from the EPA's *Soil Screening Guidance* (EPA 1996). Idaho-specific values for the Q/C dispersion factor for a 0.5-acre size source and the average wind speed for Boise were selected as default values.

Models

The default models selected to estimate the transport of chemicals between various media and within select media, such as ground water, include the following:

- The Johnson-Ettinger model (Johnson and Ettinger 1991) for transport of volatile chemicals between soil, soil vapor, or ground water and indoor air—Implementation of the model includes the effects of advection near the building and diffusion to the building from the source and infinite and finite source masses. This model does not incorporate biodegradation of chemicals during transport from the source into the indoor air.
- The dilution attenuation factor model for the soil to ground water pathway implemented in the EPA *Soil Screening Guidance* (EPA 1996)—Soil leachate generated using the high infiltration rate is mixed with ground water having the Darcy velocity described above. Target levels are estimated in ground water directly below the source.
- The Domenico model for transport of chemicals in the saturated zone—This is a steady-state model that includes advection, sorption, three-dimensional dispersion, and decay (Domenico 1990). Equations for calculating dispersivity values for use in the ground water transport model are those derived by Xu and Eckstein (1995).
- The Cowherd equation for transport and dispersion of particulates as described in the EPA *Soil Screening Guidance* (EPA 1996).

Table 1. Default fate and transport parameter values

Parameter	Symbol	Units[a]	Default Value	Reference
Soil Parameters				
Unsaturated Zone Soil				
Source-building separation	LTs	cm	30	Professional judgment, see discussion
Source bottom-building separation	LTSB	cm	183	Professional judgment, see discussion
Vapor permeability	kv	cm^2	5.0E-9	Calculated
Mean particle diameter	D	cm	0.030	EPA 2003
Van Genuchten curve shape parameter	n	—	1.449	EPA 2003
Thickness of capillary fringe zone	hcap	cm	25	EPA 2003
Dilution attenuation factor (DAF) in the unsaturated zone (user-defined)	DAFunsat	—	1	No attenuation in the unsaturated zone is assumed to occur.
Total soil porosity in the vadose zone	θT	cm^3/cm^3-soil	0.39	EPA 2003
Volumetric water content in vadose zone	θws	cm^3/cm^3	0.17	Professional judgment, see discussion
Volumetric air content in vadose zone	θas	cm^3/cm^3	0.22	Calculated
Dry soil bulk density	ρs	g/cm^3	1.64	Nielson and Rogers 1990; Hers 2002
Fractional organic carbon content in the vadose zone	foc	g-C/g-soil	0.001	Carsel et al. 1988
Volumetric water content in the foundation/wall cracks	θwcrack	cm^3/cm^3	0.17	Assumed equal to that in the adjacent soil
Volumetric air content in the foundation/wall cracks	θacrack	cm^3/cm^3	0.22	Calculated
Volumetric water content in capillary fringe zone	θwcap	cm^3/cm^3	0.32	EPA 2003
Volumetric air content in capillary fringe zone	θacap	cm^3/cm^3	0.07	EPA 2003
Saturated Zone Soil				
Dry soil bulk density	ρss	g/cm^3	1.64	Nielson and Rogers 1990; Hers 2002
Fractional organic carbon content	focs	g-C/g-soil	0.001	Professional judgment, see discussion
Total soil porosity	θTs	cm^3/cm^3-soil	0.39	Nielson and Rogers 1990; Hers 2002

Parameter	Symbol	Units[a]	Default Value	Reference
Volumetric water content	θwss	cm^3/cm^3	0.39	Equivalent to total porosity
Volumetric air content	θass	cm^3/cm^3	0.0	
Air Property				
Viscosity of air		g/cm-sec	1.8E-4	
Ground Water Parameters				
Water table-building separation	LTgw	cm	30	Professional judgment, see discussion
Ground water Darcy velocity	Ugw	cm/year	3340	DEQ 1996
Ground water mixing zone thickness	δgw	cm	153	DEQ 1996
Length of ground water source parallel to ground water flow direction	Lmz	cm	1220	Equivalent to source area dimensions
Width of ground water source perpendicular to ground water flow direction	Wgw	cm	1220	Equivalent to source area dimensions
Infiltration rate	I	cm/year	25	Hammel et al. 1995
Enclosed Space Parameters				
Area of the Enclosed Space Below Grade				
Residential—Slab on Grade	AB	cm^2	1488400	Calculated
Residential—Basement	AB	cm^2	2464400	Calculated
Nonresidential	AB	cm^2	4652649	Calculated
Enclosed Space Foundation/Wall Thickness				
Residential	Lcrack	cm	15	EPA 2003
Nonresidential	Lcrack	cm	15	EPA 2003
Total area of Cracks				
Residential	Acrack	cm^2	744	Calculated
Nonresidential	Acrack	cm^2	2326	Calculated
Number of Air Exchanges per Hour				
Residential	ER	1/hour	1	MDEQ 1998
Nonresidential	ER	1/hour	1	ASHRAE 2004
Length of Enclosed Space				
Residential	LB	cm	1220	DOE 1995
Nonresidential	LB	cm	2157	DOE 2001

Parameter	Symbol	Units[a]	Default Value	Reference
Width of Enclosed Space				
Residential	WB	cm	1220	DOE 1995
Nonresidential	WB	cm	2157	DOE 2001
Height of Enclosed Space				
Residential—Slab on Grade	HB	cm	244	EPA 2003
Residential—Basement	HB	cm	366	EPA 2003
Nonresidential	HB	cm	244	Professional judgment
Floor-Wall Seam Perimeter				
Residential	Xcrack	cm	4880	Calculated
Nonresidential	Xcrack	cm	8628	Calculated
Crack depth below grade	Zcrack	cm	15	Calculated
Equivalent crack radius	rcrack	cm	0.1	EPA 2003
Pressure differential between enclosed space and soil surface beneath	ΔP	$g/cm\text{-}sec^2$	40	EPA 2003
Cowherd Particulate Emission Model				
Inverse of the mean concentration at the center of a square source	Q/C	$(g/m^2\text{-}sec)/(kg/m^3)$	69.41	EPA 1996
Fractional vegetative cover	V	m^2/m^2	0.5	EPA 1996
Mean annual wind speed	Um	m/sec	3.98	EPA 1996
Equivalent threshold value of wind speed at 7 meters	Ut	m/sec	11.32	EPA 1996
Wind speed distribution function from Cowherd et al. 1985	F(x)	—	4.95E-2	EPA 1996
Averaging Time For Vapor Flux				
Resident child	AT	sec	1.89E8	Equal to exposure duration
Resident adult	AT	sec	9.46E8	Equal to exposure duration
Age Adjusted Resident	AT	sec	7.57E8	Equal to exposure duration
Nonresidential adult worker	AT	sec	7.88E8	Equal to exposure duration
Construction worker	AT	sec	3.15E7	Equal to exposure duration
Ground Water Protection				
Distance to the point of exposure	Xpoe	cm	0	Professional judgment
Distance to the point of compliance	Xpoc	cm	0	Professional judgment

[a] cm = centimeters; g = grams; C = carbon; m = meters; sec = seconds; kg = kilograms

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Appendix C: Default Physical and Chemical Properties

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Chemicals	CAS Number	Molecular Weight	Water Solubility (milligrams/ liter)	Henry's Law Constant (liters air/ liters water)	Organic Carbon Adsorption Coefficient Koc (milliliters/gram)	Vapor Pressure (millimeters mercury)[a]	Diffusion Coefficient in Air (square centimeters/ second)	Diffusion Coefficient in Water (square centimeters/ second)
Acenaphthene	83-32-9	154.2	3.9	7.5E-03	5027	1.6E-03	0.051	8.3E-06
Anthracene	120-12-7	178.2	0.0434	2.3E-03	16360	2.0E-04	0.039	7.9E-06
Benzene	71-43-2	78.1	1790	2.3E-01	145.8	9.5E+01	0.09	1.0E-05
Benzo(a)anthracene	56-55-3	228.3	0.0094	4.9E-04	176900	1.1E-07	0.026	6.7E-06
Benzo(a)pyrene	50-32-8	252.3	0.0016	1.9E-05	587400	5.5E-09	0.048	5.6E-06
Benzo(b)fluoranthene	205-99-2	252.3	0.0015	2.7E-05	599400	5.0E-07	0.048	5.6E-06
Benzo(k)fluoranthene	207-08-9	252.3	0.0008	2.4E-05	587400	9.6E-11	0.048	5.6E-06
Chrysene	218-01-9	228.3	0.002	2.1E-04	180500	6.3E-09	0.026	6.7E-06
1,2-Dichloroethane	107-06-2	99.0	8600	4.8E-02	40	8.7E+01	0.086	1.1E-05
Ethylbenzene	100-41-4	106.2	169	3.2E-01	446	1.0E+01	0.068	8.5E-06
Ethylene Dibromide	106-93-4	187.9	3910	2.7E-02	40	1.1E+01	0.043	1.0E-05
Fluoranthene	206-44-0	202.3	0.26	3.6E-04	55450	5.0E-06	0.028	7.2E-06
Fluorene	86-73-7	166.2	1.69	3.9E-03	9160	1.0E-04	0.044	7.9E-06
MTBE	1634-04-4	88.2	51000	2.4E-02	12	2.49E+02	0.075	8.6E-06
Naphthalene	91-20-3	128.0	31	1.8E-02	1544	2.3E-01	0.06	8.4E-06
Pyrene	129-00-0	202.3	0.135	4.9E-04	54340	6.9E-07	0.028	7.2E-06
Toluene	108-88-3	92.1	526	2.7E-01	234	2.2E+01	0.078	9.2E-06
Total Xylenes	1330-20-7	106.2	106	2.7E-01	383	8.8 E+00	0.069	8.5E-06

Note: Values for physical and chemical properties (with the exception of vapor pressure) are taken from the U.S. Environmental Protection Agency regional screening levels website (accessed May 2018) chemical specific parameter supporting table

[a] Values for vapor pressure at 20–25 degrees Celsius were obtained from the *Groundwater Chemicals Desk Reference, Volume 1* by John H. Montgomery and Linda M. Welkom (1991, Lewis Publishers) and the *Groundwater Chemicals Desk Reference, Volume 2* by John H. Montgomery (1991, Lewis Publishers).

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Appendix D: Default Toxicity Values

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The table below provides a list of the default carcinogenic and noncarcinogenic toxicity factors and oral and dermal relative absorption factors used in the risk evaluation process. All toxicity factor values, oral relative absorption factors, and dermal relative absorption factors for polynuclear aromatic hydrocarbons were obtained from the U.S. Environmental Protection Agency (EPA) regional screening level website and are current as of May 2018:

http://www.epa.gov/reg3hwmd/risk/human/rb-concentration_table/Generic_Tables/index.htm

In their *Risk Assessment Guidance for Superfund, Volume I: Human Health Evaluation Manual* (Part E, Supplemental Guidance for Dermal Risk Assessment), the EPA did not provide dermal relative absorption factors for volatile organic compounds based on the rationale that these compounds would tend to be volatilized from the soil on skin. Based on this rationale, the dermal relative absorption factors for volatile organic compounds is assumed to be zero.

Chemicals	CAS Number	Oral Slope Factor (kg-day/mg)[a]	Unit Inhalation Risk ($\mu g/m^3$)[b]	Oral Reference Dose (mg/kg-day)[c]	Inhalation Reference Concentration (mg/m^3)[d]	Oral Relative Absorption Factor	Dermal Relative Absorption Factor
Acenaphthene	83-32-9	NA	NA	6.0E-2	NA	1	0.13
Anthracene	120-12-7	NA	NA	3.0E-1	NA	1	0.13
Benzene	71-43-2	5.5E-2	7.8E-6	4.0E-3	3.0E-2	1	0
Benzo(a)anthracene	56-55-3	0.1	1.1E-4	NA	NA	1	0.13
Benzo(a)pyrene	50-32-8	1	1.1E-3	0.0003	NA	1	0.13
Benzo(b)fluoranthene	205-99-2	0.1	1.1E-4	NA	NA	1	0.13
Benzo(k)fluoranthene	207-08-9	0.01	1.1E-4	NA	NA	1	0.13
Chrysene	218-01-9	0.001	1.1E-5	NA	NA	1	0.13
1,2-Dichloroethane	107-06-2	9.1E-2	2.6E-5	6.0E-3	7.0E-3	1	0
Ethylbenzene	100-41-4	1.1E-2	2.5E-6	1.0E-1	1.0E0	1	0
Ethylene Dibromide	106-93-4	2.0E0	6.0E-4	9.0E-3	9.0E-3	1	0
Fluoranthene	206-44-0	NA	NA	4.0E-2	NA	1	0.13
Fluorene	86-73-7	NA	NA	4.0E-2	NA	1	0.13
MTBE	1634-04-4	1.8E-3	2.6E-7	NA	3.0E0	1	0
Naphthalene	91-20-3	NA	3.4E-5	2.0E-2	3.0E-3	1	0.13
Pyrene	129-00-0	NA	NA	3.0E-2	NA	1	0.13
Toluene	108-88-3	NA	NA	8.0E-2	5.0E0	1	0
Total Xylenes	1330-20-7	NA	NA	2.0E-1	1.0E-1	1	0

[a] kg-day/mg = kilogram-day per milligram
[b] $\mu g/m^3$ = microgram per cubic meter
[c] mg/kg-day = milligram per kilogram-day
[d] mg/m^3 = milligram per cubic meter

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Appendix E: Models and Equations

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1 Target Levels for Non-Residential and Construction Worker Exposures

1.1 Indoor Inhalation of Vapor Emissions

Carcinogenic effects

$$RBTL_{ai} = \frac{TR \times AT_c \times 365}{ED \times EF \times ET_i \times IUR \times 1000}$$

Noncarcinogenic effects

$$RBTL_{ai} = \frac{THQ \times AT_{nc} \times 365}{ED \times EF \times ET_i \times \left(\frac{1}{RfC}\right)}$$

Source: EPA 2009, modified from equations 6 and 11

Where:

$RBTL_{ai}$	=	Risk-based target level for indoor air inhalation [mg/m^3]
TR	=	Target risk or the increased chance of developing cancer over a lifetime due to exposure to a chemical [-]
THQ	=	Target hazard quotient for individual constituents [-]
AT_c	=	Averaging time for carcinogens [years]
AT_{nc}	=	Averaging time for noncarcinogens [years]
ED	=	Exposure duration [years]
EF	=	Exposure frequency [days/year]
ET_i	=	Exposure time for indoor inhalation [hours/day]
RfC	=	Chemical-specific inhalation reference concentration [mg/m^3]
IUR	=	Chemical-specific inhalation unit risk [(µg/m^3)$^{-1}$]
365	=	Conversion factor [days/year]

1.2 Outdoor Inhalation of Vapors and Particulates from Surficial Soil

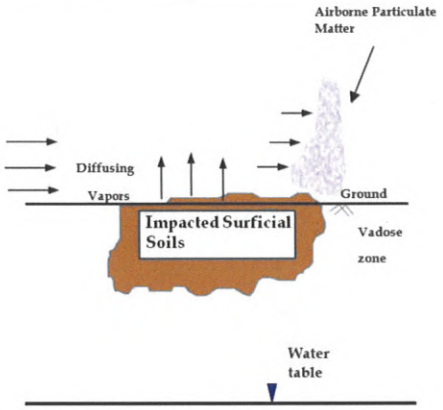
Carcinogenic effects

$$RBTL_{SS} = \frac{TR \times AT_c \times 365}{ED \times EF_d \times ET \times IUR \times \left(\frac{1}{VF} + \frac{1}{PEF}\right) \times 1000}$$

Noncarcinogenic effects

$$RBTL_{SS} = \frac{THQ \times AT_{nc} \times 365}{ED \times EF_d \times ET \times \left(\frac{1}{RfC}\right) \times \left(\frac{1}{VF} + \frac{1}{PEF}\right)}$$

Source: EPA 2011



Where:

$RBTL_{SS}$	=	Risk-based target level for outdoor inhalation of vapors and particulates from surficial soil [mg/kg dry weight]
TR	=	Target risk or the increased chance of developing cancer over a lifetime due to exposure to a chemical [-]
THQ	=	Target hazard quotient for individual constituents [-]
VF	=	Surficial soil to ambient air volatilization factor [$(m^3$-air)/(kg-soil)]
PEF	=	Particulate emission factor [$(m^3$-air)/(kg-soil)]
AT_c	=	Averaging time for carcinogens [years]
AT_{nc}	=	Averaging time for noncarcinogens [years]
ED	=	Exposure duration [years]
EF_d	=	Exposure frequency for direct contact pathway [days/year]
ET	=	Exposure time [hours/day]
RfC	=	Chemical-specific inhalation reference concentration [mg/m^3]
IUR	=	Chemical-specific inhalation unit risk [$(\mu g/m^3)^{-1}$]
365	=	Conversion factor [days/year]

1.3 Direct Ingestion of Surficial Soil

Carcinogenic effects

$$RBTL_S = \frac{TR \times BW \times AT_c \times 365}{SF_o \times EF_d \times ED \times IR_s \times RAF_o \times 10^{-6}}$$

Noncarcinogenic effects

$$RBTL_S = \frac{THQ \times BW \times AT_{nc} \times 365}{EF_d \times ED \times \left(\frac{1}{RAF_o \times RfD_o}\right) IR_s \times 10^{-6}}$$

Source: EPA 1996, p. 19

Where:

$RBTLs$	=	Risk-based target level for the ingestion of soil [mg/kg-wet soil]
TR	=	Target risk or the increased chance of developing cancer over a lifetime due to exposure to a chemical [-]
THQ	=	Target hazard quotient for individual constituents [-]
BW	=	Body weight [kg]
AT_c	=	Averaging time for carcinogens [years]
AT_{nc}	=	Averaging time for noncarcinogens [years]
ED	=	Exposure duration [years]
EF_d	=	Exposure frequency [days/year]
IR_s	=	Soil ingestion rate [mg/day]
RAF_o	=	Oral relative absorption factor [-]
RfD_o	=	Chemical-specific oral reference dose [mg/(kg-day)]
SF_o	=	Chemical-specific oral cancer slope or potency factor [mg/(kg-day)]$^{-1}$
365	=	Conversion factor [days/year]
10^{-6}	=	Conversion factor [kg/mg]

1.4 Dermal Contact with Surficial Soil

Carcinogenic effects

$$RBTL_{DC} = \frac{TR \times BW \times AT_c \times 365}{SF_o \times SA \times M \times RAF_d \times ED \times EF_d \times 10^{-6}}$$

Noncarcinogenic effects

$$RBTL_{DC} = \frac{THQ \times BW \times AT_{nc} \times 365}{SA \times M \times \left(\frac{1}{RfD_o \times RAF_d}\right) \times ED \times EF_d \times 10^{-6}}$$

Source: Modified from EPA 1989, p. 6-41; See also EPA 2007, Appendix D, p. D-6

Where:

$RBTL_{DC}$	=	Risk-based target level for dermal contact with soil [mg/kg-wet soil]
TR	=	Target risk or the increased chance of developing cancer over a lifetime due to exposure to a chemical [-]
THQ	=	Target hazard quotient for individual constituents [-]
BW	=	Body weight [kg]
AT_c	=	Averaging time for carcinogens [years]
AT_{nc}	=	Averaging time for noncarcinogens [years]
ED	=	Exposure duration [years]
EF_d	=	Exposure frequency for direct contact pathway [days/year]
RAF_d	=	Dermal relative absorption factor [-]
SA	=	Skin surface area [cm^2/day]
M	=	Soil to skin adherence factor [mg/cm^2]
RfD_o	=	Chemical-specific oral reference dose [mg/(kg-day)]
SF_o	=	Chemical-specific oral cancer slope or potency factor $[mg/(kg\text{-}day)]^{-1}$
365	=	Conversion factor [days/year]
10^{-6}	=	Conversion factor [kg/mg]

1.5 Combined Direct Contact Soil Pathway: Ingestion, Inhalation of Vapors and Particulates, and Dermal Contact

Carcinogenic effects

$$RBTL_{ss-combined} = \frac{TR \times BW \times AT_c \times 365}{ED \times EF_d \times SF_o \times 10^{-6}\left[\left(IR_s \times RAF_o\right) + \left(SA \times M \times RAF_d\right)\right]} + \frac{TR \times AT_c \times 365}{ED \times EF_d \times ET \times IUR \times \left(\frac{1}{VF} + \frac{1}{PEF}\right) \times 1000}$$

Noncarcinogenic effects

$$RBTL_{ss-combined} = \frac{THQ \times BW \times AT_{nc} \times 365}{ED \times EF_d \times 10^{-6} \times \frac{1}{RfD_o}\left[\left(IR_s \times RAF_o\right) + \left(SA \times M \times RAF_d\right)\right]} + \frac{THQ \times AT_{nc} \times 365}{ED \times EF_d \times ET \times \frac{1}{RfC}\left(\frac{1}{VF} + \frac{1}{PEF}\right)}$$

Note: All parameters are defined under the individual pathway equations above (sections 1.2–1.4).

1.6 Subsurface Soil Concentrations Protective of Indoor Vapor Inhalation

$$RBTL_{si} = \frac{RBTL_{ai}}{\alpha} * EF$$

Where:

$RBTL_{si}$ = Risk-based target level for indoor inhalation of vapors from subsurface soils [mg/kg-dry soil]

$RBTL_{ai}$ = Risk-based target level for indoor inhalation of air [mg/m^3-air]

α = Chemical-specific attenuation factor from subsurface soil to indoor (enclosed space) air derived from the Johnson-Ettinger model [-]

EF = Equilibrium factor to convert vapor target level to total soil target level

$$= \frac{\theta_{ws} + (K_D \rho_s) + (H \theta_{as})}{(H \rho_s)} * 0.001$$

Where:

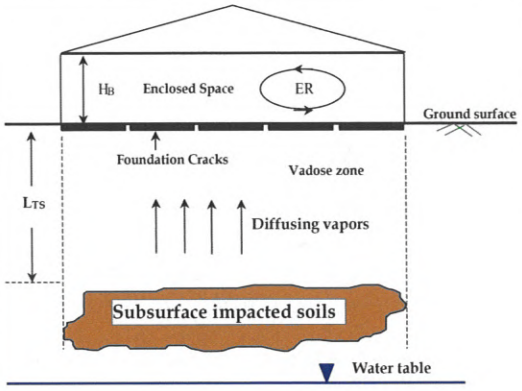
ρ_s = Dry soil bulk density [g-soil/cm^3-soil]

H = Chemical-specific Henry's Law constant [(L-H_2O)/(L-air)]

θ_{as} = Volumetric air content in the vadose zone soils [cm^3-air/cm^3-soil]

θ_{ws} = Volumetric water content in vadose zone soils [cm^3-H_2O/cm^3- soil]

K_D = $f_{oc} \times K_{oc}$ = Chemical-specific soil-water sorption coefficient [cm^3-H_2O/g-soil]



1.7 Ground Water Concentrations Protective of Indoor Vapor Inhalation

$$RBTL_{wi} = \frac{RBTL_{ai}}{\alpha} * EF$$

Where:

$RBTL_{wi}$ = Risk-based target level for indoor inhalation of vapors from ground water [mg/L-H_2O]

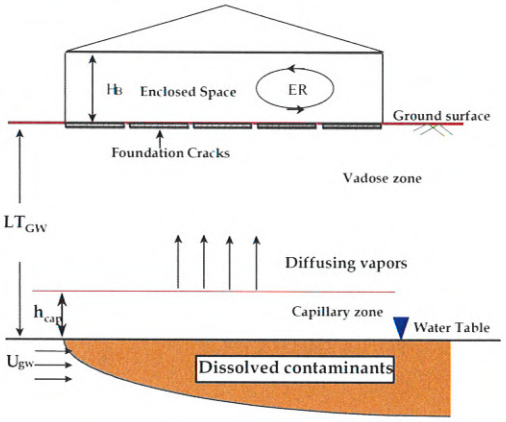
$RBTL_{ai}$ = Risk-based target level for indoor inhalation of air (mg/m^3-air)

α = Chemical-specific attenuation factor from ground water to indoor (enclosed space) air derived from the Johnson-Ettinger model [-]

EF = Equilibrium factor to convert vapor target level to water target level
= (1/H)*0.001m^3/L

Where:

H = Henry's Law Constant [-]



1.8 Direct Ingestion of Ground Water

Carcinogenic effects

$$RBTL_w = \frac{TR \times BW \times AT_c \times 365}{IR_w \times ED \times EF \times SF_o}$$

Noncarcinogenic effects

$$RBTL_w = \frac{THQ \times BW \times AT_{nc} \times 365}{IR_w \times \left(\frac{1}{RfD_o}\right) \times ED \times EF}$$

Source: Modified from EPA 1989, p. 6-35

Where:

$RBTL_w$	=	Risk-based target level for ingestion of ground water [mg/L-H_2O]
TR	=	Target risk or the increased chance of developing cancer over a lifetime due to exposure to a chemical [-]
THQ	=	Target hazard quotient for individual constituents [-]
BW	=	Body weight [kg]
AT_c	=	Averaging time for carcinogens [years]
AT_{nc}	=	Averaging time for noncarcinogens [years]
IR_w	=	Water ingestion rate [L/day]
ED	=	Exposure duration [years]
EF	=	Exposure frequency [days/year]
RfD_o	=	Chemical-specific oral reference dose [mg/(kg-day)]
SF_o	=	Chemical-specific oral cancer slope or potency factor $[mg/(kg\text{-}day)]^{-1}$
365	=	Conversion factor [days/year]

1.9 Johnson and Ettinger Infinite Source Model

The model predicts the vapor concentration inside a building from the measured soil-vapor, soil, or ground water concentration.

$$C_{building} = \alpha \times C_{source}$$

Where:

$$C_{source} = \frac{H \times C_{soil} \times \rho_s}{\theta_{ws} + K_d \times \rho_s + H \times \theta_{as}}$$

OR

$$C_{source} = H \times C_w$$

OR

C_{source} = Measured soil-vapor concentration [mg/L]

$$\alpha = \frac{\frac{D_T^{eff} A_B}{Q_{building} L_T} \times EXP\left(\frac{Q_{soil} L_{crack}}{D_{crack}^{eff} A_{crack}}\right)}{EXP\left(\frac{Q_{soil} L_{crack}}{D_{crack}^{eff} A_{crack}}\right) + \frac{D_T^{eff} A_B}{Q_{building} L_T} + \frac{D_T^{eff} A_B}{Q_{soil} L_T} \times \left[EXP\left(\frac{Q_{soil} L_{crack}}{D_{crack}^{eff} A_{crack}}\right) - 1\right]}$$

Source: EPA 2003

$C_{building}$	=	Steady-state vapor-phase concentration in the building [mg/L]
α	=	Attenuation coefficient in the vapor phase [-]
C_{source}	=	Vapor-phase concentration at the source [mg/L]
C_{soil}	=	Concentration in soil [mg/kg]
C_w	=	Concentration in ground water [mg/L]
H	=	Chemical-specific Henry's Law constant [(L-H_2O)/(L-air)]
ρ_s	=	Dry soil bulk density [g-soil/cm^3-soil]
θ_{ws}	=	Volumetric water content in vadose zone soils [cm^3-H_2O/cm^3-soil]
K_d	=	$f_{oc} \times K_{oc}$
	=	Chemical-specific soil-water sorption coefficient [cm^3-H_2O/g-soil]
θ_{as}	=	Volumetric air content in vadose zone soils [cm^3-air/cm^3-soil]
D_T^{eff}	=	Total overall effective diffusion coefficient [cm^2/s]
D_{crack}^{eff}	=	Effective diffusion coefficient through cracks [cm^2/s]
A_B	=	Area of the enclosed space below grade [cm^2]
$Q_{building}$	=	Building ventilation rate [cm^3/s]
L_T	=	Source-building separation [cm]
Q_{soil}	=	Volumetric flow rate of soil gas into the enclosed space [cm^3/s]
L_{crack}	=	Enclosed space foundation or slab thickness [cm]
A_{crack}	=	Total area of cracks [cm^2]

1.9 Johnson and Ettinger Infinite Source Model (continued)

Where:

$$Q_{building} = L_B W_B H_B ER$$

$$Q_{soil} = \frac{2\pi \Delta P k_v X_{crack}}{\mu \ln\left(\frac{2Z_{crack}}{r_{crack}}\right)}$$

For vapor release from soil:

$$D_T^{eff} = \frac{L_T}{\sum_{i=0}^{n} \frac{L_i}{D_i^{eff}}}$$

For vapor release from ground water:

$$D_T^{eff} = D_s^{eff} \qquad D_{crack}^{eff} = D_s^{eff}$$

$$D_T^{eff} = D_{ws}^{eff} = \frac{L_T}{\frac{h_{cap}}{D_{cap}^{eff}} + \frac{(L_T - h_{cap})}{D_s^{eff}}} \qquad h_{cap} = \frac{0.75}{D}$$

$Q_{building}$	=	Building ventilation rate [cm^3/s]
L_B	=	Length of building [cm]
W_B	=	Width of building [cm]
H_B	=	Height of building [cm]
ER	=	Air exchange rate [1/s]
Q_{soil}	=	Volumetric flow rate of soil gas into the enclosed space [cm^3/s]
π	=	3.14159
ΔP	=	Pressure differential between the soil surface and the enclosed space [$g/cm\text{-}s^2$]
k_v	=	Soil vapor permeability [cm^2]
X_{crack}	=	Floor-wall seam perimeter [cm]
μ	=	Viscosity of air [g/cm-s]
Z_{crack}	=	Crack depth below grade [cm]
r_{crack}	=	Equivalent crack radius [cm]
D_T^{eff}	=	Total overall effective diffusion coefficient [cm^2/s]
L_T	=	Source-building separation [cm]
L_i	=	Thickness of soil layer *i* [cm]
D_i^{eff}	=	Effective diffusion coefficient in soil layer *i* [cm^2/s]
n	=	Number of soil layers [-]
D_s^{eff}	=	Effective diffusion coefficient in soil [cm^2/s]
D_{ws}^{eff}	=	Effective diffusion coefficient in capillary fringe [cm^2/s]
h_{cap}	=	Thickness of capillary fringe zone [cm]
D_{cap}^{eff}	=	Effective diffusion coefficient in the capillary fringe soil [cm^2/s]
D_{crack}^{eff}	=	Effective diffusion coefficient in the foundation/wall cracks [cm^2/s]
D	=	Mean particle diameter [cm]

1.10 Johnson and Ettinger Finite Source Model

The model predicts the vapor concentration inside a building from the measured soil concentration when the thickness of soil contamination is known.

$$C_{building} = \alpha \times C_{source}$$

Where:

$$C_{source} = \frac{H \times C_{soil} \times \rho_s}{\theta_{ws} + K_d \times \rho_s + H \times \theta_{as}}$$

$$\alpha = \frac{\rho_s \; C_{soil} \; \Delta H_c \; A_B}{Q_{building} \; C_{source} \; \tau} \left(\frac{L_T^0}{\Delta H_c} \right) \left[\left(\beta^2 + 2 \; \psi \; \tau \right)^{1/2} - \beta \right]$$

$$\beta = \left(\frac{D_T^{eff} \; A_B}{L_T^0 \; Q_{soil}} \right) \left[1 - \exp\left(- \frac{Q_{soil} \; L_{crack}}{D_{crack}^{eff} \; A_{crack}} \right) \right] + 1$$

$$\psi = \frac{D_T^{eff} \; C_{source}}{\left(L_T^0 \right)^2 \; \rho_s \; C_{soil}}$$

$$\tau_D = \frac{\left[\Delta H_c / L_T^0 + \beta \right]^2 - \beta^2}{2 \; \psi}$$

Source: EPA 2003

$C_{building}$	=	Steady-state vapor-phase concentration in the building [mg/L]
α	=	Attenuation coefficient in the vapor phase [-]
C_{source}	=	Vapor-phase concentration at the source [mg/L]
C_{soil}	=	Original concentration in soil [mg/kg]
H	=	Chemical-specific Henry's Law constant [(L-H_2O)/(L-air)]
ρ_s	=	Dry soil bulk density [g-soil/cm^3-soil]
θ_{ws}	=	Volumetric water content in vadose zone soils [cm^3-H_2O/cm^3-soil]
K_d	=	$f_{oc} \times K_{oc}$
	=	Chemical-specific soil-water sorption coefficient [cm^3-H_2O/g-soil]
θ_{as}	=	Volumetric air content in vadose zone soils [cm^3-air/cm^3-soil]
ΔH_c	=	Initial thickness of contamination [cm]
τ_D	=	Time for source depletion [seconds]
τ	=	Exposure interval [seconds]
D_T^{eff}	=	Total overall effective diffusion coefficient [cm^2/s]
D_{crack}^{eff}	=	Effective diffusion coefficient through cracks [cm^2/s]
A_B	=	Area of the enclosed space below grade [cm^2]
$Q_{building}$	=	Building ventilation rate [cm^3/s]
L_T^0	=	Source-building separation at time = 0 [cm]
Q_{soil}	=	Volumetric flow rate of soil gas into the enclosed space [cm^3/s]
A_{crack}	=	Total area of cracks [cm^2]
L_{crack}	=	Enclosed space foundation or slab thickness [cm]

2 Target Levels for Residential Exposures

2.1 Indoor Inhalation of Vapor Emissions

Carcinogenic effects

$$RBTL_{ai\text{-}res} = \frac{TR \times AT_c \times 365}{EF_r \times ED_r \times ET_{ra} \times IUR}$$

Noncarcinogenic effects

$$RBTL_{ai\text{-}res} = \frac{THQ \times AT_{nc} \times 365}{EF_r \times ED_r \times ET_{ra} \times \left(\frac{1}{RfC}\right)}$$

Source: EPA 2009, modified from equations 6 and 11

Where:

$RBTL_{ai\text{-}res}$	=	Residential risk-based target level in indoor air [mg/m^3]
TR	=	Target risk or the increased chance of developing cancer over a lifetime due to exposure to a chemical [-]
THQ	=	Target hazard quotient for individual constituents [-]
AT_c	=	Averaging time for carcinogens [years]
AT_{nc}	=	Averaging time for noncarcinogens [years]
ED_r	=	Exposure duration for resident [years]
EF_r	=	Residential exposure frequency [days/year]
ET_{ra}	=	Indoor residential exposure time [hours/day]
RfC	=	Chemical-specific inhalation reference concentration [mg/m^3]
IUR	=	Chemical-specific inhalation unit risk [µg/m^3]$^{-1}$
365	=	Conversion factor [days/year]

2.2 Outdoor Inhalation of Vapors and Particulates from Surficial Soil

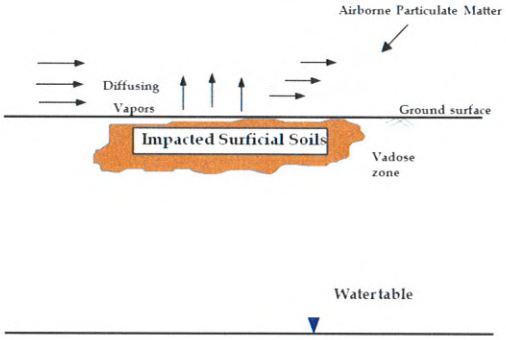
Carcinogenic effects

$$RBTL_{SS} = \frac{TR \times AT_c \times 365}{ED_r \times EF_{res} \times ET_{o-r} \times IUR \times \left(\frac{1}{VF} + \frac{1}{PEF}\right) \times 1000}$$

Noncarcinogenic effects

$$RBTL_{SS} = \frac{THQ \times AT_{nc} \times 365}{ED_c \times EF_{res} \times ET_{o-r} \times \left(\frac{1}{RfC}\right) \times \left(\frac{1}{VF} + \frac{1}{PEF}\right)}$$

Source: EPA 1996



Where:

$RBTL_{SS}$	=	Risk-based target level in surficial soil [mg/kg]
TR	=	Target risk or the increased chance of developing cancer over a lifetime due to exposure to a chemical [-]
THQ	=	Target hazard quotient for individual constituents [-]
VF	=	Surficial soil to ambient air volatilization factor [(m^3-air)/(kg-soil)]
PEF	=	Particulate emission factor [(m^3-air)/(kg-soil)]
AT_c	=	Averaging time for carcinogens [years]
AT_{nc}	=	Averaging time for noncarcinogens [years]
ED_c	=	Exposure duration for child [years]
ED_r	=	Residential exposure duration [years]
EF_{res}	=	Residential exposure frequency for direct contact pathway [days/year]
ET_{o-r}	=	Residential outdoor exposure time [hours/day]
RfC	=	Chemical-specific reference concentration [mg/(m^3)]
IUR	=	Chemical-specific inhalation unit risk [$\mu g/m^3]^{-1}$
365	=	Conversion factor [days/year]

2.3 Direct Ingestion of Surficial Soil

Carcinogenic effects

$$RBTLs_{-adj} = \frac{TR \times AT_c \times 365}{SF_o \times IR_{s-aa} \times RAF_o \times 10^{-6} \times EF_{res}}$$

Where:

$$IR_{s-aa} = \frac{ED_c \times IR_{s-c}}{BW_c} + \frac{(ED_{res} - ED_c) \times IR_{s-a}}{BW_a}$$

Noncarcinogenic effects

$$RBTLs = \frac{THQ \times AT_{nc} \times 365 \times BW_c}{IR_{s-c} \times \left(\frac{1}{RfD_o}\right) \times 10^{-6} \times EF_{res} \times ED_c}$$

Source: EPA 1996, p. 20

Where:

$RBTL_{s-adj}$	=	Age-adjusted risk-based target level for ingestion of soil for carcinogenic effects [mg/kg soil]
$RBTLs$	=	Risk-based target level for ingestion of soil for noncarcinogenic effects [mg/kg-soil]
TR	=	Target risk or the increased chance of developing cancer over a lifetime due to exposure to a chemical [-]
THQ	=	Target hazard quotient for individual constituents [-]
AT_c	=	Averaging time for carcinogens [years]
AT_{nc}	=	Averaging time for noncarcinogens [years]
RAF_o	=	Oral relative absorption factor [-]
RfD_o	=	Chemical-specific oral reference dose [mg/(kg-day)]
SF_o	=	Chemical-specific oral cancer slope or potency factor $[mg/(kg\text{-}day)]^{-1}$
IR_{s-aa}	=	Age-adjusted soil ingestion rate [mg-yr/kg-day]
IR_{s-c}	=	Resident child soil ingestion rate [mg/day]
IR_{s-a}	=	Resident adult soil ingestion rate [mg/day]
BW_c	=	Resident child body weight [kg]
BW_a	=	Resident adult body weight [kg]
ED_c	=	Resident child exposure duration [year]
ED_a	=	Resident adult exposure duration [year]
ED_{res}	=	Resident exposure duration [year]
EF_{res}	=	Exposure frequency for a resident for direct contact pathway [days/year]
365	=	Conversion factor [days/year]
10^{-6}	=	Conversion factor [kg/mg]

2.4 Dermal Contact with Surficial Soil

Carcinogenic effects

$$RBTL_{DC\text{-}adj} = \frac{TR \times AT_c \times 365}{SF_o \times SA_{aa} \times RAF_d \times 10^{-6} \times EF_{res}}$$

Where:

$$SA_{aa} = \frac{ED_c \times M_c \times SA_c}{BW_c} + \frac{ED_a \times M_a \times SA_a}{BW_a}$$

Noncarcinogenic effects

$$RBTL_{DC} = \frac{ED_c \times THQ \times AT_{nc} \times 365 \times BW_c}{RAF_d \times EF_{dc} \times ED_c \times M_c \times SA_c \times \left(\frac{1}{RfD_o \times RAF_o}\right) \times 10^{-6}}$$

Source: EPA 2007, Appendix D, p. D-6

Where:

$RBTL_{DC\text{-}adj}$	=	Age-adjusted risk-based target level for carcinogenic effects of dermal contact with soil [mg/kg soil]
$RBTL_{DC}$	=	Risk-based target level for noncarcinogenic effects of dermal contact with soil [mg/kg soil]
TR	=	Target risk or the increased chance of developing cancer over a lifetime due to exposure to a chemical [-]
THQ	=	Target hazard quotient for individual constituents [-]
AT_c	=	Averaging time for carcinogens [years]
AT_{nc}	=	Averaging time for noncarcinogens [years]
EF_{res}	=	Exposure frequency for a resident for direct contact pathway [days/year]
RAF_d	=	Chemical-specific dermal relative absorption factor [-]
RAF_o	=	Oral relative absorption factor [-]
M_c	=	Resident child soil-to-skin adherence factor [mg/cm^2]
M_a	=	Resident adult soil-to-skin adherence factor [mg/cm^2]
RfD_o	=	Chemical-specific oral reference dose [mg/(kg-day)]
SF_o	=	Chemical-specific oral cancer slope or potency factor [mg/(kg-day)]$^{-1}$
SA_{aa}	=	Age-adjusted skin surface area [mg-yr/ kg-day]
BW_c	=	Resident child body weight [kg]
BW_a	=	Resident adult body weight [kg]
ED_c	=	Resident child exposure duration [year]
ED_a	=	Resident adult exposure duration [year]
SA_c	=	Resident child skin surface area [cm^2/day]
SA_a	=	Resident adult skin surface area [cm^2/day]
365	=	Conversion factor [days/year]
10^{-6}	=	Conversion factor [kg/mg]

2.5 Combined Direct Contact Soil Pathway: Ingestion, Inhalation of Vapors and Particulates, and Dermal Contact

Carcinogenic effects

$$RBTL_{ss-combined} = \frac{TR \times AT_c \times 365}{SF_o \times 10^{-6} \times \left[\left(IR_{s-aa} \times RAF_o\right) + \left(SA_{aa} \times RAF_d\right)\right]} + \frac{TR \times AT_c \times 365}{ED_r \times EF_{res} \times ET_{o-r} \times IUR \times \left(\frac{1}{VF} + \frac{1}{PEF}\right) \times 1000}$$

Noncarcinogenic effects

$$RBTL_{ss-combined} = \frac{THQ \times AT_{nc} \times 365}{\frac{1}{RfD_o} \times 10^{-6} \times \left[\left(\left(\frac{ED_c + EF_{res} + IR_{s-c}}{BW_c}\right) \times RAF_o\right) + \left(\left(\frac{ED_c + EF_{res} + M_c + SA_c}{BW_c}\right) \times RAF_d\right)\right]} + \frac{THQ \times AT_{nc} \times 365}{ED_r \times EF_{res} \times ET_{o-r} \times \left(\frac{1}{RfC}\right) \times \left(\frac{1}{VF} + \frac{1}{PEF}\right)}$$

Note: All parameters are defined under the individual pathway equations above (sections 2.2–2.4).

2.6 Subsurface Soil Concentrations Protective of Indoor Vapor Inhalation

$$RBTL_{si} = \frac{RBTL_{ai}}{\alpha} * EF$$

Where:

$RBTL_{si}$ = Risk-based target level for indoor inhalation of vapors from subsurface soils [mg/kg-dry soil]

$RBTL_{ai}$ = Risk-based target level for indoor inhalation of air [mg/m^3-air]

α = Chemical-specific attenuation factor from subsurface soil to indoor (enclosed space) air derived from the Johnson-Ettinger model [-]

EF = Equilibrium factor to convert vapor target level to total soil target level

$$= \frac{\Theta_{ws} + (K_D \rho_s) + (H \Theta_{as})}{(H \rho_s)} * 0.001$$

Where:

ρ_s = Dry soil bulk density [g-soil/cm^3-soil]

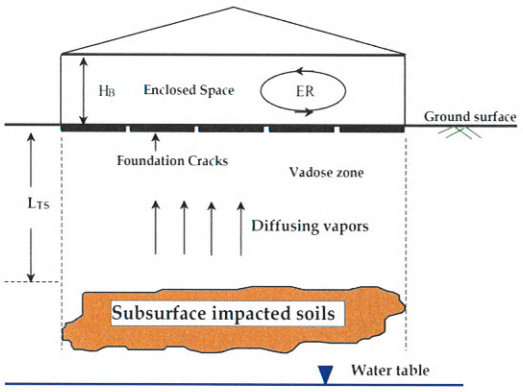
H = Chemical-specific Henry's Law constant [(L-H_2O)/(L-air)]

θ_{as} = Volumetric air content in the vadose zone soils [cm^3-air/cm^3-soil]

θ_{ws} = Volumetric water content in vadose zone soils [cm^3-H_2O/cm^3- soil]

K_D = $f_{oc} \times K_{oc}$ = Chemical-specific soil-water sorption coefficient [cm^3-H_2O/g-soil]

Source: Modified from EPA 2003



2.7 Ground Water Concentrations Protective of Indoor Vapor Inhalation

$$RBTL_{wi} = \frac{RBTL_{ai}}{\alpha} * EF$$

Where:

$RBTL_{wi}$ = Risk-based target level for indoor inhalation of vapors from ground water [mg/L-H_2O]

$RBTL_{ai}$ = Risk-based target level for indoor inhalation of air (mg/m^3-air)

α = Chemical-specific attenuation factor from ground water to indoor (enclosed space) air derived from the Johnson-Ettinger model [-]

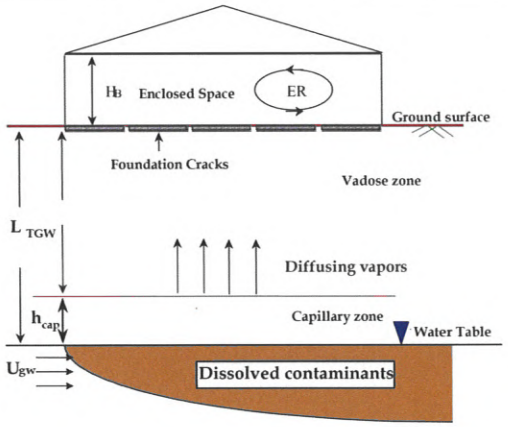
EF = Equilibrium factor to convert vapor target level to water target level

= (1/H)*0.001m^3/L

Where:

H = Henry's Constant [-]

Source: Modified from EPA 2003



2.8 Direct Ingestion of Ground Water

Carcinogenic effects

$$RBTL_{w\text{-}adj} = \frac{TR \times AT_c \times 365}{IR_{w\text{-}aa} \times SF_o}$$

Where:

$$IR_{w\text{-}aa} = \frac{ED_c \times EF_{res} \times IR_{w\text{-}c}}{BW_c} + \frac{ED_a \times EF_{res} \times IR_{w\text{-}a}}{BW_a}$$

Noncarcinogenic effects

$$RBTL_w = \frac{THQ \times AT_{nc} \times 365 \times RfD_o \times BW_a}{IR_{w\text{-}a} \times EF_{res} \times ED_a}$$

Source: Modified from EPA 1989, p. 6-35

Where:

$RBTL_{w\text{-}adj}$	=	Age-adjusted risk-based target level for ingestion of ground water [mg/L-H_2O]
$RBTL_w$	=	Risk-based target level for ingestion of ground water [mg/L-H_2O]
TR	=	Target risk or the increased chance of developing cancer over a lifetime due to exposure to a chemical [-]
THQ	=	Target hazard quotient for individual constituents [-]
AT_c	=	Averaging time for carcinogens [years]
AT_{nc}	=	Averaging time for noncarcinogens [years]
RfD_o	=	Chemical-specific oral reference dose [mg/(kg-day)]
SF_o	=	Chemical-specific oral cancer slope or potency factor [mg/(kg-day)]$^{-1}$
$IR_{w\text{-}aa}$	=	Age-adjusted ground water ingestion rate [L/kg]
$IR_{w\text{-}c}$	=	Resident child ground water ingestion rate [L/day]
$IR_{w\text{-}a}$	=	Resident adult ground water ingestion rate [L/day]
BW_c	=	Resident child body weight [kg]
BW_a	=	Resident adult body weight [kg]
ED_c	=	Resident child exposure duration [year]
ED_a	=	Resident adult exposure duration [year]
EF_r	=	Exposure frequency for a resident [days/year]
365	=	Conversion factor [days/year]

3 Target Levels for Ground Water Resource Protection

3.1 Domenico Model: Dilution Attenuation Factor (DAF) in the Saturated Zone

Domenico model for multi-dimensional transport with decay and infinite source:

$$\frac{C(x,y,z,t)}{C_o} = (1/8)\ exp\left[\frac{x}{2\,\alpha_x}\left[1-\sqrt{1+\frac{4\,k\,\alpha_x}{v}}\right]\right]\times erfc\left[\frac{\left[(x-vt)\sqrt{1+\frac{4\,k\,\alpha_x}{v}}\right]}{2\sqrt{\alpha_x \times v \times t}}\right]\times$$

$$\left[erf\left[\frac{\left(y+\frac{W_{gw}}{2}\right)}{2\sqrt{\alpha_y\,x}}\right]-erf\left[\frac{\left(y-\frac{W_{gw}}{2}\right)}{2\sqrt{\alpha_y\,x}}\right]\right]\times\left[erf\left[\frac{\left(z+\delta_{gw}\right)}{2\sqrt{\alpha_z\,x}}\right]-erf\left[\frac{\left(z-\delta_{gw}\right)}{2\sqrt{\alpha_z\,x}}\right]\right]$$

Where:

C	=	Dissolved-phase concentration [mg/L]
C_o	=	Dissolved-phase concentration at the source (at $x = y = z = 0$) [mg/L]
v	=	Retarded seepage velocity [m/sec]
k	=	Overall first order bio-decay rate [1/day]
α_x	=	Longitudinal dispersivity [m] ($\alpha_x = x/10$)
α_y	=	Lateral dispersivity [m] ($\alpha_y = x/30$)
α_z	=	Vertical dispersivity [m] ($\alpha_z = x/200$)
x, y, z	=	Spatial coordinates [m]
t	=	Time [day]
x	=	Distance along the centerline to point of exposure from the downgradient edge of dissolved-plume, source zone, or source well [m]
W_{gw}	=	Ground water mixing zone width [m]
δ_{gw}	=	Ground water mixing zone thickness [m]
DAF	=	C_o/C

Source: Domenico 1990, Eqn. 17.21

At the centerline, for steady-state (after a long time) with decay the concentration can be obtained by setting $y = 0$, $z = 0$, and $x << v \times t$ as:

$$\frac{C(x)}{C_o} = exp\left[\frac{x}{2\,\alpha_x}\left[1-\sqrt{1+\frac{4\,k\,\alpha_x}{v}}\right]\right]\times erf\left[\frac{W_{gw}}{4\sqrt{\alpha_y\,x}}\right]\times erf\left[\frac{\delta_{gw}}{2\sqrt{\alpha_z\,x}}\right]$$

At the centerline, for steady-state the concentration without decay can be obtained by setting $y = 0$, $z = 0$, $x << v \times t$, and $k = 0$ as:

$$\frac{C(x)}{C_o} = erf\left[\frac{W_{gw}}{4\sqrt{\alpha_y\,x}}\right]\times erf\left[\frac{\delta_{gw}}{2\sqrt{\alpha_z\,x}}\right]$$

Retarded seepage velocity v is given by the equation:

$$v = \frac{U_{gw}}{R \times \theta_T}$$

Where:

U_{gw}	=	ground water Darcy velocity [m/s]
R	=	retardation factor in the saturated zone [-]
θ_T	=	Total soil porosity in the saturated zone

3.2 Soil to Ground Water Leaching Factor

$$LF_{SW} = \frac{1}{DAF_{Summers} \times K_{Water-soil}}$$

$$DAF_{Summers} = 1 + \frac{U_{gw} \times \delta_{gw}}{I \times W_{gw}} \quad \text{(The Summers Model)}$$

$$K_{Water-soil} = \frac{\theta_{ws} + K_d \rho_s + H \times \theta_{as}}{\rho_s}$$

Where:

LF_{SW}	=	Soil to ground water leaching factor [mg/L-H_20)/mg/kg-soil)]
$DAF_{Summers}$	=	Dilution attenuation factor in the mixing zone [-]
$K_{Water-soil}$	=	Water-soil partitioning coefficient [(mg/kg-soil)/(mg/L-H_2O)]
ρ_s	=	Dry soil bulk density [g-soil/cm^3-soil]
θ_{ws}	=	Volumetric water content in vadose zone soils [cm^3-H_2O/cm^3- soil]
K_d	=	$f_{oc} \times K_{oc}$
	=	Chemical-specific soil-water sorption coefficient [cm^3-H_2O/g-soil]
H	=	Chemical-specific Henry's Law constant [(L-H_2O)/(L-air)]
θ_{as}	=	Volumetric air content in the vadose zone soils [cm^3-air/cm^3-soil]
U_{gw}	=	Ground water Darcy velocity [cm/yr]
δ_{gw}	=	Ground water mixing zone thickness [cm]
I	=	Infiltration rate of water through soil [cm/year]
W_{gw}	=	Ground water mixing zone length [cm]

Source: EPA 1996

3.3 Soil Saturation Limit

$$C_s^{sat} = \frac{S}{\rho_s} \times [H \times \theta_{as} + \theta_{ws} + K_d \rho_s]$$

Where:

C_s^{SAT}	=	Soil concentration at which dissolved pore water and vapor phases become saturated [(mg/kg-soil)]
S	=	Pure component solubility in water [mg/L-H_2O]
ρ_s	=	Dry soil bulk density [g-soil/cm^3-soil]
H	=	Chemical-specific Henry's Law constant [(L-H_2O)/(L-air)]
θ_{as}	=	Volumetric air content in the vadose zone soils [cm^3-air/cm^3-soil]
θ_{ws}	=	Volumetric water content in vadose zone soils [cm^3-H_2O/cm^3- soil]
K_d	=	$f_{oc} \times K_{oc}$
	=	Chemical-specific soil-water sorption coefficient [cm^3-H_2O/g-soil]

Source: ASTM 1995

3.4 Soil and Ground Water Concentration for Ground Water Protection

$$\textit{Allowable soil concentration at the source} = \textit{Target groundwater concentration at the POE} \times \frac{DAF_{POE}}{LF_{SW}} \times DAF_{unsat}$$

$$\textit{Allowable groundwater concentration at the source} = \textit{Target groundwater concentration at the POE} \times DAF_{POE}$$

$$\textit{Allowable groundwater concentration at the POC} = \textit{Target groundwater concentration at the POE} \times \frac{DAF_{POE}}{DAF_{POC}}$$

Where:

POE	=	Point of exposure
POC	=	Point of compliance
DAF_{POE}	=	Dilution Attenuation Factor (in the saturated zone) between the point of exposure and the source
DAF_{POC}	=	Dilution Attenuation Factor (in the saturated zone) between the point of compliance and the source
DAF_{unsat}	=	Dilution Attenuation Factor (in the vadose zone) between water table and soil source
LF_{sw}	=	Dry soil leaching factor

Additional relationships used in the calculation of allowable soil and ground water concentration with chemical degradation:

$$\textit{First order decay rate} = \frac{0.693}{Half - Life}$$

$$\text{Retardation Factor for Organics in saturated zone} = 1 + \left(\frac{\rho_{ss} \times K_{ds}}{\theta_{TS}} \right)$$

Where:

ρ_{ss}	=	Dry soil bulk density of the saturated zone soil [g-soil/cm^3-soil]
K_{ds}	=	Chemical-specific soil-water distribution coefficient in the saturated zone [mL/g]
	=	$K_{oc} \times f_{ocs}$
Koc	=	Organic carbon distribution coefficient in the saturated zone [mL/g]
f_{ocs}	=	Fractional organic carbon content in the saturated zone [-]
θ_{TS}	=	Total soil porosity in the saturated zone [cm^3/cm^3-soil]

4 Volatilization Factor, Particulate Emission Factor, and Effective Diffusion Coefficients

4.1 Volatilization Factor from Surface Soil to Outdoor (ambient) Air

$$VF = Q/C \times \frac{\left(3.14 \times D_A \times \tau\right)^{1/2}}{\left(2 \times \rho_s \times D_A\right)} \times 10^{-4}$$

Where:

$$D_A = \frac{\left(\theta_{as}^{10/3} \times D^a \times H + \theta_{ws}^{10/3} \times D^w\right)/\theta_T^2}{\rho_s \times K_d + \theta_{ws} + \theta_{as} \times H}$$

Where:

VF	=	Volatilization factor from surface soil to outdoor (ambient) air [(m^3-air)/(kg-soil)]
Q/C	=	Inverse of the mean concentration at the center of square source [cm^2/s]
D_A	=	Apparent diffusivity [cm^2/s]
τ	=	Averaging time for vapor flux [s]
ρ_s	=	Dry soil bulk density [g-soil/cm^3-soil]
K_d	=	Chemical-specific solid-water sorption coefficient [cm^3-H_2O/g-soil]
D^a	=	Chemical-specific diffusion coefficient in air [cm^2/s]
D^w	=	Chemical-specific diffusion coefficient in water [cm^2/s]
θ_T	=	Total soil porosity in the impacted zone [cm^3/cm^3-soil]
θ_{as}	=	Volumetric air content in the vadose zone soils [cm^3-air/cm^3-soil]
θ_{ws}	=	Volumetric water content in the capillary fringe soils [cm^3-H_2O/cm^3-soil]
H	=	Chemical-specific Henry's Law constant [(L-H_2O)/(L-air)]
10^{-4}	=	Conversion factor [m^2/cm^2]

Source: EPA 1996

4.2 Particulate Emission Factor

$$PEF = Q/C \times \frac{3600}{0.036 \times (1 - V) \times \left(U_m / U_t\right)^3 \times F(x)}$$

Where:

PEF	=	Particulate emission factor [(m^3-air)/(kg-soil)]
Q/C	=	Inverse of the mean concentration at the center of square source [(g/m^2-s)/(kg/m^3)]
V	=	Fraction of vegetative cover [-]
U_m	=	Mean annual wind speed [m/s]
U_t	=	Equivalent threshold value of wind speed at 7 m [m/s]
$F(x)$	=	Function dependent on U_m/U_t derived using Cowherd et al. 1985 [-]
0.036	=	Empirical constant [m^2-hr/g]

Source: EPA 1996

4.3 Effective Diffusion Coefficients

4.3.1 Effective Diffusion Coefficient in Soil

$$D_s^{eff} = D^a \times \frac{\theta_{as}^{3.33}}{\theta_T^{2.0}} + D^w \times \frac{1}{H} \times \frac{\theta_{ws}^{3.33}}{\theta_T^{2.0}}$$

Where:

D_s^{eff}	=	Effective diffusion coefficient in soil based on vapor-phase concentration [cm^2/s]
D^a	=	Chemical-specific diffusion coefficient in air [cm^2/s]
D^w	=	Chemical-specific diffusion coefficient in water [cm^2/s]
θ_{as}	=	Volumetric air content in capillary fringe soils [cm^3-air/cm^3-soil]
θ_{ws}	=	Volumetric water content in capillary fringe soils [cm^3-H_2O/cm^3-soil]
θ_T	=	Total soil porosity in the impacted zone [cm^3/cm^3-soil]
H	=	Chemical-specific Henry's Law constant [(L-H_2O)/(L-air)]

4.3.2 Effective Diffusion Coefficient between Ground Water and Surface Soil

$$D_{ws}^{eff} = L_{TGW} \times \left[\frac{h_{cap}}{D_{cap}^{eff}} + \frac{\left(L_{TGW} - h_{cap}\right)}{D_s^{eff}} \right]^{-1}$$

Where:

D_{ws}^{eff}	=	Effective diffusion coefficient between ground water and surface soil [cm^2/s]
h_{cap}	=	Thickness of capillary fringe [cm]
D_{cap}^{eff}	=	Effective diffusion coefficient through capillary fringe [cm^2/s]
D_s^{eff}	=	Effective diffusion coefficient in soil based on vapor-phase concentration [cm^2/s]
L_{TGW}	=	Source-building separation [cm]

4.3.3 Effective Diffusion Coefficient In Capillary Fringe Soil

$$D_{cap}^{eff} = D^a \times \frac{\theta_{acap}^{3.33}}{\theta_T^{2.0}} + D^w \times \frac{1}{H} \times \frac{\theta_{wcap}^{3.33}}{\theta_T^{2.0}}$$

Where:

D_{cap}^{eff}	=	Effective diffusion coefficient for the capillary fringe [cm^2/s]
D^a	=	Chemical-specific diffusion coefficient in air [cm^2/s]
D^w	=	Chemical-specific diffusion coefficient in water [cm^2/s]
θ_{acap}	=	Volumetric air content in capillary fringe soils [cm^3-air/cm^3-soil]
θ_{wcap}	=	Volumetric water content in capillary fringe soils [cm^3-H_2O/cm^3-soil]
θ_T	=	Total soil porosity [cm^3/cm^3-soil]
H	=	Chemical-specific Henry's Law constant [(L-H_2O)/(L-air)]

Source: ASTM 1995

4.3.4 Effective Diffusion Coefficient In Foundation/Wall Cracks

$$D_{crack}^{eff} = D^a \times \frac{\theta_{acrack}^{3.33}}{\theta_T^{2.0}} + D^w \times \frac{1}{H} \times \frac{\theta_{wcrack}^{3.33}}{\theta_T^{2.0}}$$

Where:

D_{crack}^{eff}	=	Effective diffusion coefficient through foundation cracks [cm^2/s]
D^a	=	Chemical-specific diffusion coefficient in air [cm^2/s]
D^w	=	Chemical-specific diffusion coefficient in water [cm^2/s]
θ_{acrack}	=	Volumetric air content in foundation/wall cracks [cm^3-air/cm^3-total volume]
θ_{wcrack}	=	Volumetric water content in foundation/wall cracks [cm^3-H_2O/cm^3-total volume]
θ_T	=	Total soil porosity [cm^3/cm^3-soil]
H	=	Chemical-specific Henry's Law constant [(L-H_2O)/(L-air)]

4.4 Water Content in Soil in the Capillary Fringe

$$\theta_{wcap} = \theta_r + \frac{\theta_{Tcap} - \theta_r}{\left[1 + (\alpha h)^N\right]^M}$$

Where:

θ_{wcap}	=	Water content in the capillary fringe zone soil [cm^3-water/cm^3-soil]
θ_r	=	Residual soil water content [cm^3-water/cm^3-soil]
θ_{Tcap}	=	Total porosity of soil in the capillary fringe zone [cm^3-voids/cm^3-soil]
α	=	Point of inflection in the water retention curve where $d\theta_w/dh$ is maximal [1/cm]
h	=	Air-entry pressure head [cm]
	=	$1/\alpha$ and assumed to be positive
N	=	Van Genuchten curve shape parameter [-]
M	=	$1 - (1/N)$

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Appendix F: Methodology and Example Calculation for Remedial Action Target Levels

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Introduction

For each receptor, the cumulative risk for carcinogenic effects and hazard index (HI) for noncarcinogenic effects at a site for all petroleum chemicals of interest (COIs) and complete routes of exposures (ROE) (except ingestion of water) should not exceed 1×10^{-5} and 1, respectively. This appendix describes the default methodology used by the Idaho Department of Environmental Quality (DEQ) to apportion risk and derive remedial action target level (RATL) concentrations for petroleum COIs in various media at sites where the risk or hazard is estimated to exceed the acceptable target risk level or acceptable HI.

Developing Target Levels: Method

The default method for developing target levels can be summarized by the following steps:

Step 1: Based on complete or potentially complete routes of exposure identified earlier and estimated representative concentrations, calculate the corresponding risk ($Risk_{i,j}^{rep}$) and hazard quotient ($HQ_{i,j}^{rep}$) for each chemical (i) for each complete pathway (j).

Results can be used to generate a matrix of risk and hazard quotient (HQ) values as shown in Table 1 below.

Table 1. Example matrix for calculation of remedial action target levels

Petroleum Chemical of Interest	Pathway 1		Pathway 2		Pathway 3		Cumulative		Number of Pathways	
	Risk	HQ	Risk	HQ	Risk	HQ	Risk	HI	Carcino-genic	Noncarcino-genic
C1	X	N/A	X	N/A	—	N/A	SUM	SUM	2	0
C2	N/A	X	N/A	X	N/A	X	SUM	SUM	0	3
C3	N/A	X	—	X	N/A	X	SUM	SUM	0	3
C4	X	N/A	X	N/A	X	N/A	SUM	SUM	3	0
C5	X	X	N/A	X	N/A	X	SUM	SUM	1	3
Cumulative							$Risk_{site}$ = SUM(SUM)	HI_{site} = SUM(SUM)	6	9

Note: **X** indicates pathway complete
N/A indicates not applicable because there is no relevant toxicity data or physical-chemical property.
A dash (—) indicates the value was not calculated because there was no entry under representative concentrations. This could mean that the chemical is not a petroleum chemical of interest for the pathway being evaluated based on release history or based on site characterization data.

Step 2: Calculate cumulative risk (site risk) and site HI.

$$Risk_{site} = \sum_{i=1}^{n_c} \sum_{j=1}^{m_i} Risk_{i,j}$$

$$HI_{site} = \sum_{i=1}^{n_{nc}} \sum_{j=1}^{m_i} HQ_{i,j}$$

Where:

$Risk_{i,j}$ = risk from exposure to chemical i through pathway j

$HQ_{i,j}$ = hazard quotient for exposure to chemical i through pathway j

m_i = number of complete pathways for chemical i (the suffix to m indicates that the number of complete pathways can be different for different chemicals)

n_c = number of carcinogenic chemicals at the site

n_{nc} = number of noncarcinogenic chemicals at the site

If the cumulative risk and HI for all the receptors at the site are below the acceptable levels, the site does not require the development of RATL. Site closure may be appropriate if other required regulatory issues have been resolved.

Step 3: Determine the number of chemical-pathway combinations (for carcinogens and noncarcinogens separately) at the site.

For the number of chemical-pathway combinations for carcinogens,

$$N_c = \sum_{i=1}^{n_c} \sum_{j=1}^{m_i} p_{i,j}$$

For the number of chemical-pathway combinations for non-carcinogens,

$$N_{nc} = \sum_{i=1}^{n_{nc}} \sum_{j=1}^{m_i} p_{i,j}$$

Where:**Error! Objects cannot be created from editing field codes.**

$p_{i,j}$ = complete pathway for chemical i and pathway j

m_i = number of complete pathways for chemical i (the suffix to m indicates that the number of complete pathways can be different for different chemicals)

n_c = number of carcinogenic chemicals at the site

n_{nc} = number of noncarcinogenic chemicals at the site

Note that some chemicals show both carcinogenic and noncarcinogenic toxicity and should be counted in both categories. For example, chemical C5 in the example above (Table 1) has 3 complete pathways for the noncarcinogenic effects and 1 pathway for the carcinogenic effects.

Step 4: Based on equal apportioning of target cumulative risk and HI, compute allocated risk and HQ contribution by chemical *i* through pathway *j* using the following equations:

$$Risk_{i,j}^{allocated} = \frac{1 \times 10^{-5}}{N_c}$$

$$HQ_{i,j}^{allocated} = \frac{1}{N_c}$$

Step 5: Estimate the risk reduction factor (RRF) in risk or HQ required so the contribution by chemical *i* acting through pathway *j* is equal to the allocated risk or allocated HQ.

Calculate the RRF for chemical *i* acting through pathway *j* with the following equation:

$$RRF_{i,j} = \frac{Risk_{i,j}^{rep}}{Risk_{i,j}^{allocated}}$$

Calculate the hazard quotient reduction factor (HQRF) for chemical *i* acting through pathway *j* with the following equation:

$$HQRF_{i,j} = \frac{HQ_{i,j}^{rep}}{HQ_{i,j}^{allocated}}$$

Step 6: Calculate the target level (i.e., allowable concentration) for chemical *i* acting through pathway *j*.

For carcinogens,

$$C_{i,j}^{allowable} = \frac{C_{i,j}^{rep}}{RRF_{i,j}}.$$

For noncarcinogens,

$$C_{i,j}^{allowable} = \frac{C_{i,j}^{rep}}{HQRF_{i,j}}.$$

If a chemical has $C_{i,j}^{allowable}$ based on carcinogenic and noncarcinogenic toxicity, the applicable RATL for that chemical should be the lower of the two allowable concentrations.

Developing Target Levels: Example

The following is an example of the target level calculations described above. Table 2 presents fictitious representative concentrations for each of five chemicals and three pathways (two soil and one ground water).

Table 2. Fictitious representative concentrations used in target level calculation example

Petroleum Chemical of Interest	Pathway 1 (milligrams/ kilogram)	Pathway 2 (milligrams/ kilograms)	Pathway 3 (milligrams/ liter)
C1	1	2	—
C2	2	4	2
C3	3	6	3
C4	4	8	4
C5	5	10	5

Step 1: Use these representative concentrations to calculate risk and HQ for each chemical and pathway the chemical acts through. The resulting matrix of risk and HQ values are shown in Table 3.

Table 3. Example of risk/chemical-of-interest/pathway matrix for target level calculation

Petroleum Chemical of Interest	Pathway 1		Pathway 2		Pathway 3		Cumulative		Number of Pathways	
	Risk	HQ	Risk	HQ	Risk	HQ	Risk	HI	Carcino-genic	Noncarcino-genic
C1	1E-5	N/A	2E-5	N/A	N/A	N/A	3E-5	N/A	2	0
C2	N/A	1	N/A	3	N/A	1	N/A	5	0	3
C3	N/A	1	—	1	N/A	3	N/A	5	0	3
C4	1E-5	N/A	1E-5	N/A	1E-5	N/A	3E-5	N/A	3	0
C5	2E-5	1	N/A	1	N/A	1	2E-5	3	1	3
Cumulative							$Risk_{site}$ = 8E-5	HI_{site} = 13	6	9

Note: **N/A** indicates not applicable because there is no relevant toxicity data or physical-chemical property. **A dash (—)** indicates the value was not calculated because there was no entry under representative concentrations. This could mean that the chemical is not a petroleum chemical of interest for the pathway being evaluated based on release history or based on site characterization data.

Step 2: Calculate the cumulative site risk and HI for all chemicals and pathways for a given receptor. (In this case, the site risk and HI are 7×10^{-5} and 13, respectively.)

Step 3: Determine the number of chemical-pathway combinations (for carcinogens and noncarcinogens separately) at the site. In this example, the number of chemical-pathway combinations for carcinogens is 6, and the number of chemical-pathway combinations for noncarcinogens is 9.

Step 4: Based on equal apportioning of the target cumulative risk and HI, calculate the allocated risk and HQ contribution by chemical *i* through pathway *j*.

$$Risk_{i,j}^{allocated} = \frac{1 \times 10^{-5}}{6} = 1.7 \times 10^{-6}$$

$$HQ_{i,j}^{allocated} = \frac{1}{9} = 0.11$$

Step 5: Estimate the RRF in risk or HQ required so that the contribution by a given chemical acting through a particular pathway is equal to the allocated risk or allocated HQ.

The RRF for chemical *i* acting through pathway *j* is found with the following equation:

$$RRF_{i,j} = \frac{Risk_{i,j}^{rep}}{Risk_{i,j}^{allocated}}$$

The HQ reduction factor for chemical *i* acting through pathway *j* is calculated with the following equation:

$$HQRF_{i,j} = \frac{HQ_{i,j}^{rep}}{HQ_{i,j}^{allocated}}$$

The calculations of the RFs for the example are presented in Table 4. At actual sites, the reduction factors are rarely as uniform as they are in the example.

Table 4. Reduction factor example for target level calculations

Petroleum Chemical of Interest	Pathway 1		Pathway 2		Pathway 3	
	RRF	HQRF	RRF	HQRF	RRF	HQRF
C1	1E-5/1.7E-6 = 6.0	N/A	2E-5/1.7E-6 = 12	N/A	—	N/A
C2	N/A	1/0.11 = 9.0	N/A	3/0.11 = 27	N/A	1/0.11 = 9.0
C3	N/A	1/0.11 = 9.0	—	1/0.11 = 9.0	N/A	3/0.11 = 27
C4	1E-5/1.67E-6 = 6.0	N/A	1E-5/1. 7E-6 = 6.0	N/A	1E-5/1. 7E-6 = 6.0	N/A
C5	2E-5/1.67E-6 = 12	1/0.11 = 9.0	N/A	1/0.11 = 9.0	N/A	1/0.11 = 9.0

Note: **N/A** indicates not applicable because there is no relevant toxicity data or physical-chemical property.
A dash (—) indicates the value was not calculated because there was no entry under representative concentrations. This could mean that the chemical is not a petroleum chemical of interest for the pathway being evaluated based on release history or based on site characterization data.

Step 6: Calculate the target level for a chemical acting through a given pathway.

For carcinogens,

$$C_{i,j}^{allowable} = \frac{C_{i,j}^{rep}}{RRF_{i,j}};$$

and for non-carcinogens,

$$C_{i,j}^{allowable} = \frac{C_{i,j}^{rep}}{HQRF_{i,j}}.$$

The resulting RATL calculations, carcinogenic and/or noncarcinogenic, for the example are presented in Table 5. The RATL concentrations are presented in bold.

Table 5. Example remedial action target level (RATL) concentrations for target level calculations

Petroleum Chemical of Interest	Pathway 1 (milligrams/kilogram)		Pathway 2 (milligrams/kilogram)		Pathway 3 (milligrams/liter)	
	$RATL_c$	$RATL_{nc}$	$RATL_c$	$RATL_{nc}$	$RATL_c$	$RATL_{nc}$
C1	1/6.0 = **0.17**	N/A	2/12 = 0.17	N/A	—	N/A
C2	N/A	2/9.0 = 0.22	N/A	4/27= **0.15**	N/A	2/9.0 = **0.22**
C3	N/A	3/9.0 = **0.33**	—	6/9.0 = 0.67	N/A	3/27 = **0.11**
C4	4/6.0 = **0.67**	N/A	8/6.0 = 1.3	N/A	4/6.0 = **0.67**	N/A
C5	5/12 = **0.42**	5/9.0 = 0.56	N/A	10/9.0 = 1.1	N/A	5/9.0 = **0.56**

Note: **N/A** indicates not applicable because there is no relevant toxicity data or physical-chemical property.
A dash (—) indicates the value was not calculated because there was no entry under representative concentrations. This could mean that the chemical is not a petroleum chemical of interest for the pathway being evaluated based on release history or based on site characterization data.

In this example, for chemical C5 and pathway P1, both carcinogenic and noncarcinogenic RATLs are calculated. The lower of the two, 0.42 milligrams/kilogram (the carcinogenic RATL), would be used.

Appendix G: Evaluation of the Vapor Intrusion Pathway

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EPA United States Environmental Protection Agency

EPA 510-R-15-001

Technical Guide For Addressing Petroleum Vapor Intrusion At Leaking Underground Storage Tank Sites

U.S. Environmental Protection Agency
Office of Underground Storage Tanks
Washington, D.C.

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Acronyms

1,2-DCA	1,2-Dichloroethane (also known as ethylene dichloride or EDC)
ATSDR	Agency for Toxic Substances and Disease Registry
BTEX	Benzene, Toluene, Ethylbenzene, Xylenes (there are three isomers of xylene)
CFR	Code of Federal Regulations
CSM	Conceptual Site Model
EDB	Ethylene Dibromide (also known as 1,2-dibromoethane)
IUR	Inhalation Unit Risk
ILCR	Incremental Lifetime Cancer Risk
IRIS	Integrated Risk Information System
ITRC	Interstate Technology & Regulatory Council
JEM	Johnson-Ettinger Model
LNAPL	Light Non-Aqueous Phase Liquid
MTBE	Methyl Tertiary-Butyl Ether
NAPL	Non-Aqueous Phase Liquid
OIG	Office of Inspector General
OSWER	Office of Solid Waste and Emergency Response
OUST	Office of Underground Storage Tanks
PHC	Petroleum Hydrocarbon
PPRTV	Provisional Peer Reviewed Toxicity Value
PVI	Petroleum Vapor Intrusion
RBC_v	Risk-based Concentration, Soil Vapor
RfC	Reference Concentration (inhalation)
RSL	Regional Screening Level (for Chemical Contaminants at Superfund Sites)
SIM	Selective Ion Monitoring
TAME	Tertiary-Amyl Methyl Ether
TBA	Tertiary-Butyl Alcohol
TEL	Tetraethyl Lead
TMB	Trimethylbenzene
TML	Tetramethyl Lead
TPH	Total Petroleum Hydrocarbons
UST	Underground Storage Tank
VI	Vapor Intrusion
VISL	Vapor Intrusion Screening Level
VOC	Volatile Organic Compound

Disclaimer

This document presents current technical recommendations of the U.S. Environmental Protection Agency (EPA) based on our current understanding of petroleum vapor intrusion (PVI) into indoor air from subsurface sources. This document provides technical information to EPA, state, tribal, and local agencies. It also informs the public and the regulated community on how EPA intends to implement its regulations. This guidance document does not impose any requirements or obligations on the EPA, the states, or local or tribal governments, or the regulated community. Rather, the sources of authority and requirements for addressing subsurface vapor intrusion are the relevant statutes and regulations. Decisions regarding a particular situation should be made based upon statutory and regulatory authority. Decision-makers retain the discretion to adopt or approve approaches on a case-by-case basis that differ from this document. Contact information for your state's UST-implementing agency may be found at *http://www.epa.gov/oust/states/statcon1.htm*. EPA may revise this document in the future, as appropriate.

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Recommendations

This document provides technical information to regulatory personnel from the U.S. Environmental Protection Agency (EPA) and state[1], tribal, and local agencies for investigating and assessing petroleum vapor intrusion (PVI) at sites where petroleum hydrocarbons (PHCs) have been released from underground storage tanks (USTs). This document is comprised of two parts: *Recommendations*, which provides a description of EPA's recommended approach for addressing PVI, and *Supporting Technical Information*, which provides detailed technical information supporting the recommendations.

Background

In 2002, EPA's Office of Solid Waste and Emergency Response (OSWER) issued draft vapor intrusion guidance, *OSWER Draft Guidance for Evaluating the Vapor Intrusion to Indoor Air Pathway from Groundwater and Soils (Draft Vapor Intrusion Guidance)* (EPA, 2002).[2] This draft guidance explicitly states that it is not recommended for addressing petroleum vapor intrusion (PVI) at UST sites regulated under Subtitle I of the Solid Waste Disposal Act through the Hazardous and Solid Waste Amendments of 1984.

In 2009, EPA's Office of Underground Storage Tanks (OUST), at the request of partners and stakeholders, initiated a collaborative effort to develop a technical guide for petroleum vapor intrusion. Further highlighting the need for information on PVI, EPA's Office of Inspector General later that year released an evaluation report, *Lack of Final Guidance on Vapor Intrusion Impedes Efforts to Address Indoor Air Risks* (Report No. 10-P-0042).[3] The report included recommendations, one of which was for EPA to issue final vapor intrusion guidance that incorporates information on how risks from petroleum hydrocarbon vapors should be addressed. In response to stakeholder requests, EPA's Office of Underground Storage Tanks developed this technical guide, which is a companion to OSWER's more general vapor intrusion guide.[4] Together, these two documents replace the 2002 Draft Vapor Intrusion Guide.

EPA developed the two guides to address different scenarios and meet the needs of different audiences. The UST program regulates a very large universe of sites, typically gas stations, which share many similar characteristics, including small release volumes (compared to pipelines and tank farms, for example) and the potential for aerobic biodegradation of petroleum vapors. Based on these facts, and to meet the request of UST regulators and practitioners, EPA developed a guide specifically focused on petroleum UST releases. This PVI guide provides screening criteria based on physical separation distances between vapor sources and potential receptors. EPA OUST derived the screening criteria from an analysis of a large

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[1] The term *state* refers to regulatory agencies of states, territories, and the District of Columbia.
[2] The OSWER draft guidance is accessible at http://www.epa.gov/osw/hazard/correctiveaction/eis/vapor/complete.pdf
[3] The OIG report is accessible at http://www.epa.gov/oig/reports/2010/20091214-10-P-0042.pdf
[4] *OSWER Technical Guide for Assessing and Mitigating the Vapor Intrusion Pathway From Subsurface Sources To Indoor Air* (OSWER Publication 9200.2-154), accessible at http://www.epa.gov/oswer/vaporintrusion/.

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data set of samples from leaking UST sites.[5] In contrast, the OSWER Vapor Intrusion Guide addresses a wide variety of sites and a broader range of contaminants.

Overview Of Petroleum Vapor Intrusion

Vapor intrusion is the general term given to migration of volatile organic chemicals (VOCs) from any subsurface contaminant source, such as contaminated soil or groundwater, through the soil and into an overlying building. There are two general classes of VOCs that account for a large number of soil and groundwater contamination sites in the United States:

- Petroleum hydrocarbons (PHCs) and non-PHC fuel additives
- Chlorinated solvents (e.g., the dry cleaning chemical tetrachloroethylene, also known as perchloroethylene, (PCE), and the degreasing solvents trichloroethylene (TCE), 1,1,1-trichloroethane (TCA)).

In this guide, petroleum vapor intrusion (PVI) is defined as the intrusion of vapors from subsurface PHCs and non-PHC fuel additives into overlying or nearby buildings or structures.

Vapors emanating from petroleum-contaminated soil or groundwater that enter buildings may result in indoor air concentrations that pose a risk to building occupants. PVI may pose both immediate threats to safety (e.g., fire or explosion potential from petroleum vapors or methane) and possible adverse health effects from inhalation of toxic chemicals (e.g., exposure to benzene from gasoline). PVI may be associated with three groups of volatile chemicals:

- PHCs found in gasoline, diesel, and jet fuel (e.g., benzene, trimethylbenzenes (TMBs), naphthalene)
- Volatile chemicals other than PHCs that may be found in petroleum fuels, such as ethers, alcohols, and other fuel additives (e.g., methyl tertiary-butyl ether (MTBE), tertiary-butyl alcohol (TBA), ethylene dibromide (EDB), and 1,2-dichloroethane (1,2-DCA))
- Methane, which is generated from anaerobic biodegradation of PHCs and other constituents of petroleum fuels (especially ethanol), and organic matter in soil

In contrast to chlorinated solvents, PHCs generally biodegrade rapidly under aerobic conditions and if biodegradation is complete, produce only water and carbon dioxide. If biodegradation is incomplete a variety of intermediate degradation products may be formed, but these are usually less toxic than the parent PHCs.[6] If chlorinated solvents biodegrade it is usually under

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[5] *Evaluation Of Empirical Data To Support Soil Vapor Intrusion Screening Criteria For Petroleum Hydrocarbon Compounds* (EPA 510-R-13-001), accessible at http://www.epa.gov/oust/cat/pvi/PVI_Database_Report.pdf

[6] Some petroleum hydrocarbons may also degrade anaerobically and may produce methane, particularly if the source is from an ethanol-blended gasoline. A recent modeling study cautions that for releases of high ethanol fuel blends (i.e., greater than E-20) advective methane transport may result in methane buildup inside buildings and pose a risk of explosion (Ma, et al., 2014, Numerical Model Investigation for Potential Methane Explosion and Benzene Vapor Intrusion Associated with High-Ethanol Blend Releases, *Environmental Science and Technology* 48(1):474-481).

anaerobic conditions, which is slower and may produce intermediate degradation products that are more toxic than the parent compounds.

The aerobic biodegradability of PHCs typically reduces the potential for PVI and justifies a different approach for addressing PVI than for vapor intrusion from chlorinated solvents and other non-aerobically biodegradable VOCs.[7]

Scope And Applicability

This PVI guide focuses on releases of petroleum-based fuels (e.g., gasoline, diesel), including both PHCs and non-PHC fuel additives, from underground storage tanks (USTs) regulated under Subtitle I of the Solid Waste Disposal Act of 1984, which are typically located at gas stations.[8] This guide applies to new and existing releases of PHCs and non-PHC fuel additives from leaking USTs and to previously closed sites where the implementing agency has reason to suspect that there may be a potential for PVI. Although EPA developed the PVI guide based on data from typical UST sites, this technical guide may also be helpful when addressing petroleum contamination at comparable non-UST sites. Petroleum contamination at sites that are not comparable to UST sites (such as refineries, petrochemical plants, terminals, aboveground storage tank farms, pipelines, and large scale fueling and storage operations at federal facilities), or sites with releases of non-petroleum chemicals including comingled plumes of petroleum and chlorinated solvents regardless of the source, should be addressed under OSWER's more general vapor intrusion guide.

This PVI guide does not impose legally binding requirements on implementing agencies or the regulated community. Decision-makers retain the discretion to adopt or approve approaches on a case-by-case basis that differ from this technical guide.

Recommended Actions For Addressing PVI

Addressing the potential for PVI is an integral part of the normal response to a suspected or confirmed release from any Subtitle I regulated UST system. At any leaking UST site, it is important to have a thorough understanding of the release (i.e., source, composition, and magnitude) and other factors that may influence the distribution and transport of contaminants that impact human safety and health. Until it is clear that human health and the environment are adequately protected from adverse impacts caused by the release, appropriate site characterization, risk assessment, and corrective action activities should continue.

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[7] For more information on the differences between PHCs and chlorinated solvents, see *Petroleum Hydrocarbons And Chlorinated Solvents Differ In Their Potential For Vapor Intrusion* (http://www.epa.gov/oust/cat/pvi/pvicvi.pdf)

[8] EPA's UST regulations are contained in 40 CFR Parts 280, 281, and 282.50-282.105 (see http://www.epa.gov/oust/fedlaws/cfr.htm). Definitions of key terms such as UST and petroleum are found in 40 CFR 280. These definitions may change if the regulations are revised in the future.

EPA recommends the following actions for situations in which EPA, state, tribal, and local agencies are investigating releases of petroleum-based fuels (including addressing potential risks due to PVI) at leaking UST sites or where 40 CFR 280 requires[9] UST owners and operators to undertake release investigation and corrective action activities:

- ✓ **Assess and mitigate immediate threats to safety – see Section 1** (p.11)
  Identify whether there is a potential threat of explosion or fire due to the presence of flammable PHCs and non-PHC fuel additive vapors or methane[10]. A threat could be indicated by reports of the presence of odors, disagreeable taste of water, or visible signs of PHC contamination by building occupants. If so, alert first responders so they can, if necessary, evacuate these buildings until the potential threat to human safety from fire or explosion due to PVI has been assessed and mitigated as needed.

- ✓ **Conduct a site characterization and develop a conceptual site model (CSM) – see Section 3** (p.39)
  Site characterization data should be integrated into a conceptual site model (CSM). This includes characterization of the physical, biological, and chemical systems at the site, with emphasis on determining the spatial and temporal relationships between receptors and sources of contamination. The CSM should be used as the basis for planning the PVI investigation and making informed risk management decisions about the site and the threat posed by PVI to nearby receptors. EPA recommends that the site characterization include:

  - Determining the full extent and location of contamination and its nature
  - Assessing the potential for biodegradation of PHCs (and non-PHC fuel additives)
  - Defining the hydrologic and geologic characteristics of the site
  - Identifying potential receptors in the vicinity
  - Determining whether preferential transport pathways are present and connect PHC vapor sources with potential receptors[11]
  - Considering whether there are any other factors that may preclude the use of screening criteria

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[9] In the case of a suspected or confirmed release from a regulated UST system, Subparts E and F of 40 CFR 280 require owners and operators to investigate, report, and perform corrective action (including recovery of light non-aqueous phase liquid (LNAPL) to the maximum extent practicable) if contamination is present, and submit timely reports of activities and findings to the implementing agency.

[10] Note that methane cannot be detected based on odor, taste or visible signs. Methane-detecting devices must be used. For additional information on evaluating the presence of methane and potential hazards, see ASTM's "New Practice for Evaluating Potential Hazard Due to Methane in the Vadose Zone", which is accessible at *http://www.astm.org/DATABASE.CART/WORKITEMS/WK32621.htm*.

[11] Preferential transport pathways can short-circuit the protectiveness provided by the extent of the lateral inclusion zone and the vertical separation distances described in this guide. If preferential transport pathways connect a vapor source directly to a building, indoor air sampling paired with sub-slab vapor sampling is recommended.

- ✓ **Delineate a lateral inclusion zone – see Section 4** (p.44)
  Delineate a lateral inclusion zone to focus the investigation on buildings located within these boundaries. The lateral inclusion zone is based on the spacing between clean monitoring points; the closer the spacing of the clean monitoring points, the less extensive the lateral inclusion zone.

- ✓ **Determine vertical separation distances for each building within the lateral inclusion zone – see Section 5** (p.48)
  Further narrow the investigation to potential receptors (e.g., buildings) within the lateral inclusion zone and directly overlie contamination. For such buildings, determine the vertical distance between the contamination and the building basement, foundation, or slab. This distance is determined by collecting soil gas, soil, and groundwater samples as necessary. The thickness of clean soil separating contamination from the deepest point of the building basement, foundation, or slab is the vertical separation distance.

  Additional investigation is generally unnecessary if the vertical separation distance is greater than 6 feet for dissolved contamination beneath buildings of any size, or 15 feet for light non-aqueous phase liquid (LNAPL) if the overlying building has at least one side shorter than 66 feet in length. If the distance to contamination is less than the appropriate vertical separation distance (i.e., 6 feet or 15 feet; see **Section 5**), then additional investigation is recommended.

- ✓ **Evaluate vapor source and attenuation of PHC vapors – see Section 5** (p.48), **Section 8** (p.66), **Section 9** (p.75), **Section 10** (p.81), **Section 12** (p.100), **and Section 13** (p.106)
  If contamination (either dissolved, or LNAPL whether mobile or residual) is in direct contact with a building EPA recommends indoor air sampling. In the case of direct contact, sub-slab samples cannot be collected because there is no subsurface soil between the contamination and the building. Where contamination is not in direct contact with an overlying building, then choose one of two options: (1) collect near-slab (exterior) shallow soil gas samples paired with deep (source) soil gas samples, or (2) collect indoor air samples paired with sub-slab soil gas samples. If the potential for PVI cannot be ruled out based on near-slab and deep soil gas sampling, then EPA recommends indoor air sampling paired with sub-slab vapor sampling. If the attenuation factor calculated from results of analysis of the chosen pair or vapor samples indicates that there may be a potential for PVI above applicable exposure limits, EPA recommends gathering additional information and data to determine whether mitigation is appropriate.

- ✓ **Mitigate PVI, as appropriate – see Section 1** (p.11)
  Mitigation involves interruption of the transport pathway for vapors between the source of contamination and potential receptors. Select a remedial design that is appropriate for the building and site. As necessary, establish institutional controls to limit or prohibit access to affected areas. Remediate the source of the contamination, including recovery of LNAPL (if present) to the maximum extent practicable.

Community Engagement

When conducting PVI assessments and follow-up actions, it is important to consider proactive community engagement. EPA acknowledges there is no single correct approach to engage the potentially impacted community in cleanup decisions. Community engagement can occur at any step in the process and may occur more than once. It is generally recognized that earlier and more frequent communication yields positive results, particularly for sites that pose a threat to human health or the environment, or when the public expresses an elevated level of concern or interest in the site. Depending on site circumstances, obtaining meaningful community input is a sound approach that may result in better-informed decisions. EPA developed several community engagement resources, which are available on the Office of Underground Storage Tanks website: Community Engagement And The Underground Storage Tank Program.[12] Some of the resources include:

- Guidelines For Tailoring Community Engagement Activities To Circumstances At Leaking Underground Storage Tank Sites.
- Community Engagement Resources (Toolbox) For Underground Storage Tank Programs.

Table 1 and **Figure 1** briefly outline the **Recommended Actions for Addressing PVI**. Note that this process is not necessarily linear and some of these activities may occur in a different order or recur throughout the PVI investigation; this is especially true for community engagement. Additional technical information is presented in the second part of this guide, *Supporting Technical Information.*

[12] The URL for this web site is *http://www.epa.gov/oust/communityengagement/index.htm*.

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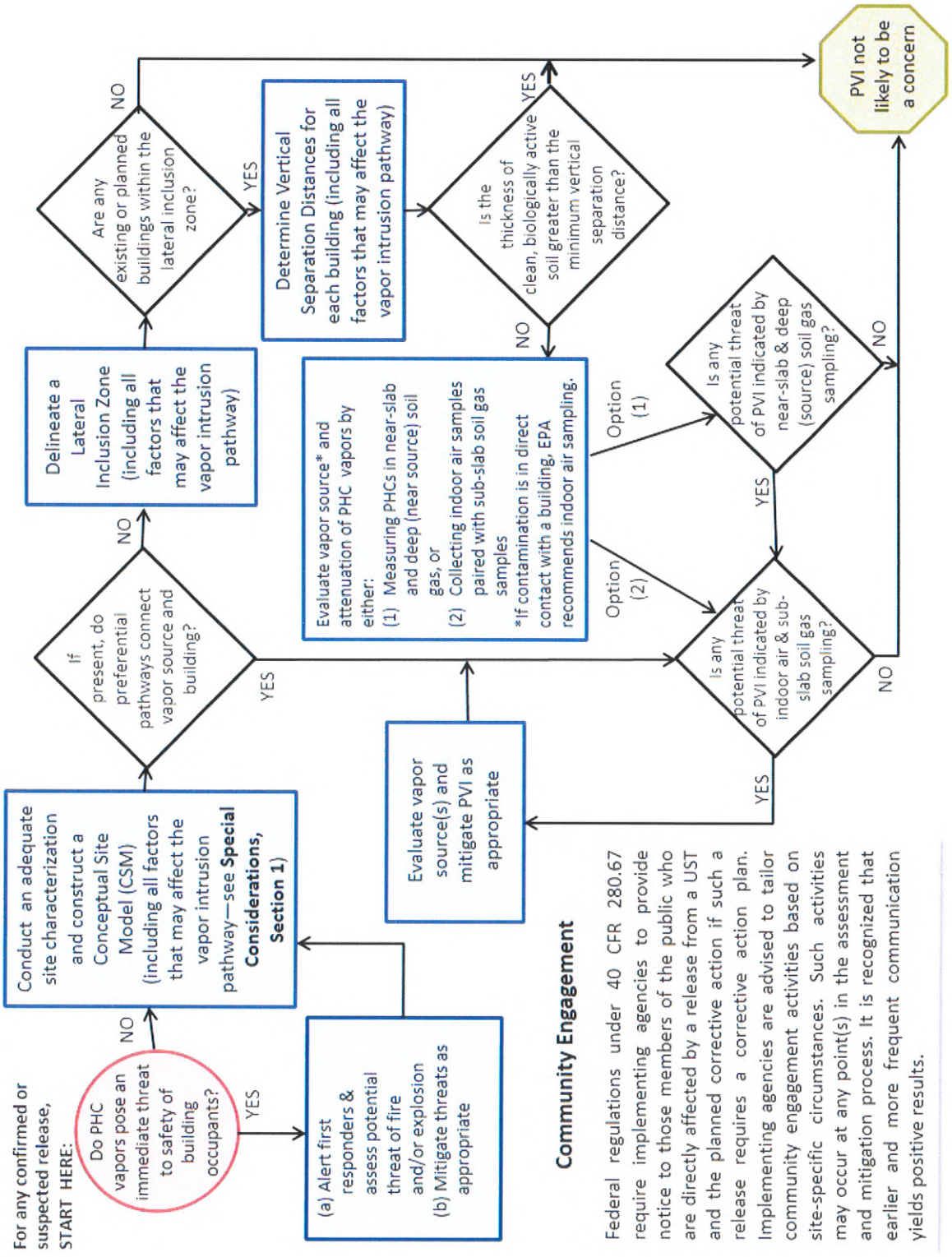
Table 1. Recommended Actions For Addressing PVI At Leaking Underground Storage Tank Sites

Recommended Actions	Purpose And Objectives	Procedures
Assess and mitigate immediate threats to safety (see Section 1, p.11)	Identify potential threat of explosion or fire due to petroleum vapors or methane. Threat may be indicated by: • LNAPL visible in building, possibly as sheen in sump • Noticeable petroleum odor; headache, dizziness, or nausea • Atypical, unusual, or disagreeable taste or smell in the water supply NOTE: Methane cannot be detected on the basis of odor, taste, or visible signs	• Investigate all reports of petroleum odors and other indicators within buildings • Detection of the presence of methane; requires specialized devices • Alert first responders so that they can, if necessary, evacuate building occupants as necessary until the potential for fire or explosion has been assessed and mitigated as needed
Conduct a site characterization and develop a conceptual site model (CSM) (see Section 3, p.39)	Characterize the physical, biological and chemical systems at the site, with emphasis on determining the spatial and temporal relationship between receptors and sources of contamination by: • Determining the full extent and location of contamination and its nature • Assessing the potential for biodegradation of PHCs • Defining the hydrologic and geologic characteristics of the site • Identifying potential receptors in the vicinity • Identifying whether preferential transport pathways are present and connect PHC vapor sources with potential receptors. Preferential transport pathways Include both natural (i.e., geologic) and man-made (i.e., underground utilities, excavations) features.	• Collect sufficient site data and information to construct CSM • Identify data gaps • Update CSM as new data become available • Where preferential transport pathways connect PHC vapor sources to receptors (e.g., buildings), indoor air sampling paired with sub-slab vapor sampling is recommended
Delineate a lateral inclusion zone (see Section 4, p.44)	Screen out buildings that are not likely to be impacted by PVI to narrow the investigation to only those buildings that have a greater potential for PVI and for which further investigation should be conducted. The lateral inclusion zone is site-specific and: • Based on the extent of contamination and distance between clean monitoring points • Decreases in extent as additional data are collected to reduce uncertainty in the CSM	• Construct lateral inclusion zone based on distance between clean monitoring points (includes consideration of the presence of preferential transport pathways)
Determine vertical separation distances (see Section 5, p.48)	Further screen out buildings that are not likely to be impacted by PVI to focus the investigation on potential receptors that overlie contamination in the dissolved, vapor, and/or LNAPL phase. The vertical separation distance is: • The thickness of clean, biologically-active soil	• For each building within the lateral inclusion zone, collect additional soil gas, soil, and groundwater samples as necessary to determine the vertical separation distance. Additional investigation is generally unnecessary

Recommended Actions	Purpose And Objectives	Procedures
	(see **Section 9**, p.75) separating contamination from overlying buildings or other potential receptors • Determined by site-specific sampling to determine the depth at which contamination is present	If the distance to contamination is greater than: • 6 feet for dissolved contamination beneath buildings of any size, or • 15 feet for LNAPL if the overlying building has at least one side shorter than 66 feet in length • If the distance to contamination is less than those indicated above, then additional investigation is recommended.
Evaluate vapor source and attenuation of PHC vapors (see Section 5, p.48, Section 8, p.66, Section 9, p.75, Section 10, p.81, Section 12, p.100, and Section 13, p.106)	Carefully evaluate the potential for PVI into those buildings identified as being the most likely to be impacted by PVI. This is a building-by-building evaluation based on sampling conducted within close proximity to the building or inside the building as necessary.	If contamination is in direct contact with building basement, foundation, or slab, then collect indoor air samples. Otherwise choose either option (1) or (2) below: 1. Collect near-slab soil gas samples coupled with deep (source) soil gas samples. If a potential threat of PVI is indicated, then proceed to option 2. If not, PVI is not likely to be a concern. 2. Collect indoor air samples paired with sub-slab soil gas samples. If these results indicate a potential threat of PVI, mitigate PVI as appropriate.
Mitigate PVI as appropriate (see Section 1, p.11)	Interrupt the pathway between the source of contamination and potential receptors. • Numerous approaches depending on building characteristics	• Select a remedial design that is appropriate for building and site • Remediate source of contamination, including recovery of LNAPL (if present) to the maximum extent practicable • Establish institutional controls to limit or prohibit access to affected areas of building, as necessary

Figure 1. Flowchart For Addressing PVI At Leaking Underground Storage Tank Sites



Supporting Technical Information

The following sections provide technical information in support of EPA's recommended actions as outlined in **Table 1** (p.7) and depicted in **Figure 1** (p.9). Each section presents information in a standardized format, which is easy to follow and allows for future revisions, as necessary.

Additional sources of information may be found in the Petroleum Vapor Intrusion Compendium (*http://www.epa.gov/oust/cat/pvi/*), located on the Office of Underground Storage Tanks (OUST) website (*http://www.epa.gov/oust/*).

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1. Petroleum Vapor Intrusion (PVI)

Description

Petroleum vapor intrusion (PVI) occurs when vapors from petroleum hydrocarbons (PHCs) migrate through the subsurface into overlying or nearby buildings. Fuels such as gasoline, diesel, aviation gasoline, and jet fuel are comprised primarily of PHCs with some non-petroleum based additives. Under certain circumstances, PVI may result in indoor air concentrations that pose a risk to building occupants. PVI may pose immediate threats to safety (e.g., fire or explosion potential from petroleum vapors or methane) or possible adverse health effects from inhalation of toxic chemicals (e.g., exposure to benzene from gasoline). Vapor concentrations generally decrease with increasing distance from a subsurface vapor source due to aerobic biodegradation, and eventually at some distance the concentrations become negligible.

Composition Of Petroleum Fuels

Petroleum fuels are comprised of hundreds of individual compounds. PHCs present in petroleum fuels generally belong to one of two major groups: aromatics and aliphatics. The aromatic PHCs are characterized as having one or more benzene rings. Benzene, toluene, ethylbenzene, and the three isomers of xylene are collectively referred to as BTEX. The aliphatics are non-aromatic PHCs consisting of straight-chains, branched chains, or non-aromatic rings. Although BTEX represent the group of PHCs that receive the most attention at typical leaking underground storage tank (UST) sites, they are not the only compounds that may pose a risk to human health.[13] Petroleum fuels may also contain a variety of non-PHC volatile organic chemicals (VOCs) as additives to enhance performance. Fuel oxygenates such as methyl

[13] The federal UST program does not prescribe human health values for contaminants; implementing authorities should use exposure values and attenuation factors appropriate for the contaminants present and the characteristics of exposure (e.g., residential vs industrial). Although there is a lack of toxicological data for many PHCs, EPA provides some information that may be applicable. For example, EPA provides vapor intrusion screening levels (VISLs) for a variety of volatile chemicals known to pose a potential cancer risk or noncancer hazard through the inhalation pathway. These VISLs, which are calculated by the VISL Calculator (EPA, 2014b), are generally recommended, medium-specific, risk-based screening-level concentrations intended for use in identifying areas or buildings that may warrant further investigation and mitigation of vapor intrusion, as appropriate. VISLs are calculated for concentrations of volatile chemicals in groundwater, soil gas (exterior to buildings and sub-slab), and indoor air for default target risk levels and exposure scenarios. The VISL Calculator does not account for biodegradation so attenuation factors may need to be adjusted for biodegradable chemicals. The VISL Calculator draws on toxicity values from Regional Screening Levels (RSLs) for Chemical Contaminants at Superfund Sites, accessible at http://www.epa.gov/reg3hwmd/risk/human/rb-concentration_table/index.htm. Both the *VISL Calculator User's Guide* (EPA, 2014a) and *VISL Calculator* (EPA, 2014b) may be downloaded from EPA's web site: http://www.epa.gov/oswer/vaporintrusion/guidance.html. RSLs are drawn from a variety of sources according to EPA's three-tiered hierarchy of toxicity data (see "Human Health Toxicity Values in Superfund Risk Assessments" OSWER Directive 9285.7-53, 2003). Tier 1 (highest quality data) is EPA's Integrated Risk Information System (IRIS), accessible at http://www.epa.gov/iris/. Tier 2 are Provisional Peer Reviewed Toxicity Values (PPRTVs), accessible at http://hhpprtv.ornl.gov/ (also see EPA, 2009). Tier 3 include toxicity values from other sources such as the Agency for Toxic Substances and Disease Registry (ATSDR). Several states have also developed toxicity values, including California (CA DTSC, 2009), Hawai'i (HI DOH, 2008, 2012), Massachusetts (MA DEP, 2003), New Jersey (NJ DEP, 2013), and Washington (WA DEC, 2006). Links to these sources are provided under *References Cited* at the end of this section.

tertiary-butyl ether (MTBE) and tertiary-butyl alcohol (TBA), and the lead scavengers[14] ethylene dibromide (EDB), and 1,2-dichloroethane (1,2-DCA), plus other PHCs (e.g., naphthalene), may also pose a risk to human health. If present, their vapor intrusion potential should be assessed (see **Section 10**, p.81). The presence of biodegradable VOCs other than benzene may result in depletion of oxygen that is necessary for aerobic biodegradation of benzene, potentially resulting in farther migration of benzene vapors.

Phase Partitioning

When petroleum fuels are released into the subsurface from a leaking UST, PHCs may partition into several phases:

- Globules of light non-aqueous phase liquid (LNAPL) trapped within soil pore spaces (i.e., residual LNAPL)
- Dissolved in soil moisture
- Adhered onto the surface of, or absorbed into, soil solids
- Vapors in soil gas
- Accumulations of mobile LNAPL on and in the capillary fringe[15]
- Dissolved in groundwater

Low volume releases may result in contamination of only soil (including soil gas and soil moisture) and remain in the vadose zone. If the volume of a fuel release is sufficient, the fuel may accumulate on and in the capillary fringe and become mobile LNAPL. The mobile LNAPL generally spreads in the direction of groundwater flow, and may accumulate in monitoring wells. Temporal fluctuations in the elevation of the water table typically create a vertical smear zone of residual LNAPL contamination both above and below the average water table elevation. The more soluble components of the LNAPL mass dissolve into groundwater and are transported down gradient by the flowing groundwater as an aqueous phase. The remaining LNAPL mass will contain a sizeable fraction of aliphatic and relatively insoluble PHCs (e.g., naphthalene), especially if the source is large or unweathered (Lahvis, et al., 2013; EPA, 2013a). PHCs in the residual phase (both above and below the water table), the mobile phase (i.e., free product, LNAPL plume), and the dissolved phase (i.e., contaminant plume) all can serve as sources of PHC vapors. **Figure 2** illustrates the typical distribution of petroleum fuels in the subsurface resulting from a leaking UST. See **Section 2** (p.33) for a more detailed discussion of typical PVI scenarios.

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[14] Older sites, where leaded gasoline was released to the subsurface, should be assessed for EDB and 1,2-DCA as they may represent a potential source of vapors (see **Section 10**). For more information about lead scavengers, see Appendix F in *Evaluation Of Empirical Data To Support Soil Vapor Intrusion Screening Criteria For Petroleum Hydrocarbon Compounds* (EPA, 2013) and EPA's Lead Scavengers web site at *http://www.epa.gov/oust/cat/leadscav.htm*.

[15] Mobile LNAPL is often referred to as free product, especially in older documents and 40 CFR 280.

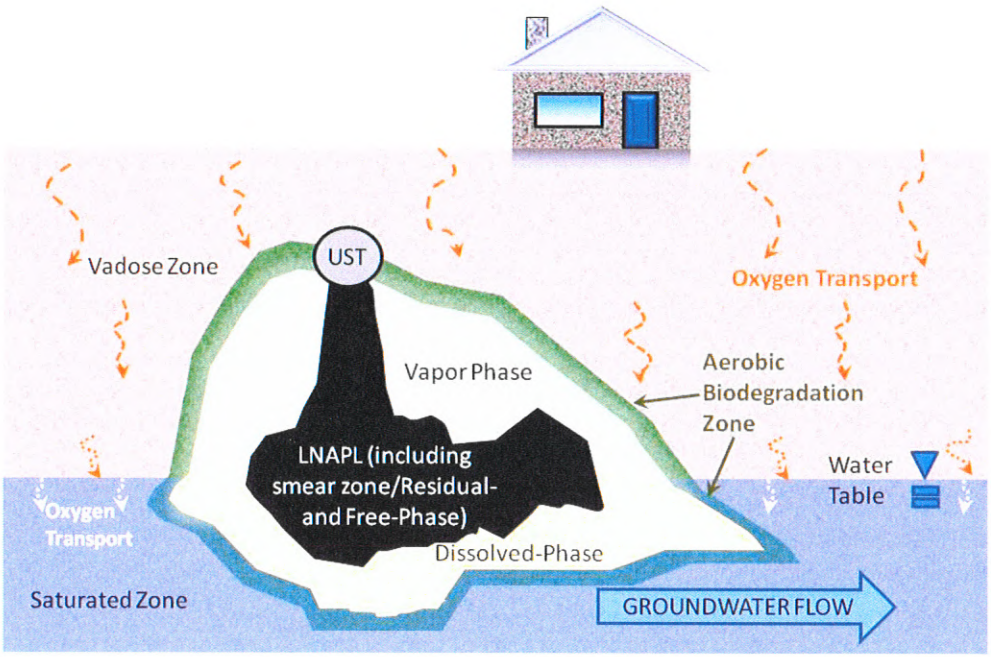

Figure 2. Conceptual Model Of Typical Petroleum Hydrocarbon Release

Aerobic biodegradation of PHCs along the perimeter of the vapor and dissolved plumes may limit the spread of subsurface contamination. Effective oxygen transport (dashed arrows) maintains aerobic conditions in the biodegradation zone. Petroleum LNAPL collects at the capillary fringe between the saturated and unsaturated zones (EPA, 2012).

Vapor Migration

Vapor migration results from two processes: diffusion and advection. Diffusion is the process whereby net transport of vapors from a source area of higher concentration (e.g., LNAPL, residual LNAPL, or dissolved plume) to an area of lower concentration occurs as a result of random molecular motion. Diffusion can also lead to chemical migration into buildings directly through a dirt floor or crawlspace, or through openings in the building slab and foundation such as passages for utility lines, sumps, and elevator pits. Also, intact concrete has appreciable permeability to diffusive gas movement (Kobayashi and Shuttoh, 1991; Sanjuan and Munoz-Martialay, 1996; and Tittarelli, 2009) and the permeability increases substantially when cracks are present (Daoud and Renken, 1999; EPA, 1995).

Advection refers to the movement of soil gas in response to pressure gradients. Advection can be an important mechanism for drawing soil gas and contaminant vapors through cracks in the basement floor or foundation into the building or back into the soil beneath the building. Heating and cooling systems can create differential pressures inside the building. When the pressure inside the building is lower than the pressure in the subsurface, vapors are drawn into the building. Conversely, when the pressure inside the building is greater than the pressure in

the subsurface, air within the building may be forced into the subsurface causing some degree of reoxygenation (Lundegard, Johnson, and Dahlen, 2008). Wind or changes in barometric pressure may also drive advective transport of oxygen into the subsurface beneath the building (Lundegard, Johnson, and Dahlen, 2008; Patterson and Davis, 2009; McHugh, DeBlanc, and Pokluda, 2006; Luo and Johnson, 2011; Robinson, Sextro, and Riley, 1997; Luo, et al., 2009; and Hong, Holton, and Johnson, 2012) (see **Section 11**).

Biodegradation Of PHCs

Biodegradation of PHCs is recognized as one of the primary mechanisms by which petroleum and other hydrocarbon pollutants are removed from the environment (Baedecker, Cozzarelli, and Hoppel, 1987; Leahy and Colwell, 1990). The biodegradability of PHCs often reduces the potential for human exposure from PVI (McHugh, et al., 2010; EPA, 2012; Interstate Technology & Regulatory Council [ITRC], 2014). Microorganisms are widely distributed in the environment and most are recognized as having some ability to metabolize PHCs (Gale, 1951; Ward, Singh, and Van Hamme, 2003; Prince, 2010). Although most microbes degrade a narrow range of organic compounds, they typically exist as a mixed consortium that collectively can biodegrade a wide range of organic compounds. Biodegradation progresses through stages with certain microbes being predominant until environmental conditions (e.g., availability of specific hydrocarbons, micronutrients, electron acceptors) become unfavorable for them at which time different microbes then become dominant (Wang and Deshusses, 2006; Suflita and Mormile, 1993; Corseuil, et al., 1998; Moyer, et al., 1996; Boopathy, 2004; Alexander, 1980; Prince, Parkerton, and Lee, 2007; Prince, 2010; and Bekins, et al., 2001). Thus, aerobic and anaerobic microbes may coexist with one class essentially dormant while the other is active.

Gasoline and diesel fuel (including biodiesel) may be completely biodegraded under aerobic conditions (Hult, 1987; Prince and Douglas, 2010; Prince, Parkerton, and Lee, 2007; Marchal, et al., 2003), though diesel fuel is more difficult and slower to biodegrade (Marchal, et al., 2003).[16] The end products of complete biodegradation (mineralization) of PHCs are water and carbon dioxide. Mineralization of PHCs is almost always the consequence of microbial activity (Alexander, 1981). If aerobic biodegradation of PHCs is incomplete, a variety of intermediate degradation products may be formed, but none of these are more toxic than the parent PHCs.

Aerobic biodegradation is well documented for many individual PHCs and classes of PHCs including:

- N-alkanes (Bouchard, et al., 2005; Prince, Parkerton, and Lee, 2007; Bailey, Jobson, and Rogers, 1973; Hult, 1989; Baedecker, et al., 2011)
- Branched alkanes (Prince and Douglas, 2010; Prince, Parkerton, and Lee, 2007); cycloalkanes (Bouchard, et al., 2005)

[16] The rate of aerobic biodegradation slows down with decreasing concentration of oxygen. Many aerobic microorganisms continue to function at concentrations as low as 0.1 mg/L of available oxygen, which is equivalent to an air concentration of 0.2%. For more information see research by Alagappan and Cowan (2004), Miralles-Wilhelm, Gelhar, and Kapoor (1997), and Mohamed, Saleh, and Sherif (2010).

- Aromatics (Wang and Deshusses, 2007; Phelps and Young, 1999; Landmeyer and Bradley, 2003; Lahvis, Baker, and Baehr, 2004; Lahvis, Baehr, and Baker, 1999; Bailey, Jobson, and Rogers, 1973; ZoBell, 1946; Corseuil, et al., 1998; Richnow et al., 2003)
- Naphthenes (Prince, Parketon, and Lee, 2007; Bailey, Jobson, and Rogers, 1973; Anderson, et al., 1999; ZoBell, 1946)
- Phenols (ZoBell, 1946; Basha, Rajendran, and Thangavelu, 2010)
- Trimethylbenzenes (Chen, et al., 2009)

Though aerobic biodegradation has been studied for over a century, anaerobic biodegradation of PHCs has been recognized only within the past three decades (Widdel, Boetius, and Rabus, 2006; Spormann and Widdel, 2000; and Townsend, et al., 2003). Anaerobic microorganisms degrade PHCs by using an electron acceptor other than oxygen (e.g., sulfate, nitrate, ferrous iron, or carbon dioxide). Anaerobic biodegradation is a slower process than aerobic biodegradation (Widdel, Boetius, and Rabus, 2006; Bailey, Jobson, and Rogers, 1973; and Lanham et al., 2013) and anaerobes grow slower than their aerobic counterparts (Widdel, Knittel, and Galushko, 2010). Instead of water and carbon dioxide, complete anaerobic biodegradation of PHCs (and naturally-occurring organic matter in soil, such as peat) can produce methane (Zengler, et al., 1999), especially with a release of an ethanol-blended gasoline (Jewell and Wilson, 2011; Ma, et al., 2012; Ma, et al., 2014). Incomplete anaerobic biodegradation of PHCs can produce compounds of higher toxicity, but these vapors are readily biodegraded in the vadose zone under aerobic conditions, and thus should not present a threat of vapor intrusion. Anaerobic biodegradation is typically the predominant mechanism of biodegradation in the source zone (Anderson and Lovley, 1997). Additional references documenting anaerobic biodegradation of PHCs are listed under *Additional Information* at the end of this section.

Importance

Important factors cited by Lahvis and Baehr (1996) and Suarez and Rifai (1999) as being influential for aerobic biodegradation of PHC vapors include:

- Vapor source hydrocarbon concentration, flux, and composition (including methane)
- Oxygen demand (i.e., the oxygen required to biodegrade the available hydrocarbons and any other organic matter present) and oxygen availability
- Soil type and properties (including texture and moisture content)
- Availability of essential micronutrients
- Ambient temperature in the subsurface
- The pH of the soil and groundwater

Additional factors cited by EPA (2012) as influencing the potential for PVI include:

- Size and characteristics of the building and adjacent land surface
- Distance between the vapor source and the building

Assessment

An assessment of the potential for PVI is not an isolated activity, but rather an integral part of the normal response to a suspected or confirmed release of PHCs from a leaking UST. At any leaking UST site (including abandoned sites or those that will be redeveloped for other uses), it is important to have a thorough understanding of the nature and magnitude of the release; the physical, biological, and chemical characteristics of the subsurface environment; an understanding of the preferential pathways for contaminant transport; and locations of receptors in the vicinity of the release. This is determined through collection and analysis of samples of soil, soil gas, groundwater, and sometimes LNAPL. Any other conditions (e.g., seasonal, weather-related; see **Section 11**, p.96) that may influence the transport of contaminants and potentially impact the safety and health of nearby building occupants should also be investigated.

Vapors emanating from dissolved-phase sources are primarily water soluble compounds, the more soluble aromatic hydrocarbons (e.g., BTEX) and other volatile and semi-volatile hydrocarbons and fuel additives (Lahvis, et al, 2013; EPA, 2013a). Vapors emanating from LNAPL sources contain a significantly larger fraction of aliphatic compounds and relatively insoluble hydrocarbons, especially if the source is large or unweathered (Lahvis, et al., 2013; EPA, 2012). Analyses of samples of soil, soil gas, groundwater, and LNAPL collected during site characterization (see **Section 3**, p.39) will provide information on specific contaminants that may warrant assessment for potential vapor intrusion.

Special Considerations

Several factors may preclude the effectiveness of aerobic biodegradation to mitigate the threat of vapor intrusion. They include:

- Source volume and composition (including PHCs and non-PHC fuel additives)
- Soil properties (moisture content, permeability, high organic carbon content, especially peat)
- Large building size
- Extensive impermeable surface covering (e.g., asphalt, concrete)
- Preferential transport pathways (including both natural and man-made)

If present, these factors may reduce the potential for biodegradation of PHC vapors and warrant additional investigative steps (e.g., collection of soil gas samples—see **Section 8**, p.66) to determine if the use of screening criteria (e.g., vertical separation distance) is appropriate.

The age and volume of release should be determined or estimated. When the release is relatively recent or if the volume of the release is relatively large[17], there is greater potential for PVI than for smaller or older releases, which may be more weathered. Large volume PHC

[17] The adjective *large* refers to either the total volume of the release or the areal extent (footprint) of the LNAPL mass in the subsurface.

releases may require a greater separation distance for biodegradation to be effective due to increased oxygen demand (EPA, 2013a).

Biodegradation of recent releases of high ethanol blended gasoline (i.e., E-20 or greater) may consume oxygen that would otherwise be available for biodegradation of PHCs resulting in an increased potential for PVI (Ma et al., 2014). In addition, the biodegradation of ethanol may result in the advective transport of methane and a potential risk of explosion. Thus, larger separation distances may be necessary to mitigate the threat of explosion or PVI at sites where high ethanol blended fuel has been released into the subsurface (Ma et al., 2014).

Preferential transport pathways may be either natural (e.g., fractures in rock, solution channels in karst terrain, bedding planes, joints, high permeability layers) or man-made (e.g., utility corridors including sewer lines themselves, trenches, excavations). Because they increase the speed at which the contaminants move through the subsurface, preferential transport pathways can potentially short circuit protectiveness that would otherwise be provided by biodegradation of PHCs and other fuel additives in homogeneous soils. Typically, it is difficult to detect and map natural preferential transport pathways, and contamination may present itself in unexpected locations. Local government offices have maps of utility corridors that can provide information on the presence and location of man-made preferential transport pathways.[18]

Recommended Steps For Addressing The Potential Risk From PVI

EPA recommends the following actions for situations in which EPA, state, tribal, and local agencies are investigating releases of petroleum-based fuels (including addressing potential risks due to PVI) at leaking UST sites or where 40 CFR 280 requires[19] UST owners and operators to undertake release investigation and corrective action activities:

- ✓ ***Assess and mitigate immediate threats to safety***

Some releases from UST systems are discovered through noticeable sensory indicators on neighboring properties. Indicators may include sight, smell, taste, or physiological effects (e.g., dizziness, headache, nausea, vomiting, and confusion). The presence of odors does not necessarily correspond to adverse health or safety impacts from PVI, as the odors could be the result of indoor vapor sources. However, it is generally prudent to investigate any reports of odors in close proximity to UST systems as the odor threshold for some chemicals exceeds their acceptable health-based concentrations. PHC odors are a nuisance and may trigger the need

[18] A federally mandated national call center was established to ensure that utility lines are marked before digging or boring. Dial 811 to have the locations of utilities marked before conducting site work that involves digging or boring. For more information, visit http://www.call811.com/default.aspx

[19] In the case of a suspected or confirmed release from a regulated UST system, Subparts E and F of 40 CFR 280 require owners and operators to investigate, report, and perform corrective action (including recovery of LNAPL to the maximum extent practicable) if contamination is present, and submit timely reports of activities and findings to the implementing agency.

for abatement or mitigation even if the concentration in indoor air is below acute or chronic health-based levels.

In confined spaces, the presence of flammable PHC vapors and non-PHC fuel additive vapors or methane may pose a threat of fire or explosion and endanger building occupants. Federal regulations (40 CFR 280.61) require that immediate action be taken to prevent any further release of the regulated substance into the environment and that fire, explosion, and vapor hazards be identified and mitigated (*Federal Register*, 1988). Section 280.64 requires that free product (mobile LNAPL) be recovered to the maximum extent practicable and that records be kept of the volumes recovered. First responders, typically fire department personnel, should be notified if there are reports of either odor from petroleum or the presence of an oily sheen on basement floors or in sumps, drains, or elevator pits. It may be necessary to evacuate building occupants until the threat from fire or explosion has been mitigated. Since methane is odorless and colorless, monitoring devices are required if methane is suspected.

✓ ***Conduct a site characterization and develop a conceptual site model (CSM)***

Once the immediate threats to safety have been mitigated (or it is determined that immediate threats do not exist), determine whether there is a long-term threat to human health and the environment from intrusion of petroleum vapors. Site characterization[20] and CSM development provide information about the full extent and location of the contamination; the nature and characteristics of the contamination; the characteristics of the site that influence contaminant migration, including the potential for biodegradation of PHCs; and the locations of receptors. Information derived from the CSM helps ensure that sources, pathways, and receptors throughout the site are considered; this knowledge can lead to selection of the most appropriate sampling locations and techniques. A systematic soil gas sampling program may also aid in defining the full extent and location of contamination, detecting the presence of preferential transport pathways, and locating pockets of PHC vapors. Preferential transport pathways are avenues of least resistance to the migration of contaminants whether in the dissolved phase, LNAPL phase, or vapor phase. They include both natural and man-made features such as:

Natural

- gravel lenses and channels
- solution channels in karst terrain
- bedding planes
- fractures, joints, and faults in consolidated rock

Man-made

- utility corridors (including sewer lines themselves) and trenches
- elevator pits
- sumps and drainage pits
- other types of excavations

[20]The term *site characterization* is used throughout this document for consistency. *Site characterization* is often used interchangeably with *site assessment*, *site evaluation*, *site investigation*, and sometimes *site check* as they all mean assembling and collecting information and data about a site.

Preferential transport pathways increase the speed at which contamination moves through the subsurface such that contaminants may not biodegrade by the time they reach receptors. They can also allow atypical movement, which in some cases may be opposite groundwater flow (ITRC, 2014). Because preferential transport pathways can short-circuit the protectiveness provided by lateral and vertical separation distances described in this PVI guide, indoor air sampling is recommended in situations where they connect vapor sources and receptors. See **Section 3** (p.39) for more information about site characterization and CSMs.

✓ ***Delineate a lateral inclusion zone***

Based on the CSM, delineate a lateral inclusion zone. The lateral inclusion zone is the area surrounding a contaminant mass through which petroleum vapors may travel, intrude into buildings, and potentially pose a threat to human health and the environment. Buildings directly above contamination sources, whether as mobile LNAPL, residual LNAPL, or PHCs dissolved in groundwater, are considered within the lateral inclusion zone. Buildings outside this zone generally may be excluded from further assessment for PVI unless:

- Site conditions change (e.g., groundwater flow direction changes, contaminant plume migrates beyond the lateral inclusion zone, development or redevelopment of nearby properties)
- Preferential transport pathways are present

In such instances, additional investigation may be warranted to more fully evaluate the risk from PVI. See **Section 4** (p.44) for more information on delineating a lateral inclusion zone.

✓ ***Determine vertical separation distances***

The vertical separation distance is the thickness of clean, biologically active soil (see **Section 9**, p.75) between a contaminant mass and the lowest point of an overlying receptor (e.g., building basement floor, foundation, or crawl space surface). Consolidated rock is not soil and should not be included in the vertical separation distance. For example, for a situation in which there is 3 feet of soil above fractured rock and the depth to contaminated groundwater is 7 feet, the vertical separation distance is 3 feet, not 7 feet. Some buildings within the lateral inclusion zone will overlie PHC contamination that exists as either a mobile LNAPL mass, residual soil contamination (including the smear zone), or dissolved in a groundwater plume. However, not all of these buildings will be threatened by PVI due to aerobic biodegradation of PHCs provided there is sufficient vertical separation distance between the receptor and the vapor source. The vertical separation distance between contamination and overlying buildings is determined as part of the normal site characterization process. The full extent and location of contaminant sources should have been adequately mapped in the subsurface and the nature and characteristics of the contamination should have been determined during site characterization and conceptual site model development (see **Section 3**, p.39).

EPA (2013a) presents analysis of petroleum vapor source data and soil gas data from a number of leaking UST sites across the United States. The report findings support screening criteria for dissolved and LNAPL PHC releases from leaking USTs. For dissolved PHC sources that are separated from overlying buildings by more than 6 feet of clean, biologically active soil, the potential threat of PVI is negligible and further investigation for PVI is generally unnecessary. For LNAPL sources that are separated from overlying buildings by more than 15 feet of clean, biologically active soil, the potential threat of PVI is negligible and further investigation for PVI is generally unnecessary. These separation distances are believed to be sufficiently protective in most situations because they include a number of built-in safety factors, which are discussed in more detail in **Section 5** (p.48). If the distance separating the source of PHC vapors and overlying buildings is less than 6 feet for dissolved sources and 15 feet for LNAPL sources, additional investigation is recommended.

EPA (2013a) recognizes that there are a number of precluding factors that may justify a greater vertical separation distance in some cases. These factors include:

- Influence of methanogenesis on oxygen demand (especially for higher ethanol blends of gasoline)
- Effect of extensive high organic matter content soils (e.g., peat) with potentially high natural oxygen demand
- Reduced oxygen flux caused by certain geologic conditions (e.g., low permeability surface layer overlying coarse-grained soils, soil moisture from precipitation (Luo et al., 2009))
- Limited knowledge of vapor attenuation behavior in fractured rock
- Limited soil gas data for non-UST (e.g., petroleum refinery, fuel terminal) sites
- Limited data on vapor attenuation behavior of aliphatic compounds
- Lack of soil vapor data for the lead scavengers ethylene dibromide (EDB) and 1,2-dichloroethane (1,2-DCA) (see **Section 10**, p.81, for more information on these contaminants)

Other site characteristics that may warrant additional investigation include exceptionally dry soils (<2 percent soil moisture), areas covered by extensive impervious paving or large buildings, and presence of preferential transport pathways (see **Section 3**, p.39). Also, soil gas movement may vary seasonally in response to differential pressures created by heating and cooling of overlying buildings (see **Section 11**, p.96).

✓ ***Evaluate vapor source and attenuation of PHC vapors***

Where contamination is not in direct contact with an overlying building, EPA recommends one of two options: (1) collection of near-slab (exterior) shallow soil gas samples paired with deep (near source) soil gas samples, or (2) collection of indoor air samples paired with sub-slab soil

gas samples to evaluate attenuation of PHC vapors and the potential for PVI.[21] When collecting soil gas samples[22], use option 1 under the following conditions (EPA, 2013b):

- A building, with the shortest side no longer than 66 feet, overlies LNAPL and the vertical separation distance is less than 15 feet, but not in direct contact with the building basement floor, foundation, or crawl space surface.
- A building, of any dimension, overlies dissolved PHC contamination and the vertical separation distance is less than 6 feet, but not in direct contact with the building basement floor, foundation, or crawl space surface.

Use option 2 for buildings larger than 66 feet on a side or if near-slab soil gas samples from around smaller buildings do not clearly demonstrate that biodegradation is sufficient to mitigate the threat of PVI by reducing PHC concentrations to below applicable human health thresholds (see Footnote #13).

The purpose of collecting paired samples is to enable determination of a building-specific vapor intrusion attenuation factor. Generic attenuation factors that do not account for biodegradation of PHCs are conservative and, likely overestimate the transfer of contaminants from soil gas to indoor air in most buildings. Attenuation factors (see **Section 12**, p.100) that account for biodegradation can be derived from models such as *BioVapor* or *PVIScreen* (see **Section 13**, p.106). Additional information may be found in Wilson *et al.* (2014).

If contamination (either dissolved, or LNAPL whether mobile or residual) is in direct contact with a building basement floor, foundation, or crawlspace surface, EPA recommends indoor air sampling (these samples cannot be paired with subsurface soil gas samples because there is no clean, biologically active soil between the contamination and the building). Information on collecting and analyzing sub-slab vapor samples and indoor air samples is beyond the scope of this document, but is provided in other documents, for example ITRC (2014) and EPA (2015).

Indoor air in many buildings will contain detectable levels of a number of vapor-forming compounds whether or not the building overlies a subsurface source of vapors, because indoor air can be impacted by a variety of indoor and outdoor sources. The composition of outdoor air surrounding a building is referred to as ambient air throughout this document. The combined contribution of indoor and outdoor sources of vapors to indoor air concentrations is referred to as background throughout this document. To differentiate and quantify the relative contribution of contaminants from PVI versus background sources, indoor air samples must be collected in conjunction with sub-slab (or near-slab, as appropriate) soil gas samples. ITRC

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[21] Implementing authorities may opt for sub-slab soil gas and indoor air sampling in any situation they deem necessary to protect the safety and health of building occupants.

[22] Soil gas samples should be analyzed for oxygen, carbon dioxide, PHCs (and any other fuel constituents likely to be present including fuel additives), and methane. As a quality assurance/quality control check, nitrogen can be added to the analyte list at a nominal cost. This will enable determination of whether significant concentrations of other gases are unaccounted for as these gases should account for nearly 100 percent of the total present. (See **Section 8**).

(2014) and EPA (2015) provide information on background sources, techniques, and methods to account for background contributions to indoor air concentrations.

Information on historic concentrations of background vapors is presented in *Background Indoor Air Concentrations of Volatile Organic Compounds in North American Residences (1990 – 2005): A Compilation of Statistics for Assessing Vapor Intrusion* (EPA, 2011b). In addition, the Montana Department of Environmental Quality (MT DEQ, 2012) conducted an extensive investigation of the indoor air quality of typical uncontaminated buildings in Montana. The objective of these studies is to illustrate the ranges and variability of VOC concentrations in indoor air resulting from sources other than vapor intrusion. While these studies provide expected ranges of indoor air contaminants, EPA recommends building-specific sampling (rather than using literature values) to characterize actual contaminant levels. If measured indoor air concentrations are found to greatly exceed the historic range of background levels, there is a greater likelihood that the indoor air concentrations are the result of vapor intrusion. Studies such as EPA (2011) and MT DEQ (2012) can be employed to determine whether measured indoor air concentrations exceed the historic range of background concentrations.

If the attenuation factor calculated from results of analysis of the chosen pair or vapor samples indicates that there may be a potential for PVI above applicable exposure limits, EPA recommends additional investigation to determine whether mitigation is appropriate.

✓ ***Mitigate petroleum vapor intrusion, as appropriate***

If contaminant concentrations represent a potential threat of fire or explosion (i.e., vapor concentrations are more than 10% of the lower explosive limit), or indoor air sampling indicates that PVI is occurring, EPA recommends that active mitigation measures be immediately initiated. ITRC (2014) and EPA (2015) provide information on mitigation and remediation of vapor intrusion. In addition, the source of contamination should be remediated per Subpart F of the Federal Regulations (40 CFR 280.60 through 280.67) (Federal Register, 1988). In particular, 40 CFR 280.64 requires the recovery of LNAPL to the "maximum extent practicable".

See the following sections for more information on the factors discussed in the paragraphs above:

- **Section 3** (p.39) Site Characterization and Conceptual Site Model (CSM)
- **Section 4** (p.44) Lateral Inclusion Zone
- **Section 5** (p.48) Vertical Separation Distance
- **Section 6** (p.57) Mobile and Residual Light Non-Aqueous Phase Liquid (LNAPL)
- **Section 7** (p.61) Groundwater Flow and Dissolved Contaminant Plumes.
- **Section 8** (p.66) Soil Gas Profile
- **Section 9** (p.75) Clean, Biologically Active Soil

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2. Typical PVI Scenarios

Description

The potential for PVI is primarily a function of the location of the contamination source relative to a potential receptor, source volume and strength, and the source mass distribution in the subsurface. Source concentrations are typically much higher for LNAPL sources than for dissolved-phase sources. Higher source concentrations will generate higher rates of mass diffusion (flux). The higher mass flux will also be more sustained over time because LNAPL sources will contain significantly more mass compared to dissolved-phase sources. Oxygen demand and the potential for encountering anaerobic conditions are also uniquely different between LNAPL and dissolved-phase sources. For both dissolved and LNAPL sources, the biodegradation reaction front is relatively narrow, but it occurs higher in the unsaturated zone (closer to land surface) over an LNAPL source than it does over a dissolved-phase source (**Figure 3**).

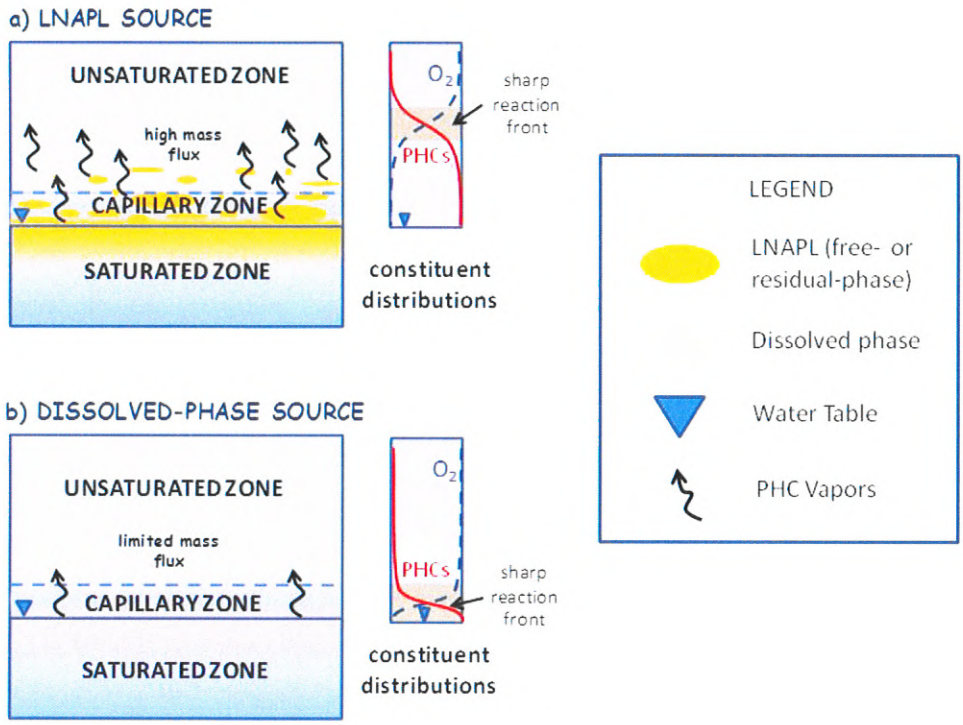

Figure 3. Difference In Potential For PVI Based On Type Of Source: a) LNAPL, b) Dissolved Phase (Source: Lahvis, et al., 2013. Reprinted from *Groundwater Monitoring & Remediation* with permission of the National Ground Water Association. Copyright 2013.)

LNAPL sources may be distributed both above and below the capillary fringe as a result of smearing from water-table fluctuations. This phenomenon will tend to enhance mass flux to the unsaturated zone because of direct partitioning between LNAPL (residual) and vapor phases. Conversely, the mass flux will be more limited for dissolved-phase sources because vapor transport through water is reduced relative to diffusion in soil gas (Golder Associates, 2006; Lahvis and Baehr, 1996). Vapor diffusion is limited by low effective air-phase porosity (i.e., high moisture saturation) and biodegradation in the capillary zone.

Importance

Relatively few confirmed occurrences of PVI at petroleum sites are reported in the literature (EPA, 2013, Section 2.6, p.9). The most likely scenarios for PVI to occur are shallow PHC sources directly beneath buildings and mobile LNAPL or groundwater plumes with high concentrations of PHCs that are in direct contact with buildings (Davis, 2009; and McHugh, et al., 2010). A study by Peargin and Kolhatkar (2011) suggests that a dissolved source with benzene greater than 1 mg/L may behave like a LNAPL source in terms of vapor-generating capability.

Assessment

Recommended steps for investigating PVI are discussed in **Section 1** (p.11). Application of the screening criteria allow for the determination of which buildings are threatened by PVI. Using this approach, resources can be appropriately focused on those buildings potentially impacted by PVI.

Figure 4 presents typical scenarios of the spatial relationship between PHC sources and potential receptors. However, it is not intended to be a comprehensive depiction of all possible configurations of such a relationship.

Table 2 summarizes the characteristics of these six scenarios relative to lateral and vertical distances from contamination and necessary investigation activities.

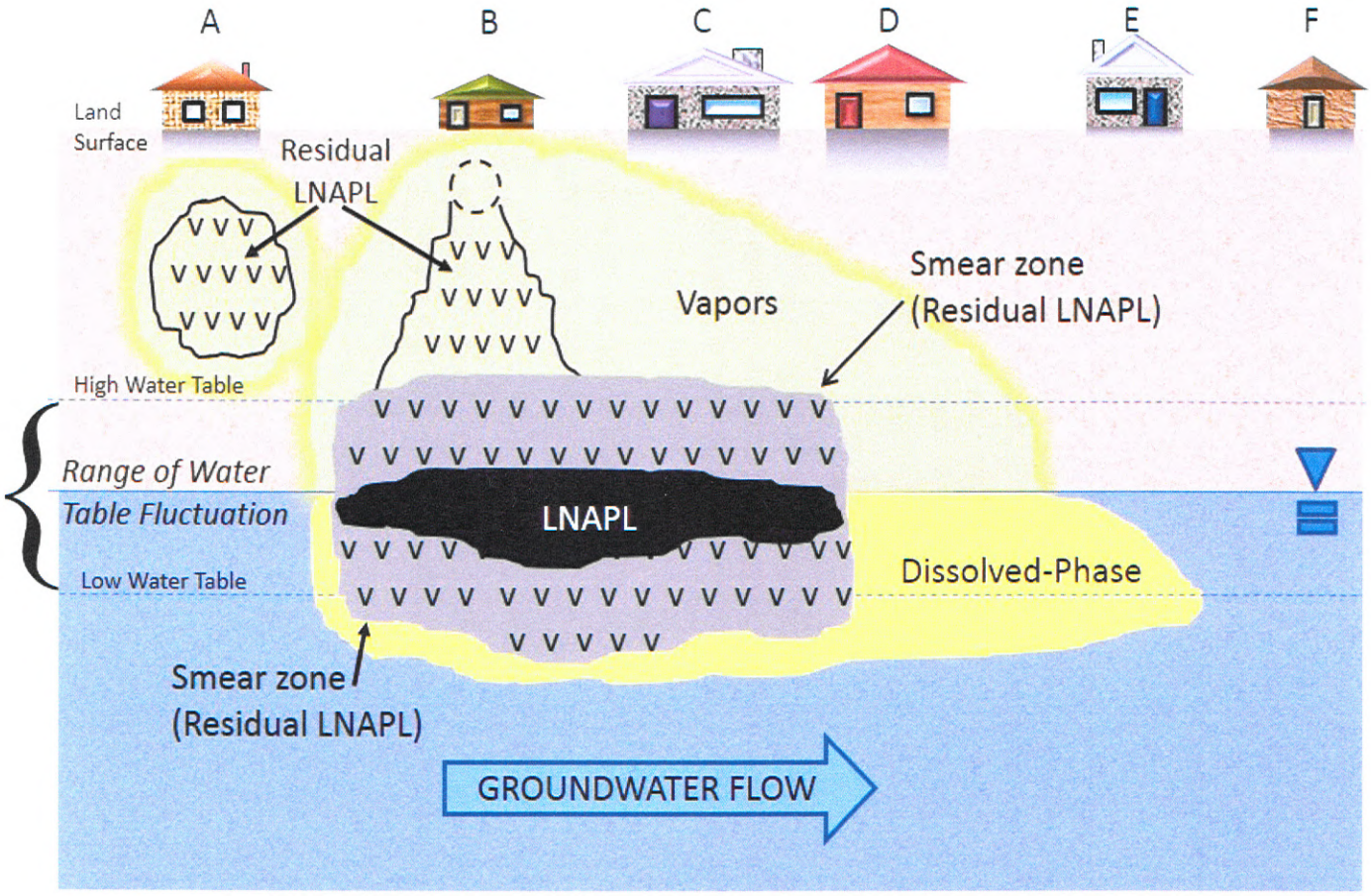

Figure 4. Typical Scenarios Of Potential PVI Sources And Potential Receptors

Table 2. Summary Of Characteristics Of Typical Scenarios Of Petroleum Vapor Sources And Potential Receptors.

Scenario (as illustrated in Figure 4)	Contamination Beneath Building? (building is within lateral inclusion zone)	Potential For PVI	Near-Slab* Soil Gas Sampling Recommended?
A	Yes; shallow residual LNAPL in the vadose zone	High	Yes, if vertical separation distance is less than 15 feet from the top of residual LNAPL, otherwise No
B	Yes; residual including smear zone, LNAPL, dissolved in groundwater	High	Yes, if vertical separation distance is less than 15 feet from the top of the smear zone, otherwise No
C	Yes; smear zone, LNAPL, dissolved in groundwater	Medium	Yes, if vertical separation distance is less than 15 feet from the top of the smear zone, otherwise No
D	Yes; dissolved in groundwater	Low	Yes, if vertical separation distance is less than 6 feet from the historical high water table elevation, otherwise No
E	Maybe; plume may be diving beneath water table	Low – None	Yes, if vertical separation distance is less than 6 feet from the historical high water table elevation, otherwise No
F	No	None	No

*Near-slab soil gas samples should be collected from each side of the potentially impacted building and as close to the building as possible. These samples should be paired with deep (near source) soil gas samples. If these samples do not clearly demonstrate that biodegradation is sufficient to mitigate the threat of PVI into the building, EPA recommends collection of indoor air samples paired with sub-slab soil gas samples.

Special Considerations

While biodegradation may reduce the potential for human exposure to petroleum vapors, its effectiveness in mitigating PVI may be limited by precluding factors such as:

- Migration of contaminants, especially plumes in flowing groundwater
- Presence of non-PHC chemicals that biodegrade too slowly (or the rate is not known with certainty)
- Presence of preferential transport pathways
- Extensive impermeable surface cover, or very large buildings
- Presence of higher blends of ethanol in gasoline that consumes oxygen that would otherwise be available for aerobic biodegradation of PHCs
- Generation of methane from higher blends of ethanol in gasoline that exerts high oxygen demand and presents a vapor intrusion threat itself
- Soils with high organic content (e.g., peat) that exert a high oxygen demand
- Soil conditions that are inhospitable to microorganisms such as insufficient soil moisture
- Insufficient thickness of clean, biologically active soil
- LNAPL source is relatively unweathered and rich in volatile PHCs

Recommendation

EPA recommends conducting an adequate PVI investigation and following the steps described in **Section 1** (p.11) to determine which buildings may be at risk for PVI.

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3. Site Characterization And Conceptual Site Model (CSM)

Description

Site characterization is the process by which site-specific information and data are gathered from a variety of sources to characterize the physical, biological, and chemical systems at a contaminated site. A conceptual site model (CSM) integrates all data and information into a three-dimensional picture of site conditions that illustrates contaminant distributions, release mechanisms, migration routes, exposure pathways, and potential receptors (EPA, 2012; ITRC, 2014). The CSM uses a combination of text and graphics to portray both known and hypothetical information (EPA, 2011). The CSM documents current conditions at the site and is supported by maps, cross-sections, and site diagrams. The CSM illustrates potential human and environmental exposure through contaminant release and migration toward receptors (EPA, 1995, 1996a). The CSM should be refined as new data are collected.

Importance

At any leaking UST site, it is important to have a thorough understanding of the full extent and location of contamination (including both PHCs and non-PHC fuel additives), the characteristics of the site that influence contaminant migration (especially the presence of preferential transport pathways), and the locations of potential receptors. A CSM helps ensure that sources, pathways, and receptors throughout the site have been considered; this knowledge can lead to selection of the most appropriate sampling locations and techniques. The CSM assists the site manager in evaluating the interaction of different site features. Risk assessors use conceptual models to help plan for risk assessment activities (EPA, 1995). The CSM is the basis for making informed risk management decisions about the site and the threat posed by PVI to nearby buildings and their occupants. In addition, remedial action costs are influenced by the quality of the CSM (EPA, 1996b).

Assessment

An investigation for PVI potential is not separate from the normal response to a confirmed UST release; an adequate site characterization is essential in order to construct an accurate CSM. A primary objective of site characterization is delineation of the aerial and vertical extent of contamination in the subsurface (per 40 CFR 280.65(a)) so that lateral and vertical separation distances can be accurately determined.[23] It is also important to determine whether preferential transport pathways are present and, if so, delineate them to determine if they connect vapor sources directly to potential receptors. Site characterization generally proceeds in a systematic manner, often beginning in or near the source area and working outward and in the downgradient direction in which groundwater flows.

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[23] The separation distances described in this document (**Section 5**, Table 3, p.52) and the protectiveness provided by clean, biologically active soil against vapor intrusion by PHCs may be insufficient to protect against vapor intrusion by non-PHC fuel additives. Additional investigation should be conducted where certain additives are present (see **Section 10**, p.81).

All information and data about the site should be integrated into a CSM, which is continually updated and refined to account for changing conditions and new information. Basic activities associated with developing a CSM include:

- Identification of potential contaminants[24]
- Identification and characterization of the source of contaminants
- Characterization of the geochemical parameters that affect biodegradation
- Characterization of the geologic and hydrogeologic characteristics of the subsurface
- Delineation of potential migration pathways, including preferential transport pathways, through environmental media
- Establishment of background levels of contaminants and areas of contamination for each contaminated medium
- Identification and characterization of potential receptors
- Determination of the limits of the study area or system boundaries

Tracking contaminant migration from sources to receptors is one of the most important uses of the CSM (ASTM, 2008). Uncertainties associated with the CSM should also be identified as well as the efforts taken to reduce uncertainties to acceptable levels (ASTM, 2008). As new information and data become available, the CSM should continually be refined (EPA, 1993; ITRC, 2007). ITRC (2014), EPA (2013, 2015), and Wilson et al., (2014) provide additional information about developing CSMs.

Special Considerations

The separation distances described in this document (**Section 5**, Table 3, p.52) and the protectiveness provided by clean, biologically active soil against vapor intrusion by PHCs may be insufficient to protect against vapor intrusion by non-PHC fuel additives. Additional investigation should be conducted where certain additives are present (see **Section 10**, p.81).

The presence and locations of preferential transport pathways should be identified and incorporated into the CSM. All new information and data about a site, including potential future land uses, should also be identified to refine the CSM.

Recommendation

Per Subparts E and F in 40 CFR 280.50 through 280.67 (see *http://www.epa.gov/oust/fedlaws/cfr.htm*), EPA recommends that an adequate site characterization considers the following:

- §280.52(b) Release Investigation and Confirmation Steps:

"Owners and operators must measure for the presence of a release where contamination is most likely to be present at the UST site. In selecting sample types, sample locations, and measurement methods, owners and operators must consider the nature of the stored

[24] The list of potential contaminants should include BTEX and other PHCs as well as non-PHC fuel additives likely to have been present in the fuel stored at the site. See **Section1** (p.11) and **Section 10** (p.81) for more information.

substance, the type of initial alarm or cause for suspicion, the type of backfill, the depth of ground water, and other factors appropriate for identifying the presence and source of the release."

- §280.62(a)(5) Initial Abatement Measures and Site Checks

"Measure for the presence of a release where contamination is most likely to be present at the UST site, unless the presence and source of the release have been confirmed in accordance with the site check required by §280.52(b) or the closure site assessment of §280.72(a). In selecting sample types, sample locations, and measurement methods, the owner and operator must consider the nature of the stored substance, the type of backfill, depth to ground water and other factors as appropriate for identifying the presence and source of the release. . ."

- §280.63(a)(1-4) Initial Site Characterization

". . .owners and operators must assemble information about the site and nature of the release, including information gained while confirming the release or completing the initial abatement measures. . . This information must include, but is not necessarily limited to the following: (1) Data on the nature and estimated quantity of release; (2) Data from available sources or site investigations concerning the following factors: surrounding populations, water quality, use and approximate locations of wells potentially affected by the release, subsurface soil conditions, locations of subsurface sewers, climatological conditions, and land use; (3) Results of the site check required under §280.62(a)(5); and (4) Results of the free product investigations. . ."

- §280.64 Free product removal

"At sites where investigations under §280.62(a)(6) indicate the presence of free product, owners and operators must remove free product to the maximum extent practicable as determined by the implementing agency while continuing, as necessary, any actions initiated under §§280.61 through 280.63, or preparing for actions required under §§280.65 through 280.66. In meeting the requirements of this section, owners and operators must: . . . (d) Unless directed to do otherwise by the implementing agency, prepare and submit to the implementing agency, within 45 days after confirming a release, a free product removal report that provides at least the following information: . . . (2) The estimated quantity, type, and thickness of free product observed or measured in wells, boreholes, and excavations;"

- §280.65(a) Investigation for soil and ground water cleanup

"In order to determine the full extent and location of soils contaminated by the release and the presence and concentrations of dissolved product contamination in the groundwater, owners and operators must conduct investigations of the release, the release site, and the surrounding area possibly affected by the release. . ."

- §280.66(b)(1-6) Corrective Action Plan

"In making this determination, the implementing agency should consider the following factors as appropriate: (1) The physical and chemical characteristics of the regulated

substance, including its toxicity, persistence, and potential for migration; (2) The hydrogeologic characteristics of the facility and the surrounding area; (3) The proximity, quality and current and future uses of nearby surface water and ground water; (4) The potential effects of residual contamination on nearby surface water and ground water; (5) An exposure assessment; and (6) Any information assembled in compliance with this subpart."

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4. Lateral Inclusion Zone

Description

The lateral inclusion zone is the area surrounding a contaminant source through which vapor-phase contamination may travel and intrude into buildings. Determination of the lateral distance within which buildings and other structures may be threatened by PVI is site-specific. In general, with increasing confidence in the site characterization and the CSM, there can be a corresponding decrease in the distance the lateral inclusion zone extends from clean monitoring points.[25] All buildings within the lateral inclusion zone should be further assessed to determine if they are separated from vapor sources by an adequate vertical separation distance (see **Section 5**, p.48). Further assessment may be unnecessary for those buildings outside the lateral inclusion zone unless preferential transport pathways are present. If contaminated groundwater is the source of vapors, migration of the contaminant plume (in the longitudinal, transverse, and vertical directions) should be assessed when evaluating the potential for future risks.

Importance

The lateral inclusion zone is a screening criterion to help determine which sites should definitely be assessed further for PVI; which sites might need additional site characterization and assessment for PVI; and which sites can reliably be excluded from consideration for further evaluation of PVI. All buildings that overlie, or are reasonably expected to overlie, contamination, whether LNAPL or the dissolved phase, are considered to be within the lateral inclusion zone.

Assessment

Lateral separation distance is schematically depicted in **Figure 5**. Though in theory the length of the lateral separation distance may be on the same scale as the vertical separation distance (EPA, 2013a; ITRC, 2014), a greater lateral distance is generally warranted in the down gradient direction (Lahvis, et al, 2013; EPA, 2013a). This is because the lateral boundaries of a migrating plume are more difficult to accurately delineate, as they are not stationary. Groundwater elevations fluctuate which may result in changes in the direction and velocity of groundwater flow. The lateral and down gradient investigation should continue until the full extent and location of contamination is determined. This is typically achieved by surrounding the dissolved-phase plume with clean monitoring points.

Both mobile LNAPL and dissolved contaminant plumes are dynamic and may move from one monitoring event to the next. As discussed in **Section 7** (p.61), periodic monitoring of groundwater flow directions and plume migration should be conducted, possibly over more than one annual cycle.

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[25] A *monitoring point* is defined as a sampling point at which soil and groundwater samples are collected (typically from monitoring wells, though not exclusively) and which define the full extent and location of contamination. A *clean monitoring point* is defined by dissolved benzene concentration less than 5 µg/L and soil TPH concentration less than 20 mg/Kg.

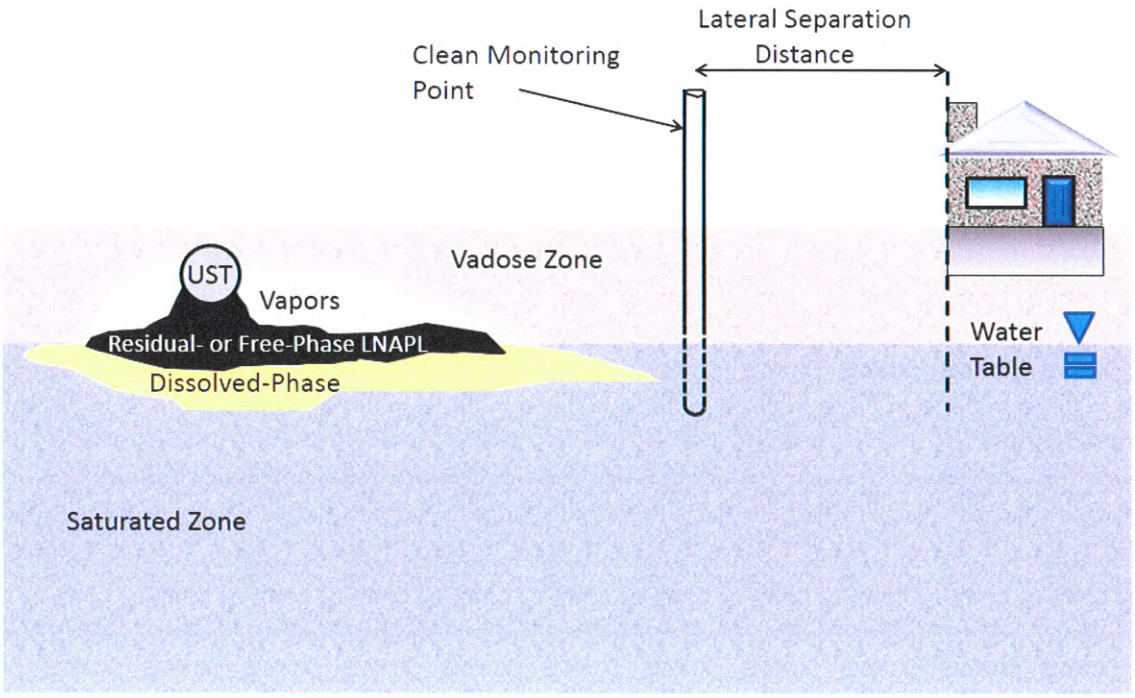

Figure 5. Lateral Separation Distance Between Source Of PHC Contamination And Hypothetical Receptor

Special Considerations

It can be difficult to accurately determine the exact location of contamination relative to potential receptors. This is in part due to the dynamic nature of contaminant plumes (both LNAPL and dissolved PHCs); the presence of heterogeneities and preferential transport pathways in geologic material; and the distance between monitoring points, such as soil borings and monitoring wells. It may be necessary to assess some nearby buildings for PVI before all site characterization activities have been completed.

It is important to consider whether, and what type of preferential transport pathways are present and could facilitate the migration of petroleum vapors. The presence of preferential transport pathways may circumvent the protectiveness that a sufficiently thick layer of clean, biologically active soil would otherwise provide. Preferential transport pathways such as utility conduits typically enter buildings through holes in the foundation or slab and can facilitate the entry of PHC vapors into the building. For example, if the transport of vapors from the source

area to the building could occur along utility conduits, then vapor sampling inside those utility conduits (e.g., sewers) should be considered. Field instrument screening at utility access points may help determine if the utility is acting as a conduit for vapors. Although specific guidance for utility sampling is beyond the scope of this document, EPA recommends that any utility sampling program include safety precautions to protect personnel (e.g., oxygen and combustible gas monitoring, confined-space entry requirements) and to avoid damage to utilities. For guidance on utility sampling, see *A Practical Strategy for Assessing the Subsurface Vapor-to-Indoor Air Migration Pathway at Petroleum Hydrocarbon Sites* (API, 2005).

Lateral separation distances that are usually protective against PVI may not be sufficiently protective in situations where methane is produced in large quantity, such as sites where high-ethanol blends of gasoline (i.e., E-20 or greater) have been released (Ma et al., 2014), and at sites where non-PHC fuel additives are present (see **Section 10**, p.81). In both of these cases, additional investigation should be conducted to assess the potential for vapor intrusion.

Another consideration is changing site conditions. Factors to consider in deciding whether to include sites for further evaluation of PVI may include future land use—that is, whether: future new buildings will be constructed within the lateral inclusion zone, utility trenches will be excavated through or near previous contamination, groundwater usage will potentially be increased, and additional releases of contaminants may occur.

Recommendation

Delineation of a lateral inclusion zone is site-specific. EPA recently published *An Approach for Developing Site-Specific Lateral and Vertical Inclusion Zones within which Structures Should be Evaluated for Petroleum Vapor Intrusion due to Releases of Motor Fuel from Underground Storage Tanks (EPA, 2013b)*. This Issue Paper describes a procedure for constructing a lateral inclusion zone that decision makers may find useful. EPA recommends that all buildings within the lateral inclusion zone be further assessed to determine if they are separated from vapor sources by an adequate vertical separation distance. Further assessment may be unnecessary for those buildings outside the lateral inclusion zone unless:

- Preferential transport pathways are present that connect PHC vapor sources to receptors
- Impermeable surface cover (e.g., concrete, asphalt, ice, very large buildings) is so extensive that there is concern whether there is sufficient oxygen in the subsurface to support biodegradation
- Soil conditions are inhospitable to microorganisms (e.g., dry soils with less than 2 percent soil moisture by dry weight) such that biodegradation is insufficient to mitigate the threat of PVI

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5. Vertical Separation Distance

Description

The vertical separation distance is the thickness of clean, biologically active soil (see **Section 9**, p.75) between the highest vertical extent of a contaminant source and the lowest point of an overlying building. This lowest point could be a building basement floor, foundation, or crawlspace surface.

Importance

If the thickness of clean, biologically active soil is sufficient and oxygen and soil moisture are present, aerobic biodegradation will usually degrade vapor-phase PHCs before they can intrude into buildings. EPA (2013a) presents a compilation and analysis of soil gas data from a large number of sites that represent many different hydrogeologic settings where gasoline was released from USTs.[26] This analysis builds on the work of Davis (2009, 2010, 2011a, and 2011b). In addition, EPA (2013a) summarizes the results of a number of parallel efforts (Lahvis, et al., 2013; Peargin and Kolhatkar, 2011; Wright, 2011, 2012). Although these studies used somewhat different data sets, there is a high degree of consistency among them. This consistency supports the establishment of vertical screening distances based on whether PHC contamination is present as LNAPL or dissolved PHCs; that is, the thickness required to aerobically biodegrade PHCs is directly related to the strength of the source. Because LNAPL sources are capable of producing higher concentrations of vapors compared to dissolved sources, the necessary separation distance between receptors and LNAPL is greater than the necessary separation distance between dissolved sources and receptors. At sites where non-PHC fuel additives are present (see **Section 10**, p.81), the vertical separation distance may not be sufficient to protect against vapor intrusion. In this case, additional investigation should be conducted to assess the potential for vapor intrusion.

Assessment

The vertical separation distance is measured from the lowest point of the overlying building basement floor, foundation, slab, or crawlspace surface and the highest vertical extent of contamination. For dissolved sources this is the historic high water table elevation; for LNAPL sources this is the top of the smear zone or residual LNAPL in the source area. Vertical separation distances for dissolved plumes and LNAPL sources are schematically depicted in **Figure 6a and 6b**, respectively. Both mobile LNAPL and dissolved contaminant plumes are dynamic and may move from one monitoring event to the next. As discussed in **Section 7** (p.61), periodic monitoring of groundwater flow directions and plume migration are recommended, possibly over more than one annual cycle.

The presence of LNAPL may be determined from direct or indirect evidence. Direct evidence includes measureable accumulations of free product in monitoring wells, an oily sheen or floating globules on the water table, and petroleum hydrocarbon-saturated bulk soil samples.

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[26] The final report (EPA, 2013a) addresses the peer review comments received. The report, database, and peer review record are accessible on EPA's PVI Compendium Web page: http://www.epa.gov/oust/cat/pvi/index.htm.

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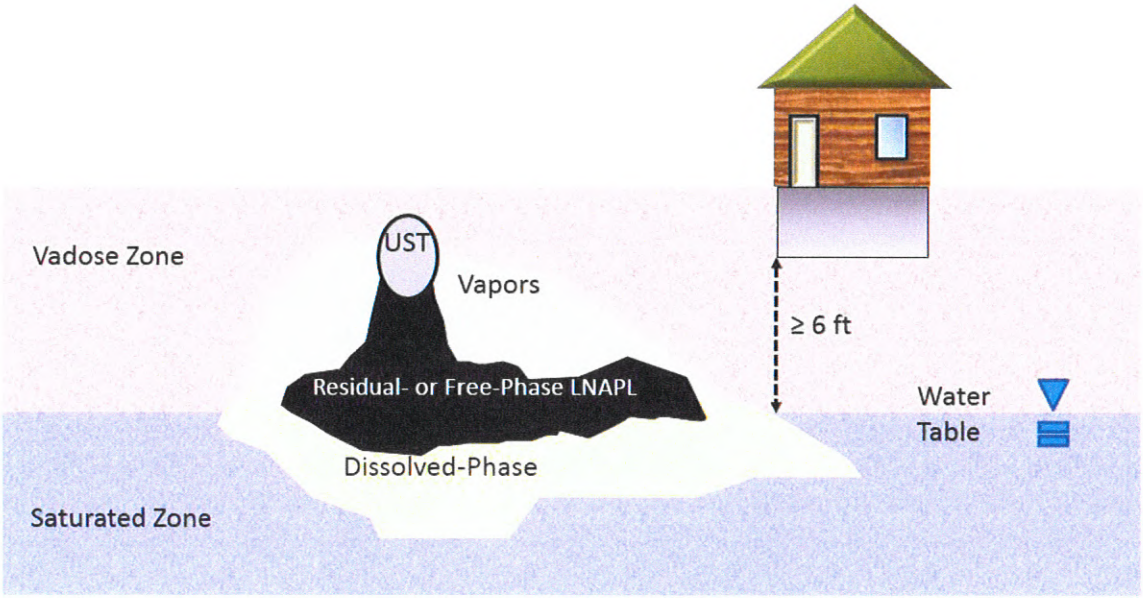
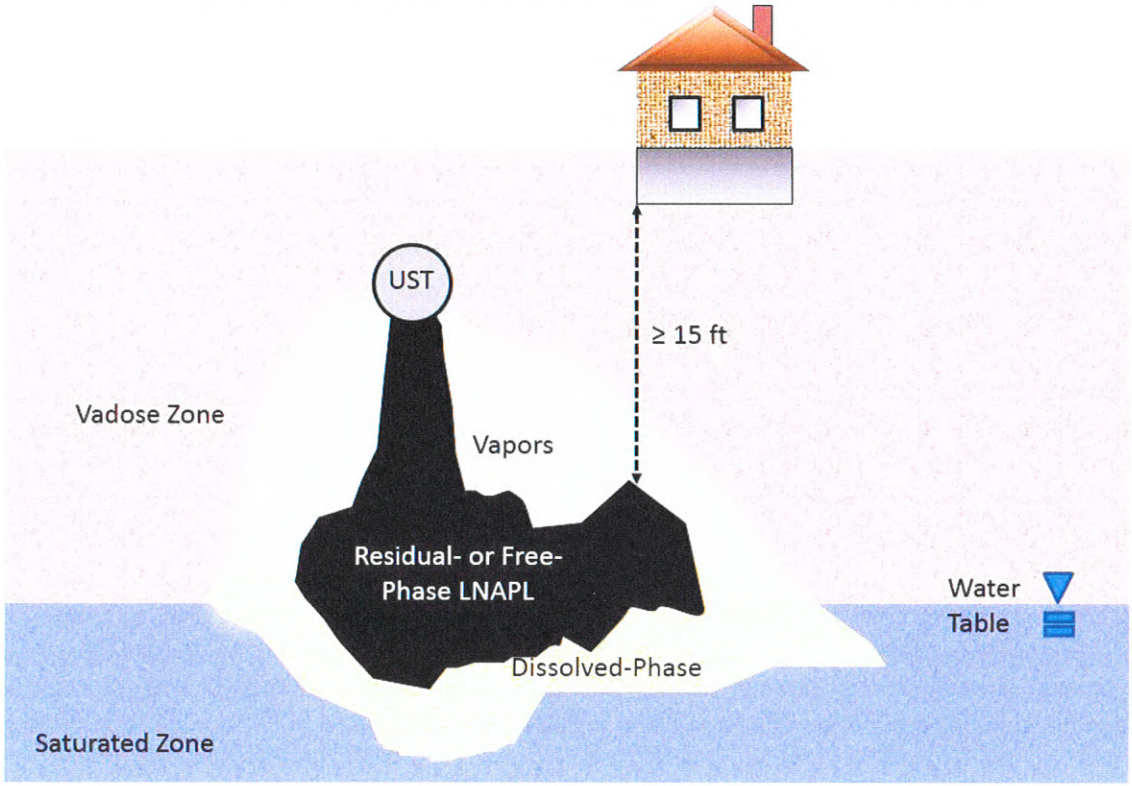


(a) Vertical separation distance for dissolved-phase source of PHCs.



(b) Vertical separation distance for LNAPL (residual or mobile phase) source of PHCs.

Figure 6. Vertical Separation Distances Between Source Of PHC Contaminants And Hypothetical Receptor: (a) Dissolved Source, (b) LNAPL Source.

Lahvis et al. (2013) caution that the presence or absence of free-phase LNAPL in monitoring wells may not be a reliable indicator of the presence of residual-phase LNAPL. The absence of LNAPL can only be determined through analysis of core samples. This is important to recognize because free-phase and residual LNAPL have a greater vapor-generating capability than dissolved sources. Indirect evidence includes high concentrations of benzene and other PHCs, often measured as TPH.[27] There is considerable variation and uncertainty in LNAPL thresholds determined from indirect evidence and Lahvis et al. (2013) suggest that multiple indicators of the presence of LNAPL be evaluated. EPA (2013a) selected a benzene concentration of 5 mg/L to differentiate between dissolved and LNAPL sources. A study by Peargin and Kolhatkar (2011) suggests that a dissolved source with benzene greater than 1 mg/L may behave like a LNAPL source in terms of vapor-generating capability. For more information on indicators of LNAPL, see **Section 6** (p.57).

Special Considerations

Preferential transport pathways such as utility conduits typically enter buildings through holes in the foundation or slab and can facilitate the entry of PHC vapors into the building. Consideration should be given to field instrument screening at utility access point(s) as an initial step to determine if the utility is acting as a conduit for vapors. If the transport of vapors from the source area to the building could occur along utility conduits, then vapor sampling inside the utility conduits, manholes, or sumps should be considered in addition to vadose zone and sub-slab soil gas sampling. Any utility sampling program should include safety precautions to protect personnel (e.g., oxygen and combustible gas monitoring, confined-space entry requirements) and to avoid damage to utilities. Specific guidance for utility sampling is available in *A Practical Strategy for Assessing the Subsurface Vapor-to-Indoor Air Migration Pathway at Petroleum Hydrocarbon Sites* (API, 2005).

Vertical separation distances that are usually protective against PVI may not be sufficiently protective in situations where methane is produced in large quantity, such as sites where high-ethanol blends of gasoline (i.e., E-20 or greater) have been released (Ma et al., 2014), or beneath very large buildings, or where the ground surface is covered by extensive impermeable material (e.g., pavement) (EPA, 2013c).

In addition, consideration should be given to whether future new buildings will be constructed within the lateral inclusion zone and whether they may be impacted by PVI.

[27] Toxicological data for TPH fractions may be found in EPA (2009, 2013b), ATSDR (1999), Tveit et al. (1999), and HI DOH (2012). More recently, Brewer et al. (2013) have developed a quantitative method for risk-based evaluation of TPH in PVI investigations.

Recommendation

EPA recommends using the criteria presented in **Table 3** to determine the necessary vertical separation distance between PHC contamination from leaking USTs and an overlying building foundation, basement, or slab. These distances are 6 feet for dissolved vapor sources (beneath buildings of any size) and 15 feet for LNAPL sources (beneath buildings up to 66 feet on the shortest side).[28] Where the respective vertical separation distance is met or exceeded, generally no further investigation for PVI is necessary if there are no precluding factors present (e.g., preferential transport pathways) and the PCH source is not a high-ethanol blend (i.e., E-20 or greater) of gasoline. If the applicable separation distance is not met and where contamination is not in direct contact with an overlying building, then choose one of two options: (1) collect near-slab (exterior) shallow soil gas samples paired with deep (source) soil gas samples, or (2) collect indoor air samples paired with sub-slab soil gas samples. If the potential for PVI cannot be ruled out based on near-slab and deep soil gas sampling, then EPA recommends indoor air sampling paired with sub-slab vapor sampling. If the attenuation factor calculated from results of analysis of the chosen pair or vapor samples indicates that there may be a potential for PVI above applicable exposure limits, EPA recommends gathering additional information and data to determine whether mitigation is appropriate.

Although biodegradation is known to occur for many individual non-PHC fuel additives and classes of additives, the rate of biodegradation in soil gas has not necessarily been rigorously quantified; this is especially true for the lead scavengers EDB and 1,2-DCA. Therefore, for these two chemicals in particular, vertical separation distances recommended in this guide may not be sufficient for petroleum fuel releases that contain EDB and 1,2-DCA and additional investigation may be necessary to assess their potential for vapor intrusion (See **Section 10**, p.81 for more information).

[28] See *3-D Modeling of Aerobic Biodegradation of Petroleum Vapors: Effect of Building Area Size on Oxygen Concentration Below the Slab* (EPA 510-R-13-002)(EPA, 2013c).

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Table 3. Recommended Vertical Separation Distance Between Contamination And Building Basement Floor, Foundation, Or Crawlspace Surface.

Media	Benzene	TPH	Vertical Separation Distance (feet)*
Soil (mg/Kg)	≤10	≤ 100 (unweathered gasoline), or ≤ 250 (weathered gasoline, diesel)	6
	>10 (LNAPL)	> 100 (unweathered gasoline) >250 (weathered gasoline, diesel)	15
Groundwater (mg/L)	≤5	≤30	6
	>5 (LNAPL)	>30 (LNAPL)	15

The thresholds for LNAPL indicated in this table are indirect evidence of the presence of LNAPL. These thresholds may vary depending on site-specific conditions (e.g., soil type, LNAPL source). The value of 5 mg/L benzene is from EPA (2013a, p.31). A study by Peargin and Kolhatkar (2011) suggests that a dissolved source with benzene greater than 1 mg/L may behave like a LNAPL source in terms of vapor-generating capability. Decision-makers may have different experiences with LNAPL indicators and may use them as appropriate. For more information, see **Section 6** (p.57) and **Figure 7** in particular.

Bulk soil samples should be analyzed for Total Petroleum Hydrocarbon (TPH) and BTEX (plus any other potential contaminants). The objective of measuring TPH is to quantify the total vapor phase concentration of PHCs. TPH may be analyzed by methods appropriate for the type of fuel released. These methods may be designated as TPH-gasoline (or sometimes gasoline range organics or GRO), TPH-diesel (or sometimes diesel range organics or DRO). Method TO-15 (see http://www.epa.gov/ttn/amtic/files/ambient/airtox/to-15r.pdf) by itself only measures a small fraction of PHCs that may be present in the vapor-phase. TO-15 analyses require a correction factor to estimate bulk TPH. An extended TO-15 analysis can provide such an estimate. For more information on TPH in vapor intrusion studies, see Brewer et al. (2013).

*The vertical separation distance represents the thickness of clean, biologically active soil between the source of PHC vapors (LNAPL, residual LNAPL, or dissolved PHCs) and the lowest (deepest) point of a receptor (building basement floor, foundation, or crawlspace surface).

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6. Mobile And Residual Light Non-Aqueous Phase Liquid (LNAPL)

Description

LNAPLs released from petroleum USTs are typically fuel products such as gasoline and diesel fuel. Fuel products are comprised of a large number of volatile and semi-volatile PHCs and synthetic additives. Among these compounds are some that are volatile and some that are semi-volatile. Newer, unweathered releases typically contain a higher proportion of more volatile PHCs than do older releases that may be more weathered and depleted in the more volatile PHCs. Similarly, gasoline contains a higher proportion of more volatile PHCs than does diesel fuel and other middle distillates such as heating oil and kerosene. Vapors emanating from dissolved-phase sources are primarily BTEX and other aromatic hydrocarbons, and relatively water-soluble PHCs. Vapors emanating from LNAPL sources contain the same constituents in addition to a sizeable fraction of aliphatic and relatively insoluble hydrocarbons (e.g., naphthalene), especially if the source is large or unweathered (Lahvis, et al., 2013; EPA, 2013).

Importance

Depending upon the volume of the release and the characteristics of the soil, PHC vapors from LNAPL sources can reach concentrations high enough to deplete oxygen needed by microorganisms to biodegrade them. Compared to a dissolved plume, a LNAPL plume from a leaking UST does not typically migrate far from the site of release (e.g., the leaking UST or connected piping). However, the larger the mass of the release the greater the potential for the LNAPL plume to migrate. When LNAPL underlies a receptor or comes into direct contact with a basement, foundation, or slab, there is increased potential for explosive levels of vapors to accumulate within the building or other structure.

Residual PHCs are non-mobile in the subsurface and occur when the release stops prior to the accumulation of a sufficient amount of LNAPL for flow to occur, or when a fluctuating water table smears the LNAPL across the water table and reduces the LNAPL saturation of the soil. This smearing inhibits the lateral migration of LNAPL. Although residual contamination is not free flowing, residual sources represent a large mass of contaminants that can persist for long periods of time and generate considerable volumes of PHC vapors as well as dissolved-phase contaminants.

Monitoring wells with residual LNAPL may not have a measurable accumulation of LNAPL so they look exactly like monitoring wells with only dissolved contamination (that is, there is no measurable LNAPL in the monitoring well). However, due to the presence of residual LNAPL, the vapor source area acts like a free-phase LNAPL source in terms of vapor-generating character (Lahvis, et al., 2013). A study by Peargin and Kolhatkar (2011) suggests that a dissolved source with benzene concentration greater than 1 mg/L may have the same vapor-generating capacity as a LNAPL source. This situation is depicted in **Figure 7**.

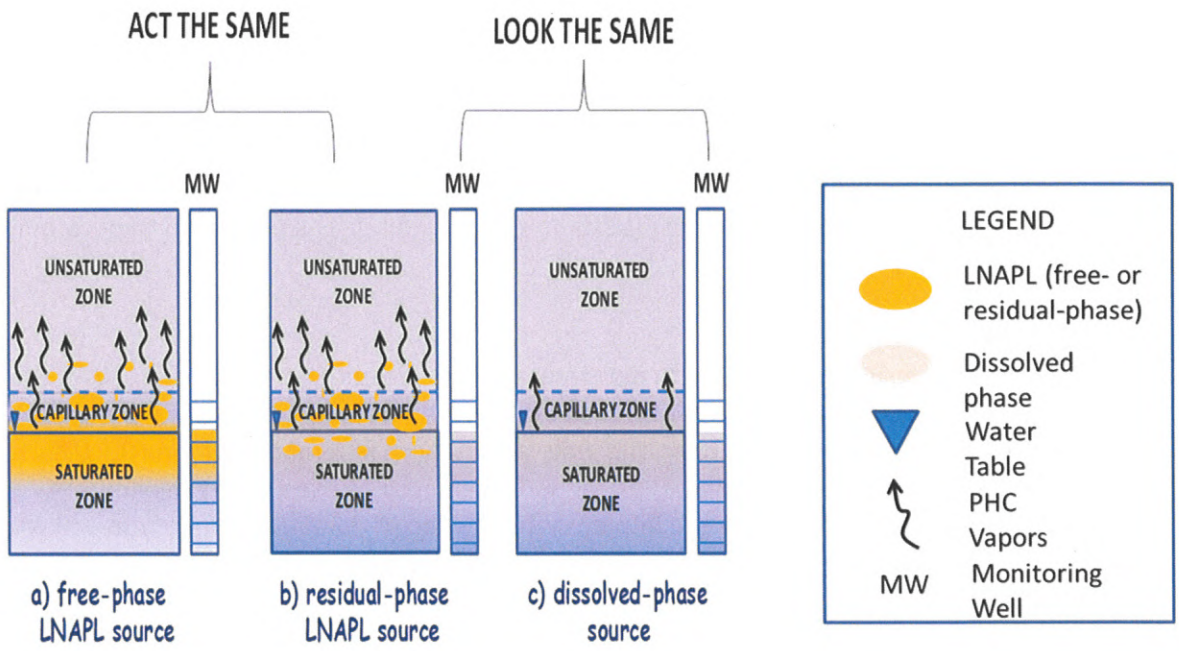

Figure 7. Conceptual Model Illustrating The Potential For Vapor Intrusion For a) Free-Phase LNAPL Source, b) Residual-Phase LNAPL Source, And c) Dissolved-Phase Source (Source: Lahvis, et al., 2013. Reprinted from *Groundwater Monitoring & Remediation* with permission of the National Ground Water Association. Copyright 2013.)

Assessment

The distinction between petroleum contamination present as LNAPL and contamination present purely as a dissolved phase is important. Unfortunately, there is no precise concentration threshold between dissolved phase PHCs and PHCs present in a mixed phase that includes LNAPL.[29] EPA (2013) used a threshold for the benzene groundwater concentration equal to 5 mg/L and a total petroleum hydrocarbon (TPH) threshold groundwater concentration of 30 mg/L for identification of LNAPL sites. The TPH threshold adopted by EPA (2013) is based on the calculated approximate average ratio of the concentration of benzene to TPH in groundwater at UST sites. A site with a LNAPL source was identified on the basis of either the benzene or TPH groundwater concentration exceeding the threshold. The thresholds adopted for identifying LNAPL sites based on soil concentrations are 10 mg/Kg benzene, 100 mg/Kg TPH for unweathered gasoline, and 250 mg/Kg TPH for diesel or weathered gasoline.

[29] Table 4 in EPA (2013) presents a variety of direct and indirect indicators of LNAPL. For example, Bruce, et al. (1991) suggest groundwater concentrations greater than one-fifth (0.2) of the effective solubility of LNAPL as indirect evidence of the presence of LNAPL. However, because the effective solubility depends on characteristics of the LNAPL mass (e.g., composition, weathering); there is uncertainty in the threshold. Additional discussions of screening concentrations for LNAPL are presented in *Evaluating Hydrocarbon Removal from Source Zones and its Effect on Dissolved Plume Longevity and Concentration* (API, 2002), and ITRC (2014).

Special Considerations

Direct means for detecting the presence of LNAPL include measurable accumulations of free product in monitoring wells, an oily sheen on the water, and saturation of bulk soil samples.[30] The presence of residual LNAPL may not be recognizable from monitoring well data. This is because the soil is not sufficiently saturated with LNAPL to allow it to flow into wells. Lahvis et al. (2013) suggest that multiple indicators (both direct and indirect) be evaluated to determine whether or not LNAPL is present.

Recommendation

EPA recommends subsurface sampling to determine the full extent and location of LNAPL (both mobile LNAPL and residual). LNAPL may be present even when there is no measureable accumulation of free product in a monitoring well. In addition, federal regulations (40 CFR 280.64) require that when free product is present, it must be "removed to the maximum extent practicable as determined by the implementing agency." Effective source removal will mitigate a long term source of PHC vapors as well as mitigate dissolved and residual LNAPL contamination.

EPA recommends analyzing bulk soil samples collected in the source area for TPH (e.g., gasoline or diesel depending on which fuels were stored on site) and specific petroleum constituents (e.g., BTEX and other volatile and semi-volatile organic chemicals, and fuel additives). EPA also recommends analysis of LNAPL samples (if present) to determine the degree of weathering and potential for vapor generation.

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[30] Consistent with the findings in EPA (2013) EPA recommends that these same thresholds also be applied for PVI investigations conducted using this guide. These thresholds are presented in **Table 3** in **Section 5** (p.52).

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7. Groundwater Flow And Dissolved Contaminant Plumes

Description

Contaminant plumes are dynamic, three-dimensional distributions of contaminants in groundwater. Contaminants dissolved in groundwater can migrate with flowing groundwater thereby spreading contamination. In some aquifers, where the direction and speed of groundwater flow are stable, the plumes are usually long and narrow. Other plumes appear to spread in both the transverse as well as the longitudinal direction. This apparent transverse dispersion may be the direct result of changes in the direction of groundwater flow. What may appear to be transverse dispersion is actually longitudinal dispersion occurring in different directions as the direction of flow changes (EPA, 2005; Wilson, 2003).

Importance

The potential for PVI from dissolved PHC contaminant plumes is typically limited to sites where there are high concentrations of dissolved contaminants or the plume is in direct contact with a building foundation, basement, or slab. A study by Peargin and Kolhatkar (2011) suggests that a dissolved source with benzene greater than 1 mg/L may have the same vapor-generating capacity as a LNAPL source.

Assessment

Contaminant plumes generally necessitate three-dimensional monitoring to assess the transient behavior of groundwater flow and the movement of contaminant plumes (EPA, 2004a, b). Contaminant plumes migrate with flowing groundwater, which can exhibit seasonal variations as well as responses to pumping, tides, or stage of a nearby river.[31] Groundwater flow directions can and often change over time, and may necessitate periodic monitoring over more than one annual cycle to understand the groundwater flow regime at a given site.

(Note: This monitoring need not delay additional investigation activities and measures to mitigate or remediate threats to safety and health.) As the plume migrates, appropriate adjustments to the sampling plan should be made to ensure that potential receptors are

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[31] Groundwater flow directions can change frequently and relatively quickly. Changes in groundwater flow directions may be more prevalent than is realized, because the variation in the direction of groundwater flow is rarely evaluated in any formal way (EPA, 2005). Wilson (2003) studied data from a site in North Carolina where groundwater flow was influenced by the stage of a nearby river. Over the course of one year of monthly monitoring, groundwater flow directions fluctuated by 120 degrees. Wilson et al. (2005) also studied data from a gas station site in New Jersey. Over a six-year period groundwater monitoring data were collected on 23 occasions; the predominant flow direction was 90-degrees from the presumed direction on which the conceptual model was constructed, and the direction of flow fluctuated by nearly 180 degrees. Mace et al. (1997) studied the variation in groundwater flow directions at 132 gas stations in Texas. Fluctuations in flow directions occurred over a range of 120 degrees. Goode and Konikow (1990) characterized a site where PHCs leaked to the water table. Groundwater flow directions changed nearly 90 degrees in less than four months in response to changing flow conditions in a nearby intermittent stream.

protected. If new PHC releases to groundwater occur, then appropriate mitigation steps can be implemented.

Plume monitoring networks should be able to detect changes in plume boundaries as well as fluctuations in the concentrations of geochemical parameters and contaminant concentrations. Collection of samples from the contaminant plume is needed to determine the extent of contamination and provide information that can be used to estimate the vapor generation capacity of the dissolved contamination. The contaminant plume should be surrounded by sampling points that are free of contamination (i.e., *clean monitoring points*).

Conventional monitoring wells may provide an incomplete picture of the true distribution of contaminants in groundwater. If the length of the screen in a monitoring well is long compared to the thickness of the plume of contamination, the sample obtained will be diluted by the inflow of clean(er) groundwater from above or below the plume. Also, plumes may dive below the screened interval of the wells leading to the false impression that the plume is shorter than it actually is (EPA, 2005).

Special Considerations

Dissolved plumes are dynamic and contamination may migrate beneath buildings over time. This is best evaluated by determining the range of fluctuation in groundwater flow direction and water table elevations beneath buildings over at least one annual cycle. However, in the interim, the remaining PVI-related activities should continue. Preferential transport pathways, if present, may facilitate the intrusion of petroleum vapors into buildings.[32] When contaminant plumes intersect preferential transport pathways, the spread of contamination can be very rapid compared to the velocity of groundwater flow through the soil.

Volatilization of contaminants from the plume into soil gas is greatly reduced when a plume dives beneath the water table surface. Volatile contaminants diffuse more slowly through the water column than through soil gas.

Recommendation

EPA recommends groundwater monitoring and sampling to determine the depth to contaminated groundwater and the vertical distribution of contaminants in the water column beneath overlying buildings[33]. Due to the transient nature of groundwater migration, EPA recommends periodic monitoring and sampling over more than one annual cycle to fully

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[32] Dissolved petroleum contaminants may threaten building inhabitant's health through their water supply rather than through vapor intrusion. Exposure may occur from wells drawing from a contaminated plume, or contamination permeating the water supply piping. Though fuel constituents generally impart a disagreeable odor and taste, building occupants may still be exposed to potentially harmful levels of contaminants. Such exposure may occur when PHCs volatilize from the dissolved phase during showering or washing clothes and dishes, or through ingesting contaminated water. Identifying the mechanism of exposure is important because methods for remediation/mitigation of PVI will be different than treatment or remediation of contaminated groundwater.

[33] If groundwater samples contain greater than 30 mg/L TPH (or greater than 5 mg/L benzene), it is possible that residual LNAPL is present (see **Section 6**, p.57).

understand the groundwater flow regime at a given site. Where the respective vertical separation distance (see **Section 5**) is met or exceeded, generally no further investigation for PVI is necessary if there are no precluding factors present (e.g., preferential transport pathways) and the PCH source is not a high-ethanol blend (i.e., E-20 or greater) of gasoline. If the applicable separation distance is not met and where contamination is not in direct contact with an overlying building, then choose one of two options: (1) collect near-slab (exterior) shallow soil gas samples paired with deep (source) soil gas samples, or (2) collect indoor air samples paired with sub-slab soil gas samples. If the potential for PVI cannot be ruled out based on near-slab and deep soil gas sampling, then EPA recommends indoor air sampling paired with sub-slab vapor sampling. If the attenuation factor calculated from results of analysis of the chosen pair or vapor samples indicates that there may be a potential for PVI above applicable exposure limits, EPA recommends gathering additional information and data to determine whether mitigation is appropriate.

Even in cases where there is no threat of PVI from contaminated groundwater, EPA recommends that the plume be assessed to determine if remediation is necessary to prevent ingestion of contaminated drinking water and protect and restore actual or potential sources of drinking water.

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8. Soil Gas Profile

Description

Aerobic biodegradation of PHC vapors occurs in many subsurface environments (Lahvis, Baker, and Behr, 1998; McHugh, et al., 2010; Roggemans, 1998; Roggemans, Bruce, and Johnson, 2002; ZoBell, 1946; Atlas, 1981; Leahy and Colwell, 1990; DeVaull, 2007). The soil gas profile can provide confirmation that aerobic biodegradation is occurring in the subsurface. Decreasing oxygen concentration and increasing carbon dioxide and methane concentrations indicate biodegradation of PHCs (Hult and Grabbe, 1988). Shallow soil gas typically contains water vapor and fixed gases: nitrogen, oxygen, carbon dioxide, carbon monoxide, and argon. These gases infiltrate into the soil from the atmosphere. Vapor phase PHC contamination may be the result of volatilization from mobile LNAPL released into the subsurface, residual soil contamination (including the smear zone), and dissolved phase contamination. The lower proportion of volatile hydrocarbon compounds in diesel fuel will lead to a comparatively smaller vapor plume in comparison to the release of a similar volume of gasoline (Prince and Douglas, 2010; Marchal, et al., 2003). In addition to PHCs, soil gas may also contain degradation products from the breakdown of PHCs and naturally occurring organic matter. The principal gases resulting from the biodegradation of PHCs are carbon dioxide (under aerobic conditions) or methane (under anaerobic conditions).

Figure 8 presents a characteristic vertical concentration profile in the unsaturated zone; oxygen concentrations decrease with depth and PHCs (including methane) and carbon dioxide

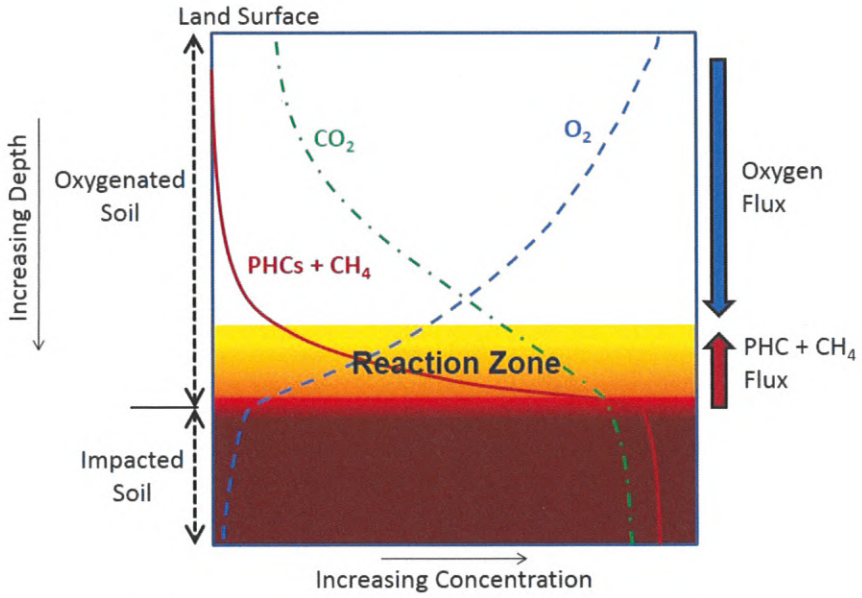

Figure 8. Typical Vertical Concentration Profile In The Unsaturated Zone For PHCs (Plus Methane), Carbon Dioxide And Oxygen

concentrations increase with depth toward the source of contamination. This typical vertical profile may vary somewhat in shape depending on site-specific conditions (Roggemans, Bruce, and Johnson, 2002). During aerobic biodegradation in unsaturated soils, PHCs degrade, oxygen is consumed, and carbon dioxide is produced. The aerobic biodegradation zone is within oxygenated soil (generally greater than 1 percent oxygen in soil gas). In the oxygenated soil zone (where aerobic biodegradation occurs between land surface and the depth of impacted soil) the decrease in PHC concentrations is typically quite rapid and occurs over a narrow interval (the reaction zone in **Figure 8**) (Abreu, Ettinger, and McAlary, 2009).

The impacted soil zone, which is anaerobic, is characterized by the maximum PHC concentrations (and often LNAPL) and biodegradation is slow (EPA, 2012a). Generally, PHC vapor concentrations will be much greater adjacent to a LNAPL source than adjacent to a dissolved hydrocarbon plume. If PHC concentrations are high enough, available oxygen may be depleted, which in turn limits aerobic biodegradation. The core of any PHC contaminant mass is typically depleted with respect to oxygen, thus anaerobic biodegradation of LNAPL or other organic sources (e.g., ethanol) can produce significant amounts of methane (Anderson and Lovley, 1997; Wiedemeier, et al., 1999; Koenigsberg and Norris, 1999; Ma et al., 2014). Methane readily biodegrades under aerobic conditions and, when present, will create an additional oxygen demand (Jewell and Wilson, 2011; Ma, et al, 2012). High concentrations of methane, oxygen, and a source of ignition can create a fire or explosion hazard in confined spaces (e.g., utility vaults and passages, basements, or garages) (Ma et al., 2014). For additional information on evaluating the presence of methane and potential hazards, see ASTM's "*New Practice for Evaluating Potential Hazard Due to Methane in the Vadose Zone*".[34]

Differences between near-slab soil gas profiles and sub-slab soil gas profiles are reported in two EPA modeling studies: the conceptual model scenarios report EPA (2012b) and the building size modeling report for PVI (EPA, 2013a). However, EPA (2012b) assumed that building foundations, basements, and slabs were impermeable and, thus, oxygen transport was not simulated through the foundation, basement, or slab into the subsurface beneath the building. Simulations presented in EPA (2013a) allowed for oxygen transport using reasonably expected oxygen permeability values for concrete (Fischer et al., 1996; McHugh, DeBlanc, and Pokluda, 2006; Lundegard, Johnson, and Dahlen, 2008; Patterson and Davis, 2009; Tittarelli, 2009). When oxygen transport is accounted for, the differences in soil gas profiles were less pronounced between near-slab and sub-slab samples very close to the building basement and slab. Thus, near-slab soil gas samples can be substituted for sub-slab samples in situations where dissolved contamination is present within 6 feet of (but not in contact with) a building basement floor, foundation, or crawlspace surface, and where LNAPL is present within 15 feet of (but not in contact with) a building basement floor, foundation, or crawlspace surface. For dissolved sources this holds for buildings of any size, and for LNAPL sources it applies to buildings with the shortest side being no longer than 66 feet (EPA, 2013a). Deep soil gas samples are needed to determine the depth to contaminated soil and the thickness of clean,

[34] The new ASTM methane guide is accessible at http://www.astm.org/DATABASE.CART/WORKITEMS/WK32621.htm

biologically active soil necessary to attenuate PHC vapors. Shallow soil gas samples should be paired with deep (near source) soil gas samples to evaluate the strength of the PHC vapor source and the attenuation of PHC vapors.

Importance

The potential for PVI is a function of the oxygen demand exerted by all biodegradable vapors, not just the key chemicals of potential concern (Jewell and Wilson, 2011; Ma, et al., 2012). When present, volatile PHCs and methane also exert an oxygen demand that may limit aerobic biodegradation of benzene (Abreu, Ettinger, and McAlary, 2009; Wilson, 2011). An estimate of the biodegradation rate can be determined from the stoichiometric relationship between the flux of oxygen, carbon dioxide, and methane (Lahvis and Baehr, 1996). PHC vapor concentrations generally decrease with increasing distance from a subsurface vapor source. At a relatively short distance from the source, concentrations of PHCs in soil gas will typically fall below potentially significant levels of concern provided that oxygen replenishment is adequate to ensure complete aerobic biodegradation. Lahvis, Baehr, and Baker (1999) observed that PHC vapors from a dissolved plume were almost completely degraded within 1 meter (3.3 feet) above the water table and that significant transport of PHC vapors may only be significant if the vapor source is LNAPL. This is consistent with the findings of EPA's (2013b) PVI database analysis report and Lahvis et al. (2013).

Assessment

Soil gas samples provide information on the distribution of contamination near the source area, whether biodegradation is occurring, and how effective it is in reducing the potential for PVI. When there is an impermeable surface cover adjacent to a building, soil gas probes should be installed beneath the surface in order for the soil gas profile to adequately characterize conditions below the surface. For very large buildings, or where there is extensive impermeable surface cover and the vapor source is relatively shallow, additional investigation is recommended to verify that biodegradation is occurring beneath the building.[35] Vapor samples should be analyzed for PHCs (and non-PHC fuel additives), methane, oxygen, and carbon dioxide (Lahvis, Baehr, and Baker, 1999).

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[35] EPA (2013a) presents modeling results for a variety of soil types, building sizes, vapor source strengths, and vertical separation distances. These results, while not exhaustive, indicate that for dissolved sources and very large buildings, an oxygen shadow does not form, thus the subsurface stays sufficiently oxygenated to support aerobic biodegradation and preclude the potential for PVI. For LNAPL sources, an oxygen shadow was not observed to form beneath buildings up to 66 feet on the shortest side. This length represents the threshold below which oxygen replenishment is sufficient to support aerobic biodegradation; above this length oxygen replenishment may be impeded and there may be insufficient oxygen present to support aerobic biodegradation. For larger buildings underlain by LNAPL within 15 feet of the foundation, basement, or slab, sub-slab soil gas sampling paired with indoor air sampling is necessary to assess whether PVI is occurring. Another potential concern for large buildings and extensive, impermeable surface cover (e.g., asphalt, concrete) is formation of a moisture shadow, which represents soil moisture content too low to support microbial biodegradation (see **Section 9,** p.75, for more information).

An estimate of the total oxygen demand can be determined in two ways: sample for methane and petroleum hydrocarbons (PHCs); or sample and measure the oxygen demand for all the organic compounds in the soil gas at the source.[36] If methane and all the PHCs in soil gas are measured, these concentrations should be converted to an equivalent concentration of benzene and summed. The total oxygen demand of the aggregate of methane and the PHCs (expressed as an equivalent concentration of benzene) can be used to determine an attenuation factor (α) that can be used along with the actual concentration of benzene in soil gas at the source to determine whether aerobic biodegradation is capable of degrading the PHC vapors to acceptable concentrations (see **Section 12,** p.106, **Figure 9**, p.101, and **Figure 10,** p.103).

In some cases, relatively shallow soil gas samples (less than five feet below ground surface) will be needed to characterize active biodegradation zones in the shallow soil (e.g., in the presence of shallow contamination sources). Some state regulatory programs do not allow soil gas sampling at depths less than 5 feet based on the concern that accurate sampling may not be possible at shallow depths because air from the surface may leak into the sample. However, recent research has shown that the collection of accurate shallow-soil gas samples is possible at depths as shallow as 2 feet below ground surface using appropriate field methods (e.g., leak testing), such as those documented in *Temporal Variation of VOCs in Soils from Groundwater to the Surface* (EPA, 2010). It is also possible under certain conditions to collect representative soil gas samples using previously installed groundwater monitoring wells (see Wilson et al., 2014).

Special Considerations

There are several factors that can limit replenishment of oxygen to deep soils. These include presence of low permeability layers, concrete or asphalt covering at the surface, high soil moisture from a recent rainfall event or from irrigation, and buildings that are so large that oxygen is depleted beneath the center of the building (Patterson and Davis, 2009). However, a recent study by EPA (2013a) indicates that for an oxygen shadow[37] to form beneath a building, the PHC vapor source must be shallow LNAPL and the building must be greater than 66 feet in length on the shortest side. For simulations with dissolved sources, no oxygen shadow formed even under a square building with sides that were 2,073 feet in length.

At sites with a new release or unweathered LNAPL source, the oxygen demand will be high. It is important to determine whether temporal variations in oxygen flux into the vadose zone will limit the effectiveness of aerobic biodegradation, potentially resulting in intermittent vapor intrusion impacts. For such sites, more than one round of soil gas monitoring may be needed to confirm that aerobic biodegradation consistently prevents PVI impacts at the site.

[36] EPA recommends using modified Method TO-15 (*see* http://www.epa.gov/ttn/amtic/files/ambient/airtox/to-15r.pdf) for organic compounds. The concentration of methane measured as a fixed gas can then be added to the results of TO-15 to give an approximation of TPH.

[37] For the purposes of this modeling study, an oxygen shadow is defined as less than 1 percent oxygen.

Recommendation

EPA recommends that soil gas samples be analyzed for PHCs, non-PHC fuel additives, methane, oxygen, and carbon dioxide. Sampling for nitrogen (and other fixed gases) in soil gas can provide a check on the quality of the analyses since the sum of these gases should be 100 percent. If they are substantially less than 100 percent, then some constituents are unaccounted for and the analyses should be interpreted with caution.

For buildings of any size within the lateral inclusion zone if the vertical separation distance between the building basement, foundation, or slab and dissolved contamination is less than 6 feet, but not in contact with the building EPA recommends that near-slab soil gas samples paired with deep (near source) soil gas be collected. For buildings up to 66 feet on the shortest side that directly overlie LNAPL masses, and the vertical separation distance is less than 15 feet (but the building is not in direct contact with LNAPL), EPA recommends collection of near-slab soil gas samples paired with deep (near source) soil gas samples. Near-slab soil gas samples should be collected from each side of the building and as close to the building as practicable. If the attenuation factor calculated from results of analysis of the chosen pair or vapor samples indicates that there may be a potential for PVI above applicable exposure limits, EPA recommends gathering additional information and data to determine whether mitigation is appropriate. If contamination is in direct contact with an overlying building (and thus, collection of shallow soil gas samples is not possible), indoor air sampling is recommended.

In addition, for very large buildings or where there is extensive impermeable surface covering, EPA recommends that near-slab or sub-slab soil gas samples be collected if there is concern that these conditions may impede the flux of oxygen to the subsurface and create an oxygen or soil moisture shadow.

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9. Clean, Biologically Active Soil

Description

For a PVI investigation, clean soil does not necessarily mean that it is contaminant-free, but rather that the level of any contamination present is low enough so that the biological activity of the soil is not diminished and the subsurface environment will support sufficient populations of microorganisms to aerobically biodegrade PHC vapors. This means that LNAPL is not present. The oxygen demand of all of the contamination present in the soil should not deplete the available supply of oxygen to such an extent that the rate of biodegradation is reduced.

Effective aerobic biodegradation of PHCs depends on the soil having sufficient oxygen and enough moisture to provide a habitat for adequate populations of active microorganisms. Although most soils contain indigenous microorganisms capable of degrading PHC vapors, typically there is an acclimation period between the time they are exposed to the PHC vapors and the time they begin to biodegrade the vapors. Prior exposure to PHCs has been observed to both increase the number of microbes and the microbial mass available for biodegradation of the PHCs and consequently speed up the degradation rate (ZoBell, 1946; Moyer, et al., 1996; Phelps and Young, 1999; and Siddique, et al., 2007).

The habitat of soil bacteria is the thin film of water held to the surface of soil particles by capillary attraction. EPA (2013a) notes that soil moisture content greater than 2 percent is adequate to support biodegradation activity (Leeson and Hinchee, 1996), although biodegradation is limited when the moisture content is at or below the permanent wilting point (Zwick, et al., 1995; Holden, Halverson, and Firestone, 1997). Adequate soil moisture is also indicated if the landscape supports the growth of non-irrigated vegetation (Riser-Roberts, 1992).

Certain geologic materials do not qualify as biologically active soil and should not be included in the vertical separation distance (see **Section 5**, p.48). These geologic materials include:

- Coarse sand and gravel with a low content of silt, clay, and organic matter, and low moisture content that is less than 2 percent dry weight
- Fractured, faulted, or jointed consolidated rock
- Consolidated rock with solution channels (i.e., karst)

Importance

Effective aerobic biodegradation of PHCs depends on a thick layer of soil having sufficient oxygen and enough soil water to provide a habitat for adequate populations of active microorganisms. If oxygen is present, these organisms will generally consume available PHCs. Furthermore, aerobic biodegradation of petroleum compounds can occur relatively quickly, with degradation half-lives as short as hours or days under some conditions (DeVaull, 2007).

Some petroleum compounds can also biodegrade under anaerobic conditions; however, above the water table, where oxygen is usually available in the soil zone, this process is less important because it is generally much slower than aerobic biodegradation (Widdel, Boetius, and Rabus, 2006; Bailey, Jobson, and Rogers, 1973; and Bruce, Kolhatkar, Cuthbertson, 2010).

Assessment

Scientific research and site characterizations have demonstrated that microorganisms capable of aerobically degrading many PHCs are present in nearly all subsurface soil environments (ZoBell, 1946; Atlas, 1981; Wilson, et al., 1986; Leahy and Colwell, 1990; Bedient, Rifai, and Newell, 1994; EPA, 1999). A number of well-characterized field studies demonstrate extensive aerobic biodegradation of PHC vapors in unsaturated soils (Kampbell, et al., 1987; Ostendorf and Kampbell, 1991; Ririe and Sweeney, 1995; Ririe, et al., 1998; Ostendorf, et al., 2000; Hers, et al., 2000; Roggemans, Bruce, and Johnson, 2002; Sanders and Hers, 2006; Davis, Patterson, and Trefry, 2009; Patterson and Davis, 2009; Lahvis, Baehr, and Baker, 1999; and Lavhis and Baehr, 1996). Several of these studies document vapor concentrations at least two to three orders of magnitude lower than would be predicted to occur merely by simple diffusion in the absence of biodegradation.

EPA (2013a) presents findings of an analysis of a large number of vapor samples from leaking UST sites. These results, which are consistent with several recent analyses of different PVI databases (and which are summarized in the report), indicate that in most settings, PHC vapors are biodegraded over relatively short distances in clean, biologically active soil.

Special Considerations

Preferential transport pathways are avenues of least resistance to the migration of contaminants whether in the dissolved phase, LNAPL phase, or vapor phase. The presence of preferential transport pathways can increase the speed at which contamination moves through the subsurface such that contaminants may not biodegrade by the time they reach receptors. Preferential transport pathways include both natural and man-made features (e.g., solution channels, gravel layers, utility corridors and excavations). Natural geologic materials such as coarse sand and gravel with a low content of silt and clay; fractured consolidated rock; or consolidated rock with solution channels, may not have enough soil moisture in contact with soil gas to support adequate densities of biologically active microorganisms. Particularly in cases with shallow contamination, site investigations should evaluate whether a sufficiently thick layer of clean, biologically active soil is present below buildings in the lateral inclusion zone.

In addition, beneath very large buildings or under areas of extensive impermeable surface cover, soil moisture content may be lower than optimal[38] to support an adequate population of biologically active microorganisms necessary to degrade PHC vapors and prevent PVI (see Tillman and Weaver, 2007; EPA, 2013b).

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[38] Such reduced soil moisture beneath large buildings is referred to as a *soil moisture shadow*.

Recommendation

Based on EPA (2013a), clean, biologically active soil does not contain LNAPL, EPA recommends LNAPL thresholds of 100 mg/Kg TPH (fresh gasoline) and 250 mg/Kg TPH (weathered gasoline and diesel). Except for the geological materials identified in *Special Considerations*, most soils contain indigenous microorganisms, sufficient oxygen, and adequate soil moisture necessary for degrading PHC vapors. Thus, it is typically not necessary to run microcosm studies or plate counts to test for microbial presence. However, if the conditions at the site are uncertain for supporting aerobic biodegradation, EPA recommends that appropriate samples be collected and analyzed to verify conditions at the site.

Due in part to difficulties in measuring this level of accuracy in the field, EPA recommends vertical separation distances of 6 feet for purely dissolved sources of PHCs and 15 feet for LNAPL sources. These distances are believed to be conservative in most environmental settings. The vertical separation distances described in this guidance (see **Table 3** in **Section 5**, p.52) should not be used at sites where the geologic materials may not have enough soil moisture in direct contact with soil gas. EPA recommends collection and analysis of adequate soil samples for soil moisture, which should be greater than 2 percent by dry weight. In situations where densities of biologically active microorganisms may not be adequate to biodegrade PHCs then soil gas samples should be collected following the recommendations in **Section 8**. If the attenuation factor calculated from results of analysis of the chosen pair or vapor samples indicates that there may be a potential for PVI above applicable exposure limits, EPA recommends gathering additional information and data to determine whether mitigation is appropriate.

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10. Non-PHC Fuel Additives

Description

Petroleum fuels are comprised of hundreds of compounds; both natural components of petroleum as well as a number of synthetic (non-PHC) additives intended to improve certain performance properties of the fuel. Contaminants other than PHCs may be present at a site as the result of releases of petroleum fuels that contain additives, including alcohols (e.g., ethanol and tertiary-butyl alcohol [TBA]), ethers (e.g., MTBE), organic lead (e.g., the tetraalkyl lead compounds: tetraethyl lead [TEL], and tetramethyl lead [TML]), and lead scavengers (e.g., ethylene dibromide [EDB] and 1,2-dichloroethane [1,2-DCA]).[39] Non-petroleum contaminants may also be from releases of substances (e.g., chlorinated solvents) other than petroleum fuels. Their presence may be from prior uses of the site or as the result of migration from an off-site source (e.g., dry cleaner, chemical plant, landfill).[40]

Importance

When assessing the potential threat of vapor intrusion, the presence of non-PHC fuel additives may pose a variety of additional challenges. Depending on the class of additive, the challenges include:

- Uncertainty regarding the aerobic biodegradation rates of some additives as well as some that do not biodegrade aerobically (or do not biodegrade quickly enough) in the shallow subsurface
- Biodegradation of an additive such as ethanol that consumes oxygen that would otherwise be available for biodegradation of other PHCs and produces a VOC (methane), which may migrate into buildings and hasten the spread of PHC vapors
- Toxicity levels of some additives are below the detection limit of conventional analytical methods

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[39] Although leaded gasoline, which also contains the lead scavengers EDB and 1,2-DCA, is no longer used for automotive fuel, it is still used for certain off-road applications such as automobile racing and in aviation fuel (Avgas). At these and older automotive fuel sites where leaded gasoline was released to the subsurface, lead scavengers may be present and could represent a potential source of vapors that should be assessed. For more information about lead scavengers, see Appendix F in *Evaluation Of Empirical Data To Support Soil Vapor Intrusion Screening Criteria For Petroleum Hydrocarbon Compounds* (EPA, 2013).

[40] While these substances are not the primary focus of a petroleum UST release investigation (including site characterization and subsequent cleanup, if necessary), there is the possibility that their presence may be detected through the use of certain analytical methods for identification of contaminants in groundwater, soil, and vapor samples. In particular, both EPA methods 8260B (EPA, 1996a) and 8021B (EPA, 1996b) can detect a number of volatile chlorinated solvents that are not associated with petroleum fuels or typically stored in USTs. The Leaking Underground Storage Tank Trust Fund cannot be used to assess or cleanup contamination from non-UST and non-petroleum sources. Volatile chlorinated solvents (e.g., PCE, TCE, TCA, Carbon tetrachloride, Chloroform) also do not biodegrade under aerobic conditions, therefore their potential for vapor intrusion should instead be assessed using the *OSWER Final Guidance For Assessing and Mitigating the Vapor Intrusion Pathway From Subsurface Sources to Indoor Air* (OSWER Publication 9200.2-154)(EPA, 2015). Should any contaminants from non-UST sources be discovered at a leaking UST site, contact the appropriate state or federal implementing agency.

The separation distances described in this document (**Section 5**, Table 3, p.52) and the protectiveness provided by clean, biologically active soil against vapor intrusion by PHCs may be insufficient to protect against vapor intrusion by non-PHC fuel additives. Additional investigation should be conducted where certain additives are present. The following narrative provides additional information on several additives and introduces the Vapor Intrusion Screening Levels (VISL) Calculator, which may be particularly useful when investigating vapor intrusion from non-PHC fuel additives.

Although biodegradation is known to occur for many individual additives and classes of additives,[41] the rate of biodegradation in soil gas has not necessarily been rigorously quantified; this is especially true for the lead scavengers EDB and 1,2-DCA. Therefore, for these two chemicals in particular, vertical separation distances recommended in this guide may not be sufficient for petroleum fuel releases that contain EDB and 1,2-DCA and additional investigation may be necessary to assess their potential for vapor intrusion. Note: Though the use of ethers and lead scavengers in gasoline has been reduced or eliminated in recent years, these compounds may still be present at some older petroleum release sites (Weaver, et al., 2005, 2008, 2009; EPA, 2008).

Alternative fuels, especially those that contain higher percentages of ethanol present a challenge because ethanol readily biodegrades to create methane (Jewell and Wilson, 2011; Ma, et al., 2012 and 2014; Freitas, et al., 2010). The use of ethanol in motor fuels is increasing. Methane generation may be more significant at sites where large volumes of ethanol-blended gasoline (and higher ethanol content fuels, greater than E-20) have been released into the subsurface (Ma et al., 2014). Methane production can increase soil gas pressures and may result in advective soil gas flow toward receptors. In such situations, intrusion of methane into confined spaces may result in the accumulation of very high concentrations creating a risk of fire and explosion. In addition, methane also biodegrades under aerobic conditions and depletes oxygen that otherwise could be available for the biodegradation of PHCs. The depletion of oxygen may result in PHC vapors being transported farther than they otherwise would be, possibly increasing the threat of PVI.

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[41] Aerobic biodegradation has been observed for the lead scavengers EDB (Prince and Douglas, 2010; Pignatello, 1986), and 1,2-DCA (Falta, 2004); the ethers MTBE (Prince and Douglas, 2010; Wang and Deshusses, 2007; Phelps and Young, 1999; Landmeyer and Bradley, 2003; Landmeyer, et al., 2010; Bradley and Landmeyer, 2006; Kuder, 2005; Lesser, et al., 2008; Baehr, Charles, and Baker, 2001) and Tertiary-amyl methyl ether (TAME) (Landmeyer, et al., 2010); the alcohols Ethanol (Powers, et al., 2001; Corseuil et. al, 1998), TBA (Wang and Deshusses, 2007; Landmeyer, et al., 2010), and Methanol (Powers, et al., 2001); and some organic lead compounds (Prince and Douglas, 2010; Gallert and Winter, 2004). Although anaerobic biodegradation is slower than aerobic biodegradation, anaerobic biodegradation may be a significant mechanism for destruction of non-PHCs fuel additives (and PHCs, especially in source areas.) Selected references on anaerobic biodegradation of various non-PHC fuel additives are listed under *Additional Information* at the end of this section.

Thus, separation distances that are usually protective against PVI may not be sufficiently protective in situations where methane is produced in large quantity (Ma et al., 2014). For additional information on sampling for the presence of methane, assessing potential risks, and how to manage the risks, see ASTM's "*New Practice for Evaluating Potential Hazard Due to Methane in the Vadose Zone*".[42]

Finally, in addition to the uncertainties regarding the rates of biodegradation of the lead scavengers EDB and 1,2-DCA,existing analytical methods are not able to detect them at very low concentrations representative of a cancer risk level of 1E-06. However, EPA (2013) suggests that although there are no soil gas data for lead scavengers in the PVI database, "a screening approach is feasible where groundwater concentrations are measured to determine the potential for vapor intrusion risks from EDB and 1,2-DCA." (see Section F.6). This approach is illustrated in the *Assessment* subsection through a sequence of equations and detailed discussion of the results for EDB and 1,2-DCA.

Assessment

Federal UST regulations (40 CFR 280.52(b)) stipulate that when conducting an investigation of a release from a regulated UST, investigators "must measure for the presence of a release where contamination is most likely to be present. In selecting sample types, sample locations, and measurement methods investigators must consider the nature of the stored substance, the type of initial alarm or cause for suspicion, the type of backfill, the depth of groundwater, and other factors appropriate for identifying the presence and source of release". Results of this sampling should also identify which contaminants should be assessed for potential vapor intrusion.

Once the candidate contaminants have been identified, the next step is to determine the target indoor air screening level for each of them. While the federal UST program does not prescribe human health values for contaminants, implementing authorities should use exposure values appropriate for the contaminants present and the characteristics of exposure (e.g., residential vs industrial). EPA provides a source of such exposure values in the Vapor Intrusion Screening Levels (VISL) Calculator.[43] VISLs for human health protection are generally recommended, medium-specific, risk-based screening-level concentrations intended for use in identifying areas or buildings that may warrant further investigation and mitigation as appropriate.

These VISLs are calculated and documented in the VISL Calculator and are based on:

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[42] The new ASTM methane guide is accessible at http://www.astm.org/DATABASE.CART/WORKITEMS/WK32621.htm

[43] The VISL Calculator provides recommended, but not mandatory, screening levels for use in evaluating the vapor intrusion pathway at Comprehensive Environmental Response, Compensation and Liability Act (CERCLA) and Resource Conservation and Recovery Act (RCRA) sites. The user's guide for the VISL Calculator provides additional information about derivation of the indoor air and subsurface screening levels (EPA, 2014a). Both the VISL Calculator (EPA, 2014b) and user's guide may be downloaded from EPA's website: http://www.epa.gov/oswer/vaporintrusion/guidance.html.

Current toxicity values selected considering OSWER's hierarchy of sources for toxicity values (EPA, 2003)[44]

- Physical-chemical parameters for vapor forming chemicals
- EPA recommended approaches for human health risk assessment

The VISLs include target indoor air screening levels for long-term (i.e., chronic) exposures that consider the potential for cancer and non-cancer effects of vapor-forming chemicals. The VISLs also include subsurface screening levels for comparison to sampling results for sub-slab soil gas, "near-source" soil gas, and groundwater. These subsurface screening levels are back-calculated from the target indoor air screening levels for chronic exposures using medium-specific, generic attenuation factors that reflect generally reasonable worst-case conditions (EPA, 2015, Appendix B). VISLs are not automatically response action levels, although EPA recommends that similar calculation algorithms be employed to derive cleanup levels (see EPA, 2015, Section 7.6 for more information).

The VISL Calculator allows users to specify an exposure scenario, target risk for carcinogens (TCR) and target hazard for non-carcinogens (THQ), and the average groundwater temperature at a site, and calculates screening levels for the target indoor air concentration, sub slab and exterior soil gas concentrations, and ground water concentration.

In the VISL Calculator, target indoor air concentrations are calculated using the equations presented in **Table 4**. For carcinogens, the inhalation unit risk (IUR) is the appropriate toxicity value. For non-carcinogens, the reference concentration (RfC) is the appropriate toxicity value. Each of these toxicity values is weighted by the appropriate exposure factors to determine the target indoor air screening concentrations. The smaller value (between $C_{ia,c}$ and $C_{ia,nc}$) is used as the target indoor air screening value.

Example calculations using the equations in **Table 4** are presented in **Table 5** for EDB and 1,2-DCA in indoor air under a residential exposure scenario. Note that the cancer screening levels ($C_{ia,c}$) are consistently lower than the non-cancer screening levels ($C_{ia,nc}$), thus the cancer screening levels would generally be used to assess risk to receptors for a given chemical.

[44] OSWER's toxicity data hierarchy is three-tiered. Tier 1 are values from EPA's Integrated Risk Information System (IRIS). The IRIS database is web accessible at *http://www.epa.gov/iris/*. Tier 2 are Provisional Peer Reviewed Toxicity Values (PPRTVs), which are accessible at *http://hhpprtv.ornl.gov/*. Tier 3 are "Other"sources, such as the Agency for Toxic Substances and Disease Registry (ATSDR), and various states (e.g., California (CA DTSC, 2009), Hawai'i (HI DOH, 2011, 2012), Massachusetts (MA DEP, 2009), New Jersey (NJ DEP, 2013), Washington (WA DEC, 2006). Links to these sources are provided under *References Cited* at the end of this section.) EPA's Regional Screening Levels (RSLs) for Superfund Sites compiles available toxicity information based on this hierarchy. The VISL Calculator draws on these RSL tables for toxicity values that are used to calculate VISLs. RSLs are accessible at *http://www.epa.gov/reg3hwmd/risk/human/rb-concentration_table/index.htm*.

Table 4. Equations For Target Indoor Air Screening Concentrations For Volatile Chemicals

Cancer	$C_{ia,c} = \frac{TCR \cdot ATc \cdot 365\ (days/year) \cdot 24(hours/day)}{EF \cdot ED \cdot ET \cdot IUR}$
Non-Cancer	$C_{ia,nc} = \frac{THQ \cdot RfC \cdot ATnc \cdot 365 \cdot 24 \cdot 1000(ug/mg)}{EF \cdot ED \cdot ET}$
$C_{ia,c}$ is the indoor air concentration for cancer risk, and $C_{ia,nc}$ is the indoor air concentration for non-cancer risk; the smaller value is used as the indoor air screening value. ATc and ATnc are the averaging times for cancer and non-cancer, respectively, and EF, ED and ET are exposure parameters (exposure frequency, duration, and time). The exposure factors should be consistent with those in Human Health Evaluation Manual, Supplemental Guidance: Update of Standard Default Exposure Factors OSWER Directive 9200.1-120 *http://www.epa.gov/oswer/riskassessment/pdf/superfund-hh-exposure/OSWER-Directive-9200-1-120-ExposureFactors.pdf*	

Table 5. Example Target Residential Indoor Air Concentrations For EDB And 1,2-DCA

Chemical	**$C_{ia,c}$ ($\mu g/m^3$)**	**$C_{ia,nc}$ ($\mu g/m^3$)**
1,2-Dibromoethane (EDB)	4.7E-03	9.4
1,2-Dichloroethane (1,2-DCA)	1.1E-1	7.3
Values (and units) of other variables used in these example residential calculations (equations in **Table 4**) are:		
Variable	Cancer (c)	Non-Cancer (nc)
IUR(c) or RfC(nc) (EDB)	6.0E-04 $(\mu g/m^3)^{-1}$	9 (mg/m^3)
IUR(c) or RfC(nc) (1,2-DCA)	2.6E-05 $(\mu g/m^3)^{-1}$	7 (mg/m^3)
TCR(c) or THQ(nc) (unitless)	10^{-6}	1.0
ATc or ATnc (years)	70	26
ED (years)	26	26
EF (days/year)	350	350
ET (hours/day)	24	24

After target indoor air screening levels (C_{ia}) have been established, the next step is to determine vapor source concentrations and assess whether these are high enough to potentially pose a threat of vapor intrusion. The equations in **Table 6** are used by the VISL Calculator to calculate groundwater and soil gas screening levels based on target indoor air screening levels. These groundwater and soil gas screening levels can then be compared to actual field measurements of groundwater and/or soil gas concentrations. If the measured concentrations are greater than the screening levels, then there is a potential for vapor intrusion, otherwise not.[45]

Table 6. Equations For Groundwater And Soil Gas Screening Levels Based On Target Indoor Air Screening Levels.

Ground Water Concentration	$C_{gw} = \frac{C_{ia}}{\alpha_{gw} \cdot 1000 \cdot HLC}$
Soil Gas Concentration	$C_{sg} = \frac{C_{ia}}{\alpha_{sg}}$

C_{ia} is the target indoor air screening level concentration (µg/m^3).
Cgw is the screening concentration in groundwater (µg/L).
Csg is the screening concentration in soil gas (µg/m^3).
HLC is the unitless Henry's Law constant.
α_{gw} and α_{sg} are the groundwater and soil gas vapor intrusion attenuation factors, respectively (both unitless).
1,000 is the number of liters per m^3 (to convert from units of µg/m^3 to µg/L).

[45] An individual subsurface sampling result that exceeds the respective, chronic screening level does not establish that vapor intrusion will pose an unacceptable human health risk to building occupants. Conversely, these generic, single-chemical VISLs do not account for the cumulative effect of all vapor-forming chemicals that may be present. Thus, if multiple chemicals that have a common, non-cancer toxic effect are present, a significant health threat may exist at a specific building or site even if none of the individual substances exceeds its VISL (see discussion of non-cancer hazard index in EPA (2015) Section 7.4.1).

These equations also may be rearranged to calculate a potential upper-bound indoor air screening concentration based on actual field measurements of groundwater and/or soil gas concentrations. For groundwater, the equation is rearranged like this:

$$(upper\ bound)C_{ia} = C_{gw} \cdot \alpha_{gw} \cdot 1000 \cdot HLC$$

Note that in order to calculate a screening level concentration in groundwater, a value for Henry's Law constant (HLC) is necessary.[46]

For soil gas the equation is rearranged like this:

$$(upper\ bound)C_{ia} = C_{sg} \cdot \alpha_{sg}$$

Appropriate values for the field measured concentration in groundwater or soil gas, and for the respective attenuation factors are plugged into the equation to yield an upper bound indoor air screening level for C_{ia}. The respective upper-bound indoor air screening level (derived from either groundwater or soil gas sampling data) is then compared to the target indoor air screening concentration (C_{ia}) from the VISL Calculator. If the upper-bound value is greater than the target value, then there is a potential for vapor intrusion, otherwise not (see Footnote #45).

In both cases, if there is a potential for vapor intrusion and where contamination is not in direct contact with an overlying building, then paired vapor samples should be collected to assess vapor attenuation. These paired samples should either be (a) near-slab (exterior) shallow soil gas samples paired with deep (source) soil gas samples, or (b) indoor air samples paired with sub-slab soil gas samples.

Table 7 presents example screening concentrations of EDB and 1,2-DCA in groundwater and soil gas using the equations in **Table 6**. These values represent the upper-bound concentrations according to Henry's Law that could be present in groundwater and soil gas, respectively, and not result in indoor air concentrations in excess of the target screening levels (i.e., VISLs) presented in **Table 5**. If concentrations measured in groundwater (C_{gw}) exceed these thresholds, it is possible that the target indoor air concentration will also be exceeded and mitigation may be necessary.

[46] The VISL Calculator is one source of Henry's Law constants. Because these constants are temperature dependent, the VISL Calculator automatically calculates the correct constant based on a temperature that is selected by the user.

Table 7. Example Screening Concentrations For EDB And 1,2-DCA In Groundwater And Soil Gas

Chemical	C_{gw} (µg/L)	C_{sg} (µg/m^3)
1,2-Dibromoethane (EDB)	0.18	.16
1,2-Dichloroethane (1,2-DCA)	2.2	3.7
Target residential indoor air concentrations ($C_{ia,c}$) are from **Table 5**. Selected attenuation factors (α) are 0.001 for groundwater and 0.03 for soil gas. These are taken from the VISL Calculator and do not account for biodegradation. Dimensionless Henry's Law constants (HLC) for groundwater at 25°C are 0.0266 for EDB and 0.048 for 1,-DCA. These values are also taken from the current version of the VISL Calculator.		

The lead scavengers present an additional challenge in that existing analytical methodology is not able to detect them at very low concentrations representative of a cancer risk level of 1E-06 for either EDB or 1,2-DCA. As shown in **Table 8**, Selective Ion Monitoring (SIM) is able to achieve a detection limit representative of the 1.0E-04 risk level for EDB and 1.0E-05 for 1,2-DCA. Commercial low level is able to achieve a detection limit representative of the 1.0E-05 risk level for 1,2-DCA. However, an analytical detection limit does not impact the risk level for a certain chemical. The chemical may be present at a concentration greater than the appropriate risk level concentration, but below the limit of detection, which may result in undetected risk to potential receptors. Approaches to compensate for such analytical limitations include using available modeling data and professional judgment to evaluate whether the chemical may be present and having samples reanalyzed by special analytical services. For the screening level assessment, the chemical should be carried through assuming that it is present at the concentration equivalent to the quantitation limit. This allows the risk at the quantitation limit to be compared to the risks associated with other chemicals at the site. At minimum, the chemical should be addressed qualitatively. These topics are beyond the scope of this PVI guide; additional information may found in EPA's *Risk Assessment Guidance for Superfund* (RAGS).[47]

[47] The *Risk Assessment Guidance for Superfund (RAGS)* document is accessible at http://www.epa.gov/oswer/riskassessment/ragsa/index.htm. In particular see Section 5.3 in Part A, and Part F: Supplemental Guidance for Inhalation Risk Assessment.

Table 8. Comparison Of Risk Levels And Achievable Analytical Detection Limits For The Lead Scavengers EDB And 1,2-DCA In Indoor Air.

Compound	Target Indoor Air Concentration			Analytical Method		
	Risk Level 1.0E-04	Risk Level 1.0E-05	Risk Level 1.0E-06	Commercial conventional	Commercial low level	Commercial SIM
EDB	0.47	0.047	0.0047	3.8	0.77	0.23
1,2-DCA	11	1.1	0.11	2.0	0.40	0.12

NOTE: all values in $\mu g/m^3$
1.0E-04 = increased lifetime cancer risk of 1 per 10,000
1.0E-05 = increased lifetime cancer risk of 1 per 100,000
1.0E-06 = increased lifetime cancer risk of 1 per 1,000,000
Commercial conventional = EPA Method TO-15 (see http://www.epa.gov/ttn/amtic/files/ambient/airtox/to-15r.pdf)
Commercial low level = EPA Method TO-15 (modified)
SIM = Selective Ion Monitoring
The achievable detection limits in this table are representative of the general state of the technology as of the present date. Some laboratories may be able to achieve lower detection limits using modified techniques. Future technological improvements may also result in lower detection limits.
Achievable
Not Achievable

Special Considerations

VISL Calculator screening levels do not include the effects of biodegradation on the concentrations of vapors in soil that could potentially intrude into indoor air. The generic attenuation factors used in calculating VISLs (i.e., 0.001 for groundwater, 0.03 for soil gas) are conservative, and may overestimate the transfer of some contaminants (e.g., those that biodegrade aerobically) from soil gas to indoor air in some buildings. As a result these screening levels will usually overestimate the true indoor air concentrations of aerobically-biodegradable volatile contaminants (e.g., PHCs). Decision-makers may choose to use alternate approaches (e.g., attenuation factors that account for biodegradation) that may be more appropriate for specific sites where circumstances do not match the underlying assumptions used in calculating the VISLs.

When Information is available on the separation distance between the source of contamination and the receptor, on the total concentration of biodegradable compounds in soil gas, and on the rate constant for degradation of contaminant vapors in soil, it is possible to refine the estimate of the attenuation factor (α) between soil gas and indoor air for some VOCs and PHCs. Approaches to refine the estimate of the attenuation factor (α) for PHCs are discussed in **Section 12** (p.100) and by Wilson et al. (2014). Also see **Section 13** (p.106) for information on the use of models to estimate attenuation factors. However, until more is known about the rates of biodegradation of EDB and 1,2-DCA in soil gas, the separation distances for PHCs shown in Section 5 and the approaches described in **Section 12** or **Section 13** for determining attenuation factors are not recommended for these two contaminants.

In addition to concerns discussed earlier, other potential concerns with increasing ethanol content are in relation to (re)mobilization of LNAPL (McDowell, et al., 2003; Yu, et al., 2009) and increased solubility of PHCs (Powers, et al., 2001). The implications of these impacts may extend beyond vapor intrusion; see **Section 7** (p.61) for information about LNAPL and **Section 6** (p.57) for information about dissolved contaminant plumes.

Recommendation

EPA recommends that groundwater samples be analyzed for PHCs and non-PHC fuel additives (e.g., alcohols, ethers, organic lead, lead scavengers) typically found in petroleum-based fuels, when appropriate. At the present level of knowledge, the groundwater and soil gas screening levels in **Table 7** are the best values to use to determine whether indoor air target levels will be exceeded for EDB and 1,2-DCA. If measured concentrations of EDB and 1,2-DCA in groundwater exceed the screening levels in **Table 7**, EPA recommends gathering additional information and data to determine whether mitigation is appropriate. The methodology illustrated in the *Assessment* subsection above can be applied to any non-PHC (or any VOC for that matter) for which an appropriate toxicity value and attenuation factor are available.

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11. Seasonal And Weather Effects

Description

The generation and movement of petroleum vapors are subject to seasonal effects such as temperature trends and fluctuations; and weather effects such as precipitation, barometric pressure changes, and wind (Lundegard, Johnson, and Dahlen, 2008). Cycling of heating and cooling systems inside buildings in response to seasonal and weather effects may also influence vapor intrusion.

Importance

Biological processes slow down with decreasing temperatures, though microorganisms continue to biodegrade PHCs at environmentally significant rates even when temperatures are near freezing (Bradley and Chapelle, 1995; Bradley, Richmond, and Chapelle, 2005; Hers, et al., 2011). Bradley and Landmeyer (2006) documented microbial degradation of MTBE in the wintertime when groundwater temperatures were below 5˚C.

There is conflicting evidence as to whether, and under what additional conditions, frozen or ice-covered soil reduces the movement of oxygen into the subsurface. Hers, et al. (2011) studied a residential site in Canada where subsurface oxygen readings taken throughout the winter did not indicate a decrease in oxygen content of soil gas and there was evidence that biodegradation was occurring. However, the residence was above a crawl space and the soil below the house was never covered by ice or snow. It is known that the air permeability of a snow layer is a complex function of pore size, grain size, ice fraction, and density (Armstrong, 2008; Bender, 1957; Conway and Abrahamson, 1984). Rike (2003) observed ongoing biodegradation in frozen arctic soils. In that study, a lengthy period of subfreezing soil temperatures at a petroleum contaminated site did not result in decreasing oxygen concentrations. In contrast, Freyman (1967) and Yanaia (2010) report that oxygen depletion has been observed in other studies of soils under ice sheets and snow cover. More study is needed to resolve this issue.

Precipitation events can impact biodegradation of petroleum vapors. A certain amount of soil moisture is necessary for microorganisms to live; not enough and they are not actively degrading PHC vapors; too much and reoxygenation is impeded, possibly leading to anaerobic conditions at greater depths (Silver, 1999; Ludemann, 2000; Pezeschki, 2001). Wind and barometric pressure changes can produce pressure gradients inside buildings. Negative pressure inside buildings can result in enhanced intrusion of PHC vapors. Positive pressure inside buildings can both prevent intrusion of PHC vapors into buildings and facilitate oxygen transport through cracks in the foundation into the subsurface. This can result in reoxygenation of the soil beneath the building that would otherwise be depleted of oxygen (Lundegard, Johnson, and Dahlen, 2008).

Heating systems in buildings, which operate most frequently during winter months, can create a chimney effect, whereby PHC vapors are pulled into buildings at much higher rates than they would ordinarily. Cooling systems, which operate only during summer months, can have the opposite effect, creating positive pressure gradients in basements that both prevent intrusion of PHC vapors into buildings and allow oxygen to enter the soil (Lundegard, Johnson, and Dahlen, 2008).

Assessment

Seasonal and weather conditions can influence the characteristics of PHC vapor migration over time. Data on temporal changes in temperature, barometric pressure, wind speed and direction, relative humidity, and precipitation can aid in correctly identifying trends and result in a more accurate CSM.

In addition, site characteristics that may indicate susceptibility to the effects of seasonal and weather factors should be assessed. These include:

- Poor drainage around the building indicated by flooded soils
- Area subject to permafrost/long lasting snow cover (based on altitude or latitude)
- Shallow and highly variable water table

Special Considerations

Seasonal effects may also influence the formation and migration of dissolved plumes and LNAPL. Changes in water table elevation can create a smear zone of residual LNAPL contamination. LNAPL in the smear zone can act as a long-term source of dissolved contamination during periods of high water table elevation and as a source of petroleum vapors during periods of low water table elevation when contaminants reemerge from a previously submerged condition. Groundwater levels in the vicinity of USTs may also be subject to the influence of water within the tank pit. After rainfall events (and potentially snowmelt) water levels within tank pits are typically above the level of ambient groundwater; consequently a groundwater recharge mound may form. This mound disrupts the local groundwater flow field and contaminants can migrate away from the tank excavation, potentially in all directions.

Recommendation

During site characterization activities, weather conditions such as temperature, barometric pressure, and wind speed/direction should be recorded to aid in recognizing the cause of trends or anomalies in the PVI data and not merely attributed to unknown factors. This information may be obtained from the National Oceanic and Atmospheric Administration (NOAA) (see *http://www.noaa.gov/wx.html*) or a nearby airport where weather data are recorded hourly.

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http://pubs.usgs.gov/of/1998/0287/report.pdf

Web Resources

U.S. Geological Survey's Soil Surveys
http://websoilsurvey.nrcs.usda.gov/app/HomePage.htm

U.S. Department of Homeland Security Federal Emergency Management Agency's flood plain maps *https://msc.fema.gov/portal*

2012 U.S. Department of Agriculture Plant Hardiness Zone Map
http://planthardiness.ars.usda.gov/PHZMWeb/

12. Vapor Intrusion Attenuation Factor (α)

Description

When Johnson and Ettinger (1991) published their vapor intrusion model they introduced a parameter to relate the vapor concentration of a volatile chemical inside a building to its vapor concentration at the subsurface source. The parameter, designated alpha (α), is also called the vapor intrusion attenuation factor. It is defined mathematically as the concentration in indoor air divided by the concentration in soil gas at the source (with concentrations in the same units). The source is defined as the region of highest vapor concentration in the vadose zone. Large values of α (i.e., values approaching one) indicate that little attenuation is taking place, whereas small values of α (i.e., values much smaller than one) indicate that significant attenuation is taking place.

Importance

As part of a risk evaluation, the concentrations of a chemical in indoor air can actually be measured, or they can be predicted. The attenuation factor is used as a part of a risk evaluation to predict or estimate the concentration of a chemical in indoor air from the concentration measured in soil gas below or near a building. To predict the indoor air concentration, the measured concentration in soil gas is multiplied by the suitable attenuation factor.

Assessment

U.S. EPA (2013, Table 6-1) provides recommended vapor attenuation factors for risk-based screening of the vapor intrusion pathway for residential buildings. For example, the generic values of α in EPA (2015) are 1.0E-03 (0.001) for groundwater, 3.0E-02 (0.03) for sub-slab soil gas, and 3.0E-02 (0.03) for deep (near-source) soil gas. These values of α are derived from measurements made during case studies of the vapor intrusion of chlorinated solvents such as trichloroethylene (TCE), which are not biologically degraded in aerobic unsaturated soil or sediment. Likewise, values for concentrations in indoor air that are derived from the model of Johnson and Ettinger (1991) also do not include any consideration of biodegradation. As a result, the generic values of α in U.S. EPA (2015) and values for indoor air that are calculated using the Johnson and Ettinger model (JEM) overestimate the indoor air concentrations of PHCs. Thus, these values of α are not applicable to PVI from leaking USTs.[48] For additional information on estimation of sub-slab attenuation factors, see Brewer et al. (2014).

To provide estimates of α that are more suitable for PHCs, Abreu, Ettinger, and McAlary (2009) developed a three-dimensional computer model to predict the effects of biodegradation in the unsaturated zone below a building on the concentrations of chemicals in the indoor air of the building. They performed a series of model simulations to estimate semi-generic values of α from site-specific information on the vertical separation distance between the receptor building

[48] Attenuation factors that account for biodegradation can be derived from models such as *BioVapor* or *PVIScreen* (see **Section 13**, p.106 for more information). Additional guidance may be found in Wilson *et al.* (2014).

and the source, and the total concentration of biodegradable compounds in soil gas at the source of the hydrocarbons. **Figure 9** compiles the computer simulations conducted by Abreu, Ettinger, and McAlary (2009) of the attenuation factor during vapor intrusion into a building with a basement. This figure presents the concentration of biologically degradable hydrocarbon in an unconventional unit (mg/L as benzene).

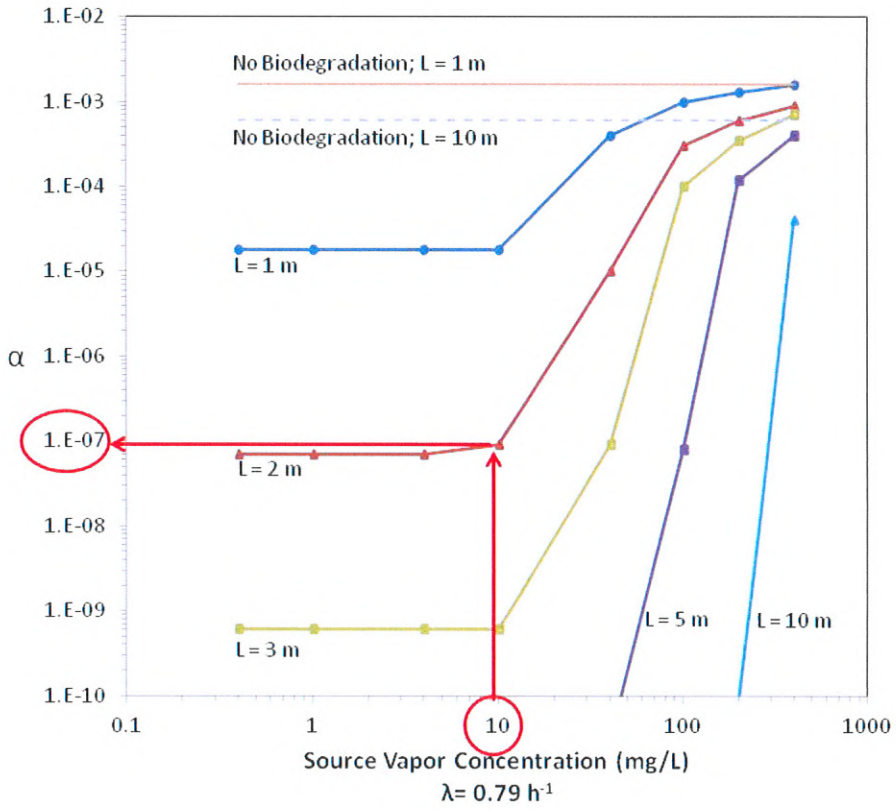

Figure 9. Relationship Between Source Vapor Concentration And Vapor Intrusion Attenuation Factor (α) As A Function Of Vertical Separation Depth Between Contaminant Source And Base Of Building (Receptor) (Source: modified from Abreu, Ettinger, and McAlary, 2009, Figure 7, page 114. Reprinted from *Groundwater Monitoring & Remediation* with permission of the National Ground Water Association. Copyright 2009.)

To generate **Figure 9**, Abreu, Ettinger, and McAlary (2009) used conservative assumptions for the rate of biodegradation. In this particular set of simulations, the first order rate constant for biodegradation (λ) was set at 0.79 h^{-1}, a reasonable average rate based on the range of rates published in the literature (DeVaull 2007). Model simulations assume the building has a basement and that it is surrounded by homogeneous, uniform sandy soil that is directly exposed to the atmosphere and that preferential pathways for vapor migration into the building or through the vadose zone are not present. As a result, the concentration of oxygen

in the soil gas in the topmost layer of exposed soil is the concentration of oxygen in the atmosphere. Compared to silty or clayey soils, sandy soils have more air filled porosity and as a result, vapors diffuse more rapidly through them (and they also allow more oxygen to diffuse from the atmosphere). The simulations assumed that the square building was 10 meters (33 feet) on each side.

Figure 9 can be used to estimate the value of α for situations where the total concentration of vapors at the source and the vertical separation distance between the contaminant source and the bottom of the building are known and all of the other input parameters match site conditions. For example, for a source vapor concentration of 10 mg/L and a vertical separation distance (L) of 2 meters (6.6 feet), the estimated value of α would be approximately 1.0E-07. To complete the exposure assessment, the measured concentration of benzene in soil gas at the source of contamination is multiplied by the value of α, to predict the indoor air concentration in a building.

Figure 10 is a redraft of **Figure 9**, where the source concentration of vapors is expressed in more conventional units for vapors in soil gas ($\mu g/m^3$). The oxygen demand of all the hydrocarbons that might be in soil gas is expressed as the concentration of TPH (gasoline) plus the concentration of methane. The concentration of TPH (gasoline) can be determined by modified EPA Method TO-15 (see *http://www.epa.gov/ttn/amtic/files/ambient/airtox/to-15r.pdf*) referenced to heptane. The concentration of methane can be determined as a fixed gas or by EPA Method 3C. The concentration of methane is multiplied by 1.136 to correct for the differences between the theoretical oxygen demand of methane and heptane.

Special Considerations

Figure 9 or **Figure 10** should only be used for UST sites with the same characteristics that were simulated by Abreu, Ettinger, and McAlary (2009). These conditions were relatively conservative. **Figure 9** and **Figure 10** are not appropriate for use at sites where the oxygen flux from the surface is impeded.

Some documents define the vapor intrusion attenuation factor differently than defined by Johnson and Ettinger (1991) and discussed in this section. The JEM (see **Section 13**, p.106) ignores background sources when estimating the indoor air concentration arising from vapor intrusion. When used in this PVI guide, the Greek letter alpha (α) refers strictly to attenuation during vapor intrusion, which might be observable if there were no background (ambient) vapor sources. In contrast, some empirical attenuation factors (sometimes designated *AF*) are based on indoor air concentrations that include both background sources and vapor concentrations that intrude into the building from a subsurface vapor source. Thus, when there is a measurable contribution from an ambient source, an attenuation factor such as *AF* (which includes the contribution of ambient sources) would be somewhat greater than the Johnson & Ettinger alpha (α), which would indicate less attenuation than is actually occurring.

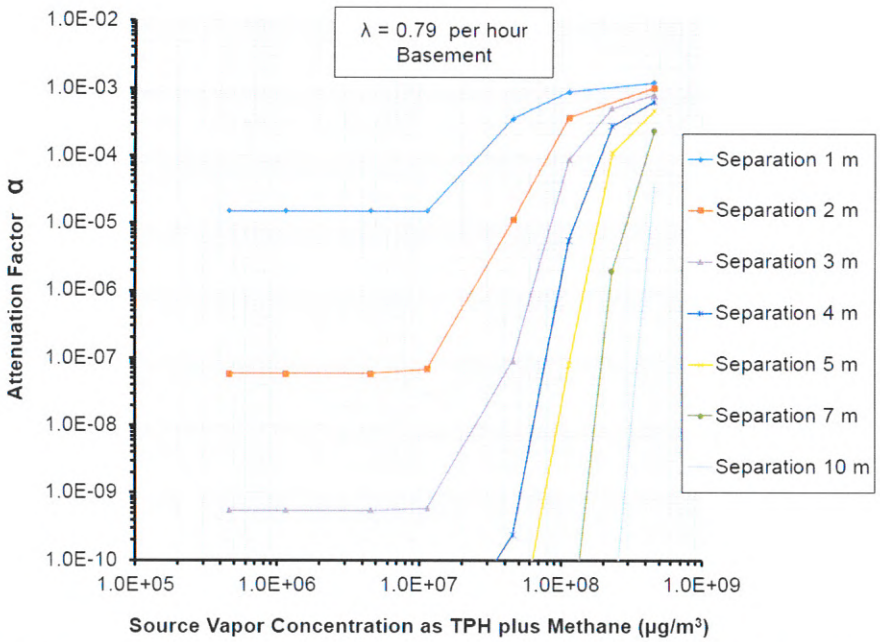

Figure 10. Rescaled Figure 9 That Expresses The Source Vapor Concentration In Conventional Units.

Recommendation

When evaluating the vapor source and attenuation of PHC vapors, paired vapor samples are required to measure the actual attenuation that occurs due to aerobic biodegradation. Where contamination is not in direct contact with an overlying building, choose one of two options: (1) collect near-slab (exterior) shallow soil gas samples paired with deep (source) soil gas samples, or (2) collect indoor air samples paired with sub-slab soil gas samples. Note that for option 2 if the measured concentration of vapor in indoor air is below the applicable allowable indoor concentration there is no need to measure sub-slab vapor concentration. If contamination is in direct contact with a building basement, foundation, or slab, it is necessary to collect indoor air samples as it will not be feasible to collect sub-slab vapor samples. If a generic vapor intrusion attenuation factor and the measured concentration of a PHC in shallow soil gas predict an acceptable concentration in indoor air, that prediction may be adequate to support a screening decision. However, generic attenuation factors may not be appropriately representative of conditions at a particular site.

Models may provide better estimates of α, but only if the actual conditions at a specific site match the assumptions of a particular model. For biodegradable PHCs it would be better to implement a transport and fate model that is designed to simulate the contribution of biodegradation. The three-dimensional models of Abreu, Ettinger, and McAlary (2009) and Verginelli and Baciocchi (2014) are potential options. BioVapor, a model developed by the American Petroleum Institute, is another option. U.S. EPA is developing a model called PVIScreen that is intended for this purpose. See **Section 13** (p.106) for more discussion of the appropriate use of computer models for PVI investigations.

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13. Computer Modeling Of Petroleum Vapor Intrusion

Description

A number of models have been developed and applied in estimating transport of volatile chemicals from subsurface soil and groundwater to indoor air (Bekele, et al. 2013). Lahvis (2011) presents a summary of 35 different analytical screening-level models, including a discussion of features, and assumptions. Models generally used for simulation of PVI are either the Johnson-Ettinger model (JEM) or BioVapor.

Johnson-Ettinger Model (JEM)

Johnson and Ettinger introduced one of the first vapor intrusion models in 1991. This model is referred to as the Johnson-Ettinger Model or JEM. Features of the JEM include:

- A steady or transient source of subsurface vapors from groundwater or residual chemicals
- Gaseous-phase diffusive vapor flow through a layer of soil
- Vapor transport through a slab-on-grade or basement foundation
- Building air exchange

The JEM presumes that the concrete foundation is impermeable and vapor movement occurs only through cracks and other openings. However, concrete is permeable to vapors and gases. Effective diffusion rates for intact air-dry concrete have been measured for hydrocarbons, oxygen, methane, and radon with an overall measured range from 1.08 to 15.6 cm^2/hr (Haghighat, et al., 2002; Patterson and Davis, 2009; Kobayashi and Shuttoh, 1991; Tittarelli, 2009; Yu, et al., 1993). Thus, diffusive vapor flow for typical foundation areas and thicknesses can be significant (McHugh, de Blanc, and Pokluda, 2006; Luo, et al., 2012). Actual measurement of differential pressure across varied building foundations show a significantly variable component over time (Nazaroff, et al., 1985; Hintenlang and Al-Ahmady, 1992; Robinson, et al., 1997a,b; McHugh , de Blanc, and Pokluda, 2006; Lundegard, Johnson, and Dahlen, 2008; Patterson and Davis, 2009; Luo and Johnson, 2011).

For sites where PHCs are present and aerobic biodegradation of PHCs occurs in the vadose zone, comparisons to JEM consistently show the model to over-predict indoor air concentrations by at least several orders of magnitude (Fitzpatrick and Fitzgerald, 2002; Sinke, 2001; Ririe, Sweeny, and Daugherty, 2002; Hers, et al., 2003; Davis, 2006; Golder Associates, 2008; Davis 2009). The potential for over-prediction is greatest for sites with low concentrations of PHCs in soil and groundwater (API, 2009; Davis, 2009; Energy Institute, 2009).

The original model has been revised numerous times to attempt to account for biodegradation, which was not included in the original JEM (see Johnson, Kemblowski, and Johnson, 1998; Ririe, et al., 1998; Johnson, Hermes, and Roggemans, 2000; Spence and Walden, 2010; Parker, 2003; Environmental Systems and Technologies, 2004; DeVaull, 2007a; Mills, et al., 2007; Turczynowicz and Robinson, 2007; API, 2010; Lahvis, 2011). EPA also revised the original JEM.

The most current information on EPA's revised model may be found on EPA's website at http://www.epa.gov/oswer/riskassessment/airmodel/johnson_ettinger.htm.

BioVapor

The BioVapor model (DeVaull, 2007a; API, 2010) is a Microsoft Excel© macro that uses a conceptual model similar to the JEM. BioVapor includes the following features:

- A steady subsurface petroleum vapor source.
- Gaseous-phase diffusive vapor flow through a layer of soil.
- Vapor transport through a slab-on-grade or basement foundation.
- Building air exchange.

In contrast to JEM, BioVapor accounts for oxygen-limited, aerobic biodegradation. Aerobic biodegradation is included as a coupled reaction between petroleum vapors and oxygen. Oxygen availability in the subsurface is dictated by transport through and around the building foundation, and by diffusion into the soil. The BioVapor model requires estimates of chemical-specific aerobic degradation rates for vadose zone soils. DeVaull (2007a,b) provides default values based on measured data. DeVaull (2011) provides improved estimates of both median values and observed ranges for an expanded set of specific chemicals.

PVIScreen

PVIScreen (Weaver, 2015) is based on the equations of BioVapor but is coded in Java to improve computational efficiency and allow for implementation of algorithms to automate uncertainty analysis. Most computer models must be run multiple times with varying input parameters in order to conduct a typical sensitivity analysis. PVIScreen automates this function by treating input variables as ranges and then conducting a Monte Carlo analysis. The results, which are provided in a matter of seconds, are presented as the probability that the indoor air concentration is less than a risk-based level. This is in contrast to most models that provide single values for various output parameters. PVIScreen also allows for flexible unit choices and presents results in an automatically-generated report.

Importance

Vapor intrusion models that include oxygen limited biodegradation support development of petroleum-specific exclusion distance criteria (i.e., lateral inclusion zone—see **Section 4**, p.44; vertical separation distance—see **Section 5**, p.48). Model results are consistent with empirical exclusion distance values derived from several PVI field investigations. These include Lahvis, et al. (2013); Davis (2009); Peargin and Kolhatkar (2011); Wright (2011); McHugh, et al. (2010), and Verginelli and Baciocchi (2014). Site assessment and field data including the depth to contamination, source strength, and type (LNAPL or dissolved) are key parameters for determining these exclusion distance criteria.

Estimates using the BioVapor model indicate that for moderate or weak sources (especially dissolved plumes), biodegradation effectively eliminates the potential for PVI. Conversely, where vapor sources are both high in concentration and in close proximity to the bottom of a foundation, the BioVapor model predicts significant potential for PVI.[49] Notably, in these cases the BioVapor model predicts significantly higher potential for PVI below a foundation, where oxygen availability is more limited, than adjacent to the foundation where the soil surface is open to air and oxygen availability is greater. This prediction is consistent with measured vertical profiles of hydrocarbons and oxygen for high concentration vapor sources taken both below a foundation and beside a foundation (Patterson and Davis, 2009; Laubacher, et al., 1997).

Weaver (2012) presents results of a sensitivity analysis that indicates when biodegradation occurs, it dominates the other processes included in the BioVapor model. In these cases, the parameters representing aerobic biodegradation, source depth, and source strength dominate the model results. In the other cases where biodegradation is insignificant, building parameters become more important, as they are in the JEM (Tillman and Weaver, 2007).

More complex numerical models including oxygen-limited biodegradation have been developed and applied. Abreu and Johnson (2006) present results for a three-dimensional model. With matched model parameters, there is reasonable agreement between the three dimensional results and those predicted with the BioVapor model (DeVaull, 2007b) and PVIScreen (Weaver, 2015). Each of these model results show similar sensitivities to changes in model parameters, and support the use of exclusion distances such as those recommended in this document (see **Section 4**, p.44, lateral inclusion zone, and **Section 5**, p.48, vertical separation distance).

Assessment

When selecting an appropriate computer model, the mathematical formulation needs to be consistent with conditions at the site and the CSM. If the computer model is not matched to conditions at the site, then error is likely introduced into the computer model results. This means that input parameters for the computer model should be representative of the actual physical, chemical, and biological properties of the site. Typically all factors influencing vapor intrusion are not included in currently available models. Even with more advanced modeling, resource limitations would prevent the detailed characterization necessary to determine representative values for some of the input parameters. Some of these factors include subsurface heterogeneity, variation in building operation, subsurface moisture content, variations in weather and others. For most other types of environmental models, limitations in characterization are mitigated by calibration to known endpoints, typically concentration distributions. Though calibration results may not be unique (that is the same results could potentially be obtained using different values for the same suite of input parameters), when these results match field conditions, a model is deemed to be useful for predictive simulations.

[49] Moderate or weak sources are associated with dissolved plumes. Strong sources are associated with LNAPL. **Table 3** on page 52 presents concentration thresholds associated with dissolved plumes and LNAPL.

Special Considerations

Most of the parameters describing model processes will not be known with certainty. A common limitation is that field measurements of all the input parameters (e.g., biodegradation rates, soil moisture content beneath buildings, air exchange rates) are typically not available, and those that are (e.g., source concentration) may be spatially or temporally variable. Literature values are typically substituted for site-specific data. This leads to uncertainty as to whether parameter values are truly representative of site conditions. Model results will likewise inevitably lack certainty (Bekele, et al, 2013). The importance of these (and other) parameters is determined through an uncertainty analysis. By determining the impact of parameter variability on the model results, the uncertainty analysis adds confidence to the conclusions drawn from the model.

Recommendation

An appropriate framework for the use of a mathematical model and understanding of model characteristics is critical when using the results of mathematical models for regulatory purposes (Hers, et al., 2003). The appropriate role for a model in a PVI investigation is as a means to explain observed behavior. EPA recommends the use of a model that considers aerobic biodegradation when assessing the potential for PVI. Regardless of which model is used to simulate PVI, EPA recommends that an uncertainty analysis be conducted to provide error bounds on predictions of the computer model.

Model results obtained by using site-specific inputs can provide results that inform decision-making. In particular, model results can be used to demonstrate that: sufficient oxygen exists to degrade petroleum contaminants, contaminant vapor distributions are plausible given conditions at the site, estimates of the vapor attenuation anticipated in the subsurface due to biodegradation are reasonable. Models may also be used for purposes such as improving a site-specific sampling strategy, validation (or refutation) of the CSM by comparing a model to measured soil gas data, and in estimating the effect of varied or changed site conditions (e.g., including construction of a new building on a brownfields site).

Model results can thus be used as one line of evidence that a building is not likely to be impacted by PHC vapors. At the present time and state of knowledge, EPA cautions that model results should not be used as the sole rationale for determining that a building is not threatened or impacted by PVI.

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Glossary

Note: Most of these definitions are from EPA's on-line glossaries (see http://iaspub.epa.gov/sor_internet/registry/termreg/searchandretrieve/termsandacronyms/search.do).

Absorption: the penetration of atoms, ions, or molecules into the bulk mass of a substance. In contrast, adsorption is the retention of atoms, ions, or molecules onto the surface of another substance

Advection: the process of transfer of fluids (vapors or liquid) through a geologic formation in response to a pressure gradient that may be caused by changes in barometric pressure, water table levels, wind fluctuations, or infiltration

Aerobic: able to live, grow, or take place only when free oxygen is present

Anaerobic: able to live, grow, or take place where free oxygen is not present

Analyte: the element, ion, or compound that an analysis seeks to identify; the element of interest

Attenuation: the reduction or lessening in amount (*e.g.*, a reduction in the amount of contaminants in a plume as it migrates away from the source)

Biodegradability (or biodegradation potential): the relative ease with which organic chemicals will degrade as the result of biological metabolism. With respect to petroleum hydrocarbons, although virtually all petroleum hydrocarbons are biodegradable, biodegradability is highly variable and dependent somewhat on the specific type of hydrocarbon. In general, biodegradability increases with increasing solubility; solubility is inversely proportional to molecular weight.

Biodegradation: a process by which microbial organisms transform or alter (through metabolic or enzymatic action) the structure of chemicals introduced into the environment

Biologically active soil: in the context of a PVI investigation means that the subsurface soil environment will support populations of microorganisms that are present in sufficient quantities to aerobically degrade PHC vapors before they intrude into a receptor. Effective aerobic biodegradation of petroleum hydrocarbons depends on the soil having sufficient oxygen and enough soil water to provide a habitat for adequate populations of active microorganisms. The presence of sufficient oxygen must be determined by the collection and analysis of soil gas. Soil that is too dry will not support microbial life. The soil generally will not be too dry for bacteria if the depth to the water table is less than 300 feet, or if the soil around the receptor supports the growth of plants characteristic of temperate climates. (NOTE that in hot, arid climates lack of soil moisture may inhibit biodegradation of PHCs) Concentrations of carbon dioxide which are ten-fold higher than concentrations in the atmosphere are an acceptable indication that conditions support microbial respiration. The actual habitat of soil bacteria is the thin film of water held to the surface of soil particles by capillary attraction. Coarse sand and gravel with a low content of silt or clay or organic matter, or fractured consolidated rock, or consolidated rock with solution channels, may not have enough soil water in intimate contact with soil gas to support adequate densities of biologically active microorganisms. These geological materials do not qualify as "biologically active soil."

BTEX: acronym for the aromatic hydrocarbons benzene, toluene, ethylbenzene, and xylenes (three isomers)

Capillary fringe: the zone of a porous medium above the water table within which the porous medium is saturated by water under pressure that is less than atmospheric pressure. See also *vadose zone* and *unsaturated zone*.

Clean monitoring point: Concentration thresholds for "clean" monitoring points are: the BTEX concentration in groundwater is equal to or less than the respective maximum contaminant level (e.g., 5 µg/L for benzene); the TPH concentration in soil is less than 20 mg/Kg; there is no potential presence of liquid or residual phase LNAPL; the oxygen concentration is greater than 0.2 percent; and the combustible gas concentration in soil gas is less than 100 ppm (v/v).

Clean soil: In the context of a PVI investigation, clean soil does not necessarily mean that the soil is free from all contamination, but rather that any contamination present is at concentrations low enough that the biological activity of the soil is sufficient to biodegrade PHC vapors before they reach a receptor.

Computer model: a mathematical representation of a physical process or system. Computer models are based upon sound conceptual site models to provide meaningful information. As the complexity of computer models increases, so does the amount of data required, and the quality of the output from computer models is directly related to the quality of the input data. Because of the complexity of natural systems, models necessarily rely on simplifying assumptions that may or may not accurately represent the dynamics of the natural system. Calibration and sensitivity analyses are important steps in the appropriate use of models.

Conceptual site model (CSM): a three-dimensional representation that conveys what is known or suspected about potential contamination sources, release mechanisms, and the transport and fate of those contaminants. The conceptual model provides the basis for assessing potential remedial technologies at the site. "Conceptual site model" is not synonymous with "computer model"; however, a computer model may be helpful for understanding and visualizing current site conditions or for predictive simulations of potential future conditions.

Contamination: in the context of a PVI investigation, contamination means that: the BTEX concentration in groundwater is greater than the respective MCL; or the TPH concentration in soil is greater than 100 mg/Kg; or there is potential presence of liquid or residual phase LNAPL; or the combustible gas concentration in soil gas is greater than 100 ppm (v/v).

Diffusion: the process by which molecules in a single phase equilibrate to a zero concentration gradient by random molecular motion (Brownian motion). The flux of molecules is from regions of high concentration to low concentration and is governed by Fick's Second Law.

Dispersion: the process by which a substance or chemical spreads and dilutes in flowing groundwater or soil gas

Downgradient: in the direction of decreasing potentiometric head; the general direction of groundwater flow

First responder: refers to those individuals who in the early stages of an incident are responsible for the protection and preservation of life, property, evidence, and the environment. Typically these are police, firefighters, or emergency medical personnel.

Fixed gases: refers to the gases nitrogen, oxygen, argon, carbon dioxide, and carbon monoxide. The volume of these gases together accounts for virtually 100 percent of the composition of the earth's atmosphere. Presence and concentration of these gases are determined using gas chromatography (GC).

Flux: the rate of movement of mass through a unit cross-sectional area per unit time in response to a concentration gradient or some advective force

Free product: a petroleum hydrocarbon in the liquid ("free" or non-aqueous) phase (see also light non-aqueous phase liquid, LNAPL)

Gradient: the rate of change in value of a physical or chemical parameter per unit change in position For example, hydraulic gradient is equal to the difference in head measured at two points (usually wells) divided by the distance separating the two points. The dimensions of head and distance are both lengths, therefore the gradient is expressed as a dimensionless ratio (L/L).

Groundwater: the water contained in the pore spaces of saturated geologic media

Henry's law constant: the ratio of the concentration of a compound in air (or vapor) to the concentration of the compound in water under equilibrium conditions

Henry's law: the relationship between the partial pressure of a compound and the equilibrium concentration in the liquid through a proportionality constant known as the Henry's law constant

Heterogeneous: varying in structure or composition at different locations in space

Homogeneous: uniform in structure or composition at all locations in space

Hydraulic gradient: the change in total potentiometric (or piezometric) head between two points divided by the horizontal distance separating the two points

Hydrocarbon: chemical compounds composed only of carbon and hydrogen

Inclusion zone: the area surrounding a contaminant mass through which vapor-phase contamination may travel and intrude into buildings and potentially result in adverse health effects to inhabitants

Indian country: (1) All land within limits of any Indian reservation under the jurisdiction of the United States government, notwithstanding the issuance of any patent, and, including rights-of-way running through the reservation; (2) All dependent Indian communities within the borders of the United States whether within the original or subsequently acquired territory thereof, and whether within or without the limits of a state; and (3) All Indian allotments, the Indian titles to which have not been extinguished, including rights-of-way running through the same.

Indigenous: living or occurring naturally in a specific area or environment; native

Isotropic: the condition in which hydraulic properties of an aquifer are equal when measured in any direction

Lateral inclusion zone: the area surrounding a contaminant mass and for which all buildings within its boundaries should be assessed for potential PVI. By definition, all buildings that overlie contamination in any phase are within the lateral inclusion zone.

Light non-aqueous phase liquid (LNAPL): contaminants that remain as the original bulk liquid with a density less than that of water (see also free product)

Microorganisms: microscopic organisms including bacteria, protozoans, yeast, fungi, mold, viruses, and algae

Permeability: a qualitative description of the relative ease with which rock, soil, or sediment will transmit a fluid (liquid or gas). Often used as a synonym for hydraulic conductivity or coefficient of permeability.

Petroleum: 40CFR280.12 defines the term *petroleum* to include crude oil or any fraction thereof that is liquid at standard conditions of temperature and pressure (60 degrees Fahrenheit and 14.7 pounds per square inch absolute).

Petroleum hydrocarbons (PHCs): hydrocarbons (i.e., compounds comprised of combinations of hydrogen and carbon atoms) that are components of petroleum (crude oil), including the various products that result from distillation of crude oil

Petroleum vapor intrusion (PVI): intrusion of petroleum hydrocarbon vapors into buildings or other structures

Porosity: the volume fraction of a rock or unconsolidated sediment not occupied by solid material but usually occupied by water or air (gas)

Preferential transport pathways: pathways through which contaminants may be transported at a higher rate than through surrounding materials. Preferential transport pathways are heterogeneities within geologic media and include features that are natural (such as facies changes, sand or gravel stringers, solution channels in karst, bedding planes and weathered surfaces, fractures, and joints) as well as man-made (such as utility corridors, trenches, other types of excavations).

Regulated substance: (a) Any substance defined in section 101(14) of the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA) of 1980 (but not including any substance regulated as a hazardous waste under subtitle C), and (b) Petroleum, including crude oil or any fraction thereof that is liquid at standard conditions of temperature and pressure (60 degrees Fahrenheit and 14.7 pounds per square inch absolute). The term regulated substance includes but is not limited to petroleum and petroleum-based substances comprised of a complex blend of hydrocarbons derived from crude oil through processes of separation, conversion, upgrading, and finishing, such as motor fuels, jet fuels, distillate fuel oils, residual fuel oils, lubricants, petroleum solvents, and used oils.

RfC (reference concentration, inhalation): an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure of a chemical to the human population through inhalation (including sensitive subpopulations), that is likely to be without risk of deleterious noncancer effects during a lifetime

Selective ion monitoring (SIM): a mass spectrometry scanning mode in which only a limited mass-to-charge ratio range is transmitted or detected by the instrument, as opposed to the full spectrum range

Semi-volatile organic compound (SVOC): an organic compound which has a boiling point higher than water and which may vaporize when exposed to temperatures above room temperature. Semi-volatile organic compounds include phenols and polynuclear aromatic hydrocarbons (PAHs).

Site assessment: see site characterization

Site characterization: (verb) the process by which site-specific information and data are gathered from a variety of sources to characterize the physical, biological, and chemical systems at a contaminated site. A primary objective of site characterization is delineation of the areal (both horizontal—longitudinal and lateral—transverse) and vertical extent of contamination. This includes changes in plume boundaries, changes in geochemical parameters that affect biodegradation, and contaminant mass (or concentration) increases or decreases. (noun) The product (e.g., CSM, report) resulting from the site characterization process. (Note: Site assessment, site investigation, site evaluation, and site check are all synonyms of site characterization.)

Site check: see site characterization

Site evaluation: see site characterization

Site investigation: see site characterization

Soil moisture: the water contained in the pore spaces in the unsaturated zone

Solubility: the amount of mass of a compound that will dissolve in a unit volume of solution

Sorption: a general term used to encompass the processes of absorption, adsorption, ion exchange, and chemisorption

Source material: material that includes or contains contaminants that act as a reservoir (either stationary or mobile) for migration of contamination to the ground water, to surface water, to air, (or other environmental media), or acts as a source for direct exposure. Contaminated ground water generally is not considered to be a source material although non-aqueous phase liquids (NAPLS [occurring either as residual- or free-phase]) may be viewed as source materials.

Source zone: the impacted area immediately surrounding the source of a release of regulated substances comprising source materials

Total petroleum hydrocarbons (TPH): a measure of the concentration or mass of petroleum hydrocarbon constituents present in a given amount of air, soil, or water. (Note: The term total is a misnomer, in that few, if any, of the procedures for quantifying hydrocarbons are capable of measuring all fractions of petroleum hydrocarbons present in the sample. Volatile hydrocarbons are usually lost in the process and not quantified. Additionally, some non-petroleum hydrocarbons may be included in the analysis.)

Travel time: the time it takes a contaminant to travel from the source to a particular point downgradient

Tribe: Indian tribe or tribe means an Indian or Alaska Native tribe, band, nation, pueblo, village, or community that the Secretary of the Interior acknowledges to exist as an Indian tribe pursuant to the federally Recognized Indian Tribe List Act of 1944, 25 U.S.C. 479a.

Underground storage tank (UST): 40CFR280.12 defines an *underground storage tank* as any one or combination of tanks (including underground pipes connected thereto) that is used to contain an accumulation of regulated substances, and the volume of which (including the volume of underground pipes connected thereto) is 10 percent or more beneath the surface of the ground. This term does not include any: (a) Farm or residential tank of 1,100 gallons or less capacity used for storing motor fuel for noncommercial purposes; (b) Tank used for storing heating oil for consumptive use on the premises where stored; (c) Septic tank; (d) Pipeline facility (including gathering lines) regulated under: (1) The Natural Gas Pipeline Safety Act of 1968 (49 U.S.C. App. 1671, *et seq.*), or (2) The Hazardous Liquid Pipeline Safety Act of 1979 (49 U.S.C. App. 2001, *et seq.*), or (3) Which is an intrastate pipeline facility regulated under state laws comparable to the provisions of the law referred to in paragraph (d)(1) or (d)(2) of this definition; (e) Surface impoundment, pit, pond, or lagoon; (f) Storm-water or wastewater collection system; (g) Flow-through process tank; (h) Liquid trap or associated gathering lines directly related to oil or gas production and gathering operations; or (i) Storage tank situated in an underground area (such as a basement, cellar, mine working, drift, pit, or tunnel) if the storage tank is situated upon or above the surface of the floor. The term underground storage tank or UST does not include any pipes connected to any tank which is described in paragraphs (a) through (i) of this definition.

Unsaturated zone: the zone between land surface and the capillary fringe within which the moisture content is less than saturation and pressure is less than atmospheric. Soil pore spaces also typically contain air or other gases. The capillary fringe is not included in the unsaturated zone.

Vadose zone: the zone between land surface and the water table within which the moisture content is less than saturation (except in the capillary fringe) and pressure is less than atmospheric. Soil pore spaces also typically contain air or other gases. The capillary fringe is included in the vadose zone.

Vapor intrusion attenuation factor (α): a parameter defined by Johnson and Ettinger (1991) to relate the vapor concentration of a volatile chemical inside the building to its vapor concentration at the subsurface source. This parameter, designated alpha (α), is defined mathematically as the vapor concentration in indoor air divided by the vapor concentration in soil gas at the source (with concentration being in the same units), and thus it is a ratio. The source is defined as the region of highest vapor concentration. Therefore, α values are always less than one. The vapor intrusion attenuation factor is an inverse measurement of the attenuation: α values *decrease* with *increasing* attenuation and α values *increase* with *decreasing* attenuation. In other words, α values represent the fraction of soil gas contaminant that reaches indoor air. Large α values (i.e., values approaching 1) indicate that a large fraction of the soil gas contaminant has reached the indoor air; therefore, little attenuation is taking place, whereas small α values indicate that a small fraction of the soil gas contaminant has reached the indoor air; therefore, significant attenuation is taking place.

Vapor pressure: the force per unit area exerted by a vapor in an equilibrium state with its pure solid, liquid, or solution at a given temperature. Vapor pressure is a measure of a substance's propensity to evaporate. Vapor pressure increases exponentially with an increase in temperature.

Vertical separation distance: the thickness of clean, biologically active soil that separates the source of contamination from a building basement, foundation, or slab

Volatile: is a tendency of a substance to vaporize or the speed at which it vaporizes. Volatility is indicated by a substance's vapor pressure. Substances with a higher vapor pressure will vaporize more readily at a given temperature than substances with a lower vapor pressure. A volatile organic compound is an organic compound which has a boiling point below that of water and which can easily vaporize or volatilize.

Volatile organic compound (VOC): organic compound that at room temperature and normal atmospheric pressure produces vapors that escape easily from volatile liquid chemicals. Volatile organic compounds include a variety of chemicals such as gasoline, benzene, toluene, xylene, formaldehyde, tetrachloroethylene, and perchloroethylene.

Volatilization: the process of transfer of a chemical from the aqueous or liquid phase to the gas phase. Solubility, molecular weight, and vapor pressure of the liquid and the nature of the gas-liquid interface affect the rate of volatilization.

Water table: the water surface in an unconfined aquifer at which the fluid pressure in the pore spaces is at atmospheric pressure

Weathering: the process during which a complex compound is reduced to its simpler component parts, transported via physical processes, or biodegraded over time

Wilting point: the minimal point of soil moisture the plant requires not to wilt. Wilting point values under field conditions are not constant for any given soil, but are determined by the integrated effects of plant, soil and atmospheric conditions.

Appendix I: Estimation of Exposure Point Concentrations in Soil and Ground Water

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1 Background

Exposure point concentrations (EPC) are the **average** chemical concentrations to which receptors are exposed over a specified duration within a specified geographical area. The geographical area about which a receptor moves and contacts contaminated media during the specified exposure duration is termed an exposure unit (EU). EPCs are also often referred to as representative concentrations.

This appendix describes the concept and methodology that should be used to estimate EPCs. This guidance provides general recommendations on procedures to accurately determine EPCs. These recommendations may not apply to all sites, particularly large, complex sites. Site-specific circumstances may require consultation with the Idaho Department of Environmental Quality (DEQ), the application of professional judgment, and reference to the more detailed literature cited herein. Other useful references are also included at the conclusion of this appendix.

In the site-specific application of the risk evaluation process, EPCs are used as input parameters in estimating the risk to a specified receptor for each complete route of exposure identified in the site conceptual exposure model (SCM) and each petroleum chemical of interest (COI). Risk management decisions are then made based on a comparison of the estimated risk with the regulatory specified target risk. This comparison is termed a forward-mode calculation. EPCs can also be used in what are termed backward-mode calculations when they are compared with calculated target levels for each complete route of exposure and each petroleum COI. In either mode, the calculation of EPCs is critical in the outcome of the risk evaluation.

Complications in the calculation of the EPCs may arise because the concept of EPC is often mistakenly associated with a site as opposed to an exposure pathway or the source. Since there may be several complete pathways at a site, several EPCs, one for each complete pathway, should be estimated. For example, estimation of the soil EPC for the pathway involving soil leaching and protection of ground water ingestion typically considers data over the entire soil profile from the source area. At the same site, soil EPC estimates for the direct contact route of exposure involving surficial soil would typically consider only the upper several feet of the soil profile and would focus on the portions of the site where receptors may travel. The accurate estimation of EPCs is complicated by several factors, including the following:

- Spatial variability in the concentrations
- Temporal variability in the concentrations
- Lack of sufficient, appropriately located, site-specific concentration data
- Poor definition or uncertainty in the location, size, or other characteristics of the EU

The uncertainty in the EPC introduced by some of these factors can be reduced by considering them during the development of the SCM and the sampling and analysis plan.

After samples have been collected and analyzed, the results need to be appropriately evaluated to produce sound estimates of EPCs. This evaluation includes assessing the following:

- Data quantity
- Data quality (which data are acceptable for use)
- Statistical methods (which methods to use)
- Which usable data apply to a specific EU

This guidance focuses primarily on the latter two issues.

2 Statistical Considerations for Estimating Exposure Point Concentrations

Numerous statistical methods can be employed to develop estimates of the exposure point (average) chemical concentration to which a receptor will be exposed. These methods include examining the maximum detected concentration, upper confidence limit (UCL) of the mean (for example the 95% UCL), arithmetic average, geometric average, area-weighted average, depth-weighted average, and volume-weighted average concentration (very rarely used). Associated with each of these methods are certain advantages, disadvantages, and constraints on their appropriate use. There is no uniformly accepted statistical methodology to estimate the EPC. Implicit in the decision to use any particular method is the need to acknowledge and account for the representativeness of the samples collected, the homogeneity of the defined EU, the statistical distribution of the data, the minimum data requirements of the statistical method used, and the uncertainty in the resultant data used to derive the estimated concentration.

From a practical perspective, several factors common to petroleum release sites may make the use of statistical methods to develop EPCs at a given site unrealistic, particularly for ground water. These factors include the following:

- Small release areas
- Dominantly subsurface releases, often at great depth
- Focus on source areas and not exposure pathways
- Limited sample numbers due to temporal/spatial constraints

2.1 Maximum Detected Concentration

The use of the maximum detected chemical concentration is required for comparison to screening levels during the screening level evaluation (see Section 3, Screening Level Evaluation, in the main body of the document). Depending on the quality of the site characterization data available, the maximum detected concentration can be used as EPCs in site-specific risk evaluations and will typically represent a conservative estimate of the average concentrations, particularly when sample numbers are low (i.e., four or less).

The effort necessary to calculate EPCs for certain complete pathways can be avoided by using the maximum media-specific concentrations when they do not exceed the target

levels or when the cumulative risk, calculated using maximum concentrations, does not exceed the target risk.

2.2 Upper Confidence Limit

The true population mean is a unique value that can be calculated only if the entire population has been sampled (i.e., the entire contaminated media analyzed). Since the entire population is almost never sampled, the true mean is never known. Thus, at best, only an estimate of the true population mean concentration is possible.

To account for the uncertainty associated with the estimated mean concentration, a confidence interval about the true but unknown mean is often constructed. The interval estimate includes a range and an associated degree of confidence that the true unknown mean lies within this range. In risk assessment applications, instead of calculating a two-sided confidence interval, a one-sided confidence interval is most often estimated.

For the calculation of EPCs, the U.S. Environmental Protection Agency (EPA) has recommended, in most cases, using the 95% upper confidence limit (UCL) of the mean (EPA 1992a). The upper limit for a one-sided 95% confidence interval of the mean is defined as a value that, when calculated repeatedly for randomly drawn subsets of site data, equals or exceeds the true mean 95% of the time. Alternatively, the true mean exceeds the UCL only 5% of the time. Ideally, a minimum of 8 to 10 samples is desirable to generate a 95% UCL. Although the UCL can be determined with fewer samples, doing so tends to results in the 95% UCL estimate being larger (large variances) than the arithmetic average and will sometimes exceed the maximum measured concentration. In these instances, the maximum measured concentration can be substituted for the 95% UCL or the user can decide to collect more samples to reduce the sampling variance.

Several issues commonly arise with environmental data sets that complicate the development of the confidence limit and should be evaluated through the use of an exploratory analysis prior to performing the calculation. These issues include the following:

- Determination of the distribution of the data chosen to represent the EU (normal, lognormal, or nonparametric [i.e., not conforming to a specific distribution]). This determination includes decisions as to what analysis and statistical tests to perform, how to interpret the test results, and how to treat the data once a determination is made.
- How to handle censored data and/or skewed data (typically due to non-detect [ND] values).

Depending on the nature of the underlying distribution of the data (or lack thereof), the one-sided 95% UCL can be calculated using a number of methodologies. The details regarding these methodologies are beyond the scope of this guidance.

EPA has developed technical guidance, a user's guide, and computer software (ProUCL 4.1) for calculating the UCL based on parametric (normal and lognormal distributions) and nonparametric distributions and when data sets have ND observations

(EPA 2011a, 2011b). The ProUCL technical guidance (Sections 1.7.1 and 1.7.2) describes the minimum data set conditions under which the ProUCL software will perform UCL calculations. These guidelines generally involve data set sizes greater than or equal to five with more than one detected value.

For samples collected using a multi-increment sampling approach, data set sizes as small as three may be sufficient to calculate a UCL. The Interstate Technology Regulatory Council (ITRC) has developed a guide for incremental sampling methodology (ITRC 2012).

For simpler data sets (with few or no ND values), DEQ has developed the IdahoUCL software, which is available at http://www.deq.idaho.gov/risk-evaluation-manual.

2.3 Arithmetic Average

Using the arithmetic average (or mean) is similar to the UCL with the disadvantage that no estimate of the uncertainty, variability of the average, or information regarding the underlying distribution of the population is incorporated into the value generated. For a population that is normally distributed, the estimates generated using the 95% UCL versus the mean tend to converge as the number of samples approaches 20 to 30 (EPA 1992a).

2.4 Geometric Average

The geometric average is sometimes used as an estimate of the mean of lognormally distributed variables. It represents the value in the original scale of the mean of the transformed variable. It is, however, a biased estimate of the mean, and statistical texts such as *Statistical Methods for Environmental Pollution Monitoring* (Gilbert 1987) caution against its use in environmental applications. *Statistical Methods for Environmental Pollution Monitoring* (Gilbert 1987) or *ProUCL 4.1 Technical Guide* (EPA 2011a) should be consulted when attempting to develop an unbiased estimate of the mean of a lognormally distributed variable. Exploratory data analysis should be conducted to confirm an assumption that the variable is lognormally distributed prior to calculating an EPC. As with the arithmetic average, no estimate of the uncertainty or variability is incorporated into the value generated by the geometric average and it may not be conservative.

2.5 Area-Weighted Average

Where sampling locations are unevenly spaced, area-weighted averaging methods can be employed to generate an estimate of the average concentration across an area. This calculation is done by generating an area (or Thiessen polygon) associated with each sampling location, assigning a "weight" to each data point based on the area of the polygon associated with that point, and summing the weighted data point values. One advantage of the method is that it is useful in characterizing areas where the number of sample points is low.

The method also has several disadvantages. First, the shape, and consequently the contribution of an area associated with a sample location to the "average," is totally dependent on the spatial distribution of all data points and may not be reflective of the true distribution of contaminants at a site. Second, since each polygon is associated with one sample point, no estimate of the accuracy or error in the average value is possible. Finally, the method, unlike several other interpolation schemes, does not assume that points that are closer together are more similar than points that are farther apart. The method for calculating an area-weighted average using Thiessen polygons is discussed in section 5.

2.6 Depth-Weighted Average

Depth-weighted averaging methods are used to develop an average or EPC for a specific borehole where multiple samples at varying depth intervals have been obtained. In characterizing a source area with multiple boreholes, the depth-weighted averages from each borehole can be used in a 95% UCL calculation. The methodology for depth-weighted averaging is described in EPA's *Soil Screening Guidance: User's Guide* (EPA 1996, section 2.3).

2.7 Volume-Weighted Average

Volume-weighted averaging methods are a combination of area- and depth-weighted averaging techniques. They are rarely used in risk assessment evaluations.

3 General Considerations for Estimating Exposure Point Concentrations

Estimating EPCs requires considering several issues. Prior to performing the computations, consider the information in the following sections.

3.1 Surface and Subsurface Soil Concentrations

When evaluating exposure point soil concentrations consider the following:

- The spatial resolution of the data must be sufficient. While the exact number of necessary samples cannot be specified, data should be available from areas of known or likely sources, and the EU should be defined for a given pathway and receptor.
- Historical data should be examined closely prior to inclusion in the EPC estimate, particularly if the petroleum COIs are susceptible to biodegradation (such as petroleum hydrocarbons), volatilization, or leaching. If sufficient new data are collected, they may be used for risk evaluation and the old data may be disregarded. A new release requires the collection of additional data.
- If there is a "high" density of soil samples (>30) for a homogeneous EU and sample locations are approximately equally spaced, the arithmetic average may be

used instead of the 95% UCL or the area-weighted average. This method is acceptable because the area-weighted average, arithmetic average, and UCL concentrations will tend to converge (EPA 1992a) if the underlying population can be assumed to be normally distributed. The >30 value mentioned above should also be considered in relation to the size of the EU and may not be appropriate for very large EUs.

- ND soil samples located at the periphery of the EU (e.g., the footprint of a building) should not be used.
- ND samples (also referred to as left-censored data) located within the EU require special treatment. The EPA has recently discouraged using replacement methods (such as half the detection limit) (EPA 2011a). The proportion of ND samples in the subject data set and whether multiple detection limits exist will affect the specific methods used to generate summary statistics and the UCL. EPA ProUCL 4.1 software has several options for handling left-censored data. Consult the technical guidance accompanying the software to determine which method is most appropriate for the specific data set and how to treat the censored data (EPA 2011a).
- If multiple surficial soil samples and/or multiple subsurface soil samples are available from the same borehole within the EU, the depth-weighted average or arithmetic average concentration of these samples may be used. If the samples are equally spaced, the depth-weighted average concentration will be the same as the arithmetic average concentration.
- An alternative to using discrete soil samples to calculate the UCL is to use incremental sampling methodologies (USACE 2009; Hawaii DOH, section 4 2008; Alaska DEC 2009; ITRC 2012). Incremental sampling is a sampling approach to obtain a pooled sample for analysis that has an analyte concentration representative of the EU. While it is similar to composite sampling, the incremental approach takes into account sample size to reduce variability and also allows for the calculation of a UCL while only requiring a few samples for laboratory analysis. It typically requires greater up-front planning with respect to sampling design, methodology, and defining of data quality objectives than traditional composite sampling.
- If vapor intrusion is a potentially complete pathway, collecting soil vapor data, in lieu of soil samples, for characterizing the potential risk should be considered. Consult Appendix G (Evaluation of the Vapor Intrusion Pathway) and section 4.5 of this appendix for sampling details.

3.2 Ground Water Concentrations

Follow the guidelines listed below to account for the temporal and spatial variation in ground water concentrations. These recommendations apply primarily to evaluation of ground water data for the purpose of estimating EPCs for risk evaluation.

They are not intended for cases where other monitoring objectives, such as determining compliance with cleanup criteria or site closure, are the primary goals.

- For wells with a clear increasing or a decreasing trend, data from the most recent 12 months or the 4 most recent measurements should be averaged (use whichever covers the longer duration). Note that for wells with increasing trends, continued monitoring may be needed until the trend stabilizes or decreases. The need for additional monitoring is a site-specific determination that is dependent on a number of factors, including the magnitude of measured concentrations in relation to risk-based criteria, the degree to which samples are representative and address site factors such as seasonality, and the estimated travel time of contamination from the release area to ground water and to potential receptors. For example, four measurements, taken at appropriate intervals over the course of a year, show an increasing trend but are all below applicable risk criteria. Further monitoring to develop an EPC may not be necessary.
- For wells with stable or fluctuating concentrations with no apparent trend, data from either the most recent 24 months or the 8 most recent measurements should be used to develop a 95% UCL.
- If site ground water analytical data are limited (number of wells or number of sampling events) and prevent adequate statistical analysis, using the maximum concentrations is preferred. Using the average concentration is discouraged, particularly if the plume stability status (increasing, decreasing, or stable) with respect to the release is unknown or the representativeness of the available data is in question.
- While developing the EPC for wells described by the first two bullets above, the treatment of left-censored data (concentrations below detection limits) deserves special consideration and may require specialized analysis techniques. Replacement techniques (such as using half the detection limit) are currently discouraged by the EPA (EPA 2011a). If the percentage of ND values is a significant percentage of the total number of data points (>25%), the representativeness of the data set for the EU in question should be evaluated.
- Wells with concentrations consistently below detection limits in the periphery of the EU should not be used.
- For wells that contain free product where it is not possible to obtain a representative dissolved phase sample, the use of the effective solubility of petroleum COIs should be considered as a conservative surrogate for their chemical concentration in estimating EPCs.

Two useful documents that provide guidance on the statistical evaluation of ground water monitoring data are the EPA's unified guidance (EPA 2009) and DEQ's *Statistical Guidance for Determining Background Ground Water Quality and Degradation* (DEQ 2009).

4 Calculation of Exposure Point Concentrations

An EPC is necessary for each complete exposure pathway at a site. Based on the pathways typically considered in the risk evaluation process, the EPCs listed below are typically needed for each media.

4.1 Surficial Soil (0–1 Foot below Ground Surface)

The risk evaluation process requires consideration of two pathways of exposure associated with the surficial soil: 1) the ingestion of chemicals in ground water due to leaching of residual chemicals present in the surficial soil and 2) the accidental ingestion of soil, outdoor inhalation of vapors and particulates from surficial soil emissions, and dermal contact with surficial soil. These two pathways are referred to as the ground water protection and direct soil contact pathways, respectively. Thus, at most, two different surficial soil EPCs are required, though typically one EPC estimate can be used for both pathways.

4.1.1 Exposure Point Surficial Soil Concentration for the Ground Water Protection Pathway

Figure 1 shows a schematic of the soil leaching to ground water pathway. The evaluation of this pathway for surficial soil assumes that the contamination does not extend greater than 1 foot below ground surface. If this is not the case, then samples taken in the surficial soil zone should be included with those from greater depth and evaluated together.

The conceptual model for this pathway also assumes that the leachate from the surficial (or subsurface) soil source travels vertically downwards to the water table without any lateral or transverse spreading. Thus, the horizontal dimensions of the surficial (or subsurface) soil source and the ground water source are identical. Estimating the source dimensions requires considerable professional judgment. Factors typically considered in making these estimates include historical knowledge of where a spill or source was located, visual clues such as soil discoloration, and laboratory data (taking care not to include samples with ND results.

Irrespective of the manner in which the source area is identified, it is important to indicate the dimensions of the source on a map. The exposure point surficial soil source concentration should be estimated using only the surficial soil data collected within the delineated source zone. The method used to derive the EPC should typically be either the UCL of the mean (when the quantity and characteristics of the data available allow a statistical analysis) or the values derived from an incremental sampling approach.

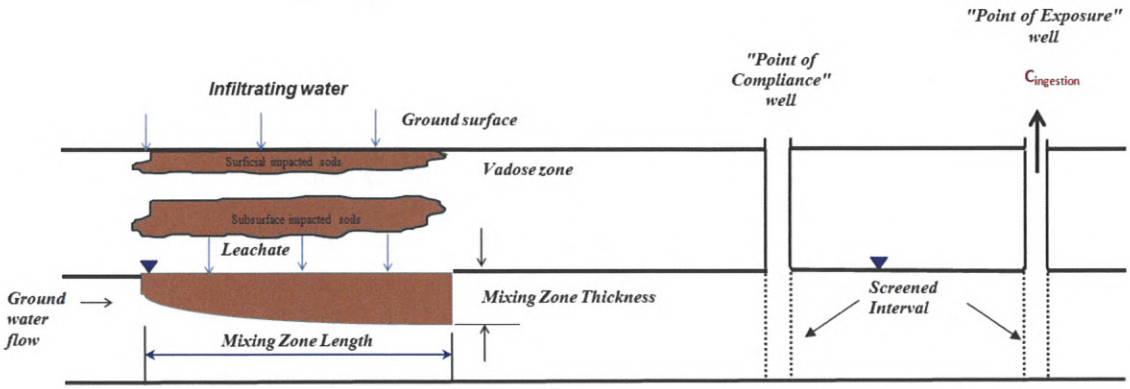


Figure 1. Schematic of soil leaching to ground water

4.1.2 Exposure Point Surficial Soil Concentrations for the Direct Contact Pathway

For this pathway, the exposure point surficial soil concentration has to be based on the receptor's EU (i.e., the area over which the receptor may be exposed to the surficial soil). The exact location of this area is often difficult to estimate since it must be representative of a period of time equal to the receptor's exposure duration (for example, up to 30 years for residential land use and about 7 years for nonresidential land use). In most cases, it is reasonable to assume that the receptor will access all portions of the EU in a random manner. Under current conditions, in the absence of specific information about the receptor's activities, the unpaved portion of the site may be considered as the receptor's approximate EU. Where volatile organic compounds (VOCs) are included in the list of potential petroleum COIs and/or the paved portion is in poor condition or consists of a material that does not limit VOC migration, this guide would not apply. For potential future exposures, if current condition cannot be assumed to continue, the assumption should be made that the pavement is removed, exposure to surficial soil is possible, and the entire site should be considered as the EU.

If the possibility exists that, for a future use residential scenario, contaminated subsurface soil existing under a current nonresidential scenario may be brought to the surface and result in direct contact residential exposures at the surface, the appropriate subsurface data should be included in the estimate of the EPC.

To estimate the EPC for this pathway, it would be necessary to estimate the receptor's area of exposure and determine the number of soil samples available within this EU. This information should be used to estimate the 95% UCL or an area-weighted average concentration using the procedures discussed in section 5. The use of an incremental sampling approach for characterizing EPCs for this route of exposure may be particularly well-suited and efficient.

4.2 Subsurface Soil (Greater Than 1 Foot below Ground Surface)

The risk evaluation process includes two pathways of exposure associated with subsurface soil: 1) the ingestion of chemicals in ground water or exposure to surface water impacted by discharge of contaminated ground water resulting from leaching of chemicals in subsurface soil and 2) indoor inhalation of vapor emissions. These two pathways are referred to as the ground water protection and vapor intrusion pathways, respectively. Thus, two different subsurface soil EPCs are required (one for each complete pathway). Additional EPCs may be required if the receptor's EU for current and future conditions is different.

4.2.1 Exposure Point Subsurface Soil Concentration for Ground Water Protection Pathway

The leachate from the subsurface soil source is assumed to travel vertically downwards without any lateral or horizontal spreading (Figure 1). Thus, the EPC for this pathway should be based on the subsurface soil concentrations measured within the source area.

As in the case of the surficial soil concentration protective of ground water (section 4.1.1), the exposure point subsurface soil source concentration would be the average concentration calculated using the data within the soil source area. If the source area is small (several tens of feet across), typically smaller numbers of soil samples are available. In this case, the 95% UCL should first be calculated if the sample numbers for applicable data are adequate. If the 95% UCL exceeds the maximum concentration, it may be appropriate to use the maximum concentration.

4.2.2 Exposure Point Subsurface Soil Concentration for Vapor Intrusion Pathway

The use of soil concentration data and development of exposure point soil concentrations for evaluation of vapor intrusion, while allowable, is not as desirable as the use of soil vapor data. The use of soil vapor data is discussed in more detail in Appendix G (Evaluation of the Vapor Intrusion Pathway) and in section 4.5 of this appendix.

The default methodology and model used to estimate the risks resulting from the indoor inhalation of vapors emanating from a contaminated subsurface soil source is the Johnson and Ettinger model (Johnson and Ettinger 1991). The Johnson and Ettinger model assumes that the chemicals volatilize from a subsurface soil source, travel vertically upwards via diffusion without any lateral or transverse spreading, and enter the building via advection through cracks in the foundation. Because this model does not account for biodegradation (an important attenuation process for petroleum hydrocarbon chemicals), the predictions are generally considered conservative for these chemicals. Other models that do incorporate biodegradation, such as the BioVapor model (API 2010) may also have applicability.

To be completely consistent with the Johnson and Ettinger conceptual model, the EPC for this pathway would be based on the soil concentrations measured in the soil directly below the enclosed space. In many cases, this is not possible. Furthermore, depending on site conditions (such as the location of pavement, preferential pathways, and site lithology), vapors from source areas adjacent to but not under an existing structure may contribute to indoor inhalation exposures. The goal should be to characterize the average soil concentration in the source area that may potentially contribute vapors to any existing or potential future structures. If the pathway is considered complete for current conditions, appropriate samples for EPC estimates should be selected to achieve this goal. Samples should be focused in the immediate vicinity of any existing structures as well as within 50 feet of the structure. If free product is suspected or known to exist in the area around the structure, sampling locations should be extended to 100 feet. If current and reasonably anticipated future land uses are the same, the EPC calculation is unchanged for future uses.

To evaluate EPCs for potential future vapor intrusion (e.g., in the event that an enclosed structure is constructed on top of contaminated soil), it is necessary to determine the nature of any future structure and estimate the size (footprint) of the structure and its location.

If the location and characteristics of future structures are known, the EPC should be conservatively estimated using samples from that vicinity, including the buffers mentioned above for existing structures. If the nature of future structures is not known, the assumption should be made that a structure could be placed anywhere on the property in question and potentially located directly over the source. The size of the structure would be assumed to be similar to that of the likely future land use, in most cases either residential or nonresidential. The default size of a residential structure assumed in this guidance is approximately 40 feet by 40 feet. For sites where the footprint of the current and likely future enclosed spaces are different, different exposure point subsurface soil concentrations (one for current conditions and one for future conditions) may be necessary. The 95% UCL or area-weighted average methods may be used, as appropriate. Where multiple boreholes with several depth interval samples are available, a depth-weighted average from individual boreholes can be developed.

4.3 Exposure Point Concentration for Protection of a Construction Worker

The risk evaluation process includes the evaluation of one pathway of exposure for construction workers: accidental ingestion, dermal contact, and outdoor inhalation of vapors and particulates from soil.

For the construction worker, no distinction is made between the surficial and subsurface soil because subsurface soils may be exposed during construction. To estimate the EPC for the construction worker, it is necessary to identify the depth, areal extent, and number of samples taken within the zone of construction. The potential future depth of construction can be estimated by contacting local construction firms and identifying the typical depth of utilities on and adjacent to the site, contacting local utility companies, or

using as-built plans for proposed facilities if they exist. If the areal extent of the construction area is not known, it may be conservatively estimated as the source area. If sample results are available for several depth intervals, these should be averaged using depth weighting. The depth-weighted averaged values from multiple boreholes could then be combined to calculate a 95% UCL or area-weighted average, as appropriate. The EPC would be the depth-weighted average concentration within this zone of construction.

4.4 Ground Water

The risk evaluation process requires evaluating two routes of exposure associated with shallow ground water: 1) ingestion of ground water and 2) indoor inhalation of vapor emissions from ground water. Where multiple aquifers are present, the shallowest aquifer is typically the aquifer first considered for both pathways. Site-specific circumstances—such as the disappearance of the shallow aquifer or transport of contamination to the deeper aquifer—may require evaluation of both aquifers. Characterization of petroleum COIs in both aquifers should still be performed. At a minimum, two different ground water EPCs, one for each complete pathway, are required.

4.4.1 Exposure Point Compliance Well Concentration for Ground Water Protection Pathway

For the ingestion of ground water pathway, maximum contaminant levels (MCLs) or equivalent concentrations have to be met at the point of exposure location. Often, the point of exposure well location is hypothetical and data may not be available. Alternatively, if a point of exposure well is present, an upgradient sentry or compliance well is often used as an early warning monitoring location. In both of these cases, ground water transport models are used to calculate the predicted concentrations at the point of exposure based on source area concentrations, the allowable concentrations in the source area, or an alternate point of compliance location concentration that will result in acceptable concentration at the point of exposure. In any case, EPCs will need to be estimated for the source area or for the alternate point of compliance location. In addition, one or more compliance wells have to be identified, and target compliance well concentrations (typically higher than the exposure well concentration) have to be calculated at these wells.

To evaluate this pathway, the EPCs in the source area, point of compliance, or point of exposure locations should be calculated based on the measured concentrations as discussed below. In most cases, a rule of thumb is that measurements taken more frequently than quarterly would not be considered statistically independent samples, would not be accepted to meet the specified number of measurements, and should not be used for statistical analysis and hypothesis testing (DEQ 2009). Methods to evaluate temporal independence are discussed in EPA 2009 and DEQ 2009.

- For wells with no clear trend, the EPC should be estimated as the 95% UCL if the data permit. Where the calculated 95% UCL exceeds the maximum concentration or if the data are not suitable for statistical analysis, the maximum concentration should be used as the EPC. For compliance wells with stable, clearly decreasing,

or clearly increasing trends, the EPC is estimated as the 95% UCL of the most recent 1 year of data or most recent 4 measurements, whichever represents the longer time duration. For wells with an increasing concentration trend, continued monitoring may be needed until the trend stabilizes. Quarterly data for at least 1 year is recommended. The data should be pooled for source area characterization where multiple wells are available (DEQ 2009). Wells clearly not part of the source area of contamination should not be included in the calculations.

4.4.2 Exposure Point Ground Water Concentration for Protection of Indoor Inhalation Pathway

Ground water concentrations protective of indoor inhalation are commonly estimated using the Johnson and Ettinger model (Johnson and Ettinger 1991). This model assumes no lateral or transverse spreading or attenuation of the vapors as they migrate upward from the water table through the capillary fringe, the unsaturated zone, and into the enclosed space. Thus, the EPCs for this pathway should be based on the ground water concentration measured within and adjacent to the footprint of the building. Refer to section 4.2.2 for discussion related to the future land use footprints and their relationship to the impacted area.

For the indoor inhalation of vapor emissions from ground water, multiple EPCs may be required if the plume has migrated below several current or potential future buildings. For example, if a plume has migrated or is likely to migrate below two different buildings (for example on-site and off-site buildings), separate on-site and off-site EPCs should be estimated.

If the plume has migrated below several buildings with similar receptors (residential or commercial), it may be sufficient to evaluate this pathway only for the building below which the concentrations are the highest and/or the depth to ground water is the lowest. If this building is protective of indoor inhalation exposures, it may not be necessary to evaluate other buildings.

The plume may not be in the proximity of current structures. If assumed future land use includes the possibility of building structures in the vicinity of the plume, a similar calculation of EPCs and risk should be made using appropriate assumptions about the location and type of future structures.

While the target ground water concentrations are based on the assumption of no lateral or transverse spreading of the vapors as they diffuse upwards to the building, site characteristics such as site lithology and preferential pathways may result in lateral migration towards a structure. For this reason, the EPCs should be conservatively based on data gathered adjacent to the structure. After identifying the locations of the building footprints and the appropriate ground water monitoring data within and adjacent to each footprint, the 95% UCL or area-weighted average concentration within each footprint may be estimated, as discussed in section 5.

4.5. Soil Vapor

Soil vapor is used exclusively to evaluate the risk posed via the vapor intrusion pathway. Many of the same considerations discussed for the development of EPCs using soil data in section 4.2.2 also apply to soil vapor data. However, one important difference is that, similar to ground water concentrations, the number of soil vapor sample locations is typically fewer than with soil data and the use of statistical methods is precluded. In most cases, because of the variability commonly observed with vapor measurements and the uncertainty of vapor flow paths from the subsurface into indoor spaces, it is preferable to use the maximum concentrations measured within the defined EU. Where multidepth sampling of soil vapor has demonstrated attenuation of concentrations and the presence of a sufficient thickness of oxygenated soil conditions, the use of lower concentrations may be acceptable. Sufficient sample numbers are more often available where source areas or the buildings under consideration are large. In these situations, the use of area-weighted averaging or other statistical methods may be appropriate.

5 Estimating Area-Weighted Exposure Point Concentrations

Area-weighted EPCs can be estimated using the Thiessen polygon method (Fetters 1993; Linsley et al. 1975). If the available data are located on a uniform grid, the area-weighted average would be the same as the arithmetic average. If the dimensions of the source and the receptor's EU are relatively small (several tens of feet across) and very few (1 to 6) soil samples are available within the soil source, the arithmetic average concentration may be used as an approximation of the area-weighted average concentration.

5.1 Step 1: Identify the Exposure Unit

The first and most critical step is to identify the size and location of the EU over which the area-weighted EPC has to be estimated. The location and size of this EU will often vary depending on the pathway being evaluated. Specific guidance on the location of the receptor's area of exposure has been discussed in sections 3 and 4. Area-weighted concentrations can only be estimated if multiple samples have been collected within the unit. If several samples are available just outside the EU, it may be reasonable to extend the size of the unit to include this data. If the values of these samples are ND, they should not be included. This exclusion is technically justified since at most sites the location of the EU is approximate at best.

As part of Step 1, the various EUs for which area-weighted concentrations are desired should be drawn on a site map. The location of data points (soil borings, monitoring wells, etc.) should also be clearly labeled on the map.

If the borings or monitoring wells within the EU are located in a regular grid, the calculation of an area-weighted average is unnecessary and the user should proceed with an EPC calculation using a different method, such as the 95% UCL.

5.2 Step 2: Subdivide the Exposure Unit

The EU, identified in Step 1, is discretized into polygonal elements by connecting the sampling points within each EU (also identified in Step 1) and drawing perpendicular bisectors to these lines to form polygons. The area of each Thiessen polygon is then estimated.

5.3 Step 3: Estimate Exposure Point Concentrations for Each Thiessen Polygon

The concentration measured at the sampling location within each polygon is considered representative of the area of each polygon. As discussed in section 3, if multiple data are available from a location (either multiple depths or dates), compute the arithmetic average concentration of each petroleum COI measured at that location. The arithmetic concentration is then considered representative of the polygon.

5.4 Step 4: Estimate Area-Weighted Average Concentration for the Exposure Unit

The area-weighted average concentration for the EU is estimated using Equation 1:

$$C_{area} = \frac{\sum_{i=1}^{i=n} (A_i * C_{avg,i})}{A_{Total}} \qquad \text{(Equation 1)}$$

Where,

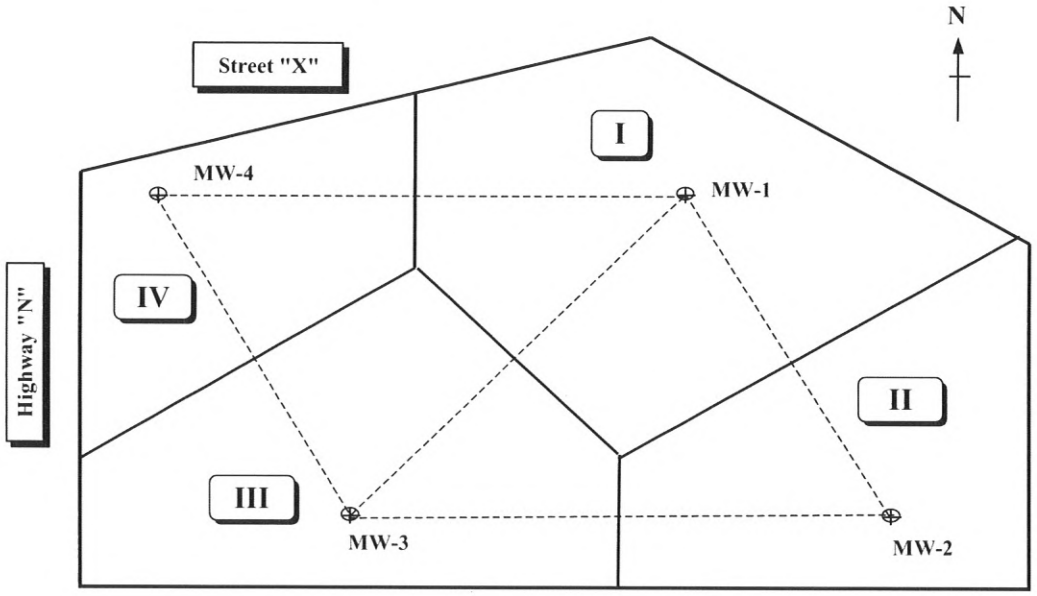
C_{area} = area-weighted average concentration over the EU [mg/kg]

A_i = area of each Thiessen polygon [m^2]

A_{Total} = total area of the polygons (i.e., area of the EU) [m^2]

$C_{avg,i}$ = mean of soil or ground water concentrations measured within the polygonal element *i* [mg/kg]

An example application of the Thiessen polygon method is schematically shown in Figure 2.



Polygonal Element	Mean Soil Concentration $C_{avg,i}$ mg/kg	Area of the Element A_i m^2	$A_i * C_{avg,i}$ m^2 - mg/kg	Area Weighted Average Concentration mg/kg
I	2	604	1208	
II	1.8	398	716.4	
III	1.2	578	693.6	
IV	1	234	234	
	TOTAL	**1814**	**2852**	
Area Weighted Average Concentration = $C_{area} = \frac{\sum_{i=1}^{i=n}(A_i * C_{avg,i})}{A_{Total}}$				**1.57**

Figure 2. Thiessen polygon method

6 Recommendations

- For most pathways, 95% UCL techniques are recommended for development of EPC estimates of average concentrations. For cases where the number of samples is low (four or fewer) and/or the number of ND values is high, the use of the maximum concentration may be most appropriate. The use of the maximum may also be appropriate when the calculated 95% UCL exceeds the maximum concentration measured at the site and the collected data are considered representative of site and EU conditions.
- The use of area-weighted average methods is not recommended for most pathways, but may be justified in developing EPCs for the surficial soil pathways. The inclusion of methods that evaluate and incorporate spatial uncertainty into the area-weighted average calculation increases the validity of the estimate derived (Burmaster and Thompson 1997).

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Appendix H: Application of Natural Attenuation

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Introduction

This appendix presents general guidance on the applicability and implementation of remediation by natural attenuation (RNA) at petroleum release sites in Idaho. Its primary focus is on attenuation of ground water contamination. Attenuation of petroleum hydrocarbons has also been documented in other media such as soil and soil vapor. Attenuation in soil vapor is addressed in Appendix G, which discusses evaluation of the vapor intrusion pathway. This appendix is divided into three parts:

- Part I presents a brief overview of the science of natural attenuation (NA)
- Part II presents the regulatory requirements for implementing NA as a remedial option
- Part III discusses the techniques available to support, quantify, and implement NA as a remedial option

This document should be used in conjunction with the *Idaho Risk Evaluation Manual for Petroleum Releases* (REM) and publicly available literature when implementing RNA. Additional information is available in the references provided at the end of this document.

PART I: The Science of Natural Attenuation

Part I presents an overview of the science of NA, including the following topics:

- A brief overview of the processes that constitute NA (section 2)
- A description of how biodegradation operates in attenuating petroleum hydrocarbons (section 3)
- A description of the indicators of NA of hydrocarbon plumes (section 3.5)

1 The Concept of Natural Attenuation

The term natural attenuation refers to the reduction in concentration or mass of chemicals in a media due to the effects of various environmental fate and transport processes. NA occurs without human intervention. Although NA is applicable to a reduction in concentration in any medium (e.g., air, surface water, ground water), in this appendix it refers to the reduction in concentration of a dissolved ground water contaminant plume. For a ground water plume, environmental fate and transport processes include physical processes (advection, dispersion, dilution, sorption, and volatilization); chemical processes (hydrolysis, oxidation, and reduction); and biodegradation processes (aerobic and anaerobic). Physical processes are nondestructive in that they redistribute the chemicals in the environment without affecting the total mass of the individual chemical. Chemical transformation processes and biodegradation result in the transformation of the parent chemical into other chemicals referred to as daughter products.

The only human action involved in RNA is monitoring to demonstrate that concentration reduction is occurring at a reasonable rate. Depending on site-specific conditions, RNA may be used as a stand-alone corrective action strategy or in combination with other engineered remediation alternatives.

This guidance focuses on using NA on sites contaminated with petroleum products. NA has also been used at sites with other classes of contaminants, such as metals, explosives, and pesticides (USACE 1999; SNL 1997). The same concepts for evaluation, requirements for site characterization, and demonstrations as to effectiveness are required regardless of the class of contaminant. A general approach to the evaluation of the bioremediation aspects of NA for a range of biotreatable compounds is described in ITRC 2002.

2 Overview of Natural Attenuation Processes

Although each contaminated site is unique, for this discussion it is useful to consider a generic site where a petroleum spill has occurred. The soil immediately below and around the point of release becomes contaminated, and the contaminant front moves downward. The downward movement of the contaminant front continues until one of the following three conditions occurs:

- The soil sorption capacity exceeds the amount of contaminant available.
- An impermeable barrier is encountered and the contaminant spreads horizontally.
- The contaminant reaches the water table and, if it is a light non-aqueous phase liquid (LNAPL), spreads horizontally.

The term LNAPL relates to the density of the released contaminant. LNAPLs are chemicals that are liquid at ambient temperature but lighter than water. For example, the density of toluene is 0.866 grams per cubic centimeter (g/cc) compared to a density of 1 g/cc for water.

After the contaminant movement has stopped, the soil through which it traveled is contaminated with residual chemicals that act as a contaminant source for the ground water plume. Figure 1 shows a schematic of a LNAPL moving through the soil to the ground water.

When rainwater infiltrates through the residual contaminated soils, it dissolves and leaches out the soluble components. For petroleum hydrocarbons, the toxic soluble chemicals include, but are not limited to, benzene, toluene, ethylbenzene, and xylene (BTEX); the soluble additives methyl tertiary butyl ether (MTBE) and ethylene dibromide; and smaller fractions of other less-soluble constituents. After undergoing NA processes in the unsaturated zone, these dissolved chemicals reach the water table, mix with ground water, and move with the ground water to form a dissolved plume. At sites where the spill is of a sufficient quantity to reach the water table and form an LNAPL layer on the water table, soluble constituents from the LNAPL gradually dissolve in ground water and form a dissolved ground water plume.

Additionally, vapors of volatile hydrocarbons (chemicals with a Henry's Law constant greater than 1×10^{-5} atm-m^3/mole) will spread outwards from the contaminated soil and dissolve in soil moisture and ground water.

As the dissolved plume moves through the unsaturated and the saturated zones, its concentration decreases due to the combined influence of several NA processes. Each of these processes is briefly discussed below.

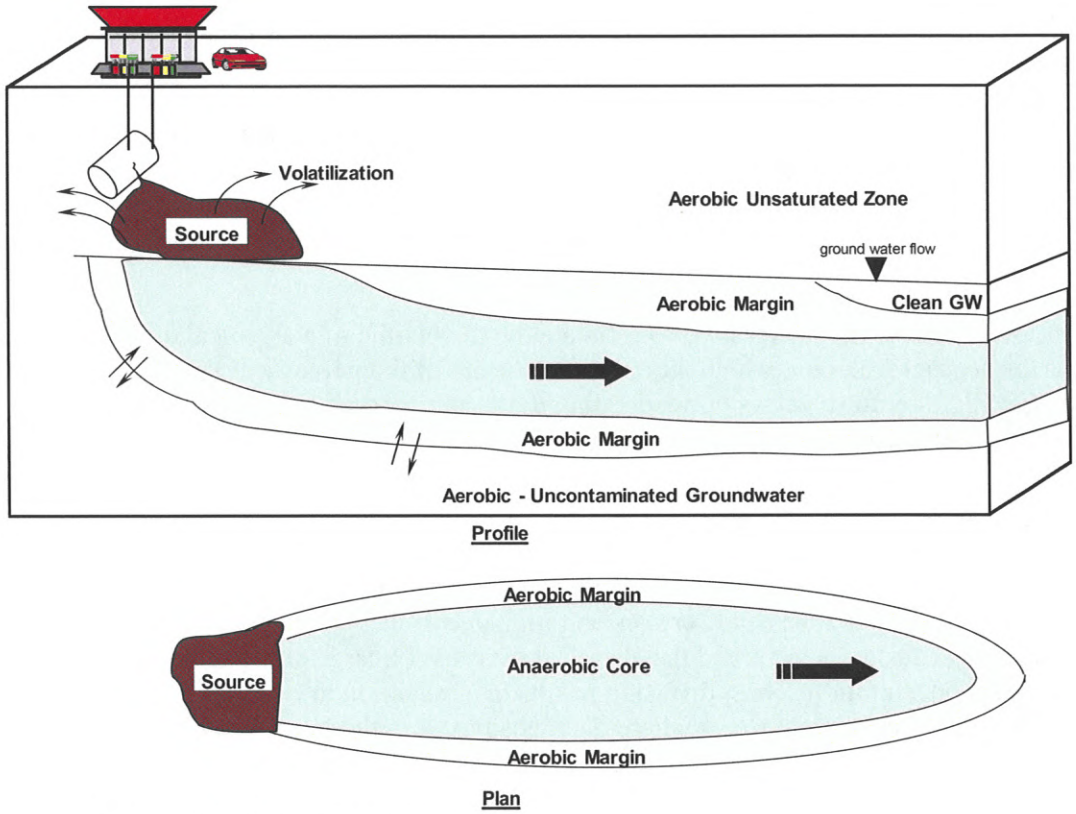


Figure 1. Schematic of a hydrocarbon release

2.1 Advection

Advection refers to the bulk movement or flow of water caused by differences in density, temperature, or pressure. In most aquifers, flow occurs predominantly due to hydraulic gradients, which may be natural—resulting in regional ground water movement—or man-made, caused by pumping or artificial recharge. In saturated zones, hydraulic gradients may exist in horizontal and vertical directions, resulting in complex three-dimensional flow patterns. However, at most sites there exists a predominant flow direction that results in the migration of most mass.

As water moves in the saturated zone, it carries with it the dissolved constituents. The process results in the migration of dissolved constituents in the saturated zone without a change in concentration and is termed advection.

Parameters required to estimate the volume of water moving through a saturated zone include the Darcy velocity and the cross-sectional flow area. Darcy velocity is estimated using hydraulic conductivity and hydraulic gradient.

Hydraulic conductivity may be estimated using a variety of methods, including slug tests, pump tests, grain size distribution, and literature values corresponding to the site stratigraphy. For most saturated zones, hydraulic conductivity varies in the horizontal and vertical directions.

Site-specific values of hydraulic gradients are estimated based on water-level measurements in monitoring wells, or piezometers. When estimating horizontal hydraulic gradients, it is important to compare data from wells screened in the same saturated zone. Wells screened in different zones or at different depths (e.g., cluster wells) can be used to estimate the vertical hydraulic gradient between the zones. Site-specific hydraulic gradients may exhibit seasonal and spatial variations (in magnitude and direction) due to a variety of factors such as pumping, seasonal flow in surface water bodies, and seasonal variations in rainfall.

Another related parameter used to estimate the travel time of a chemical due to advection is the seepage velocity, which requires an estimate of the porosity of the media. Typically, literature values corresponding to the aquifer type (e.g., sand or silt) are used to estimate porosity.

2.2 Molecular Diffusion

Molecular diffusion refers to the transport of chemical mass from a zone of higher concentration to a zone of lower concentration due to the movement of molecules. The effect of diffusion is to spread the chemical mass over a large area and hence reduce the overall concentration. Thus, diffusion results in a reduction in concentration by dilution. In most ground water systems where there is advection, the attenuation in concentration or the chemical mass transport due to diffusion is small and often negligible. However, in no-flow or low-flow situations, diffusion can be an important attenuation mechanism.

Molecular diffusion is quantified using Fick's Law, and the parameter required to quantify diffusion is the effective diffusion coefficient of the chemical (Freeze and Cherry 1979).

2.3 Mechanical Dispersion

Mechanical dispersion refers to the spreading of the contaminant plume that occurs due to variations in the flow velocity. In the saturated zone, velocity variations occur due to a variety of factors, including inter-pore and intra-pore velocity variations and the tortuosity of the porous media. The net effect of mechanical dispersion is that the chemical spreads both horizontally and vertically, thus reducing the overall concentration in the plume. Thus, like diffusion, dispersion is a dilution process.

The transport of mass due to mechanical dispersion is quantified using Fick's Law. The key parameters are the dispersivity coefficients in the three cardinal (x, y, and z) directions. Dispersivity values have been measured using tracers at several research sites, based on which empirical dispersivity relationships have been developed (EPRI 1985; Xu and Eckstein 1995). For most site-specific applications of fate and transport models, these empirical relationships are used. Higher dispersivity values result in larger plumes, which result in increased dilution and lower concentrations.

2.4 Hydrodynamic Dispersion

The term hydrodynamic dispersion refers to the sum of molecular diffusion and mechanical dispersion. In most ground water systems where there is advection, hydrodynamic dispersion is approximately equal to mechanical dispersion, since the effect of molecular diffusion is negligible.

2.5 Sorption

Sorption refers to the transfer or distribution of mass between the liquid and solid phases. Sorption has the overall effect of reducing the mobility of the chemical, which increases its residence time in the subsurface and hence the amount of microbial degradation. This distribution is quantified by the soil water partition coefficient. For organic chemicals, the partition coefficient depends on the chemical-specific normalized organic carbon partition coefficient and the organic carbon content in the soil. The partition coefficient is used to estimate the retardation factor for the chemical, which is a measure of the "stickiness" of the chemical to the formation. Parameters required to estimate the retardation factor include porosity, organic carbon content of soil, bulk density of soil, and chemical-specific normalized organic partition coefficient.

2.6 Volatilization

Volatilization refers to the transfer of chemical from the LNAPL or dissolved phase to the vapor phase. Vapors can migrate by diffusion alone (in the absence of a pressure gradient) and by diffusion and advection if a pressure gradient exists in the formation. Chemicals volatilizing from the dissolved plume occupy the pores in the unsaturated zone and migrate outwards due to the combined influences of molecular diffusion and vapor-phase advection if pressure gradients exist. Thus, volatilization can result in a net loss of chemical from the dissolved phase or from the LNAPL.

The chemical-specific factors controlling volatilization from a dilute solution and LNAPL are the Henry's Law constant and saturated vapor pressure, respectively. These factors are sensitive to the temperature of the media where volatilization occurs.

2.7 Biodegradation

Biodegradation refers to the destruction of chemicals by indigenous microorganisms present in the aquifer. For petroleum hydrocarbons, biodegradation is the primary

destruction mechanism. Due to the significance of biodegradation within the overall process of NA, biodegradation is discussed at length in section 3. In certain situations, additional compounds (e.g., ozone, oxygen, peroxide); nutrients; or microorganisms may be added to the contaminant plume to enhance the rate of biodegradation.

2.8 Overall Effect of Natural Attenuation Processes

As explained above, the process of NA refers to a combination of advection, molecular diffusion, dispersion, sorption, volatilization, chemical reactions, and biodegradation.

The combined effect of these processes is to spread or reduce the chemical mass in the dissolved plume. Thus, the concentration of the chemical decreases as distance from the source increases. Figure 2 shows the concentration profiles in actual monitoring wells down-gradient of a source and the expected concentrations under ideal conditions. Although such patterns have been observed at several sites, fluctuations in water levels, flow direction, and climatic conditions often result in nonideal behavior. Additional complications occur due to errors in data collection, analytical measurements, and the existence of multiple sources (in space and time) at a site.

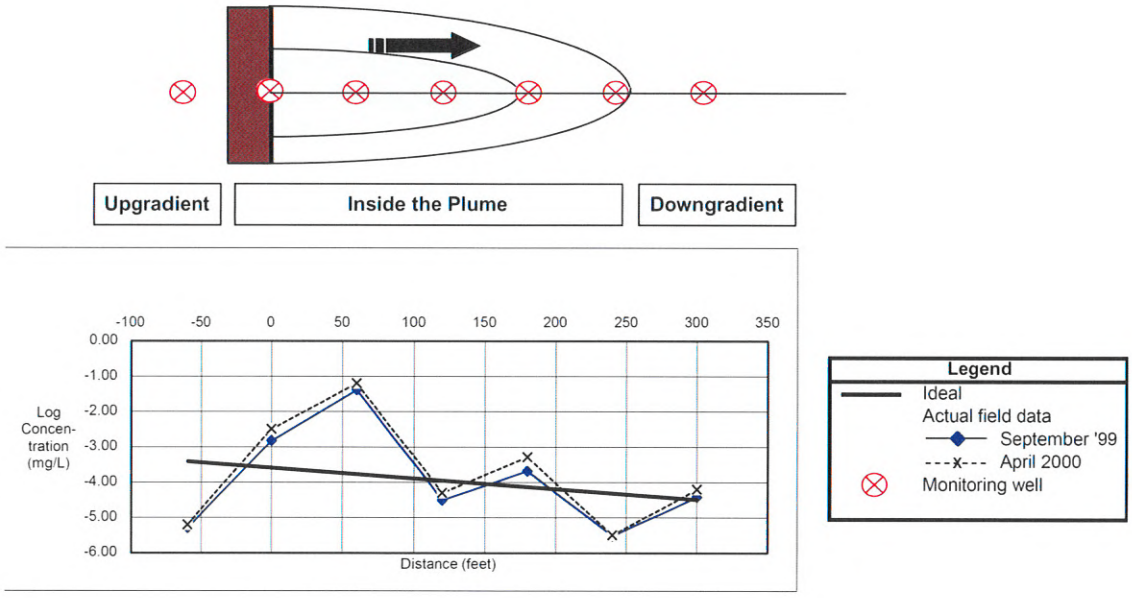


Figure 2. Concentration profile as a function of distance (ideal behavior and data from an actual site)

Depending on the overall rate of NA and the on-going contribution of chemicals to the ground water plume from the residual soil source, ground water plumes may be classified as expanding, stable, or shrinking. These concepts are discussed below.

2.8.1 Expanding Plume

An expanding plume is characterized by increasing concentrations within the plume and/or an outward movement of the plume that increases the size of the plume. An expanding plume occurs when the chemical mass loading to the plume from leaching or dissolution of residual LNAPL exceeds the mass loss due to NA processes.

In an expanding plume, NA processes continue to occur but at a rate too slow to prevent the increase in concentrations or the size of the plume.

2.8.2 Stable Plume

A stable plume is characterized by stable concentrations within the plume and at the periphery of the plume (i.e., the concentrations do not show a decreasing or increasing trend). For a plume to be stable in size or concentration, the rate of chemical mass addition to the plume from the source is equal to the rate of chemical mass loss by NA processes. The source may be the chemicals leaching from adsorbed and residual concentrations in the capillary/water table fluctuation zone or in the vadose zone or the dissolution of chemicals from the LNAPL source.

2.8.3 Shrinking Plume

A shrinking plume is characterized by decreasing ground water concentrations within the plume, decreasing concentrations at the periphery of the plume, or a decrease in the area of the plume. For a shrinking plume, the addition of chemical mass from the source is less than the mass lost due to NA processes. Thus, unless site-specific conditions change that result in an increase in chemical mass addition to the plume or a decrease in the rate of NA, the plume will eventually disappear.

2.8.4 Lifecycle of a Plume

Initially, when a chemical reaches the ground water and a plume forms, it is an expanding plume. The plume continues to expand as long as the addition of chemical mass from the source exceeds mass loss by NA processes. As the plume expands and occupies an ever-increasing portion of the aquifer, the loss of mass by NA processes increases. Thus, a point is reached when the mass addition equals mass lost, and the plume becomes stable. Because of the phenomenon of NA, most BTEX plumes resulting from service station spills become stable at lengths less than 500 feet, as demonstrated by numerous plume studies (Buscheck et al. 1996; Rice et al. 1995). At most sites, the chemical source is finite; in time, the mass loading from the source to the dissolved plume decreases. Meanwhile, the rate of mass loss due to NA processes increases or stays the same, so eventually the plume begins to shrink.

Under ideal conditions, all dissolved chemical plumes would follow the above lifecycle; however, real plumes may not follow this pattern due to a number of confounding factors, including the following:

- Variations in ground water velocities that affect the rate of NA
- Fluctuations in the water table that affect the source mass loading due to the release of chemicals trapped in the capillary fringe
- Variations in climatic conditions that affect the rate of NA
- Variations in rainfall and infiltration that affect mass loading to ground water
- Additions to the plume from new releases and spills from operating facilities

Because of the above complications, it is important to collect and evaluate all the site data and look at multiple lines of evidence to understand the plume behavior and predict its future behavior (see section 3.5).

3 Biodegradation of Petroleum Hydrocarbons

This section discusses the biodegradation of dissolved petroleum hydrocarbons and identifies the various indicators that should be measured to confirm biodegradation.

The biodegradation of hydrocarbons is the process by which naturally occurring subsurface microorganisms biodegrade contaminants. The process of biodegradation, as facilitated by microorganisms, can be represented by the general reaction:

Hydrocarbon + Electron Acceptors + Nutrients YIELDS *Carbon Dioxide + Water + Microorganisms + Waste Products*

The above biologically mediated reaction produces energy for cell growth and reproduction of the microbial population. The process of electron transfer results in the oxidation of the donor (hydrocarbon), reduction of the electron acceptor, and the production of usable energy for the organisms. Based on the principles of thermodynamics, biologically mediated reactions that yield the most energy are favored over reactions that yield less usable energy for the organisms. For hydrocarbons, biologically mediated reactions ideally occur in the following order:

1. Dissolved oxygen in the ground water is used as the electron acceptor.
2. After all oxygen has been depleted and anaerobic conditions exist within the dissolved plume, dissolved nitrate is used as the electron acceptor.
3. After the depletion of dissolved oxygen and nitrate, ferric iron is used as an electron acceptor and is reduced to ferrous iron.
4. After the depletion of oxygen, nitrate, and iron, sulfate is used by sulfate-reducing bacteria to degrade the hydrocarbons.
5. Finally, methanogenesis degrades the hydrocarbons.

While all petroleum hydrocarbons are biodegradable, the rate of biodegradation can differ significantly from site to site depending on the composition and amount of hydrocarbons; type and amount of available electron acceptors; type, number, and characteristics of the microorganisms; and quantity and quality of nutrients.

Site-specific measurements of these factors, comparison of these factors within and outside the plume, and temporal variations in these factors can be used to demonstrate the occurrence of biodegradation. Each of these factors is discussed below.

3.1 Composition and Amount of Hydrocarbons

Almost all petroleum hydrocarbons are biodegradable under aerobic conditions. The ease of biodegradation depends on the type of hydrocarbon. Low molecular weight hydrocarbons (e.g., C10 to C24 alkenes) and single-ring aromatics are the most easily biodegradable. As molecular weight increases, resistance to biodegradation also increases. Individual compounds degrade at different rates under aerobic and anaerobic conditions.

For most hydrocarbon-impacted sites, the primary chemicals of interest (from a risk perspective) are BTEX, MTBE, and naphthalene. Naphthalene and BTEX are readily degradable under aerobic conditions. Benzene typically degrades slower than other BTEX hydrocarbons under anaerobic conditions. The biodegradation and NA of MTBE has been a topic of current research (Moyer and Kostecki 2003; EPA 2005; API 2007). MTBE degrades under both aerobic and anaerobic conditions. However, the rates of MTBE degradation and controlling factors have not yet been firmly established.

3.2 Available Electron Acceptors

The biodegradation of hydrocarbons is essentially an oxidation-reduction reaction. In this reaction, the hydrocarbon donates the electron (i.e., the hydrocarbon is oxidized) and a second compound (the electron acceptor) is reduced. Of the several electron acceptors available in the subsurface environment, oxygen, because of its high energy yield, is typically used first by microorganisms. Anaerobic bacteria can use other electron acceptors, including the following:

- Nitrate (NO_3^-) that is reduced to nitrogen (N_2)
- Manganese (Mn^{4+}) that is reduced to water soluble Mn^{2+}
- Ferric iron (Fe^{3+}) that is reduced to water soluble Fe^{2+}
- Sulfate (SO_4^{--}) that is reduced to sulfide (S^-)
- Carbon dioxide (CO_2) that may be used by methanogens to yield methane (CH_4)

As the biodegradation of hydrocarbons occurs, the concentration of the electron acceptors decreases and the concentration of the products formed increases. This concept can be used to demonstrate the occurrence of biodegradation (i.e., secondary line of evidence, see section 3.5.2). Table 1 shows the expected relationship between the BTEX concentration and the electron acceptors and the products of the oxidation reduction reaction.

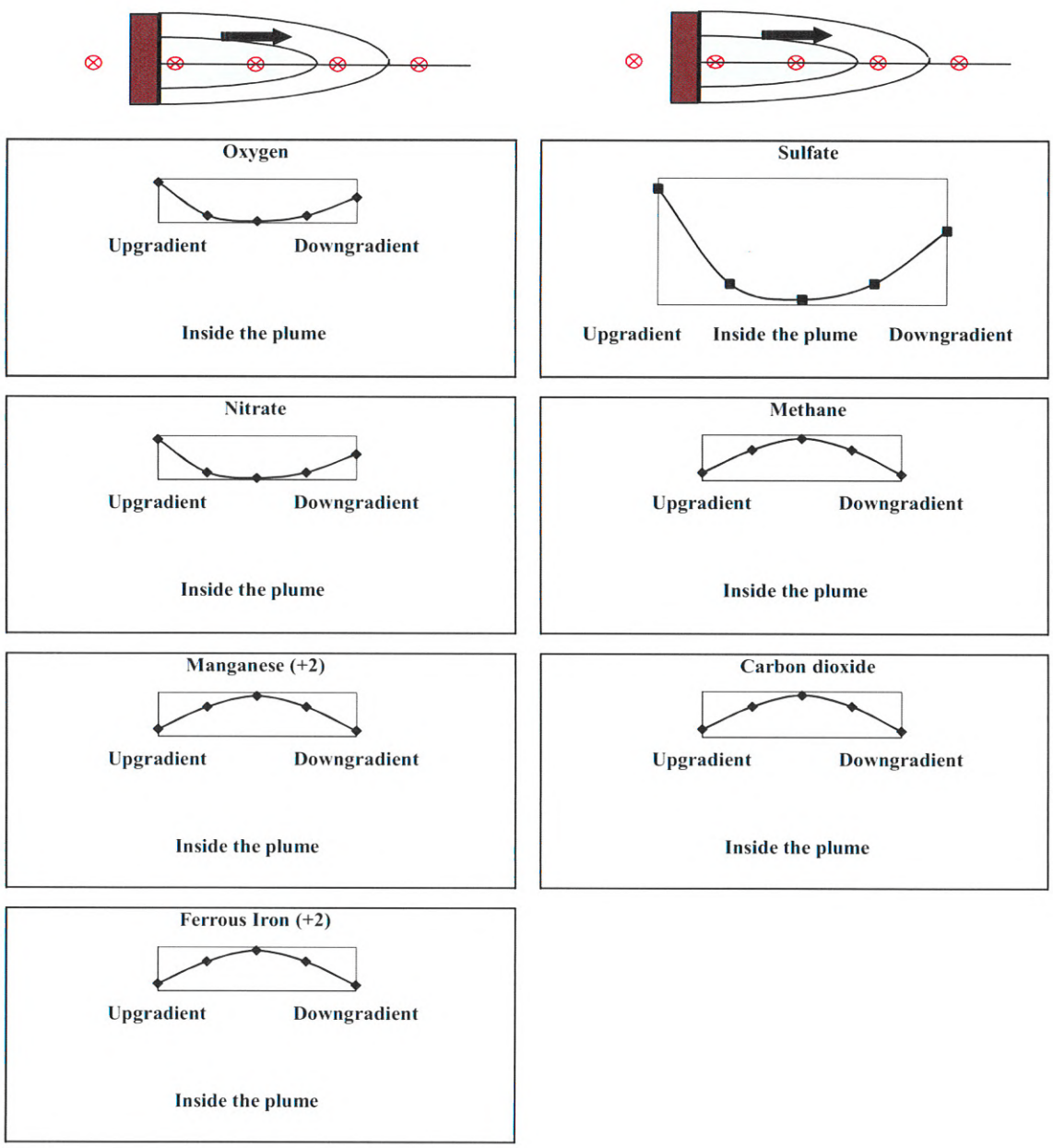


Figure 3. Expected pattern of natural attenuation indicators (secondary line of evidence)

3.3 Quantity and Quality of Nutrients

In addition to the electron acceptors, microorganisms also require nutrients. These nutrients are incorporated into the biomass and are necessary to form cells. The nutrients nitrogen and phosphorous are required in relatively large amounts. Small amounts of micro-nutrients—such as sulfur, manganese, and magnesium—are also required.

Certain compounds, such as nitrates and sulfates, can serve either as nutrients or electron acceptors. Nutrients are rarely a limiting factor in the subsurface biodegradation of petroleum hydrocarbons. A decrease in nutrient levels within the zone of degradation can indicate biodegradation.

3.4 Characteristics of Microorganisms

The ability of microorganisms to degrade a wide variety of petroleum hydrocarbons is well documented. Hydrocarbon-degrading microorganisms are widespread in the environment, as they occur in fresh water, salt water, soil, and ground water. The number of cells per milliliter of water can also be used as an indicator of biodegradation. As hydrocarbons degrade, the cell count for hydrocarbon-degrading bacteria increases. McKee et al. (1972) found 50,000 or more hydrocarbon-degrading bacteria per milliliter of water in samples from wells containing traces of gasoline, while a noncontaminated well had only 200 microorganisms per milliliter.

3.5 Indicators of Natural Attenuation of Hydrocarbon Plumes

Based on the information presented above, concentrations of several substances (hydrocarbons, electron acceptors, microorganisms, nutrients, and carbon dioxide) can be measured to demonstrate the occurrence of NA.

These measurements are typically divided into three tiers, or "lines of evidence" (i.e., primary, secondary, and tertiary lines of evidence), to demonstrate NA. Data collected under each line of evidence can be evaluated qualitatively or quantitatively.

3.5.1 Primary Line of Evidence

The purpose of the primary line of evidence of NA is to demonstrate the loss of chemical mass by evaluating measured petroleum hydrocarbon concentrations. Of all the methods available to demonstrate the occurrence of NA, this is perhaps the simplest and most useful to demonstrate site-specific reductions in risk. Site-specific application of the primary line of evidence requires an adequate number of correctly installed sampling points (monitoring wells), an adequate amount of chemical data from these points, and a thorough evaluation of these data. These issues are discussed in Parts II and III of this document.

Although the primary line of evidence can show whether the concentration of a plume is attenuating, it does not show whether the decrease is due to destructive mechanisms or merely dilution. Secondary lines of evidence are necessary to determine whether the decrease is due to biodegradation.

3.5.2 Secondary Line of Evidence

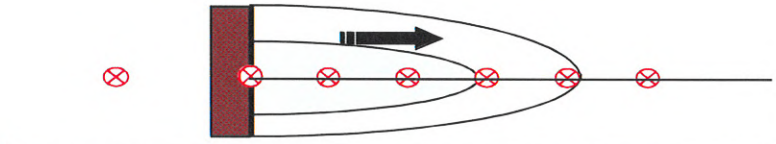
Secondary evidence of NA refers to measurements of electron acceptors and products of metabolism within the plume and their comparison with concentrations in the unimpacted area of the aquifer, where no biodegradation activity would be expected to occur.

Parameters that are typically measured in the field include dissolved oxygen, REDOX potential, dissolved nitrates, manganese, ferrous iron, sulfate, and methane. These parameters should be measured at up-gradient locations, inside the plume near the source, and at down-gradient locations. Expected patterns of these parameters that are indicative of biodegradation are shown in Table 1 and Figure 3.

As microorganisms consume chemicals, there is a corresponding consumption of the compounds that serve as electron acceptors. Thus, the concentration of these compounds would decrease in the portion of the plume where biodegradation is occurring. For example, under aerobic biodegradation, the concentration of oxygen would decrease, assuming oxygen is not being added to the plume. Similarly, under anaerobic conditions, a depletion of nitrate, ferric (III) iron, and sulfate can be expected.

Biodegradation also results in an increase in the concentration of metabolic byproducts. For example, increased concentrations of nitrite and ferrous (II) iron within the plume would be indicative of biodegradation.

Table 1. Expected pattern of natural attenuation indicators (secondary line of evidence)



	Upgradient	Inside the plume		Downgradient
BTEX	ND	High	Low	ND

Type of Reaction	Geochemical Indicator	Geochemical Indicator Concentration		
Aerobic	Oxygen	High	Low	High
Anaerobic	Nitrate	High	Low	High
	Manganese	Low	High	Low
	Ferrous Iron	Low	High	Low
	Sulfate	High	Low	High
	Methane	Low	High	Low
	Carbon dioxide	Low	High	Low

The secondary line of evidence demonstrates the occurrence of biodegradation only. It does not provide any data on the occurrence of other NA processes.

3.5.3 Tertiary (Optional) Line of Evidence

The tertiary (optional) line of evidence involves performing microbiological studies, such as identifying the microorganisms present in the formation and counting their cells, in an effort to demonstrate the occurrence of NA. Thus, the objectives of secondary and tertiary lines of evidence are similar. In the portion of the plume where NA is occurring, the ratio of petroleum degraders to the total number of bacteria should be higher than in

the uncontaminated portion of the plume due to the readily available petroleum energy source. Tertiary lines of evidence are seldom required at petroleum hydrocarbon impacted sites and are not discussed further.

PART II: Process for the Implementation of Remediation by Natural Attenuation

Remediation by natural attenuation refers to the achievement of site-specific cleanup goals using NA. As discussed in Part I, NA consists of several processes that occur at all contaminated sites at varying rates. As with any other remedial option, the site-specific applicability of RNA must be carefully evaluated before it is selected as the remedial alternative of choice. RNA should not be considered a presumptive remedy; rather, it is one of several available strategies that should be evaluated to ensure its applicability based on site-specific conditions.

The first step in any evaluation of NA is the collection of appropriate site characterization data. In general, the data collected need to confirm the occurrence of NA, the effectiveness of RNA, and that the receptors are not exposed to unacceptable risk throughout the period when the site is being remediated by NA. The data collected should help answer the following questions and support the activities described in the questions.

- Has the full horizontal and vertical extent of the source and the plume been delineated?
- Is the plume at steady state and is it stable or shrinking in size?
- Can contaminant degradation be demonstrated and quantified?
- Can the long-term behavior of the source and the plume be modeled?
- Can the time frame to achieve remedial cleanup goals be estimated?
- What is the impact of source removal/reduction on the remedial time frame?

Once the site has been characterized to document the feasibility of NA, an evaluation as to the site-specific appropriateness of NA as the preferred remedy should be performed. RNA is applicable only at the following types of sites:

- Sites where immediate threats to human health, safety, and the environment do not exist or have been mitigated
- Sites where "active" sources, such as leaking tanks, drums, etc., have been removed
- Sites where the projected time frame to achieve remedial objectives is "reasonable," as defined in section 7
- Sites where the plume is stable or shrinking and is not likely to impact current receptors or sensitive habitat
- Sites where active remediation has removed the bulk of the contaminants and the role of RNA is to perform the "final touchup"
- Sites where any necessary institutional controls can be reliably implemented

Upon selection of RNA as part or all of the preferred remedy, a corrective action plan will be developed to document the selection process and provide details about implementation of the remedy. The Idaho Department of Environmental Quality (DEQ) must approve this corrective action plan. At all sites, RNA will be accompanied by long-term monitoring to demonstrate that RNA is occurring at the rate anticipated when RNA

was selected as the remedial option. Monitoring will continue until the specified cleanup goals have been achieved. If the monitoring data indicate that RNA is not occurring at an acceptable rate, the remedial plan will need to be modified.

4 Risk Management Plan for Remediation by Natural Attenuation

At sites where RNA is part of the preferred remedial option, the responsible party should include a discussion in the corrective action plan that addresses the following elements:

- A summary of site characterization activities that demonstrates a thorough understanding of the nature and extent of the source and the nature and extent of the impacts, provides data supporting the likely effectiveness of RNA, and discusses any source removal/control activities performed at the site
- A discussion of remedial endpoints and points of compliance, and the manner in which these were determined
- A discussion of the time frame over which the endpoints are expected to be achieved
- A demonstration that during this time frame, risks to human health and the environment are acceptable
- A discussion of monitoring locations, the rationale for monitoring location selection, and the type and frequency of data that will be collected to monitor the performance of RNA and the achievement of remedial goals
- A description of the tools to be used to evaluate/analyze the monitoring data
- A description of the institutional controls that may be required and documentation of their implementation
- A description of a contingency plan that will be implemented if the monitoring results indicate that RNA is not sufficiently effective or is not proceeding at the expected rate
- A description of the frequency and form of the reports to be submitted to DEQ during the course of implementing RNA

A brief discussion of critical components of the RNA portion of the corrective action plan is presented below.

5 Source Characterization and Control

Characterizing and controlling the source are important aspects of RNA. Sufficient data should be collected during the site investigation phase to delineate the nature and extent of the source and estimate the source lifetime. The term "nature" refers to an evaluation of the chemicals of interest and a determination that the chemicals are amenable to NA. The extent refers to the physical dimensions of the source as well as a determination of the mass of residual chemicals present in the source. An estimate of the lifetime of the source can be made by calculating the mass flux out of the source area (using ground water flow characteristics and contaminant concentrations in the source area) and

comparing this to the total contaminant mass in the source area (including free phase product, soils, and ground water).

DEQ requires that all active sources (e.g., leaking pipes, tanks, spills) be stopped and any free phase product in ground water be removed, to the maximum extent practicable. It is best to reduce the source and remediate soils containing residual product that are significant sources of contamination to ground water. Such control measures will reduce the time required to achieve remedial objectives. At a minimum, sufficient source material should be removed to ensure a declining plume. The amount of active remedial activity necessary should be determined on a case-by-cases basis and clearly presented in the risk management plan.

6 Plume Characterization

The goals of collecting data to characterize the plume are to demonstrate the magnitude and direction of contaminant transport and the stability status of the plume, to confirm degradation is occurring, and to estimate the contaminant degradation rate or the ability of the aquifer to assimilate the contamination.

To achieve these goals, the responsible party must construct wells to account for aquifer heterogeneity and dominant zones of contaminant transport, select appropriate monitoring locations, collect samples at an adequate frequency, and collect and evaluate the appropriate analytical data. How to determine the appropriate monitoring locations, sampling frequency, and data is discussed below.

The location and number of ground water samples collected and analyzed must be determined based on site-specific conditions.

At a minimum, sampling points should be located so as to achieve the following:

- Locate the distribution of contaminants within the plume
- Locate the plume boundaries
- Track plume movement and migration

While they do help define the extent of the plume, sampling points at nondetect locations provide little useful information for documenting plume characteristics for an NA evaluation. Most sampling points need to be located within the plume boundaries for NA evaluation purposes.

Monitoring wells should be located up-gradient of the source, within or immediately down-gradient of the source area, and within the plume aligned along the plume axis. Data should be collected from an unimpacted down-gradient well also. A down-gradient clean well can be used to help characterize the extent of the plume and may be used to protect down-gradient receptors by providing early detection of plume movement. This function is described in section 8. Wells delineating the sides of the plume assist in determining if there are significant seasonal changes in ground water flow direction.

As discussed in sections 3.5.1 and 3.5.2, data related to the primary and secondary lines of evidence should be collected. In rare cases, it may be necessary to collect data to demonstrate tertiary lines of evidence as well. Based on the data collected, a determination should be made whether the plume is expanding, stable, or shrinking. The specific analytical tools that may be used to conduct this characterization are discussed in Part III of this document.

Expanding plumes require continued monitoring. Depending on site conditions, such as the risk to current or potential future receptors and the rate at which the plume is expanding, additional assessment of the plume and/or source removal and reduction may be necessary. An expanding plume typically requires active remediation.

Plumes documented to be stable or shrinking are candidates for the use of NA. These plumes will also require continued monitoring, though perhaps at a lower frequency than expanding plumes. Depending on site conditions and the time frame of remediation, a stable plume may require residual source characterization or removal.

The frequency and duration of monitoring during the plume characterization phase should be determined on a site-specific basis and in consultation with DEQ. However, in most cases, 1–2 years of quarterly monitoring data are necessary to evaluate the degree of seasonal variations in water levels and flow directions present at a site. This information is necessary to characterize a plume as expanding, stable, or shrinking and to estimate degradation rates. As clear trends emerge in the data, the monitoring frequency may be modified. The actual duration of sampling will depend on the time it takes to demonstrate a clear trend in the concentrations.

7 Reasonable Time Frame Determination

The determination as to what constitutes a reasonable time frame for RNA is a complex, site-specific determination not amenable to simple rules of thumb or quantification. In making this determination, DEQ will take into account factors that include, but are not limited to, the following:

- The time frame for RNA compared to that for other remedies being evaluated
- The time frame in which affected portions of the aquifer might be needed for various uses
- The likelihood that impacted ground water will be utilized
- The degree of uncertainty in site characterization and NA estimates
- The reliability of institutional controls over the time frames for which they may be required to function
- The ability of the responsible party to maintain the required monitoring and plume evaluation required when NA is used as a remedy

8 Monitoring to Demonstrate the Effectiveness of Remediation by Natural Attenuation

Due to the uncertainties associated with the site-specific implementation of RNA, long-term monitoring is necessary to demonstrate its effectiveness. Long-term monitoring is used to ensure that the behavior of the plume does not change (EPA 1999) and that predictions of plume behavior are accurate. The objectives of long-term monitoring are to demonstrate NA is continuing to occur, human health and the environment are being protected, and the plume is not expanding.

The specifics of the monitoring plan (e.g., the location, frequency, and type of samples to be collected and the analytical procedures to be used) should be determined on a site-specific basis. The primary factors that should be considered when designing a long-term monitoring program include the following:

- Distance to potential receptor exposure points
- Ground water seepage velocity and direction
- Types of contaminants
- Aquifer heterogeneity
- Three-dimensional distribution of chemicals of interest
- Areas of unique geochemical conditions
- Surface water impacts
- Effects of active remediation systems (Wiedemeier et al. 2000)

The secondary factors that should be considered include the following:

- Access issues
- Property lines
- Contaminant contributions from offsite sources (Wiedemeier et al. 2000)

Two types of wells are required for any long-term monitoring program: performance monitoring wells and contingency monitoring wells. Performance monitoring wells are used to demonstrate that NA is proceeding according to expectations; document that geochemical conditions continue to be adequate to support NA processes; identify any toxic products resulting from NA processes; determine if plume conditions remain stable or are shrinking; identify changes in ground water conditions, such as change in flow direction, recharge, etc.; and document that cleanup criteria have been met.

Contingency monitoring wells are placed beyond the predicted down-gradient boundary of the plume and up gradient from known or potential receptor exposure points. Their purpose is to provide an "early-warning" if unexpected plume expansion occurs and allow implementation of a contingent remedy if needed. Multiple contingency wells may be needed, particularly if seasonal variations in ground water flow direction are known to occur.

Sampling frequency should be based on the following factors:

- The natural variability observed in contaminant concentrations
- The distance and travel time from the source to the point of compliance
- The reduction in concentrations needed to meet target levels

9 Contingency Measures

The RNA corrective action plan should include a contingency plan to be implemented if the site data indicate that RNA is not occurring at the expected rate or the exposure conditions at the site have changed, resulting in an unacceptable risk to human health or the environment.

Contingency measures will prevent delays in site remediation and provide a clear roadmap for site remediation. Triggers should be established and included in the plan that would cause the responsible party to implement alternative active strategies to enhance RNA. The triggers should be as objective and quantitative as possible. Examples of triggers that would cause the responsible party to implement alternative strategies include, but are not limited to, the following:

- A consistent increase in concentrations in one or more wells
- A failure of any of the institutional conditions necessary to protect human health and the environment during the period of RNA
- A change in the exposure conditions (e.g., removal of pavement)
- Continued expansion of the plume
- Unacceptably low rates of RNA

PART III: Techniques Available to Demonstrate Natural Attenuation

Several techniques are available to evaluate the data collected to demonstrate NA or to design and implement an RNA program. These techniques can be divided into three categories: techniques to demonstrate the occurrence of NA, techniques to estimate the site-specific rate of NA, and techniques to quantify the future behavior of the plume. The available techniques for each of these evaluations are presented below.

10 Techniques to Demonstrate the Occurrence of Natural Attenuation

The occurrence of NA may be demonstrated by using graphical and/or statistical techniques. The specific techniques used will vary depending on site conditions and the specifics of the data. To the extent possible, multiple techniques should be used to provide added insight into the NA process.

10.1 Graphical Techniques

Chemicals-of-interest data collected from strategically located monitoring wells can be used to draw site-wide contour maps of individual constituent concentrations for each monitoring event, create concentration-versus-time plots for each well with detectable constituent levels and at least four rounds of data, and create concentration-versus-distance plots along the flow direction for several monitoring events. Depending on the variability in the concentrations, it may be better to plot the natural logarithm of concentration versus time and distance. An example plot is shown in Figure 4. When creating these plots, care should be taken to ensure that the selected scale clearly demonstrates the trend. Since the concentrations are affected by water level fluctuations, it is important to also plot water levels as a function of time.

These plots can indicate whether the concentration trend is decreasing, stable (no significant trend), increasing, or mixed. The latter refers to a situation where different wells (source wells versus periphery wells) exhibit different trends. Increasing concentrations in the source well and decreasing concentrations in the down-gradient wells may occur due to a variety of reasons. For example, the mass loading to the source may cause an increase in the source wells due to an increase in the infiltration rate, or the rate of biodegradation near the source may be reduced due to a depletion of oxygen.

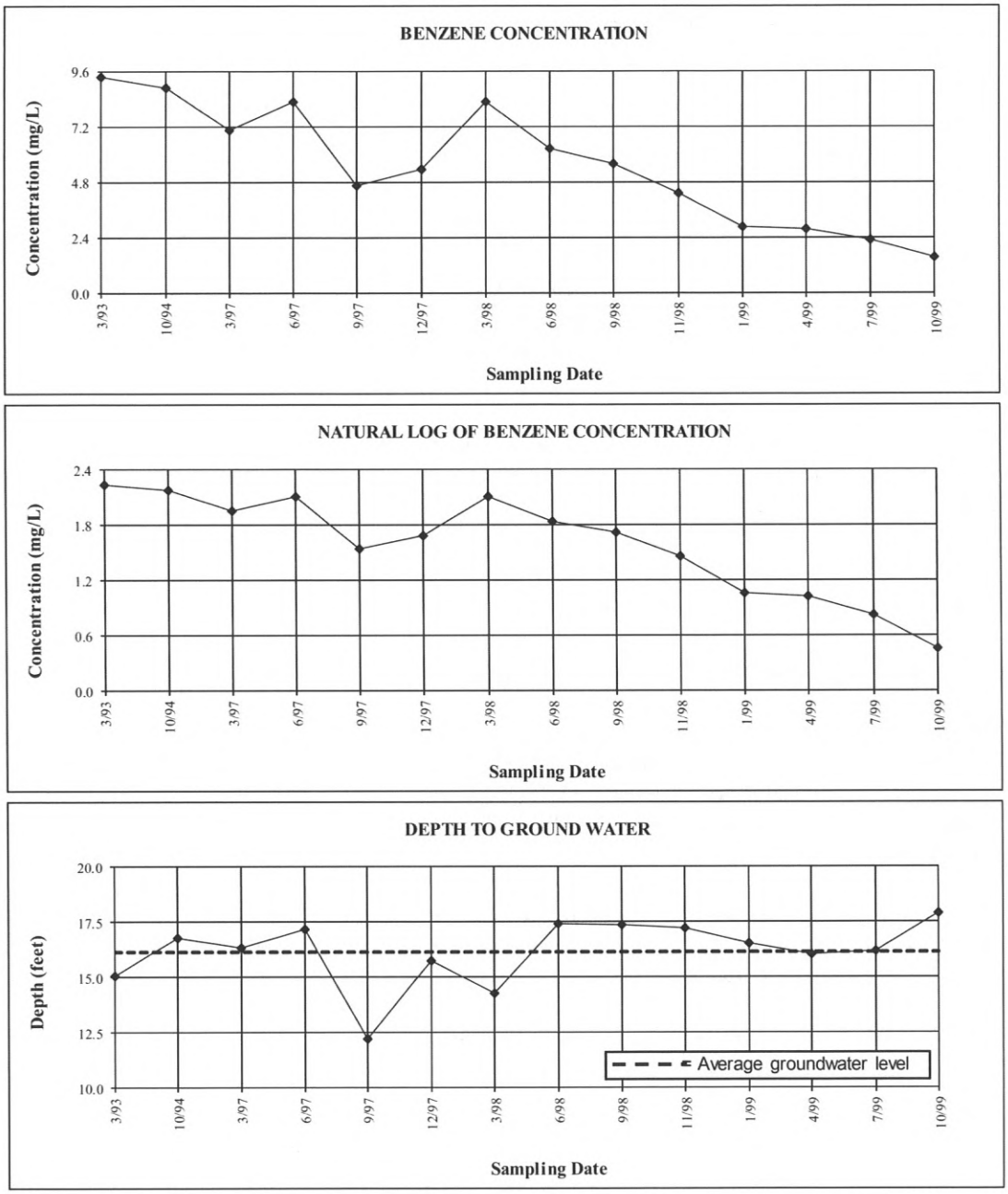


Figure 4. Concentration-versus-time plot of benzene

Conversely, increasing concentrations in down-gradient wells and decreasing concentrations near the source may indicate that the plume is moving but the source has depleted. Conclusions related to concentration trends based on visual observations of the data must be supported by statistical analysis.

In addition to the chemical-of-interest concentrations, indicator chemical concentrations should be plotted along the plume axis (in the concentration-versus-distance plots) along with the hydrocarbon concentrations. The observed pattern of concentrations can be used

to demonstrate NA. For example, low dissolved oxygen concentrations within the plume and higher concentrations up-gradient and down-gradient of the source are indicative of biodegradation within the plume.

10.2 Statistical Evaluations

Statistical tools may be used to determine and quantify the concentration trend. These tests can be used to test a null hypothesis and an alternative hypothesis. A null hypothesis might be that there is no time trend in the concentrations-versus-distance or time, and the alternative hypothesis might be that there is a downward trend. Application of the statistical test would then result in accepting or rejecting the null hypothesis at a specified level of significance.

A nonparametric test, called the Mann-Kendall test, is often used to determine whether a trend exists in the data. This test is particularly useful for environmental data for several reasons:

- The test is nonparametric, which implies that the test is applicable irrespective of the underlying distribution of the data.
- The test is simple to implement.
- Concentration values below the detection limit can be used.
- The results are not affected by missing data.

The Mann-Kendall test is applicable only when there is no seasonality in the data. This is the case if the data do not show any seasonal variations or the data were collected from one season. When data indicate seasonality, the seasonal Kendall test may be used. For details on both of these tests, refer to Gilbert (1987), Gibbons (1994), or other books on statistical analysis.

DEQ strongly recommends the use of the Mann-Kendall test to determine the trend in nonseasonal data except in situations where a visual plot of data indicates without **any** ambiguity that a trend exists in the data.

If the concentration-versus-time or concentration-versus-distance data indicate a decreasing trend, a regression analysis may be used to estimate the slope of the best-fit line.

As explained in section 11.2 and 11.3, the slope of the line can be used to estimate the NA or the biodegradation rate. For additional information on regression analysis, refer to any statistics textbook.

11 Techniques to Estimate the Site-specific Rate of Natural Attenuation

The data collected to demonstrate the primary line of evidence of NA can be used to estimate site-specific NA rates and biodegradation rates. Since NA includes multiple processes in addition to biodegradation, the NA rate would be higher than the

biodegradation rate. The latter can be used as an input into a ground water fate and transport model, such as Domenico's model (Domenico 1987), to estimate the future migration of the plume, and to estimate a site-specific dilution attenuation factor. Three methods are available to estimate the NA rate: 1) mass balance analysis for expanding, stable, or shrinking plumes; 2) plume concentration-versus-time plots; and 3) plume concentration-versus-distance plots. Descriptions of each of these methods are presented below. An excellent discussion of the calculation and use of rate constants for use in NA evaluations is presented in EPA (2002). This section also includes a discussion of calculating biodegradation rates using recalcitrant tracers.

11.1 Mass Balance Analysis

This method of estimating the NA rate is based on the concept of mass balance. For a stable plume, the mass entering the ground water plume must equal the mass lost by NA. Thus, if the mass entering the plume can be estimated, it should be possible to estimate the NA rate. A detailed description of the application of mass balance analysis to estimate the NA rate of a petroleum release is described in Section X6.1 of the *Standard Guide for Remediation of Groundwater by Natural Attenuation at Petroleum Release Sites* (ASTM 2004).

11.2 Well Concentration-versus-Time Plot

The estimate of the overall attenuation rate for a shrinking plume can be calculated assuming a first-order decay rate and is represented mathematically by Equation 1:

$$\frac{dC}{dt} = exp^{(-kt)} \qquad \text{(Equation 1)}$$

Where:
C = concentration
t = time [years]
k = NA rate [1/yr]

The solution to the above differential equation results in the familiar exponential decay equation (Equation 2):

$$C(t) = C(t=0)\,exp^{(-kt)} \qquad \text{(Equation 2)}$$

Where:
$C(t)$ = Concentration at any time t (mg/L)

Taking the natural logarithms of both sides of Equation 2 results in Equation 3:

$$ln\,C(t) - ln\,C(t=0) = -kt \qquad \text{(Equation 3)}$$

Thus, a plot of natural log of concentration versus time would be a straight line with a slope equal to k (the NA rate).

11.3 Well Concentration-versus-Distance Plot

Advective travel time can be expressed as below (Equation 4):

$$t = \frac{x}{v} \qquad \text{(Equation 4)}$$

Where:
x = Advective travel distance (cm)
v = Seepage velocity (cm/yr)

Substituting Equation 4 in Equation 2 results in Equation 5:

$$C(t) = C(t=0)\,exp^{(-k\frac{x}{v})} \qquad \text{(Equation 5)}$$

Taking the natural log of both sides of the equation results in Equation 6:

$$ln[C(t=0)] - ln[C(t)] = -k\frac{x}{v} \qquad \text{(Equation 6)}$$

For a shrinking plume that follows the first-order attenuation rate presented above, a plot of log concentration versus distance would be a straight line with a slope of k/v. By multiplying the slope with the seepage velocity, the NA rate (k) can be estimated.

Buscheck and Alcantar (1995) used the solution of the one-dimensional transport equation with biodegradation to estimate the biodegradation rate based on the slope of the log concentration-versus-distance plot. Specifically, they derived the following expression (Equation 7) for the biodegradation rate:

$$\lambda = \frac{v}{4\alpha_x}\left\{\left[1+2\alpha_x\left(\frac{k}{v}\right)\right]^2 - 1\right\} \qquad \text{(Equation 7)}$$

Where:
λ = Biodegradation rate, assumed to occur at equal rates in the dissolved and sorbed phases
α_x = Longitudinal dispersivity (0.1x)

Zhang and Heathcote (2003) modified this method to account for situations with finite source size and lateral dispersion to improve the estimates of the biodegradation rate.

The following step-by-step description of the biodegradation rate estimation process can be implemented on a site-specific basis.

Step 1: Determine the ground water flow direction based on the water level measurements for each monitoring event.

Step 2: For each monitoring event, identify the wells located along the direction of flow (i.e., along the plume center line). Since the flow direction may vary seasonally, different wells may be used for different monitoring events.

Step 3: Tabulate the concentrations of the chemicals of interest and calculate the natural log concentrations.

Step 4: Plot the natural log concentrations on the *y*-axis and the distance along the *x*-axis.

Step 5: Calculate the slope of the best-fit line and the confidence in this estimate by examining the 95% confidence limits of the slope.

Step 6: Estimate the ground water seepage velocity.

Step 7: Multiply the slope of the best-fit line calculated in Step 5 with the seepage velocity. The result will represent the overall NA rate. This NA rate represents the reduction in concentration due to the combined influence of the various NA processes mentioned in section 2. This decay rate should not be confused with the biodegradation rate (λ) that is an input to ground water models.

Step 8: Estimate the biodegradation rate from Equation 7.

Steps 1–8 should be completed for each time period for which data are available and the results presented as a range of NA and biodegradation rates. The latter can be used as an input to the Domenico model (Domenico 1987) to estimate the dilution attenuation factor. Due to confounding factors such as seasonal variations in ground water velocity, fluctuations in water levels, and errors in sampling and analysis methods, the NA and biodegradation rates may vary significantly (by as much as a factor of 10). Therefore, it is best to present the range as well as the average rates.

11.4 Evaluation of Plume Behavior with a Recalcitrant Tracer

Physical, chemical, and biological processes act together to decrease contaminant concentrations away from a source. However, monitored NA requires that accurate biodegradation rates for a site be known. To estimate accurate biodegradation rates, conservative tracers can be employed. The concentrations of these tracers are not affected by biodegradation processes and so can be used to delineate between the effects of biodegradation and other NA processes such as dilution and sorption. Generally, tracers are biologically recalcitrant and have chemical properties similar to the contaminant of interest. Examples of common tracers include MTBE for petroleum hydrocarbon plumes.

12 Techniques to Quantify the Future Behavior of the Plume

The future behavior of the plume can be estimated by using fate and transport models. A number of analytical and numerical models are available. Commonly used analytical

models include the Domenico model (Domenico 1987) and BIOSCREEN. BIOSCREEN can be downloaded from www.epa.gov/ada/csmos/models/bioscrn.html.

These models can be used to estimate plume length, concentrations at down-gradient receptor locations, and dilution attenuation factors and can be calibrated to site-specific ground water data. The correct application of fate and transport models requires experience and specialized knowledge that is beyond the scope of this document.

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Appendix J: Sample Table of Contents for a Risk Evaluation Report

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Introduction

During the risk evaluation process when collecting media-specific chemical concentration data and establishing remediation standards, situations may arise where practical quantitation limits (PQLs) for specific chemicals and samples may exceed screening levels or site-specific, risk-based concentrations. Section 500 of IDAPA 58.01.24, Application of Risk Based Corrective Action at Petroleum Release Sites, delineates the following factors that may be used to allow the use of PQLs as remediation standards:

- Analytical method
- Method detection limit
- Sampling procedures
- Estimated risk levels
- Other

This appendix provides background on the concepts of PQLs, MDLs and Remediation Standards and provides guidance on using the above factors when a REM user is proposing PQLs as remediation standards.

Background— Practical Quantitation Limits, Method Detection Limits and Remediation Standards

What are PQLs and MDLs?

A PQL is defined in part in 58.01.24.010 as "The lowest concentration of a chemical that can be reliably quantified among laboratories within specified limits of precision and accuracy for a specific laboratory analytical method during routine laboratory operating conditions." The method detection limit (MDL) is defined as "The minimum concentration of a substance that can be reported with 99% confidence is greater than zero."

How are PQLs Derived?

PQL values are derived in a number of ways, and there is no consensus as to the process used to develop them. In some cases, they are derived as a fixed multiplier applied to the MDL value or the standard deviation of samples used to develop the MDL. The multiplier commonly ranges from 3 to 5 and may be as great as 10. In other cases, PQLs may be derived by analysis of data from actual laboratory performance studies. In these cases, PQL values are a function of analytical methods, a given laboratory's equipment, operating protocols, operating conditions, quality assurance/quality control procedures, and sampling and media considerations. Values are sometimes reported by laboratories at levels between the MDL and the PQL and are commonly qualified as estimated quantities. The closer the estimated value is to the PQL, the more confidence in the estimated value.

How did DEQ derive the PQLs and MDLs in Table 1?

For the petroleum chemicals of interest (COI) listed in the rule, the common analytical methods for soil and water employed at petroleum release sites are established by the U.S. Environmental Protection Agency (EPA) in SW-846 (EPA 2011). For soil vapor and ambient air other EPA methods are applied (EPA 1999).Table 1 lists these methods employed in the analysis of the petroleum COI along with typically achieved detection and quantitation limits.

These detection and quantitation values were obtained from sample laboratory reports for site investigations done for the Idaho Department of Environmental Quality (DEQ) at a number of sites where petroleum COI were suspected. In their method descriptions, EPA lists examples of lower limits of quantitation for individual analytes but indicates that they are instrument-dependent and influenced by sample preparation/introduction technique (EPA 2006) or highly matrix-dependent and are provided for guidance only (EPA 2007).

For a given media, sampling considerations may have an impact on achievable detection limits. For example, when sampling soil vapor or ambient air with certain methods, the achievable quantitation limit can be a function of the amount of vapor or air sampled. Quantitation limits are commonly reduced as the amount of air sampled increases.

Specialized analytical techniques can sometimes provide lower MDL and PQL values. Table 1 illustrates this with a comparison of values achieved with the use of standard method 8270 for semivolatile compounds versus employing 8270 using selective ion monitoring (SIM). PQL values are 6 times lower for soils and 20 times lower for water samples.

Depending on the petroleum product released, levels of contamination, chemicals present, and media in question (soil, water, and vapor), interferences to analytical detection and quantitation may be present. Procedures such as sample dilution may allow quantification of petroleum COI concentrations but will also result in elevated detection and quantitation limits.

Remediation Standard

A remediation standard is defined in IDAPA 58.01.24 as a "media specific concentration which, when attained, is considered to provide adequate protection of human health and the environment."

Remediation standards are established at petroleum release sites where corrective action has been determined to be required. The need for corrective action is commonly determined after completion of a risk evaluation. Remediation standards are commonly established as part of a risk evaluation or an approved corrective action plan (CAP).

The magnitude of a remediation standard that is established for a given chemical and the potential that it may be exceeded by a PQL is dependent on a number of factors, including, but not limited to, the following:

- Assumptions regarding current and future site land use, both on and off site
- What petroleum products were released and the relative distribution of chemicals detected
- The magnitude and distribution of contamination (which media are impacted)
- The routes of exposure determined to pose the greatest threats

The two risk evaluation scenarios where elevated PQL values may require the reevaluation of initially selected remediation standards are as follows:

1) Screening Level Evaluation
The screening level evaluation described in IDAPA 58.01.24 employs the simplest and most straightforward use of remediation standards in the form of the residential use screening levels. The screening levels are conservative, calculated, risk-based concentrations determined to be protective of unrestricted use exposures.

Because laboratory analytical technology is continually changing, these media-specific chemical concentrations are established without consideration of the ability of standard laboratory methods to detect and quantify these values. For the petroleum COI in Table 1, the compounds benzo(a)anthracene (BAA) and benzo(b)fluoranthene (BBF) in water and ethylene dibromide (EDB) in soil pose the greatest potential challenges with respect to PQL values meeting screening level concentrations.

For BAA and BBF, common practical quantitation limits in water using EPA Method 8270 with SIM (0.00005 mg/liter) slightly exceed the groundwater screening levels (0.00003 mg/liter) while the method detection limits (0.00002 mg/liter) are slightly below the screening values. At petroleum release sites where these chemicals are COI and groundwater analytical results for these chemicals are reported either as estimated values (between the quantitation and detection limits) or below the detection limit the screening levels will be assumed to have been achieved. Additional support for this determination is provided if all other PAH chemicals are also reported at concentrations below screening levels.

The most commonly used analytical method for EDB in soils (EPA Method 8260) has typical quantitation (0.001 mg/kg) and detection (0.0003 mg/kg) limits that exceed the soil screening level concentration (0.00014 mg/kg). The soil screening level for EDB is based on protection of groundwater. The groundwater quantitation limit for EDB is below groundwater screening level. Examination of Table 2 of the guidance shows that for EDB the soil quantitation limits are low enough to evaluate the other relevant pathways and routes of exposure, 0.27 mg/kg for direct contact and 0.001 mg/kg for vapor intrusion. At petroleum release sites where EDB is a COI and groundwater is potentially impacted and representative groundwater samples report EDB below the screening level but soil quantitation limits are above the soil screening level the groundwater results will take precedence.

In the screening level evaluation, the user must compare maximum media-specific concentrations measured during site assessment activities to the screening levels. If the measured concentrations do not exceed the screening levels, the site may be eligible for site closure. If the measured concentrations do exceed screening levels, the user may select screening levels as the remediation standards upon which corrective action is based and develop a CAP. The user may also choose to conduct additional investigation or evaluation and perform a site-specific risk evaluation. Samples may also have results reported as undetected at a concentration that is less than the PQL but higher than the screening level. In this case, a potentially unacceptable risk would be indicated.

2) Site-Specific Risk Evaluation
During the site-specific risk evaluation process, media-specific chemical concentration data are collected and used, along with assumptions regarding exposure pathways and receptors, to calculate risk to expected receptors. If the calculated risk is unacceptable, media-specific, risk-based chemical concentrations are established. These risk-based concentrations become the remediation standards for site corrective action. Samples are then taken during and after corrective action to demonstrate the standards have been attained.

PQLs for selected analytes in a given media sample may exceed one or more of the calculated risk-based remediation standards, making the demonstration that the standard has been attained problematic. It is also problematic when samples with results below a PQL are included in the calculation of exposure point concentrations and risk.

Remediation standards are oftentimes the lowest at sites where:

- screening levels have been selected as the standards,
- unrestricted use is the desired corrective action land use goal,
- contamination has migrated offsite in groundwater,
- on-site vapor intrusion risk is determined to exist, or
- diesel fuel contamination (and polynuclear aromatic hydrocarbon chemicals) is present in surface soil or in close proximity to surface water.

Accordingly, PQL-related issues often arise at such sites.

Table 1. Method detection limit (MDL) and practical quantitation limit (PQL) soil, water, and vapor concentrations for petroleum chemicals of interest using selected analytical methods

	SOIL			WATER			VAPOR		
CHEMICALS	Method	MDL (mg/kg)	PQL (mg/kg)	Method	MDL (mg/L)	PQL (mg/L)	Method	MDL ($\mu g/m^3$)	PQL ($\mu g/m^3$)
Acenaphthene	8270(SIM)	0.0087 (0.0016)	0.036 (0.006)	8270(SIM)	0.0004 (0.000013)	0.001 (0.00005)	NA		
Anthracene	8270(SIM)	0.0074 (0.0008)	0.036 (0.006)	8270(SIM)	0.00036 (0.000012)	0.001 (0.00005)	NA		
Benzo(a)anthracene	8270(SIM)	0.0093 (0.0011)	0.036 (0.006)	8270(SIM)	0.0004 (0.000023)	0.001 (0.00005)	NA		
Benzo(a)pyrene	8270(SIM)	0.0098 (0.0008)	0.036 (0.006)	8270(SIM)	0.00053 (0.000013)	0.001 (0.00005)	NA		
Benzo(b)fluoranthene	8270(SIM)	0.0098 (0.0011)	0.036 (0.006)	8270(SIM)	0.00046 (0.000024)	0.001 (0.00005)	NA		
Benzo(k)fluoranthene	8270(SIM)	0.0089 (0.0005)	0.036 (0.006)	8270(SIM)	0.00036 (0.000020)	0.001 (0.00005)	NA		
Chrysene	8270(SIM)	0.013 (0.0006)	0.036 (0.006)	8270(SIM)	0.00028 (0.000018)	0.001 (0.00005)	NA		
Fluoranthene	8270(SIM)	0.011 (0.0008)	0.036 (0.006)	8270(SIM)	0.0004 (0.000020)	0.001 (0.00005)	NA		
Fluorene	8270(SIM)	0.0078 (0.0018)	0.036 (0.006)	8270(SIM)	0.00042 (0.000012)	0.001 (0.00005)	NA		
Pyrene	8270(SIM)	0.010 (0.0006)	0.036 (0.006)	8270(SIM)	0.00035 (0.000022)	0.001 (0.00005)	NA		
1,2-Dichloroethane	8260	0.00053	0.001	8260	0.00027	0.001	TO-17	--	0.4
Ethylene Dibromide	8260	0.0003	0.001	8011	0.0000057	0.00001	TO-15 SIM	--	0.8
Benzene	8260	0.00033	0.001	8260	0.00029	0.001	TO-17	--	0.32
Ethylbenzene	8260	0.00023	0.001	8260	0.00022	0.001	TO-17	--	0.43
Toluene	8260	0.0012	0.005	8260	0.00027	0.005	TO-17	--	0.38
Total Xylenes	8260	0.00046	0.003	8260	0.00086	0.003	TO-17	--	0.43
MTBE	8260	0.00028	0.001	8260	0.00019	0.001	TO-15 SIM	--	0.5
Naphthalene	8260	0.0004	0.005	8260	0.00017	0.005	TO-17	--	0.05

Checklist for Proposals to Use PQLs as Remediation Standards

Proposals to DEQ for the use of PQLs as remediation standards at petroleum release sites should include:

- the results of any risk evaluation,
- the remediation standards developed from that process,
- the proposed PQL, and
- the site-specific issues, with supporting information, that justify the use of the proposed PQL(s) as a remediation standard(s).

The supporting information that should be provided in the proposal is listed below along with a discussion of how DEQ will evaluate that information along with potential solutions to various issues, as they may be relevant to the site being evaluated, Given the number and variety of factors which may arise regarding PQLs in relation to remediation standards both the list and the discussion are not considered all-inclusive.

1. Risk Evaluation

- Describe the conceptual site model.
- Identify the level of risk evaluation, the chemicals, media, and pathway or route of exposure that are at issue.
- State the magnitude of the proposed PQL and MDL vs. the remediation standard.

Screening Level Evaluation

For sites where a screening level evaluation has taken place and the proposal is to use PQLs in place of screening levels as remediation standards for specific COI and media, the information provided will be reviewed in a number of ways. The proposed PQLs will first be reviewed relative to the conceptual site model and the pathway/routes of exposure, which are the basis of the screening levels for the chemicals under consideration.

- If the PQL for a chemical exceeds a soil screening level based on groundwater protection but the PQL achieves the groundwater screening level (also based on groundwater protection) for the same chemical, the soil PQL may be used as the soil remediation standard for that chemical.
- If the PQL for a chemical exceeds a soil or groundwater screening level for other routes of exposure (groundwater ingestion, vapor inhalation, or direct contact), DEQ will review the magnitude of the difference between the PQL/MDL and the screening level (whether greater than or less than the screening level) for all COI with a common route of exposure to estimate the potential impact on the cumulative risk from that pathway.
- If the pathway or route of exposure for the media-specific screening level for that chemical can be considered incomplete and the PQL is below the

screening levels for any other complete/potentially complete pathways/routes of exposure for that chemical and media the PQL may be acceptable as a remediation standard. DEQ will use Table 2 of this guidance for evaluation. Alternatively, the screening level for the most appropriate pathway or route of exposure may be considered as a remediation standard.

If only a screening level evaluation has been done completion of a site-specific evaluation may revise the remediation standards and still allow unrestricted use of the site, if that is the desired/expected future land use condition.

Site-Specific Evaluation

PQL issues may be related to cleanup criteria from a site specific risk evaluation. Site specific evaluations depend on the calculation of cumulative risk to a receptor from all pathways/routes of exposure and chemicals, based on estimated exposure point concentrations. The calculation of exposure point concentrations can be influenced by the number of chemicals with PQL issues, proportion of samples with <PQL values, the magnitude of the PQL, and how these censored data are treated in the calculation procedure. If the calculations result in unacceptable risks cleanup levels for individual COI are calculated, some of which may be low enough to be exceeded by PQLs. DEQ will evaluate whether and to what extent < PQL data were used appropriately in these calculations, if the resultant calculated risks are over or under estimated, the degree to which the < PQL data contribute to overall risk, and whether the calculated cleanup criteria can be modified to avoid the PQL issue or if use of a PQL will not materially affect the protectiveness of the cleanup.

The assumptions of the conceptual site model and risk evaluation will be reviewed to determine if the land use scenarios, receptors, and input parameter values are appropriate. For example, while an assumption of residential use may be appropriate all of the specific pathways and routes of exposure assumed to be complete may not be. Exclusion of an inappropriate pathway may eliminate the specific PQL concern. Alternatively, the pathways/routes of exposure may be appropriate but the receptor/land use scenario may not be.

If the PQL for a COI is above a remediation standard but the MDL is at or below the standard there may be instances where sample results falling between these limits can be considered to have met the remediation standard. If a sample result is reported as an estimated value and that concentration is at or below the remediation standard the standard will have been met, Sample results reported as undetected (less than the detection limit, provided the limit is at or below the standard) will have met the standard.

Additional guidance on the treatment of PQL/MDL data and issues in site-specific risk evaluation are available in the EPA *Guidance for Data Useability in Risk Assessment (Part A)* (EPA 1992), the *Risk Assessment Guidance for Superfund*,

Volume I, Part A (EPA 1989), and the EPA ProUCL statistical software technical guide (EPA 2010).

2. Analytical Issues

- Identify the analytical methods used that are the basis of the PQL
- Provide all relevant QA/QC information from the laboratory sheets for the analyses in question including data quality assessment and summaries provided by the laboratory.

When reviewing the proposal DEQ will evaluate whether the data quality assessment and QA/QC accompanying the analytical results adequately explain and support the PQLs proposed. Generally, PQL proposals should be based on PQLs derived from undiluted samples. Elevated PQLs resulting from sample dilution are typically the result of an attempt to quantitate all the COI when the concentrations of one or more chemicals (some of which may not be COI) are highly elevated, often referred to as matrix interference.

Matrix interference can also occur due to the nature of the media (soils in particular) which can impair the quantitation of a COI. The matrix spike and matrix spike duplicate portions of the laboratory QA procedures can sometimes clarify whether there are matrix interferences and whether they are causing over or underestimation of actual concentrations of a COI.

3. Sampling

- Provide information on the number of sampling events completed to support the PQL proposal.
- Provide information on the sampling procedures and QA/QC measures implemented during each of the sampling programs undertaken at the release site. Copies of quality assurance project plans and evaluations of adherence to and departure from those plans for the site in question for each event should be included.

The owner/operator may select alternative sampling procedures, which may provide for a lower PQL. The PQLs for analysis of air and vapor samples can be dramatically affected by the volume of air which is sampled.

DEQ will review the proposal for use of a specific PQL as a remediation standard as part of the overall CAP and approve or deny the request along with specifying any conditions of approval or reasons for denial.

References

EPA (U.S. Environmental Protection Agency). 1989. *Risk Assessment Guidance for Superfund, Volume 1, Human Health Manual (Part A)*. United States Environmental Protection Agency. EPA/540/1-89/002.

EPA (U.S. Environmental Protection Agency). 1992. *Guidance for Data Useability in Risk Assessment (Part A)*. United States Environmental Protection Agency. 9285.7-09A.

EPA (U.S. Environmental Protection Agency). 1999. *Compendium of Methods for the Determination of Toxic Organic Compounds in Ambient Air, Second Edition*. United States Environmental Protection Agency. EPA/625/R-96/010b.

EPA (U.S. Environmental Protection Agency). 2001. *The Relationship Between SW-846, PBMS, and Innovative Analytical Techniques*. United States Environmental Protection Agency. EPA 542-R-01-015.

EPA (U.S. Environmental Protection Agency). 2006. Method 8260C. Volatile Organic Compounds by Gas Chromatography/Mass Spectrometry (GC/MS), Revision 3, August 2006 in *Test Methods for Evaluating Solid Waste, Physical/Chemical Methods*. United States Environmental Protection Agency. SW-846.

EPA (U.S. Environmental Protection Agency). 2007. Method 8270D. Semivolatile Organic Compounds by Gas Chromatography/Mass Spectrometry (GC/MS).), Revision 4, February 2007 in *Test Methods for Evaluating Solid Waste, Physical/Chemical Methods*. United States Environmental Protection Agency. SW-846.

EPA (U.S. Environmental Protection Agency). 2010. *ProUCL Version 4.1.00 Technical Guide (Draft), Statistical Software for Environmental Applications for Data Sets with and without Nondetect Observations*. United States Environmental Protection Agency. EPA/600/R-07/041.

EPA (U.S. Environmental Protection Agency). 2011. *Test Methods for Evaluating Solid Waste, Physical/Chemical Methods*. United States Environmental Protection Agency. SW-846. Update IV of the Third Edition. Available at: http://www.epa.gov/epawaste/hazard/testmethods/index.htm

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Appendix L: Quality Assurance Project Plan Template

This appendix provides an example of the elements and general description of the content that should be included in a Quality Assurance Project Plan. It was current as of July 2012. Please contact DEQ to obtain a copy of the most current version.

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State of Idaho
Department of Environmental Quality

Quality Assurance Project Plan

Idaho Department of Environmental Quality

Title: **Enter the title of your project here**

Region/Division: Enter the name of the applicable Region or Division

Revision # Enter the document revision number. This number should increase by 1 each time the document is revised and approved.

Date: mm/dd/yyyy This date should be reasonably close to the final approval signature date

TRIM Record Number: To be filled in by staff member who enters document into TRIM

REC 4851

TR 1536

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THE INFORMATIONAL TEXT CONTAINED ON THE NEXT FEW PAGES (UP TO "SECTION 1 – TITLE AND APPROVAL PAGE") IS INTENDED FOR USE BY STAFF TASKED WITH GENERATING A NEW PROJECT QAPP, AND SHOULD BE DELETED FROM THE DOCUMENT PRIOR TO FINALIZATION.

Example/Template QAPP – Rev 1.2 – 01/13/2012

The following few pages contain important information and general instructions for all Department of Environmental Quality (DEQ) personnel assigned the task of generating, reviewing, or approving a DEQ Quality Assurance Project Plan (QAPP). A thorough understanding of these instructions will expedite the QAPP development process, and all personnel involved in these tasks are highly encouraged to read these pages prior to initiating the process. Before submission of the QAPP for approval, these four pages of instructional notes should be deleted, including this page and all the following pages up to Section 1 – "Title and Approval Page".

All DEQ staff involved in generating a project QAPP are also strongly encouraged to read the current revision of the DEQ Quality Management Plan (QMP), and the "EPA Guidance for Quality Assurance Project Plans, EPA QA/G-5" document, which explains each section of a project QAPP in more detail. These two documents can be accessed via hyperlinks located on the Inside DEQ Intranet "Quality Assurance" page, and on the last page of these instructions.

This document is intended to be both an example QAPP, and a template for use, by those who need to author a DEQ project QAPP. The format of this document is designed to comply with the DEQ Quality Management Plan, and to meet the minimum quality system requirements as established by the EPA. Previous versions of the DEQ QAPP outline should no longer be used.

In order to ensure progressive QAPP document improvement across the agency, the latest version of this example/template QAPP should be obtained from the DEQ intranet each time that a new project QAPP is to be developed. Through the incorporation of feedback and input from project personnel, this example/template QAPP will continue to improve over time.

The text in this document, which is highlighted in grey, is considered example language which must be revised and edited as necessary to reflect the needs of the actual individual project for which the new QAPP is being written. Text in this document that is NOT highlighted in grey is considered language that is critical to meeting the minimum intent of the DEQ QMP. Much of this non-highlighted language is expected to be applicable to most DEQ QAPP's. If the non-highlighted text is edited to satisfy specific project requirements, the revision must address the intent of the original text in an equivalent or superior fashion.

The format (Sections 1 through 25) of this document shall not be changed, as it is specifically designed to comply with the DEQ QMP, and to meet current EPA requirements. Please also note that all sections in the included outline must be filled out, leaving no blank sections. If a section is not applicable to the project, an explanation of why that section is not relevant is required.

REC 4853

TR 1538

Through the use of this example/template QAPP, rather than a blank template, the individual project author will have the opportunity to use portions of the existing language that are applicable to their project. This example/template document is based on a Nitrate Priority Area QAPP, originally authored by the Boise Regional Office, and further enhanced by the Idaho Falls Regional Office. The example language serves to illustrate the level of detail necessary for a typical DEQ project QAPP.

Use of this example/template QAPP is intended to make the process of creating a new DEQ project QAPP simpler, more robust, and increasingly uniform throughout the agency. For additional guidance on what information should be included in each section of the example/template QAPP, please refer to the "EPA QA/G-5 Guidance for Quality Assurance Project Plans" document, which explains each section in more detail.

Please note that this example/template QAPP is not intended to be an "off-the-shelf" completed project QAPP. It is intended as an aid for QAPP development, and to help ensure a level of consistency across the agency. While it is not possible to develop an example QAPP that will satisfy the detailed needs of all projects which may arise in the performance of DEQ project work, the provided example language will guide project personnel in their efforts to produce an acceptable QAPP.

This example/template QAPP is also based upon the assumption that the project for which a QAPP is being developed uses a laboratory to analyze samples. Not all DEQ projects gather samples in the process of gathering project data. In cases where only data is gathered, some portions of the non-shaded language may not be applicable, and should be removed. However, please remember that no section can be left blank. If a section is not applicable to the project, an explanation of why that section is not relevant is necessary.

For projects requiring the use of existing data, DEQ QAPP authors should follow the steps outlined in Chapter 3 of the EPA "Guidance for Quality Assurance Project Plans" document (EPA QA/G-5).

As mentioned previously, this document will be revised on a regular basis, based on input from Regional and State Office staff. The DEQ will also be revising the entire DEQ Quality Management Plan (QMP), based on comments received from the EPA during the September 2011 Quality System Review (QSR) of the DEQ quality assurance program.

The DEQ QMP revision process will involve frequent consultation with the EPA, and will likely result in several changes to the current program. During this transitional period, the example/template QAPP may occasionally be revised to reflect the most significant changes made to the overall DEQ quality system.

Suggestions for improvement of this document, which meet EPA requirements, are highly encouraged. Please bring all suggestions to the attention of the DEQ Quality Assurance Director.

REC 4854

TR 1539

To help alleviate confusion with respect to the general roles of various project personnel, please refer to Table 2 of the example/template QAPP for an in-depth description of these roles and responsibilities.
The following links contain resources that will provide helpful information and guidance to all DEQ personnel tasked with generating a project QAPP. The first link provided below will bring the user to the "Quality Assurance" area of the "Inside DEQ" Intranet Page.

For DEQ personnel tasked with writing a project Quality Assurance Project Plan, the **EPA QA/G-5 Guidance document** provides clear and detailed explanations on how to fill out the required sections. This example/template QAPP only provides the framework for a project QAPP, the bulk of the information must be supplied by the author of the QAPP. The EPA QA/G-5 guidance document will be of significant assistance to the QAPP author, and use of that document (see link below) is highly recommended.

Link to the DEQ intranet page which provides several links to the major EPA and DEQ QA System documents:
http://insidedeq.deq-intra/director/quality.htm

Link to the "DEQ Quality Management Plan" (QMP):
This document describes the overall quality assurance system used by the DEQ. It provides the general description of how the DEQ quality assurance system functions, what the elements of the system are, and basic requirements for DEQ quality system documents.
http://insidedeq.deq-intra/director/quality/quality_mgmt_plan_07.pdf

Link to the EPA "Guidance for Quality Assurance Project Plans" (EPA QA/G-5) document:
In conjunction with the DEQ QMP, this document provides detailed guidance to project personnel with respect to how to write a project QAPP.
http://www.epa.gov/quality/qs-docs/g5-final.pdf

Link to the EPA page listing several resources related to writing a project QAPP:
http://www.epa.gov/quality/qapps.html

Link to the EPA Agency-wide quality system document resource page:
http://www.epa.gov/quality/qa_docs.html

Link to the EPA Quality System main page:
http://www.epa.gov/quality/

Note that for most of the EPA "Requirement" documents, there is a companion EPA "Guidance" document. These guidance documents generally have the same title as the requirements document, but have the letter "G" rather than "R" associated with their title. The EPA has may other quality system guidance and requirement documents, all of which can be easily found at the EPA Quality System main internet page (see link above).

(Links verified operational on 1-13-2012)

REC 4855

TR 1540

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1. Title and Approval Page

Quality Assurance Project Plan

Title: Enter the title of your project here
Region/Division: Enter the name of the applicable Region or Division
Revision # Enter the document revision number. This number should increase by 1 each time the document is revised and approved
Date: mm/dd/yyyy This date must be the same as that used on the cover page and header. This date should be reasonably close to the final approval signature

Approval Signatures
Note: This QAPP becomes effective on the date of the last approval signature

DEQ Quality Assurance Director

Signature: *(If Required – See QAPP instruction pages)* _____
Name: Mark K. Clough, Quality Assurance Director, State Office Date

Program/Regional Manager

Signature: _____ _____
Name: Staff Name, Position, Office/Region Date

Project Quality Assurance Officer

Signature: _____ _____
Name: Staff Name, Position, Office/Region Date

Project Manager

Signature: _____ _____
Name: Staff Name, Position, Office/Region Date

Project Technical Lead / Author

Signature: _____ _____
Name: Staff Name, Position, Office/Region Date

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REC 4858

TR 1543

2. Table of Contents

The Table of Contents (Below) must be updated following the completion of the new QAPP.

This can easily be accomplished using Microsoft Word, through use of the following steps:

1. After the draft project QAPP has been completed, open the document in Microsoft Word 2010
2. Print this page so that you have these directions (if needed), then delete these shaded "table of contents directions" so that they will not be included in your newly created table of contents.
3. Using the mouse, single left click the table of contents, which will turn the table grey.
4. After a few seconds, a tab with the words "Update Table" on it will open at the top of the table of contents.
5. Click on the "Update Table" tab, and then select the "Update Entire Table" option.
6. Click "OK", and the table of contents will immediately update.
7. Click anywhere in the document, outside the table of contents, and the table of contents update procedure will be completed.

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3. DISTRIBUTION LIST

The following personnel and analytical laboratory contacts, at a minimum, will receive either an electronic copy or a hard copy of the final signed QAPP:

Table 1: Project QAPP distribution list.

Name	Project Affiliation	Organization and address/location	Contact Number
Mark K. Clough	DEQ Quality Assurance Director	Idaho DEQ – Directors Office	208-373-0528
Name	Program Manager	Idaho DEQ	###
Name	Project Quality Assurance Officer	Idaho DEQ	###
Name	Project Manager	Idaho DEQ	###
Name	Project technical Lead	Idaho DEQ	###
Contact Name	Analytical Laboratory	Laboratory Name	###
Contact Name	Analytical Laboratory	Laboratory Name	###
Contact Name	Analytical Laboratory	Laboratory Name	###

REC 4861

TR 1546

4. PROJECT/TASK ORGANIZATION

Table 2: Key project personnel and associated responsibilities.

Name	Project Title/Responsibility
Name of assigned DEQ Staff	**Program Manager:** This person is the regional manager or state office program manager who will assist in the development, review, and approval of the project QAPP. Responsible for ensuring that the project QAPP is designed to meet the data needs of the program, and references current approved program procedures and policies. The Program Manager will also select a qualified Project Quality Assurance Officer, and after obtaining approval for this selection from the DEQ Quality Assurance Director, assign this individual to the project. This process is designed to enhance impartiality, and to ensure the accuracy of the authorized Project QA Officer list maintained by the DEQ Quality Assurance Director.
Name of assigned DEQ Staff	**Project Quality Assurance Officer**: Each project is to have an assigned Project QA Officer (QAO). This person will assist in the development, review, and approval of the project QAPP, and project related documents such as Field Sampling Plans (FSPs). The Project QAO will perform periodic project reviews/audits in accordance with the DEQ QMP, and provide data verification and validation per the project QAPP and FSP. The Project QA Officer may also be part of the review team for project final reports. In matters of project quality assurance, this individual will have a direct line of communication to the DEQ Quality Assurance Director. Per EPA requirements, the Project QA Officer shall review the QAPP annually, to determine if revision is necessary. The Project QA Officer shall not be the Project Technical Lead, the Project Manager, the Program Manager, or be otherwise assigned to the project data generation efforts. Neither the Project Manager nor the Project Quality Assurance Officer may directly report to the other within the DEQ organizational structure, and both of these individuals may not be directly supervised by the same person. All assigned Project QA Officers shall, prior to signing for the approval of any project QAPP, contact the DEQ Quality Assurance Director to discuss the project. At that time, the DEQ QA Director shall also verify that the assigned Project QA Officer is on the authorized Project QA Officer list. This process is designed to ensure that all DEQ QAPPs are approved, and issued, in accordance with the DEQ Quality Management Plan.

REC 4862

TR 1547

Name	Project Title/Responsibility
Name of assigned DEQ Staff	**Project Manager:** This person is responsible for overall project planning, document development and approval, sample planning and coordination, laboratory coordination, data review and verification, reporting functions, project report/summary development, and documentation of all project activities in the TRIM system and elsewhere as required by the project documents. Responsible for ensuring all project work is conducted in accordance with the DEQ QMP, and the approved project QAPP and associated FSPs. The Project Manager is responsible for ensuring that personnel assigned to this project are appropriately trained and qualified, with the corresponding training records on file in Human Resources. This individual will also perform periodic project reviews/audits in accordance with the DEQ QMP, and provide data verification and validation per the project QAPP and associated FSPs. The Project Manager may also be part of the review team for project final reports. The Project Manager shall review the project QAPP annually, and determine if revision is necessary. If the QAPP does require revision, the revised QAPP must be submitted for approval prior to implementation, per the DEQ QMP.
Name of assigned DEQ Staff	**Project Technical Lead**: This individual is to be familiar with the technical aspects of the project, and is assigned by the Program / Project Manager to be the technical lead and to assist in the development of the project specific QAPP. This individual should have experience in the methods, procedures, and equipment to be employed in the conduct of the work described in the QAPP. Also responsible for Coordination with sample location contacts, management of day-to-day aspects of sampling; planning, data collection, sample handling, coordination with the labs for sample shipping and analysis, receipt of resulting data, and data review and verification per the approved project QAPP and associated FSPs. This individual should be familiar with the information contained in the EPA Guidance for Quality Assurance Project Plans, EPA QA/G-5 document.
Name of assigned DEQ Staff	**Laboratory Contact/Manager**: Laboratory sample receipt, analysis, and laboratory data review.

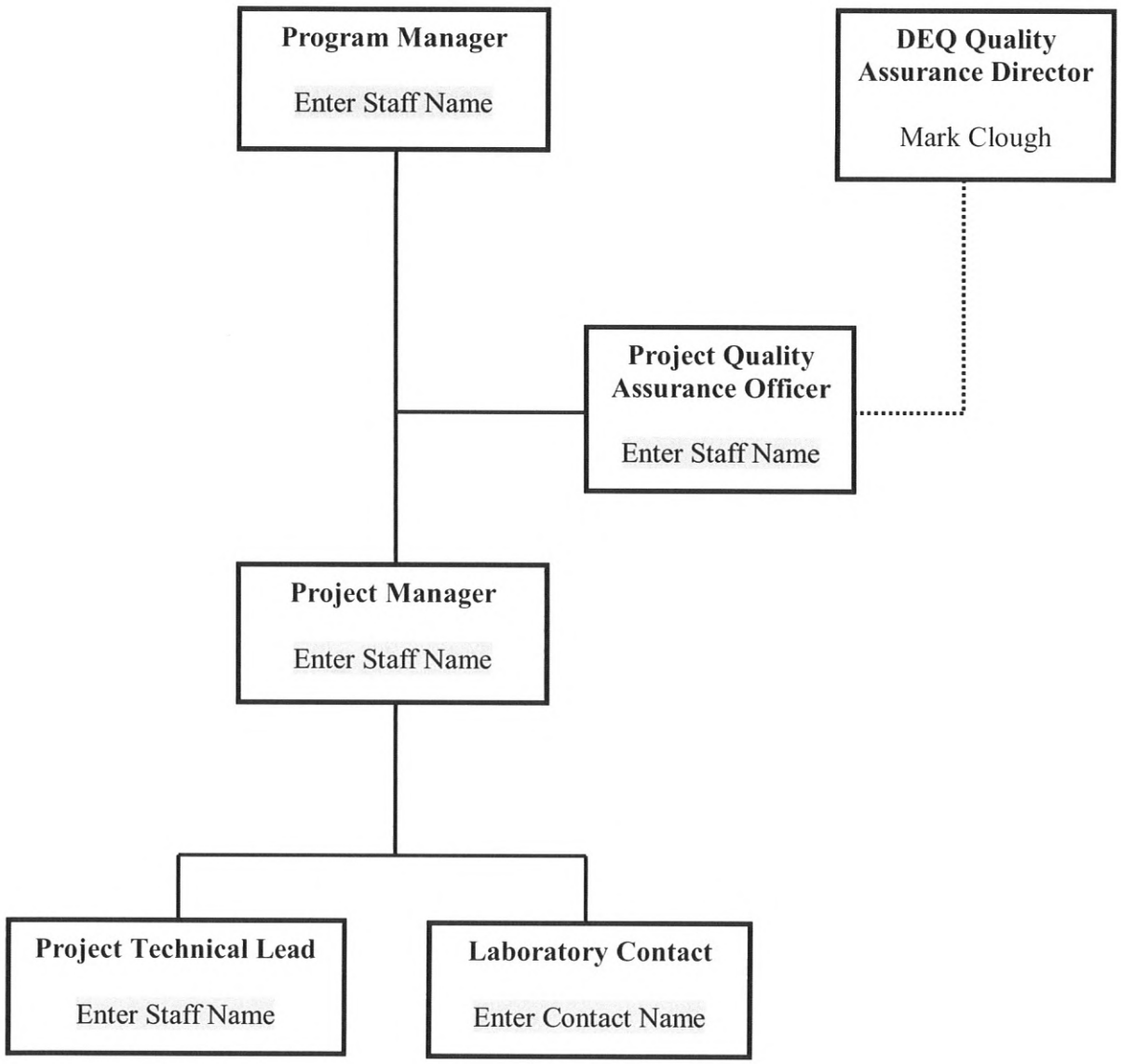

Figure 1: Project organizational chart

REC 4864

TR 1549

5. PROBLEM DEFINITION/BACKGROUND

A. Problem Statement

The Idaho Department of Environmental Quality (DEQ) is responsible for conducting regional ground water monitoring activities, per the Idaho Ground Water Quality Plan. The DEQ Idaho Falls Regional Office (IFRO) develops monitoring projects to investigate regional ground water quality issues. These issues can be the result of local public concern, regional office priority, or State-wide Departmental emphasis. Regional projects may include nitrate source or trend-related investigations focusing on Nitrate Priority Areas (NPAs), and sampling to address specific local concerns such as arsenic. The DEQ regional office is also charged with facilitating drinking water source protection. Projects may include sampling to support protection implementation strategies.

The overall rational for regional nitrate monitoring activities is to address DEQ's responsibilities under the Ground Water Quality Plan, summed up as to provide ground water monitoring data that will aid in:

- identifying areas of high vulnerability
- assess concentration trends in areas of degraded ground water quality
- identify, delineate, and explain sources of variability and degradation at regional and local levels,
- informing, directing, and prioritizing ground water protection programs and efforts, and
- Providing a means of evaluating effectiveness of best management practices, improving these best management practices, and to support regulatory decisions.

This Quality Assurance Project Plan (QAPP) provides a framework for data collection to identify potential sources of impact to ground water within the region. More specifically, this QAPP includes elements consistent for ground water monitoring events focusing on identifying potential sources of nitrate impacts to drinking water sources, primarily ground water. Nitrate-related sampling campaigns shall reference this QAPP, and include a Field Sampling Plan (FSP) detailing specific objectives, analytes, sampling strategies, pertinent background and sample locations.

REC 4865

TR 1550

B. Intended Usage of Data

The data collected for the Regional NPA Monitoring will be used to determine the nature and extent of ground water contamination due to nitrate. The sample results will be shared with Idaho State Department of Agriculture (ISDA) or other agencies, as necessary, to determine appropriate response activities. All sample results will be entered into the DEQ Ground Water Quality Database and be available through the online mapping application.

Sample results for NPA monitoring will be presented in either an annual DEQ ground water monitoring report or a campaign/project-specific report that will be included in the DEQ Ground Water Technical Report Series. Nitrate data may also be used in the NPA ranking process.

Private well owners will receive a report of analytical data from samples collected from their well. Appropriate data interpretation and recommendations may also be included.

6. PROJECT/TASK DESCRIPTION

A. General Overview of Project

Sampling projects will assess regional and local ground water quality impacts to the public due to the nitrates in ground water. The framework for monitoring to assess regional and local water quality and impacts will be described in a regional nitrate monitoring design document to be developed. A project/campaign-specific description, including network design/site selection will be included in the FSP for each monitoring campaign. Sites will be selected based on a combination of criteria, as pertinent to the specific project, including; well completion depth, location, accessibility, and historic sample results. Random or stratified random selection processes may be employed. Preference may be given to wells representative of sensitive populations and wells screened in the upper-most aquifer or portion of the aquifer. Priority may also be given to previously sampled wells to allow development/evaluation of trends.

Samples may be collected at each location for analysis of one or more of the following, as required for the specific sampling campaign:

- Major cations (e.g. calcium, magnesium, sodium, potassium)
- anions (e.g., nitrate, nitrite, sulfate, chloride, bromide, fluoride and o-phosphate)
- ammonia
- bacteria: total coliform bacteria , E. coli

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- nitrogen isotope ($\delta^{15}N$)
- oxygen/deuterium isotopic ($\delta^{2}H$- $\delta^{18}O$)
- nitrogen and oxygen isotopic for nitrate anion ($\delta^{15}N_{NO3}$, $\delta^{18}O_{NO3}$)
- tritium
- Pharmaceuticals and Personal Care Products (PPCPs)

Sample submission may follow a staged approach to maximize cost vs. diagnostic benefits; for example while samples collected for less costly analyses such as $\delta^{15}N$, and $\delta^{18}O$ may be collected and submitted for all sites, samples for more expensive analyses such as $\delta^{15}N_{NO3}$ and $\delta^{18}O_{NO3}$ or PPCPs may be collected at all sites, but not submitted for analysis unless initial results indicate that such information may confirm contamination sources or geochemical processes are occurring. These tiered analyses may aid in correctly identifying the primary factors to explain contaminant conditions observed. Holding times and sample preservation requirements would allow for this staged approach.

B. Project Timetable

The specific project timetable will be designated for each monitoring project in the FSP.

7. QUALITY OBJECTIVES AND CRITERIA

The objective of quality assurance and quality control (QA/QC) is to assure that analytical results obtained by sample analyses are representative of actual chemical and physical compositions of the ground water. Field QA/QC will consist of following a standard protocol for sample collection and by collecting and analyzing sample duplicates and field blanks. The duplicates will be used to determine both field and laboratory precision. The field blank will be used to check the integrity of the sample collection and handling process. Both the duplicate and field blank samples are stored and handled with the normal sample load for shipment to the laboratory. Project goals and sampling conditions may require additional field QC samples, including equipment blanks or spiked samples. Field QC samples will be submitted "blind". Ideally, at least one set of field quality assurance samples will accompany each sample shipment or analysis batch.

Field QC samples will comprise at least 10% of all samples with a goal of 20% QC samples.

Field screening data (e.g., field parameters of pH, temperature, specific conductivity, and dissolved oxygen) are at data quality Level I (field parameter/ screening level data). Laboratory analytical data (i.e., data from samples submitted to a laboratory for analysis) are at data quality Level III (standard laboratory procedures and data reviewed by standard Quality Assurance protocols). Specific data quality objectives or requirements will be included in the FSP if not included in the project QAPP.

A. Data Precision, Accuracy, Measurement Range

Accuracy is a measure of the closeness of the agreement between a "true" or reference value and the associated measured value. A sampling campaign may include spiked samples with a known matrix submitted blind to the laboratory or may rely on reported recoveries for Laboratory Control Samples (LCS). The recoveries of laboratory control samples (LCS), matrix spikes, and surrogate spikes will be used to evaluate the accuracy of the measurements. These recoveries are typically calculated as "percent recovery" represented by the following equations:

Spiked sample or LCS Percent Recovery:

$$\%R = C_M / C_T * 100$$

Where: C_M = Measured spike/LCS concentration
C_T = True spike/LCS concentration

Matrix Spike and Surrogate Recoveries:

$$\%R = (C_S - C_{US}) / C_T * 100$$

Where : C_S = Measured concentration of Spiked Sample
C_{US} = Measured concentration of Un-Spiked Sample
C_T = True Concentration of Spike Added

Laboratory accuracy for each analysis is set by a statistical analysis of the laboratory equipment and the acceptable accuracy range for the laboratory equipment will be indicated in the laboratory sheets. Any outliers from the acceptable range in % Recovery, as determined by the laboratory, will be flagged by the laboratory. Typical accuracy goals will be ± 20%. Accuracy goals will be specified in the FSP if not specified in the QAPP.

Precision is a measure of agreement between two measurements of the same property under prescribed conditions. Sampling campaigns may include duplicate samples (field replicates or split samples) or may rely on LCS split sample results. The Relative Percent Difference (RPD) of duplicate samples will be used to assess data precision. For laboratory duplicates, field duplicates and matrix spike duplicates, the following equation will be used to calculate Relative Percent Difference (RPD):

$$RPD = \frac{(C_1 - C_2)}{(C_1 + C_2) / 2} * 100$$

Where: C_1 = Concentration in first sample
C_2 = Concentration in the second/duplicate sample
Where both C_1 and C_2 > 5 times the laboratory Method Detection Limit (MDL).
Where one or both C_1 and C_2 are less than 5 times the MDL, the results will be considered within control limits where C_1 and C_2 are ± MDL.

For radiological samples, such as tritium, precision will be assessed by RPD where both results exceed 5 times the MDL, otherwise results will be considered within control limits when within 3 times Pooled Standard Error (PSE):

$$PSE = /R_1-R_2/ \leq 3(S_1^2 + S_2^2)^{1/2}$$

Where:

R_1 = concentration in first sample
R_2 = concentration in second/duplicate sample
S_1 = analytical uncertainty (counting error associated with laboratory measurement of the first sample)
S_2 = analytical uncertainty (counting error associated with laboratory measurement of the duplicate sample)

The goal for precision and what that precision will be based on for each sampling campaign will be included in the FSP if not included in the QAPP. In general, precision will be based on field duplicates with a goal of ± 20%.

Appropriate **Measurement Range** is determined by reviewing results with comparison to the laboratory reporting levels/MDL. Reporting requirements are determined prior to sampling through review of historical data for the analytes and region of interest, and reflected in choice of analytical laboratories, analysis methods and requested reporting levels/MDL. Assessment criteria and goals will be described in the FSP if not included in the QAPP.

B. Data Representativeness

Representativeness is defined as the degree to which the sample data accurately and precisely represent site conditions. The representativeness criterion is best satisfied by confirming that sampling locations are properly selected, sample collection procedures are appropriate and consistently followed, a sufficient number of samples are collected, and analytical results meet data quality objectives. All sampling procedures will follow the sampling procedures in the sampling protocol in Appendix A. Representativeness is evaluated by comparing the combination of data accuracy, precision, appropriate measurement range and methods, and assessing other potential sources of bias; including sample holding times, blank samples, and laboratory quality assurance review. Any additional specific assessment criteria and goals will be described in the FSP if not included in the QAPP.

C. Data Comparability

Comparability is defined as the confidence with which one data set can be compared to another data set. Using standard sampling and analytical procedures will maximize

comparability. In an effort to ensure data comparability, sample collection protocols (included in Appendix A) will be consistently followed, the same analytical procedures will be used, and the same laboratory will be used to analyze the samples throughout each project. The FSP for each project will include the laboratory to be used for each analyte.

D. Data Completeness

Completeness is defined as the percentage of valid data relative to the total possible data points. For data to be considered valid, it must meet all of the acceptance criteria, including accuracy and precision, as well as any other criteria specified by the analytical method used. The overall data quality objective for completeness for the sampling events conducted under this QAPP is 80%. Any required departure from this goal will be justified and explained in the FSP.

8. SPECIAL TRAINING/CERTIFICATION

The Project Manager and/or Program Manager is responsible for ensuring that personnel assigned to this project are appropriately trained and qualified, with the appropriate training records on file in DEQ Human Resources.

All work performed by DEQ personnel will be conducted in accordance with the State of Idaho Worker Health and Safety Plan.

No special training for ground water sample collection is required; staff will have previous ground water sampling experience and on-the-job training.

9. DOCUMENTATION AND RECORDS

Project documents will be filed electronically in TRIM, in accordance with applicable program filing procedures. The Project Manager is responsible for ensuring that the most current approved revision of the project QAPP, with related FSPs and SOPs, is available in the DEQ TRIM electronic records management system.

Field personnel will document each day's activities in field notes. Information is to be recorded as follows:

- Project data must be recorded directly, promptly, and legibly.
- Field logbook or field sheet entries must be made in black or blue permanent ink and must be signed/initialed and dated by the person making the entry.
- Changes or corrections to data must be indicated with a single line through the original entry.
- Changes must be initialed, dated, and explained.

In addition to field notes (as identified in Appendix B at a minimum), documentation is to include all data used to develop the monitoring network, well sampling permission documentation, a sampling procedures document, the reports summarizing the sampling events and results.

10. SAMPLING PROCESS DESIGN

A. Rationale for Selection of Sampling Sites

The nitrate priority area monitoring network will consist of existing private domestic, irrigation or public water system wells that are selected following the protocol (to be developed) for the IFRO Regional Ground Water Monitoring Network Design. Sampling frequency, where not described in the regional ground water monitoring design document, will be described in the associated FSP. The specific FSP will identify the number of sample locations and specify analytes, collection and analysis requirements, special handling or follow-up criteria and reporting requirements. Permission from the well owner will be obtained prior to sampling each well.

B. Sample Design Logistics

Sampling logistics will be identified in the specific monitoring campaign FSP if not identified in this QAPP.

11. SAMPLING METHODS

QA/QC procedures as specified for sample collection will be followed by sampling personnel. The QA/QC procedures will be fulfilled by adhering to all requirements detailed in this QAPP and the ground water sampling procedure located in Appendix A of this QAPP. Such adherence will be demonstrated through appropriate documentation of sampling procedures within the field logbook or field sheets as described herein. Field audits by the Project QA Officer may also be part of QA/QC procedures.

Samples collected from private domestic wells, irrigation or public supply wells will utilize the existing pump and distribution system. Water samples will be collected from a faucet or sample port nearest the well and before any treatment system. Samples collected from monitoring wells will utilize a submersible pump, peristaltic pump, or disposable bailer. If a pump is used, dedicated or disposable tubing will also be used. Equipment blanks may be included with the complement of quality assurance samples.

A portable meter will be used to measure pH, specific conductance, dissolved oxygen, and temperature at each sample location. A GPS will be used to determine the longitude and latitude of the well/sampling point.

Field work quality will be controlled by following standard sampling protocols (Appendix A) during each sampling event, using consistent sampling containers and laboratories, and collecting sample duplicates and blanks. Protocols for items such as equipment decontamination, chain of custody forms, sample blanks, etc, are found in Appendix A, and further detailed in the project FSP. Detailed field notes will be taken for quality control and proper sample identification.

Analytes, laboratories, shipping addresses, and current contract numbers as appropriate are included in Table 3. Analytical methods, sample container, preservation and holding times are identified in Section 13 and Table 4.

Table 3: Analytes, laboratories, and contract numbers.

Analytes	**Preferred analyzing Laboratory**	**Shipping address**	**DEQ Contract number**
Major anions, Major cations, nutrients	State of Idaho Bureau of Laboratories	2220 Old Penitentiary Rd Boise ID 83712	MOA
Bacteria: Total Coliforms, E. Coli	IAS-EnviroChem	3314 Pole Line Road Pocatello, ID 83201	Vendor
Stable isotopes: ^{15}N, ^{18}O, ^{2}H	University of Arizona Environmental Isotope Geosciences Laboratory	Department of Geosciences Gould-Simpson Building Tucson, AZ 85721-0077	C515
tritium	Idaho State University Environmental Monitoring Laboratory	Department of Physics 785 Sth 8th Bldg3 RmB107A Pocatello, ID 83209	research partner
Stable isotopes: $^{15}N_{NO3}$, $^{18}O_{NO3}$	University of Waterloo Environmental Isotope Laboratory	UwEILAB C/O Chemistry Stores University of Waterloo 200 University Ave. W. Waterloo, ON Canada N2L 3G1	(Update)
Stable isotopes: ^{15}N, ^{18}O, ^{2}H, $^{15}N_{NO3}$, $^{18}O_{NO3}$	Northern Arizona University Colorado Plateau Stable Isotope Laboratory	Northern Arizona University CPSIL/CPAL Room 108 115 W Dupont Ave Building 88 Flagstaff, AZ 86011 Tel: 928-853-1983	Vendor

Analytes	Preferred analyzing Laboratory	Shipping address	DEQ Contract number
Pharmaceuticals and Personal Care Products (PPCPs)	(Appropriate Laboratories and contacts will be developed as needed)	(Update)	(Update)

12. SAMPLE HANDLING AND CUSTODY

Samples will be collected by DEQ personnel into laboratory-supplied sampling containers, labeled, placed in an ice-chilled cooler and transported directly to the laboratory or shipment location. Samples collected for $^{15}N_{NO3}$ and $^{18}O_{NO3}$ analysis will be frozen at DEQ until the chemistry and other stable isotope results from the sample location are received and reviewed.

Where analytical results for a sample location exceed 5 mg/L, and/or supporting results suggest chemical evolution of nitrogen in groundwater samples collected for $^{15}N_{NO3}$ and $^{18}O_{NO3}$ analysis may be sent to University of Waterloo EIL or Northern Arizona University CPSIL for analysis. DEQ personnel will oversee proper storage and handling of all samples collected until transferred into the care of others. Properly filled out chain of custody forms will be used and maintained at all times. Protocols for chain of custody forms, sample handling, etc, are found in Appendix A, and further detailed in the project FSP. Chain of custody forms will accompany the samples from the time of sample collection throughout the duration of the shipping process.

13. ANALYTICAL METHODS

All sample containers, labels, and preservatives will be obtained from the analytical laboratory. Samples must be preserved and analyzed within the holding times. The laboratory will be notified prior to sample shipment to ensure the holding time is not exceeded. All other instructions provided by the analytical laboratory will be followed throughout the duration of each project.

Table 3 lists analytical laboratories for the NPA monitoring projects, including the potential parameters to be analyzed by that laboratory and the location of the laboratory. Samples may be sent to other laboratories as needed to achieve specific sample campaign objectives. In general, samples for major ion/common ion chemistry and nutrients will be sent to Idaho Bureau of Laboratories, Boise; bacteria to IAS-Envirochem, Pocatello; and environmental-level tritium to Idaho State University EML. Stable isotope analysis may be sent to one or more laboratories based on factors including proven quality of results, timeliness of result

receipt, cost, and convenience. Inter laboratory comparisons may be conducted to determine long-term laboratory choices. Initially, the University of Arizona Environmental Isotope Laboratory will be used for ^{15}N, ^{18}O, ^{2}H analysis. A selection of samples for $^{15}N_{NO3}$, $^{18}O_{NO3}$ will be sent to University of Waterloo EIL, with comparison samples sent to Northern Arizona University CPSIL for analysis and method comparison. Future analysis result comparisons for ^{15}N, ^{18}O, and ^{2}H may also be made between University of Arizona and Northern Arizona University.

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Table 4: Analytical method, container, preservation and sampling holding times.

Sample	Parameter	Analytical Method	Sample container	Preservative	Holding Time
Major cations	Ca, Mg, Na, K,	EPA 200.7	1 L LDPE	HNO_3, 4^0 C	6 months
Major anions	Cl, F, SO_4,	EPA 300.0	1 L LDPE	4^0 C	28 days
	Alkalinity (as $CaCO_3$)	SM2320B		4^0 C	14 days
	Total Dissolved Solids	SM2540C		4^0 C	7 days
Nutrients	NO2+NO3-N	EPA 353.2	1 L LDPE	H_2SO_4, 4^0 C	28 Days
	Ammonia	EPA 350.1		H_2SO_4, 4^0 C	28 Days
	Ortho-phosphorus	SM 4500P-E		H_2SO_4, 4^0 C	28 Days
Tritium	Low-level tritium	HASL 300	1 L HDPE	None	180 days
bacteria	Total Coli form, E. Coli bacteria	9223B	120 ml polystyrene	4^0 C	30 hours
Stable isotopes	^{15}N	TP11	1 L LDPE	Freeze samples	Unlimited if frozen
	$^{15}N_{NO3}$, $^{18}O_{NO3}$	Carlo Erba[2] 1500 EA, VG PRISM, Denitrifying[2] bacteria	2L LDPE[2], 60 ml x2 HDPE[2]	Freeze samples[2], Filter and freeze[2]	56 days[1], Unlimited[2]
	^{18}O	TP13	250 ml HDPE	None	None
	Deuterium	TP04		None	None
PPCPs	(Specific parameter, analysis methods and sampling requirements will be identified as needed)				

[1] Waterloo EIL
[2]Northern Arizona University CPSIL

14. QUALITY CONTROL

A. Field QC Checks

Field QC samples, typically duplicates and blanks, will be submitted blind (not identified as a QC sample) for analysis. The overall field QC frequency will be at least 10% of the sample load. Submission of QC samples will be scheduled to ensure that at least one QC sample set will be included with each batch of samples submitted to the laboratory. Field QC checks are to be as evenly distributed as project conditions allow between duplicates, blanks, and spikes.

Duplicates

Duplicate samples are two samples collected from the same location and representing the same sampling event and are carried through all assessment and analytical procedures in an identical manner. Duplicate can be "replicates" (samples taken one immediately after the other, separated only be the actual time required to fill the sample container), or "splits" (subsamples drawn from the same initial volume of matrix). The FSP will describe the method for obtaining duplicate samples. Field sampling procedures outlined in Appendix A will also be followed for each of the sampling events to ensure consistency in sample collection. All relevant information will be recorded for the duplicates in the field logbook or field sheet. The duplicates will allow assessment of repeatability and accuracy of the sampling procedures and will also be used to assist in assessment of any cross-contamination issues. Results from the field duplicate analysis will be presented in the analytical report.

Field and Equipment Blanks

A blank is a sample of known matrix where the specific constituents requested for analysis are known to not be present, or are present at concentrations less than the laboratory lower limit of detection.

Field blanks are samples of blank matrix, typically deionized water, prepared in the field under similar conditions, processed the same as and included for analysis as a regular sample. Field blanks are a quality control check to identify potential problems with the sample collection, handling and analysis process. Equipment blanks are blank sample matrix passed through or over non-dedicated sampling equipment to check the decontamination process between samples or sample sites.

Equipment blanks may be collected when sampling equipment requiring decontamination (portable pumps, sampling manifolds, ect.) are carried from well to well. Equipment

blanks when collected, will also be submitted blind for analysis and may be included in the overall 10% QC sample calculation.

Field spikes
Samples from a third party vendor that include a known concentration of analytes of concern may be submitted blind to the analyzing laboratory. These "spiked" samples may be included in the sample load to allow for an independent accuracy assessment or for inter laboratory comparisons. Due to the added cost of procuring or preparing field spike samples these may not be included with all sampling campaigns. Use of spiked samples will be described in the FSP.

B. Laboratory QC Checks

Laboratory quality control checks are routinely performed as part of the analysis process. Frequency and type of QC samples are often analysis method-dependent and include reagent blanks, matrix spikes, and internal laboratory splits. Analyzing laboratories will report any variance from QC control limits impacting quality of sample results and may report details of internal laboratory QC if requested. The analytical laboratory may provide appropriate sample containers, chain of custody forms, sample labels, and any necessary container seals. Laboratory QA/QC and data reports will be filed in TRIM following applicable filing protocols.

Quality control checks include internal checks for sampling analysis activities, duplicate samples and blanks. Quality Control procedures for the laboratories have been certified through the U.S. Environmental Protection Agency. The following list documents key components of the laboratory QA/QC program for this project.

Laboratory Blanks

A laboratory blank is a sample of an uncontaminated reference matrix. The laboratory blank is analyzed to evaluate the accuracy of the analysis.

Laboratory Quality Control Samples
Laboratory control samples (LCSs) are samples that contain a known concentration of analytes and are analyzed to assess the overall method performance. They undergo the same preparatory and determinative procedures as the project environmental samples and are the primary indicator of laboratory performance. LCS recoveries are used to measure accuracy. The relative percent difference (RPD) for duplicate LCS recoveries is used to measure precision.

Laboratory Duplicate Sample

A laboratory duplicate sample is a sample that is split by the laboratory into two separate and identical samples. The two samples are analyzed and a comparison of the results (RPD) is used to assess laboratory precision.

Matrix Spike and Matrix Spike Duplicate (MS/MSD) Samples
A matrix spike (MS) is a sample with known amount of the target analyte added to project matrix before analysis to assess possible matrix interferences on the analysis. Percent recoveries (%R) on MS samples should be compared to %R of LCS samples. A MS, matrix spike duplicate (MSD) pair can be used to assess precision.

C. Data Analysis QC Checks

The QC check data may be checked/reviewed for quality by the Project Technical Lead, the Project Manager, or the Project QA Officer at any time during the project, and must be checked once all of the data is collected. Corrective actions, as needed, will be documented in the event that control limits are exceeded. Data qualifiers will be assigned following appropriate data verification/validation procedures. Any qualifiers added will be defined in the project summary/technical report and will be consistent with appropriate EPA guidance, EPA QA/G-8.

15. INSTRUMENT/EQUIPMENT TESTING, INSPECTION, AND MAINTENANCE

Laboratory instrument/equipment testing, inspection, and maintenance are performed by and documented by the laboratory as required by or consistent with the State of Idaho laboratory certification process. Procedures and schedules for preventive maintenance of sampling equipment are the responsibility of the laboratory. Each instrument or item of laboratory equipment will be maintained periodically to ensure accuracy. These procedures and frequency of performance are designated in the individual instrument manuals.

Project field instrument/equipment testing, inspection, and maintenance will be performed in accordance with the individual instrument/equipment manual.

16. INSTRUMENT/EQUIPMENT CALIBRATION AND FREQUENCY

Laboratory instrument calibration is conducted, and documented by the laboratories laboratory as required by or consistent with the State of Idaho certification process.

All field monitoring equipment for the measurement of field parameters (temperature, pH, specific conductance, dissolved oxygen) will be calibrated and maintained as recommended by the manufacturer, or as found in individual instrument/equipment manuals, to ensure accuracy within specified limits. Field equipment used to collect samples will be calibrated according to manufacturers' procedures or internal guidelines at the start of each field day (at a minimum) and/or at intervals recommended by the manufacturer or found in individual instrument/equipment manuals. Calibration details will be recorded in the field logbook or field sheet.

17. INSPECTION/ACCEPTANCE OF SUPPLIES AND CONSUMABLES

The equipment and supplies required for monitoring campaigns will be consistent with the included ground water sampling procedure (Appendix A). Sampling equipment and personal protective equipment beyond that listed in the ground water sampling procedure will be documented in the FSP (i.e. if antibiotics or steroids are collected, a face mask will be used). All sample containers may be obtained from the analytical laboratory. All gloves, face masks, and sample containers will be new, and will be used once during each sample collection. Each instrument or item will be calibrated per the individual instrument/equipment manuals, and also visually inspected by field sampling personnel for damage and operability.

18. NON-DIRECT MEASUREMENTS & DATA ACQUISITION

This section addresses data obtained from existing data sources, not directly measured or generated in the scope of this project.

The laboratories shall provide DEQ with a data package that includes the analytical results of the submitted samples, the QA/QC report for the analyses, and a copy of the chain-of-custody record. Laboratories may be requested to provide results and reports in an electronic format.

No other non-direct data is expected to be acquired.

19. DATA MANAGEMENT

Hard copies of field notes and laboratory data reports will be kept at least until data review and reporting is complete. Electronic copies of all field notes and laboratory reports will be kept in TRIM. The analytical results will be uploaded to the DEQ Ground Water Quality

database after review by the Project QA officer and will be available to the public through the DEQ online mapping application.

20. ASSESSMENT AND RESPONSE ACTIONS

Assessment of the project quality control plan will be performed by reviewing field notes and laboratory reports and by conducting field audits where possible. This assessment will be completed or directed by the Project QA Officer. Any errors or inconsistencies identified in the field notes will be investigated and corrected to ensure the integrity of the data and conformation to the QAPP and FSP. Review of internal laboratory quality assurance, audits, and surveillances or other types of laboratory assessments will also be taken into account. If unexpected analytical results are reported for any reason, the laboratory will be contacted to perform an additional quality review of the data in question. The Project QA Officer will perform additional assessment of the plan independently of the Project Manager and sampling lead.

A note to the file will be included with the field notes and laboratory reports if any follow up quality assurance activities regarding field notes or laboratory reports are conducted.

The Project QA Officer shall review the QAPP annually, to determine if revision is necessary. The Project Manager should also review the project QAPP on an annual basis to ensure that the project QAPP continues to meet the needs of the data users. If the project QAPP does require revision, the revised QAPP must be submitted for approval, prior to implementation, per the DEQ QMP.

21. REPORTS TO MANAGEMENT

Sample results for NPA-related monitoring will be presented in either an annual DEQ ground water monitoring report or a site-specific report that will be included in the DEQ Ground Water Technical Report Series.

22. DATA REVIEW, VERIFICATION, AND VALIDATION

Data collected under this QAPP will be reviewed by the Project Manager, Project Technical Lead, and the Project QA Officer to ensure the data has been recorded, transmitted, and processed correctly. RPDs will be calculated for all field duplicates and the laboratory %R and RPDs will be reviewed. Review by the Project QA Officer shall include a minimum of 10 percent of all project data with a goal of 20 percent. This review will include verification/validation to the original laboratory data reports.

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Data verification and validation efforts will be recorded in project documentation.

23. VERIFICATION AND VALIDATION METHODS

DEQ personnel performing data verification and validation are encouraged to review the EPA guidance on methods for this task, found in EPA Guidance on environmental Data Verification and Data Validation, EPA QA/G-8.

Data verification will be performed by the Project Manager and/or Project Technical Lead by reviewing all chain-of-custody sheets, surrogate recoveries, method blanks and LCS and MS sample/sample duplicates to assess %R and range of RPDs. The %R and RPDs will be compared to project goals as described in the QAPP and FSP and an assessment of completeness will be made.

Data validation will be performed by the Project Manager and/or Project Technical Lead, and the Project QA Officer, extending the data evaluation beyond method and procedural compliance, to determine the analytical quality of the data set. Assignment of data validation qualifiers will be completed by the Project Manager and/or Project Technical Lead consistent with appropriate EPA guidance. Validation by the Project QA Officer will include review of data qualifiers. The intent of data validation is to determine if the data are adequate to support the objectives of the project. Items to be considered include: Does the data meet the needs of the project, does the data meet the quality objectives of the project, and are the conclusions drawn from the gathered data supportable. Data validation will also include a determination, where possible of the reasons for any failure to meet method, procedural, or contractual requirements, and an evaluation of the impact of such failure on the overall data set.

Any discrepancies from requirements of the QAPP, with respect to the data, will be noted during the verification and validation process. As determined by the Project Manager, the Project Technical Lead, or the Project QA Officer, if the data do not meet the needs of the project, or the quality objectives of the QAPP, and/or if the conclusions drawn from the data do not appear to be reasonable, the Project Manager and the Project QA Officer shall immediately report such findings to the appropriate Regional Manager and State Office Program Manager for determination of the necessary corrective actions.

24. RECONCILIATION WITH USER REQUIREMENTS

Data quality objectives (DQOs) will be discussed with the analytical laboratory as needed by the Project Manager or Project Technical Lead when DQOs are not met to insure that the laboratory is taking appropriate corrective action. Corrective actions may be initiated to suggest updates to internal laboratory QA procedures in order to rectify QA issues. If no

corrective actions are being implemented and no plan can be developed to address QA issues, the Project Manager will consider changing laboratories for future sampling events.

Data Quality Assessment (DQA) will be performed in accordance with the DEQ QMP. Additional guidance can also be found in EPA Data Quality Assessment: A Reviewer's Guide, EPA QA/G-9R, or in EPA, 2006, Data Quality Assessment: Statistical Methods for Practitioners, EPA QA/G-9S, EPA/240/B-06/003.

The DQA, performed by the Project Manager and the Project QA Officer, addresses the determination of if a data set is of the right type, quality, and quantity to achieve the objectives of the project and can confidently be used to make an informed decision.

As previously stated in Section 23, if the Project Manager, the Project Technical Lead, or the Project QA Officer, reach the conclusion that the project data do not meet the needs of the project, or the quality objectives of the QAPP, and/or if the conclusions drawn from the data do not appear to be reasonable, the Project Manager and the Project QA Officer shall immediately report such findings to the appropriate Regional Manager and State Office Program Manager for determination of the necessary corrective actions

If sampling activities require revision, the project QAPP and/or the project FSP will be revised as necessary. Following revision, and prior to implementation, the revised project QAPP and/or FSP must be re-approved in accordance with the Idaho DEQ QMP.

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25. REFERENCES

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APPENDIX A - GROUND WATER SAMPLING PROCEDURES, IFRO SAMPLING PROJECTS

Note: In this example, a standard procedure for water sampling was incorporated into the project QAPP as an appendix. Not all project QAPP's will require this, but this example illustrates how this can be done. Another way to accomplish this is to reference an approved DEQ Standard Operating Procedure (SOP).

It must be noted and understood that this "Appendix A" is NOT the Field Sampling Plan (FSP) referenced in this example QAPP. A FSP is a stand-alone document that gives project specific information and direction with respect to project sampling. This example QAPP assumes that a FSP will be written to accompany the QAPP. If the project for which a QAPP is being written (using this example/template) will not have a specific FSP written for it, then all the information that this example/template QAPP defers to the FSP will need to be included within the new project QAPP itself.

Equipment required: field log book with collection data sheets, sample labels, water-proof pens and markers, cell phone, GPS, instruments for field parameter measurement, sample collection equipment (may include hose bib, sample collection port and associated tubing, peristaltic pump, bucket, submersible pump and generator), sample containers, preservatives, sample cooler and ice, powder-free nitrile or vinyl gloves, safety glasses or face shield, paper towels, first-aid equipment, bag for trash.

1.0 Well Purging Procedures

Each well/sample point will be purged until the field parameters stabilize as defined in Section 2 of this Appendix. The volume of water and amount of time required to properly purge each well will be dependent on the size and yielding characteristics of each well.

2.0 Field Parameter Measuring Procedures

Field measurements of pH, temperature, and specific conductance will be measured throughout the purging sequence and recorded on the field data sheet or logbook. Field parameters will be recorded at least once for every five minutes while the well is purged. Stabilization of these parameters is considered successful when three successive readings (a minimum of five minutes apart) meet the following criteria:

pH :	± 0.1 standard unit
Specific Conductance:	± 10µmhos/cm or ten percent of the preceding reading

Temperature: ± 0.5° C

Measurements of field parameters will be taken using a field parameter meter that is calibrated prior to each day of sampling. Water used in field parameter measurements will be collected into a dedicated bucket or flow-through from the sampling hose connected to a faucet nearest to the wellhead. All measurements collected will be recorded in the field sheets and field logbook with appropriate times and well identification information. When possible, static water level measurements will be recorded.

3.0 Sample Collection Procedures

Once the field parameters have stabilized, collect the sample from the faucet or sample port. If a hose must be used for sample collection, a dedicated hose supplied by DEQ will be used. Samples should be collected as quickly as possible following stabilization of the field parameters. Collect the sample directly into the appropriate container. If a filtered sample is required, use an in-line filter connected with tubing at the faucet or sample port. If the sample point or conditions do not allow use of an inline filter, a peristaltic pump can be used. Collect water from the sample point in a bucket that has been triple rinsed in the sample matrix. Purge the pump line by running at least 500 ml of the water through the pump and proceed to collect samples. Samplers will wear a new pair of vinyl/nitrile gloves at each location, and will keep gloves on until samples are collected and required preservatives added. Samples should be collected and handled in a way that reduces the potential for losing the analyte from the sample matrix; for a VOC samples, reduce the discharge to a low, laminar flow, leaving a positive meniscus but not allowing the container to overflow and thereby losing preservative from the container. Typically, sample containers that are not pre-preserved should be triple rinsed with the sample matrix prior to collection.

The samples will be labeled with durable labels and water-resistant ink to provide proper identification. Labels will have the following information: unique sample identification number, date and time of collection, parameters requested, and project name/number.

Preservation of the collected samples will follow laboratory instructions. Samples to be chilled will be placed on ice in an ice chest at less than 4° C from the time of sampling until the analysis is complete. All samples will be transported in ice chests with ice packs and chain of custody forms.

4.0 Decontamination Procedures

The sample collection equipment carried from one location to another will be rinsed with deionized water or sample matrix prior to collecting measurements at the new site. Equipment that cannot be sufficiently purged with the sample matrix prior to sample collection will be rinsed with deionized water. Decontamination between sites may

require a stronger solution, depending on the nature of the contaminant. Special decontamination procedures will be detailed in the FSP.

5.0 Field sampling sheets

Field sampling sheets within a bound logbook will be completed for each well at each site visit. An example field sample sheet is included in Appendix B. At a minimum, the following information, as available, will be documented for each site visited during each sampling event:

- Identification of the well
- Total well depth
- Approximate purge volume and rate
- Date and time of sample collection
- Sample identification numbers and parameters requested
- Field parameter measurements and methods
- Field observations and remarks
- Name of collectors
- Weather conditions

6.0 Chain of Custody Forms

Once the samples have been collected, they will be placed in an ice chest (with ice) while in the field, and stored in a designated sample refrigerator until delivered or shipped to the lab. A chain of custody form will accommodate each ice chest during shipment to the lab. The chain of custody form will include the following information:

- Project name/code
- Laboratory name and address
- Sample identification number
- Date and time of collection
- Type of sample, number of containers, and analysis requested
- Sample preservation methods
- Signature of sample collector(s)/shipper
- Date and time of release to shipper/common carrier

The following procedures will be followed to ensure proper chain of custody:

- The chain of custody record will be checked for a signature
- The sample will be stored in a secure area until it is analyzed.

7.0 Quality Assurance/Quality Control

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The objective of quality assurance and quality control is to make certain that the ground water analytical results represent the actual chemical and physical composition of the ground water at the site. DEQ will be responsible for the QA/QC activities of the samples and analytical laboratories. Components of the QA/QC program are as follows:

Laboratory: The analytical laboratory will provide or assist in the sampling containers, preservatives, chain of custody, labels and seals. A laboratory QA/QC report with continuing calibration checks will accompany each data report and will be kept on file by DEQ.

Sample Collection: QA/QC procedures for sample collection will be accomplished by the sampling personnel. A standardized field logbook or field sheet will be kept for each sampling event following the format described above. It will include all label and seal numbers and documentation of QA/QC procedures related to sample collection.

Trip Blank: Trip blanks may be included if samples for VOA analysis are included with the project.

Field Blank: Field blanks will be collected at the rate of at least 5 percent.

Duplicate Samples: Duplicate samples will be collected at the rate of at least 5 percent.

Field Spike: Spikes prepared by an independent source and submitted blind to the lab may be included with field QC samples.

Field QC Sample Goals: Field QC samples (duplicates, blanks, and spikes) will constitute at least 10%-20% of samples submitted to the analyzing laboratory.

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APPENDIX B - GROUND WATER SAMPLING FIELD SHEET - IFRO

In this example, this appendix was used to supply an approved field sheet to the staff engaged in sampling efforts. Not all project QAPP's will require this appendix, but this illustrates how this type of information is included in a QAPP.

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TR 1574

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APPENDIX C - GROUND WATER SAMPLING PERMISSION FORM

In this example, this appendix was used to supply an approved access permission form to the staff engaged in sampling efforts. Not all project QAPP's will require this appendix, but this illustrates how this type of information is included in a QAPP.

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Environmental Protection
Agency

Office of Health and
Environmental Assessment
Washington DC 20460

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March 1984
Final Report

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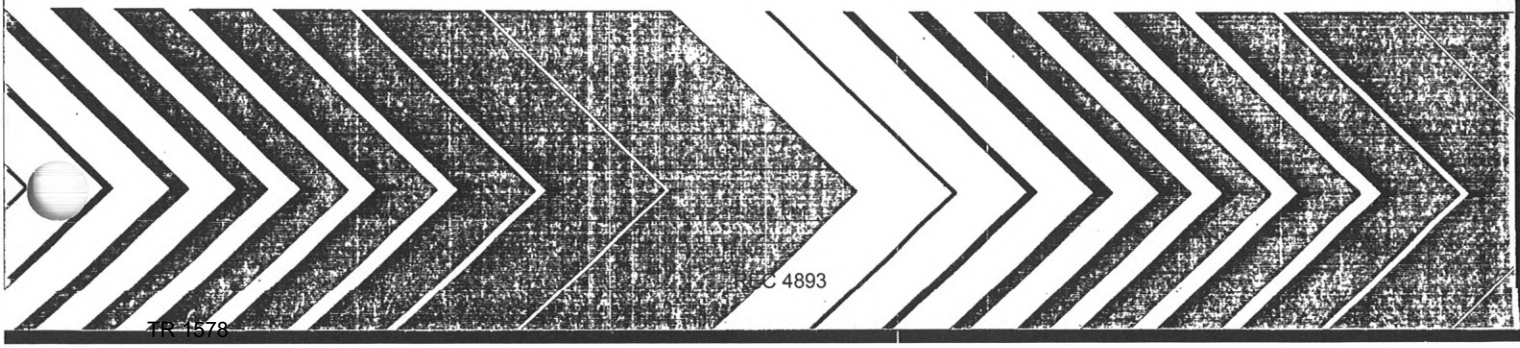
Health Assessment Document for Inorganic Arsenic

Final Report



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Final Report

Health Assessment Document for Inorganic Arsenic

FINAL REPORT

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Research and Development
Office of Health and Environmental Assessment
Environmental Criteria and Assessment Office
Research Triangle Park, NC 27711

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NOTICE

This document has been reviewed in accordance with the U.S. Environmental Protection Agency's peer and administrative review policies and approved for presentation and publication. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

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PREFACE

The Office of Health and Environmental Assessment, in consultation with other Agency and non-Agency scientists, has prepared this health assessment to serve as a "source document" for Agency-wide use. Specifically, this document was prepared at the request of the Office of Air Quality Planning and Standards.

In the development of this assessment document, the scientific literature has been inventoried, key studies have been evaluated, and summary/conclusions have been prepared such that the toxicity of arsenic is qualitatively and, where possible, quantitatively identified. Observed effect levels and dose-response relationships are discussed where appropriate in order to place adverse health responses in perspective with observed environmental levels.

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ABSTRACT

This document summarizes current scientific information regarding the effects of inorganic arsenic on man and the environment. The observed effects, as presented herein, constitute the health basis from which the U.S. Environmental Protection Agency will make determinations regarding regulatory initiatives pursuant to the Clean Air Act. Specifically, this document discusses the following topics--physical and chemical properties of inorganic arsenic; environmental distribution and cycling; inorganic arsenic metabolism; toxicology, including mutagenic and carcinogenic properties; and essentiality--and identifies the factors most germane to assessing quantitative and qualitative human health risks.

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1. INTRODUCTION

This report evaluates health effects associated with arsenic exposure, with particular emphasis placed on health effects thought to be of most concern in regard to exposure to inorganic arsenic of the general U.S. population. Organic arsenic compounds are considered only insofar as certain forms of the element arise via transformation of arsenic in man and other species, or arise by environmental transformation.

This report is organized into chapters which provide a cohesive discussion of all aspects of inorganic arsenic and delineate a logical linking of this information to human health risk. The chapters include: an executive summary (Chapter 2) of the information contained within the text of later chapters; background information on the chemical and environmental aspects of arsenic, including levels of arsenic in media with which U.S. population groups come into contact (Chapter 3); arsenic metabolism, where factors of absorption, biotransformation, tissue distribution, and excretion of inorganic arsenic are discussed with reference to the toxicity of the element (Chapter 4); arsenic toxicology, discussing the various acute, subacute, and chronic health effects of inorganic arsenic in man and animals (Chapter 5); arsenic mutagenesis, discussing the ability of inorganic arsenic to cause gene mutations, chromosomal aberrations, sister chromatid exchanges and inhibition of DNA synthesis (Chapter 6); arsenic carcinogenesis, including discussion of selected dose-effect and dose-response relationships (Chapter 7); arsenic as an essential element, which deals with the current status of inorganic arsenic as a required nutrient in at least some species of animals (Chapter 8); and a human health risk assessment for arsenic, where key information from the preceding chapters is placed in an interpretive and quantitative perspective highlighting those health effects of most concern for U.S. populations (Chapter 9).

This report is not intended to be an exhaustive review of all the arsenic literature, but is focused upon those data thought to be most useful and relevant for human health risk assessment purposes. Particular emphasis is placed on delineation of health effects and risks associated with exposure to airborne arsenic, in view of the most immediate use intended for the present report, i.e., to serve as a basis for decision making regarding the regulation of inorganic arsenic as a hazardous air pollutant under pertinent sections of the Clean Air Act, as amended in 1977. Health effects associated with the ingestion of arsenic or with exposure via other routes are also discussed, providing a basis for possible use for multimedia risk assessment purposes, as well. The background information provided at the outset on sources, emissions, and ambient concentrations of arsenic in various media is presented in order to provide a general perspective against which to view the health effects evaluations contained in later chapters of the document. More detailed exposure assessments, taking into account even more recent, up-to-date emission and ambient concentration data have been prepared separately for use in subsequent EPA regulatory decision making regarding arsenic.

The Agency recognizes that the regulatory decision-making process is a continuous one; therefore, should new information become available in the future that would warrent a reevaluation of the information contained herein, the Agency will undertake such an evaluation as part of its mandate to protect the health of the general U.S. population.

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2. SUMMARY AND CONCLUSIONS

As a toxic agent, inorganic arsenic possesses several properties that are not shared with many environmental pollutants. The element exists in various chemical states, e.g., tri- and pentavalent inorganic arsenic and methylated organic arsenic, with each having differing toxicological potential. In man, experimental animals, and other organisms, arsenic undergoes a variety of transformations, the full significance and mechanisms of which are, as yet, not well understood. Furthermore, there appears to be a nutritional requirement for low levels of arsenic in certain experimental animals and this may also be the case for man. All of these factors complicate the analyses of the toxicological effects and the risk for human health associated with environmental exposure to arsenic compounds. The following chapter summarizes these factors as they are presented in depth in the ensuing document text.

2.1 BACKGROUND INFORMATION

2.1.1 Chemical/Physical Aspects of Arsenic

It is the various compounds of arsenic which have been of most importance in the extensive history of the toxicology of the element, the zero-valent metallic form being of minor toxicological interest.

Arsenic is encountered as a component of sulfidic ores of metals such as copper, cobalt and nickel. The smelting of these ores is associated with arsenic release into the environment. Arsenic trioxide, As_2O_3, a toxicologically significant form, is a smelter product arising from air roasting of these sulfidic ores.

Arsenic trioxide, white arsenic, is only sparingly soluble in water and other solvents which do not promote chemical transformation. The compound dissolves in acidic or alkaline aqueous media to yield either the free acid or

salts, with these being soluble in a number of solvents. The oxide readily sublimes (135°C), and this factor is of importance in considering analytical methods for measuring levels of the compound.

The pentavalent arsenic pentoxide, As_2O_5, may be prepared by nitric acid oxidation of the trioxide or the element itself. This form has high solubility in water (63 g/100 g water), forming the strongly oxidizing arsenic acid, H_3AsO_4 ($E^o = 0.56V$).

Stability of the valency forms of arsenic in solution is dependent on the nature of the medium. Oxygenated media and higher pH favor the pentavalent form, while reducing and/or acidic media favor the trivalent state.

The acids of both valency forms of arsenic readily form alkali and alkaline metal salts, with the former being much more soluble than the latter. Organic ester derivatives of arsenic are quite labile to hydrolysis and this chemical behavior has biochemical/toxicological implications in the postulated role of arsenate ion in interfering with phosphorylation reactions.

Arsine (arsenic trihydride, AsH_3) is the most poisonous of the arsenicals, being a strong hemolytic agent, and it can be formed under certain restricted conditions, i.e., reduction of the oxy compounds in the presence of a strong hydrogen source.

Monomethyl and dimethyl arsenic arise by both environmental and *in vivo* transformation processes.

In high-temperature processes, arsenic is released as a vapor which is then adsorbed or condensed onto small particles. Such adherence to particles of 1-2 μm or less may result in enhanced health risk from the agent since particles in this size range are inhaled and deposited in the deepest part of the respiratory tract.

Arsenic compounds tend to form insoluble complexes with soils and sediments. In the case of soils, the interaction occurs with amorphous aluminum or iron oxides.

2.1.2 The Environmental Cycling of Arsenic

Primary smelting, biocide use and glass manufacturing constitute some of the major inputs of arsenic into the various environmental compartments. Of an estimated total release of approximately 10,000 short tons annually in the U.S., smelter activity accounts for about 50 percent, biocide (pesticide, fungicide, herbicide) use contributes 32 percent, and glass production contributes about 7.0 percent, with the remaining amount being released from various other sources.

The atmosphere is a major conduit for arsenic emitted from anthropogenic sources to the other environmental compartments via wet and dry precipitation processes. Dry and wet fall onto soils may be followed by movement through soils either into groundwater or surface water. Passage of arsenic into surface waters may be followed by transfer to sediments. Such cycling is made complex by chemical and biological transformations which have been reported as occurring in the various environmental compartments.

Trivalent arsenic in the atmosphere or in aerated surface waters can undergo oxidation to the pentavalent state, while pentavalent arsenic in media which are below pH 7.0 and contain oxidizable material can react to form the trivalent form via reduction.

Biological transformations of arsenic have been documented as occurring via both sedimentary bacteria and suspended marine algae. Several different hypotheses have been advanced to explain the biological cycling of arsenic.

Reduction and methylation of inorganic arsenic occur only to a limited extent in soils, one report noting a conversion of only 1-2 percent over a period of months.

With reference to the relative amounts of the annual environmental burden of arsenic, it has been calculated for 1974 that land is the major sink for arsenic, approximately 90 percent, with the atmosphere accounting for 7-8 percent and the smallest quantity appearing in waters.

2.1.3 Levels of Arsenic in Various Media

Available data on levels of arsenic in various media with which man interacts are generally presented as total arsenic, with limited information available for identifying specific chemical forms of arsenic.

2.1.3.1 Levels of Arsenic in Ambient Air--Based on the comprehensive data for U.S. air levels of arsenic obtained by the U.S. EPA's National Air Sampling Network, air levels of arsenic in the U.S. generally do not exceed 0.1 $\mu g/m^3$.

Generally, airborne arsenic is adhered to particulate matter. Although the immediate areas around smelters may contain some arsenic in the vapor form, data are available to indicate rapid adherence to particulate matter when sampling 2-3 km from these emission sites.

The specific chemical form(s) of airborne arsenic is still unclear. Generally, in most urban/suburban areas, arsenic is mainly in the form of a mixture of inorganic arsenic in the tri- and pentavalent states. Only in areas where methylated arsenic is used agriculturally or where biotic transformation can occur has methylated arsenic been found in air samples.

2.1.3.2 Levels of Arsenic in Drinking Water--The National Interim Primary Drinking Water Regulations, promulgated under the Safe Drinking Water Act, set the Maximum Contaminant Level (MCL) for arsenic in U.S. public water supplies at 50 µg/l. In general, arsenic is not found in drinking water at levels exceeding this MCL. Well waters in the western U.S. and Alaska, however, may have much higher levels owing to geochemical enrichment. In Lane County, Oregon, recent analyses report levels up to 2.2 ppm (2.2 mg/liter), while the

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highest figure in Alaska was 10 ppm (10 mg/liter), representing both natural and mining residue contributions.

It is reasonable to assume that the chief chemical form of arsenic in most public water supplies would be the pentavalent inorganic form, owing to both aeration and chlorination. Similarly, well waters in Alaska and the western U.S. are reported to mainly contain pentavalent inorganic arsenic.

2.1.3.3 Arsenic in Food--The most recent data base for the arsenic content of foods is the 1975-1976 survey carried out by the U.S. Food and Drug Administration. Shellfish and other marine foods have the highest levels on a food category basis. Overall, the total dietary intake of arsenic in 1975-1976 was approximately 50 μg (elemental arsenic), representing an increase from the preceding years. Whether this increase represents a trend or merely reflects analytical variation in sampling from year to year is still to be determined.

The chemical forms of arsenic in foods are varied and complex. Crustaceans and other marine life store arsenic in complex organoarsenical forms which, based on recent reports, are assimilated by man and generally excreted intact. Toxicologically, these forms are comparatively inert.

2.1.3.4 Arsenic in Soils--Background soil arsenic levels range from less than 1 ppm to over 40 ppm, the latter reflecting agricultural practices as well as air fallout. Soil arsenic is usually bound to clay surfaces, and its mobility is a function of soil pH, phosphate levels, iron and aluminum content, and soil type. The mobile fraction, usually in the pentavalent form, is of concern in terms of movement to plants and water. Little reductive methylation occurs in most soils.

2.1.3.5 Other Sources of Arsenic--Limited data on arsenic content of tobacco suggest that more recent values range from around 1.5 ppm or less, while in the past (1945) values up to 40 ppm were measured. This decrease reflects reduced use of arsenical biocides in tobacco production.

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2.2 ARSENIC METABOLISM

2.2.1 Routes of Absorption

Major routes of absorption of arsenic in the general population are inhalation and ingestion. The ingestion of arsenic may be either through the direct intake of food and water or through secondary intake via inhalation and swallowing. Arsenic uptake through the skin appears to be a minor route of exposure. Factors affecting the extent of absorption include chemical forms, particle size, and solubility.

2.2.1.1 Respiratory Absorption--Limited data from human subjects suggest that about 40 percent of most forms of inhaled arsenic is deposited in the lungs, all of which is eventually absorbed, yielding a net absorption of approximately 30 percent or greater of the inhaled amount.

Several studies of smelter workers also confirm that significant absorption of inhaled arsenic occurs, as judged by rapidly rising urine arsenic levels when exposure first occurs. Furthermore, the levels excreted are correlated with workplace air levels.

Animal data also indicate respiratory tract absorption when exposure occurs by inhalation of aerosols or by intratracheal instillation.

2.2.1.2 Gastrointestinal Absorption--Based on a number of reports using human subjects, soluble inorganic arsenic is almost totally absorbed from the gastrointestinal tract. Similar data have been obtained for such experimental animal species as the rat, pig, and monkey.

Less soluble forms of arsenic, such as arsenic trioxide in suspension, lead to considerably lower absorption while insoluble arsenic triselenide passes through the human GI tract with negligible absorption.

2.2.1.3 Transplacental Transfer--Transplacental transfer of arsenic in man appears to occur, based on autopsy data and on one report showing that newborn

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cord blood levels approximate those of the mothers. Measurable levels of arsenic in fetal tissue have been determined by the fourth month of gestation, increasing to month seven.

In animals, inorganic arsenic appears to rapidly cross the placental barrier where it is distributed in embryonic tissue.

2.2.2 Biotransformation of Inorganic Arsenic In Vivo

An understanding of inorganic arsenic metabolism in man and other species is complicated by recently revealed biotransformation processes, discovered because of the development of analytical techniques which permit the chemical speciation of arsenic into its various forms. These processes not only relate to pharmacokinetic parameters such as tissue distribution and excretion, but also figure in the toxicology of the element. The two processes of significance for consideration here are the methylation of inorganic arsenic and oxidation-reduction interconversion of inorganic arsenic.

An extensive recent literature documents the in vivo methylation of inorganic arsenic to monomethyl and dimethyl arsenic (the latter being the major methylated metabolite) in every mammalian system studied to date, including man.

While the quantitative features of this phenomenon may vary among species, one can generally state that: 1) dimethyl arsenic is the major transformation product in both humans and animals, with the amount of monomethyl arsenic, when formed, being greater in humans; 2) methylation is assumed to be a route of detoxification, the methylated forms being not only much less toxic but also more rapidly excreted; 3) the methylating capacity of a given system can persist over a range of inorganic arsenic exposure but at some point can be overwhelmed; and 4) retrospective assessment of early data on arsenic

metabolism must be reviewed in light of the current knowledge about biomethylation. In man, dimethyl arsenic represents approximately 75 percent of total arsenic excretion, with monomethyl arsenic being excreted in lesser amounts.

The demonstration of interconversion of the two valency forms of inorganic arsenic claimed in earlier literature must be considered in light of the biomethylation phenomenon, and only more recent studies addressing this problem using chemical speciation techniques can be considered reliable. Invariably, the giving of inorganic penta- or trivalent arsenic to experimental animals or human volunteers leads to predominantly methylated forms, with any inorganic arsenic being present in small amounts. These observations and supporting data showing reduction of pentavalent arsenic in vivo are consistent with a reductive biomethylation mechanism, including initial reduction of pentavalent to trivalent arsenic prior to methylation. A recent study using speciation methods and human subjects also establishes the in vivo reduction of pentavalent to trivalent arsenic in humans.

Even with sophisticated analytical methods permitting chemical speciation in biological media, the lability of arsenic in dosing solution to oxidation-reduction requires careful assessment of the actual form being administered.

2.2.3 Distribution of Arsenic in Man and Animals

Blood is the main vehicle for transport of arsenicals following absorption, and from which arsenic is cleared relatively rapidly to tissues in all species except the rat. In the rat, arsenic-erythrocyte interaction tends to preclude rapid movement to tissues, with a biological half-time of up to 90 days, versus a corresponding time of several days in all other species. Arsenic movement from blood appears to conform to a three-compartment model which must reflect in part the biomethylation of inorganic arsenic noted above.

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Exposure of various experimental animals to either tri- or pentavalent inorganic arsenic leads to initial accumulation of the element in liver, kidney, spleen, aorta, and skin. In most species, arsenic clearance from soft tissue is relatively rapid except for the skin, where the high sulfhydryl group content probably promotes tight arsenical binding.

In man, tissue partitioning data are mainly available from autopsy data. Heart, kidney, liver and lung have highest levels on a concentration basis, but skin and excretory/storage organs such as nails and hair have the highest absolute amounts. Brain tissue has levels only slightly below those of other soft tissues.

Recent data on valency and exposure level effects on tissue distribution of arsenic indicate that levels of arsenic in kidney, liver, bile, brain, skeleton, skin, and blood are 2- to 25-fold higher for the trivalent form than for the pentavalent state, and are greatly increased at higher dosing. The difference is held to be due to the relative methylating capacity of either form as well as the level of exposure.

2.2.4 Arsenic Accumulation

The long-held view of arsenic as an element which accumulates in the body was mainly based on the behavior of arsenic in the rat, an anomalous model which does not reflect the case with other species. For other species, including man, long-term accumulation does not generally occur in physiologically active compartments in the body.

In man, the only evidence for tissue accumulation is autopsy data from retired workers with a history of metal smelter exposure in which lung arsenic levels were 8-fold higher than in a control population. This suggests the existence of a very insoluble form of arsenic in smelter ambient air.

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2.2.5 Arsenic Excretion

Renal clearance appears to be the major route of excretion of absorbed arsenic in man and animals. Biliary transport of the element leads to enteric reabsorption, with little carriage in feces.

In man, inorganic arsenic is excreted rather rapidly, and in several studies in which continuous exposure resulted in the acquisition of steady state, around 60 percent of a given dose was excreted within one day.

The pattern of renal excretion reflects the *in vivo* biotransformation capacity for inorganic arsenic, one study noting that trivalent arsenic was excreted more slowly than an equivalent dose of the pentavalent form, and higher doses of both forms were cleared relatively more slowly than lower doses.

2.3 ARSENIC TOXICOLOGY

2.3.1 Acute Toxicity

Acute symptoms of arsenic poisoning are similar in both man and experimental animals. With oral exposure, the acute symptoms include severe gastrointestinal damage resulting in vomiting and diarrhea and general vascular collapse leading to shock, coma, and death. Other acute effects are muscular cramps, facial edema, and cardiovascular reactions. Airborne exposure at high levels also results in severe irritation of nasal mucosa, larynx, and bronchi. Sequelae of acute contact with inorganic arsenic include peripheral nervous system disturbances with slow recovery and reversible effects on the hematopoietic system.

Levels of exposure associated with acute arsenic toxicity vary with the valency form of the element, the trivalent state being approximately 4-fold more toxic than pentavalent arsenic. Oral LD_{50} values for trivalent arsenic

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vary from 15 to 293 mg/kg b.w. in rats and from 10-150 mg/kg in other test species.

While a number of outbreaks of acute arsenic poisoning have been described, few data exist on actual doses and type of arsenical involved. One report has estimated the human lethal dose for arsenic trioxide to be anywhere from 70 to 180 mg.

2.3.2 Chronic Toxicity

Two categories of chronic arsenic toxicity can be discerned from the available literature: 1) the mutagenicity/carcinogenicity of arsenic; and 2) various non-carcinogenic chronic effects.

2.3.2.1 Mutagenesis of Inorganic Arsenic--Various inorganic compounds of arsenic have been tested for mutagenicity in a variety of test systems ranging in complexity from bacteria to peripheral lymphocytes of exposed human beings. Although many of the data are contradictory, the weight of evidence supports the following conclusions:

1) Arsenic is either inactive or extremely weak for the induction of gene mutations in vitro.
2) Arsenic is clastogenic and induces sister chromatid exchanges (SCE) in a variety of cell types, including human cells in vitro; trivalent arsenic is approximately an order of magnitude more potent than pentavalent arsenic.
3) Arsenic does not appear to induce chromosome aberrations in vivo in experimental animals.
4) Several studies suggest that human beings exposed to arsenic demonstrate higher frequencies of SCE and chromosomal aberrations in peripheral lymphocytes; however, the quality of these studies is generally poor.

5) Arsenic may affect DNA by the inhibition of DNA repair processes or by its occasional substitution for phosphorus in the DNA backbone.

From these conclusions, it can be surmised that arsenic may have the potential to cause chromosomal changes in human beings. Although additional information is needed, it appears that the mutagenic potency of arsenic is weak compared to other known metal mutagens.

2.3.2.2 Carcinogenesis of Inorganic Arsenic--The current status of inorganic arsenic as a human and experimental animal carcinogen has been extensively and critically reviewed by public agencies such as the National Institutes of Occupational Safety and Health, scientific bodies such as the National Academy of Science and the International Agency for Research on Cancer, and in a number of individual assessments.

At present, the collective evidence for an etiological role of inorganic arsenic in human cancers is strongest for cancers of the skin and lung.

In man, chronic oral exposure to arsenic induces a sequence of changes in skin epithelium, proceeding from hyperpigmentation to hyperkeratosis characterized as keratin proliferation of a verrucose nature, and leading in some cases to late onset skin cancers. The skin cancers can be histopathologically characterized as either squamous carcinomas in the keratotic areas or basal cell carcinomas.

Arsenic-associated skin cancers, regardless of type of exposure, differ from those having an ultraviolet light etiology in that they occur on unexposed areas such as the palms and soles and occur as multiple lesions. The latency period for such lesions has been reported to range from 6 to 50 years for skin cancer induced by the administration of arsenical medicinals. The most reliable study of skin cancer associated with arsenic-contaminated drinking water found the minimum human latency period to be 24 years.

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Lung cancers associated with occupational exposure to arsenic appear to be mainly of the poorly differentiated and small-cell undifferentiated epidermoid carcinoma type, although well-differentiated epidermoid carcinoma and acinar-type adenocarcinoma have also been noted. The latency period for such lung cancer due to occupational arsenic exposure at smelters has been reported to range from 13 to 50 years.

While other visceral cancers such as hepatic angiosarcomas have also been claimed to be associated with arsenic exposure, the data base for such association is less conclusive than for cancers of the skin and lung.

2.3.2.2.1 Human Epidemiology of Arsenic Carcinogenesis. Cancer- and possible precancerous lesion-producing inorganic arsenic exposures have been demonstrated in both occupational populations, such as copper smelters, pesticide manufacturers and argricultural workers, and in non-occupational populations using arsenical drugs or consuming arsenic-contaminated drinking water and/or food.

Cancer or possible precancerous skin lesions associated with arsenic exposure include lung cancer, skin cancer, peripheral vasculopathy, hyperkeratosis, hyperpigmentation, and depigmentation. Of these, cancers of the lung and skin have received the most attention. Furthermore, epidemiologic reports of cancer or possible precancerous lesions related to arsenic exposures have a wide geographical distribution, with studies reported in the United States, Europe, Asia and South America.

Lung Cancer

An excess mortality in respiratory cancer has been noted among smelter workers and among workers engaged in the production and use of arsenical pesticides. In a number of these studies, the levels of exposure are uncertain and there is simultaneous exposure to agents such as other metals and sulfur dioxide. Furthermore, some of these studies did not take into account the effects of cigarette smoking.

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A proportionate mortality study of an English factory which manufactured arsenite as a sheep dip powder found that workers at the facility had a proportion of lung cancer deaths twice that for other workers in the geographic area. Of the total factory group, the chemical workers, who were the most closely associated with the arsenite production, accounted for all of the lung cancer deaths and had a higher proportion of deaths from all cancers than the total factory population. Air exposure information was limited, levels up to 4 mg As/m^3 having been reported only for 1945-1946. The outcome of the earlier English study has been supported by studies of two facilities in the United States. At one facility manufacturing lead-, calcium-, and magnesium arsenate and copper acetoarsenite over the period 1919-1956, the ratio of observed-to-expected lung cancer deaths among workers was evaluated on the basis of exposure level, giving ratios ranging up to 7:1 in the highest exposure category.

The second U.S. facility, in Baltimore, Maryland, has been the subject of two occupational studies. At this operation, production of lead-, calcium-, and sodium arsenate was started in the early 1950s. Air levels of arsenic were not available. In the most recent report--a follow-up of workers employed from 1946 to 1974--statistically significant increases in lung cancer deaths were found in "predominantly arsenical production workers." Information on smoking history was not obtained.

Occupational exposure to arsenic also occurs in smelters. Several reports have centered on workers at a copper smelter in the state of Washington. In the most recent publication concerning cancer deaths at this facility, an increase in overall mortality, a significant increase in cancer deaths, and a highly significant increase in deaths from lung cancer were noted. Although

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cigarette smoking data were not available, a clear lung cancer dose response by arsenic exposure was found, suggesting that smoking probably did not confound the lung cancer response believed to be due to arsenic.

Other U.S. studies have been done at smelter sites in Utah and Montana. In the Utah study, smelter workers showed a 3-fold increase in the lung cancer death rate compared to the general population of the state. Exposures to sulfur dioxide and copper, as well as arsenic, were found to be significantly higher for the lung cancer cases. Differences in smoking habits could not explain the excess lung cancer mortality. Smelter workers at the Montana smelter were found to follow a lung cancer dose response by arsenic exposure. Differences in smoking habits could not explain the differences in lung cancer mortality. Little association, if any, was found between sulfur dioxide exposure and lung cancer mortality.

Some of the evidence from the U.S. smelter studies suggests that arsenic may be acting as either a late-stage carcinogen in the multistage theory of carcinogenesis or as a promoter in the carcinogenesis process. Either hypothesis requires further study, however.

Excess lung cancer mortality has also been reported for workers in foreign smelters. Several reports have concerned the smelter facility in Sweden. In this operation, it was found that arsenic exposure was associated with increases in lung cancer deaths, the ratio being 4.6 for a work history of more than 17 years. Sulfur dioxide exposure was not found to be associated with lung cancer, nor could the results be explained by differences in smoking habits. A study of smelter workers in Japan has also reported a positive association between smelter employment and lung cancer. Workers in the highest exposure and longest follow-up category were reported to have a 25-fold increase in lung cancer mortality.

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Several studies suggest that populations surrounding arsenic-emitting sources are at a greater risk of lung cancer. One study found that lung cancer in counties with smelters was significantly higher than in counties without smelters. Another study found an association between residence in an area surrounding an arsenic pesticide plant and lung cancer mortality even after controlling for employment at the pesticide plant. Two lung cancer mortality studies of populations in the vicinity of smelters are inconclusive with regard to lung cancer risk in the general population because lung cancer deaths of workers at the smelters were included in the analyses. It should be noted that none of these studies addressed the effects of population migration, however.

Skin Cancer and Precancerous Lesions

All of the occupational studies on arsenic have been mortality studies. Because skin cancer is rarely fatal, the occupational studies, in general, do not report excesses of skin cancer. The English study referred to in the preceding section, however, did note that cancer deaths among those factory workers with skin cancer was 13.6 percent compared to a figure of 1.3 percent in the reference population.

Most of the available information on the association of arsenic with skin cancer has involved non-occupational populations in geographical areas as diverse as Taiwan, Argentina, and northern Europe, and has involved arsenic in drinking water or medicinal preparations.

In Taiwan, exposure started in 1910-1920 with the availability of water from deep wells. In the most comprehensive study of this group, 37 villages with a population of 40,421 were surveyed in 1965 and the prevalence rate of skin cancer was categorized by arsenic exposure and age. The prevalence rate of skin cancer increased with both well water arsenic and age. The greatest

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prevalence rate was in the >60-years age group (192.0/1,000 subjects) exposed to well water with an arsenic content of >0.6 ppm. There was a similar ascending gradient for hyperkeratosis, an apparent precondition for the later onset of skin cancer.

In Cordoba, Argentina, arsenical waters have also been reported to be associated with increased rates of skin cancer among the population using this water. In the various reports on this area, it has been noted that over 81 percent of persons with "arsenical-type" skin epitheliomas presenting themselves at a particular dermatology clinic came from areas where high levels of arsenic were known to be present in the water supplies and where arsenicism among individuals was known to occur. Lack of information on the size of the populations in each geographic area limits the conclusions that can be drawn from these studies, however.

In a number of epidemiological surveys conducted in Antofagasta, Chile, the presence of a relatively high level of arsenic, 0.6 ppm, in the public drinking water from 1958 to 1970, was shown to have resulted in a high number of skin lesions including hyperkeratosis which may be a precondition for skin cancer. In one report of cases seen and diagnosed from 1968 to 1971 in Antofagasta, the author reported 457 patients with various cutaneous lesions including leukoderma, melanoderma, hyperkeratosis, and squamous-cell carcinoma; all had high arsenic content in the hair. The number of cases for each diagnosis was not specified.

An investigation of the population having contact with well waters containing elevated levels of arsenic in an area of Oregon did not yield any evidence for skin cancer associated with such exposure, nor did a similar study in Utah. Factors which may have contributed to the difference in results between these studies and the studies in Taiwan, where an association between

skin cancer and arsenic in drinking water was found, include: (1) in addition to arsenic, ergotamine was found in the Taiwan drinking water, (2) the socioeconomic level of the Taiwanese who experienced skin cancer was rather low, which may have had ramifications in terms of diet, personal hygiene and medical care, and (3) racial differences between the Taiwanese and U.S. populations may have had an effect. However, the population sample sizes of the Oregon and Utah studies were too small to detect the risk from skin cancer that would have been predicted, on the basis of arsenic ingestion, from a linear model of the Taiwanese data.

The chronic ingestion of trivalent arsenic present in the medicinal preparation, Fowler's Solution, has been shown to be associated with the typical arsenic dermatopathology, including skin cancer. In one detailed study of patients with a history of Fowler's Solution use, 21 cases of skin cancer and 106 cases of hyperkeratoses were found among 262 subjects. Both the hyperkeratosis and skin cancer prevalence rates were found to increase as the total ingested amounts of the arsenical increased. The minimal latency period for hyperkeratosis was 2.5 years while the minimal latency period for skin cancer was 6 years, with an average of 14 years.

Internal neoplasms associated with arsenic exposure have been reported in subjects exposed to medicinal arsenic as well as in such occupational groups as vintners and smelter workers.

2.3.2.2.2 Experimental studies of arsenic carcinogenesis. Consistent demonstration of arsenic carcinogenicity in test animals, using different chemical forms, routes of exposure, and various experimental species, has not been observed. Part of the difficulty may lie in the selection of an appropriate animal model. The absence of skin cancers in the experimental animals used could be accounted for by their skin being poor models of human skin. Rat

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results must be considered suspect because the rat is anomalous in how it metabolizes arsenic.

Recent data indicate that tumorigenicity and possibly carcinogenicity can be demonstrated in animals if the retention of arsenic in the lung is increased. The additional observations that calcium arsenate, as reported from two laboratories, is only slowly cleared from the lung, strongly suggest that this agent may be carcinogenic.

2.3.2.3 Chronic Neurological Effects of Arsenic Exposure--Both peripheral and central nervous system effects have been documented in man and animals exposed to inorganic arsenic.

Peripheral nervous system effects have been noted in workers occupationally exposed to arsenic and in individuals accidentally exposed to food contaminated with arsenic. Some of these effects follow an insidious course, appearing months or years after onset of exposure. Effects are of both the sensory and motor types, sensory deficits manifesting themselves first. The resulting polyneuropathies tend to follow a slow course of recovery over months or years. More subtle neurological effects, such as neuromuscular disturbances and altered nerve conduction velocity, have also been reported by various investigators.

While there are documented cases of central nervous system (CNS) effects in children due to acute or subacute exposure, chronic arsenic intoxication as a factor in such abnormalities as hearing impairment has not been confirmed.

Few useful animal models exist for the central and peripheral nervous system effects seen in humans. One study has reported evidence of CNS functional deficits in rats exposed to arsenic trioxide aerosol, while a second report claims impaired behavioral responses in rats given arsenic trioxide via stomach intubation. Since rats handle arsenic differently than all other species, the significance of these data is not clear.

2.3.2.4 Cardiovascular Effects of Arsenic Exposure--Cardiovascular effects associated with chronic arsenic intake include Blackfoot disease seen in Taiwanese consuming well water having elevated arsenic. This is a peripheral vascular disease leading to gangrene of the extremities. Since ergotamine-like compounds were also present in the waters, the conclusive role for arsenic is not clear. Peripheral vascular changes have been documented among German vintners who were exposed occupationally to arsenic pesticides as well as arsenic in wine.

2.3.2.5 Other Systemic Effects of Arsenic--Non-cancerous respiratory effects of inorganic arsenic are mainly seen with occupational exposure and with arsenic trioxide. In one study of smelter workers, those handling refined arsenic showed nasal septum perforation and rhinopharyngolaryngitis, while workers in roaster, furnace, and convertor areas showed tracheobronchitis and pulmonary insufficiency.

Teratogenic effects of arsenic compounds at relatively high exposure levels have been demonstrated in a number of animal species, including hamsters, rats, and mice. Generally, such effects have been observed after parenteral administration of either arsenite or arsenate. Oral exposures of animals to these same arsenic compounds at lower doses, by contrast, have not been shown to produce any notable effects on reproduction and development. Methylated arsenic, while potentially teratogenic at high doses, is of lower potency than inorganic forms. There is little evidence that inorganic arsenic is a human teratogen.

Hepatic effects have been noted in a number of studies dealing with chronic intake of arsenic. These disturbances present as cirrhosis and portal hypertension. One complicating factor in occupational exposure assessment has been the effect of alcohol consumption.

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Chronic exposure to arsenic via well water contaminated by arsenic, medicinals, or the workplace, produces a reversible anemia. Rats, mice, and cats fed either arsenite or arsenate show reduced hemoglobin production via disturbance of the ALA-synthetase and heme-synthetase steps in the heme biosynthetic pathway.

Renal effects seen with arsenite or arsenate exposure in either man or animals have been poorly characterized.

2.3.3 Factors Affecting Arsenic Toxicity

The most widely recognized and studied interactive behavior of arsenic is with selenium, the pair being antagonistic in effect in all animal species studied. Dietary arsenic supplementation is known to protect against selenium toxicity, while selenium protects against either tri- or pentavalent arsenic. Arsenite shows a protective effect for selenite toxicity in cell cultures, but the reverse does not appear to be the case.

Few data exist for interactive relationships between arsenic and other elements. One report notes that cadmium and arsenic given simultaneously by the oral route retarded weight gain in young adult rats to a greater extent than either element given alone.

2.4 ARSENIC AS AN ESSENTIAL ELEMENT

Inorganic arsenic appears to be an essential element in certain animal species--rats, goats, chicks, and minipigs--based on the observation of detrimental effects using diets deficient in the element.

In rats, arsenic-deficient diets in pregnant dams are associated with slow growth, enlarged spleens, erythrocyte dysfunction in post-weaning offspring, and greater perinatal mortality.

In studies using goats and minipigs, diets having less than 50 ppb As produced effects in the adult animals as well as in their offspring. Morta-

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lity of adult goats was increased as was the mortality of both kids and piglets. In chicks, arsenic deprivation influenced the effects of dietary arginine, manganese, and zinc, the fluctuations of which variously affected metabolic activity.

Remaining to be independently demonstrated are a physiological role for arsenic, the existence of any specific carrier in the body, or arsenic essentiality in man.

2.5 HUMAN HEALTH RISK ASSESSMENT FOR ARSENIC

This portion of the summary contains the data summarized earlier, presented within a perspective of the possible quantitative risk posed to the general population of the United States by arsenic exposure. Categories of consideration include: (1) levels of arsenic in media relevant to the U.S. population; (2) those effects relevant to the general population; (3) indicators of exposure, specifically "internal dose" measures; (4) dose-effect and dose-response relationships which can be determined from available information; and (5) the identification of groups within the general population who may be at increased risk for the health effects of arsenic.

2.5.1 Exposure Aspects of Arsenic

Arsenic exposure in the general population of the United States occurs via inhalation and ingestion of water and food.

Respiratory intake of arsenic on a daily basis is approximately 0.12 μg, of which 0.03 μg would be absorbed, assuming 30 percent absorption and based on a 1981 national average air value of 0.006 $\mu g/m^3$ of air and a daily ventilation rate of 20 m^3.

Since much of the U.S. drinking water supply is below the 10 μg/liter level, daily consumption of water at a rate of 2 liters would lead to an intake $\leq$ 20 μg.

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Based on 1975-76 figures from the Food and Drug Administration, daily arsenic intake from food is approximately 50 μg (elemental arsenic) for adults. If one assumes at least 80 percent absorption of this daily intake, approximately 40 μg is the absorbed amount. It should be noted, however, that arsenic in certain foods is known to be in a chemically complex form that is relatively resistant to metabolism and toxicologically inert; consequently, it is rapidly excreted intact. Therefore, the amount of absorbed food arsenic considered to be toxicologically significant is relatively small compared to total arsenic intake.

Cigarette smoking contributes about 6 μg/pack of cigarettes in mainstream smoke, of which approximately 2.0 μg/pack would be absorbed.

Thus, the aggregate absorbed amount is approximately $\leq$ 60 μg for non-smokers. However, the actual amount of toxicologically significant arsenic taken in daily would probably be closer to 20 μg or less.

2.5.2 Effect/Response Aspects of Arsenic

2.5.2.1 Relevant Health Effects--General population concerns are with effects arising from long-term exposure to moderate levels of arsenic.

One can rank health effects germane to the general population as follows:

1. Respiratory tract cancer.
2. Skin cancer.
3. Non-cancerous skin lesions.
4. Peripheral neuropathological effects.
5. Cardiovascular changes.

Cancer of the respiratory system is clearly associated with exposure to arsenic via inhalation. This association has been especially noted among workers engaged in the production and usage of pesticides and among smelter workers. The latency period for lung cancer due to occupational arsenic exposure has been reported to range from 13 to 50 years.

Cancer of the skin has been found as a dose-dependent effect in a Taiwanese population with lifetime exposure to well water arsenic as well as among people who were treated with large doses of arsenite for skin disorders. Arsenic-associated skin cancers occur on areas of the body generally unexposed to the ultraviolet light of the sun, such as the palms of hands and soles of feet. The latency period for skin cancer has been reported to range from 6 to 50 years for cancers induced via administration of arsenical medicinals. In the Taiwanese drinking water study, the minimum latency period was reported to be about 24 years.

The Carcinogen Assessment Group (CAG) of the U.S. Environmental Protection Agency (EPA) has concluded that there is sufficient evidence that inorganic compounds of arsenic are both lung and skin carcinogens in humans.

Hyperkeratosis and hyperpigmentation, sometimes with precancerous changes, have been a common finding in persons ingesting arsenic. These skin lesions, like the manifest cancer, develop on surfaces usually unexposed to sunlight.

Peripheral nervous system effects range from sensory-motor deficits with higher exposure to changes in electromyography and nerve conduction velocity at long-term, low levels of contact with arsenic.

Vascular effects, such as Blackfoot disease (peripheral vasculopathy) have been noted in a Taiwanese population having life-long arsenic exposure; however, these effects may have been confounded by the presence of ergotamine-like compounds. Peripheral vascular changes have also been found in German vintners exposed occupationally to arsenic pesticides as well as arsenic in wine.

2.5.2.2 Dose-Effect/Dose-Response Relationships--The general question of how to define and employ a dose factor in attempts at quantitative assessments of human health risk for any toxicant is highly dependent upon: 1) the available

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information on the body's ability to metabolize the agent, and 2) the assessment of the relative utility of various internal indices of exposure.

The time period over which a given total intake occurs is highly important. For example, intake of one gram of arsenic over a period of years would be quite different pathophysiologically from assimilating this amount at one time, the latter probably having a lethal outcome. This time-dependent behavior is related in part to the relative ability of the body to detoxify inorganic arsenic by methylation as a function of both dose and time.

In cases of acute and sub-acute exposure, indicators of internal exposures, such as blood or urine arsenic levels, are probably appropriate for assessing the intensity of exposure.

With chronic low-level exposure, however, the available data would indicate that the total amount assimilated is probably more important than an indicator concentration without knowledge of the total exposure period. An added problem is the background level of arsenic found in some indicators due to dietary habit. Therefore, in low-level chronic exposures, arsenic levels in blood or urine would only be moderately increased over background levels. Hair arsenic levels cannot be employed as reliable indicators of exposure because no methods exist for distinguishing external contamination levels from those accumulated via absorption and metabolic distribution.

Given the above limitations concerning the use of blood, urinary or hair arsenic concentrations as internal indices of cumulative, long-term low-level arsenic exposure, the dose-effect/dose-response relationships summarized below are done so mainly in terms of external arsenic exposure levels via either inhalation or ingestion.

From available data, the Carcinogen Assessment Group (CAG) has estimated carcinogenic unit risks for both air and water exposures to arsenic. The

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quantitative aspect of carcinogen risk assessment is included here because it may be of use in setting regulatory priorities, evaluating the adequacy of technology-based controls, and other aspects of the regulatory decision-making process. However, the imprecision of presently available technology for estimating cancer risks to humans at low levels of exposure should be recognized. At best, the linear extrapolation model used (see Section 7.3) provides a rough but plausible estimate of the upper limit of risk--that is, with this model it is not likely that the true risk would be much more than the estimated risk, but it could be considerably lower. The risk estimates presented below should not be regarded, therefore, as accurate representations of true cancer risks even when the exposures involved are accurately defined. The estimates presented may, however, be factored into regulatory decisions to the extent that the concept of upper-risk limits is found to be useful.

The air estimates were based on data obtained in five separate studies involving three independently exposed worker populations. Linear and quadratic response models in both the absolute and relative form were fitted to the worker data. It was found that for the models that fit the data at the $p = 0.01$ or better level, the corresponding unit risk estimates ranged from 1.05×10^{-4} to 1.36×10^{-2}. However, linear models were found to fit better than quadratic models and absolute models fit better than relative models. The CAG also felt that exposure to trivalent arsenic was more representative of low environmental exposure than pentavalent arsenic. Restricting their unit risk estimates to those obtained from linear absolute models where exposure was to trivalent arsenic gave a range of 1.25×10^{-3} to 7.6×10^{-3}. A weighted average of the five estimates in this range gave a composite estimate of 4.29×10^{-3}.

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The unit risk estimates for water were based on an extensive drinking water study which was conducted in a rural area of Taiwan. An association between arsenic in well water and skin cancer was observed in the study population. Using the male population, who appeared to be more susceptible, the CAG estimated that the unit risk associated with drinking water contaminated with 1 µg/ℓ of arsenic was 4.3×10^{-4}.

To compare the air and water unit risks, the CAG converted the exposure units in both cases to mg/kg/day absorbed doses, which resulted in unit risk estimates of 50.1 and 15.0, respectively.

The potency of arsenic compared to other carcinogens was evaluated by noting that an arsenic potency of $2.25 \times 10^{+3}$ $(\text{mMol/kg/day})^{-1}$ lies in the first quartile of the 52 suspect carcinogens that have been evaluated by the CAG.

The U.S. EPA is presently examining information from studies on both patient and general populations which have been exposed to arsenic via medicinals or drinking water, respectively, in order to determine whether quantitative dose-response relationships can be established for non-cancerous skin lesions.

While the qualitative evidence for peripheral neurological effects and cardiovascular changes in arsenic-exposed populations is well established, the data are insufficient for determining quantitative dose-response relationships at the present time.

2.5.3 Populations at Special Risk to Health Effects of Arsenic

From a Japanese study, which reported on the poisoning of children exposed to arsenic in infant milk formula, young children may be considered at risk for acute exposure to arsenic. From the clinical reports published at the time of the mass poisoning, as well as those from follow-up studies, a

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number of signs of central nervous system involvement were noted at both the time of the episode and much later, with the follow-up studies showing behavioral problems, abnormal brain wave patterns, marked cognitive deficits, and severe hearing loss.

Because children consume more water per unit body weight than do adults, the daily intake of arsenic via drinking water per kilogram body weight would be greater in children. This might have implications regarding chronic exposure effects in children. However, it should be noted that serious health effects due to chronic exposure of arsenic in drinking water have not been found at a greater frequency in children than adults.

Individuals residing in the vicinity of certain arsenic-emitting sources, e.g., certain types of smelters, may be at risk for increased arsenic intake because of both direct exposure to arsenic in air and indirect exposure via arsenic secondarily deposited from air onto soil or other human exposure media. The relative contribution from such indirect exposures to increased risk would be difficult to define, however.

A less defined group at risk would be cigarette smokers due to some arsenic in tobacco, but it is not clear just what the quantitative increase in risk would be.

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3. BACKGROUND INFORMATION

3.1 CHEMICAL/PHYSICOCHEMICAL ASPECTS

Compounds of arsenic in various chemical forms have most prominently figured in the extensive history of the toxicology of the element. The physical properties for several of these compounds are presented in Table 3-1. In contrast, the element in the metallic, zero-valent form is of minor toxicological interest.

Geochemically, arsenic is encountered as a component of sulfidic ores, occurring as the arsenides and diarsenides of metals such as nickel, cobalt, and copper, and is present in rocks and soils at trace levels. Smelting of commercially important metal ores, therefore, often has associated with it the release into the environment of significant quantities of certain arsenic compounds. For example, arsenic trioxide, As_2O_3, a major form of the element in terms of its toxicological history, is a smelter product arising from air roasting of metallic arsenides or arsenic-containing sulfides.

Arsenic trioxide, white arsenic, is only slightly soluble in water and other solvents which do not promote chemical transformation. Its solubility in solvents which mimic physiological media may not necessarily be the same as for simple solvents, e.g., gastric juice versus water. Arsenic trioxide sublimes, the process becoming pronounced at 135°C. This property appears to have been overlooked through the years in considering analytical methods for measuring levels of the compound. Dissolution of the trioxide in aqueous media leads to formation of arsenous acid, H_3AsO_3, while alkaline treatment leads to formation of the arsenite ion, $AsO(OH)^-_2$, with both the acid and the salt being freely soluble in a number of solvents.

TABLE 3-1. PHYSICAL PROPERTIES OF ARSENIC AND ARSENIC COMPOUNDS

Chemical name	Atomic/ molecular weight	Melting point (°C)	Boiling point (°C)	Density (g/cm^3)	Crystal system	CAS Number
Arsanilic acid	217.07	232	---	1.9571^{20}	monoclinic needles from water or ethanol	98-50-0
Arsenic	74.92	817 (28 atm) (triple-point)	613 (sublimes)	5.727^{14}	hexagonal, rhombic	7440-38-2
Arsenic pentoxide	229.84	315 (dec.)	---	4.32	amorphous	1303-28-2
Arsenic sulphide	246.04	300	707	3.43	yellow or red monoclinic needles (change from yellow to red at ~170°C)	1303-33-9
Arsenic trioxide[a]	197.84	312.3	465	3.738	amorphous or vitreous	1327-53-3
Arsine	77.95	-113.5	-55 (dec. 230)	2.695 (gas)[b] 1.689^{849} (liq.)	colourless gas	7784-42-1
Calcium arsenate	398.08	---	---	3.62	amorphic powder	7778-44-1
Dimethylarsinic acid	138.00	200	---	---	prism	75-60-5
Lead arsenate	347.12	720 (dec.)	---	5.79	monoclinic leaves	7784-40-9
Methanearsonic acid, disodium salt	183.9	132-139	---	---	crystalline	144-21-8
Methanearsonic acid, monosodium salt	161.9	115-119	---	---	crystalline	2163-80-6
Potassium arsenate	180.04	288	---	2.867	tetrahedral	7784-41-0
Potassium arsenite	254.8	---	---	---	powder	13464-35-2
Sodium arsenate dodecahydrate	423.93	86.6	---	1.752-1.804	trigonal or hexagonal prism	7631-89-2
Sodium arsenite	129.91	---	---	1.87	powder	7784-46-5
Sodium cacodylate	159.98		200	---	crystalline	124-65-2

[a] Vapour pressure 0.653 (200°C)

[b] Specific gravity (air = 1)

Source: Adapted from International Agency for Research on Cancer (1980).

Arsenic pentoxide, As_2O_5, may be readily prepared by nitric acid oxidation of elemental arsenic or the trioxide. Compared to the trioxide, the pentoxide has considerable solubility in water (63.0 g/100 g water), presumably dissolving to form the relatively strong arsenic acid, H_3AsO_4. In acid media, arsenic acid has oxidizing potential (E^o=0.56V).

The relative stability of solutions of arsenic or arsenous acids to oxidation-reduction is of considerable importance in terms of valency-dependent arsenic toxicity. In oxygenated media, one would expect the pentavalent form to dominate, while reducing media would favor the trivalent state.

Arsenous and arsenic acids both form mono-, di- and tri-metal salts, the alkali-metal salts such as potassium and sodium arsenite being freely soluble in water and the alkaline salts such as calcium or magnesium arsenite being slightly soluble.

While tri-organic esters of the tri- and pentavalent arsenic acids are known, they are labile to hydrolysis and one would expect the mono- and di-organic derivatives to be even more so. This behavior has implications in the postulated role of arsenate ions in interfering with phosphorylation reactions.

Arsine (arsenic trihydride, AsH_3) is a strong hemolytic toxicant and probably the most poisonous of the arsenicals. Although generally a minor factor in the environmental chemistry of arsenicals, it can form under certain restricted conditions, i.e., via reduction in the presence of an active hydrogen-generating source.

Monomethyl and dimethyl arsenic, in the form of methylarsonous and methyl arsonic, dimethylarsinous and dimethylarsinic (cacodylic) acids, occur both in the environment and are formed via <u>in vivo</u> transformation in many mammalian

species, including man. Such organic arsenic compounds are also of commercial significance. For instance, both methylarsonic and dimethylarsinic acids, usually in the form of the mono- or dialkali salts, are employed as herbicides which, when released into the environment, may undergo reduction to the corresponding labile arsine compounds, CH_3AsH_2 (methylarsine) and $(CH_3)_2$ AsH (dimethylarsine) (Arsenic. NAS, 1977). Like trivalent inorganic arsenic, methylarsonous acid can interact with thiol groups (as can cacodylic acid) to form the CH_3-As(-S-)$_2$ and $(CH_3)_2$-As-S groups, respectively. The physical forms of arsenic in the environment depend on its mode of emission and subsequent interactions with other materials.

Arsenic, along with other trace metals, can be mobilized in association with airborne particles derived from high-temperature sources such as fossil-fueled power plants, metallurgical smelters and blast furnaces.

Arsenic compounds form insoluble complexes with soils and sediments. With soils, the interaction involves clay surfaces containing amorphous aluminum or iron oxides (Woolson, 1976).

3.2 ENVIRONMENTAL CYCLING OF ARSENIC

Inorganic arsenic is released into the environment from a number of anthropogenic sources which include primary copper, zinc and lead smelters, glass manufacturers (specifically those that add arsenic to the raw materials) and arsenic chemical manufacturers. Figure 3-1 presents a generalized scheme for the geochemical cycling of arsenic through various compartments of the environment. The atmosphere is a major conduit for arsenic emitted from anthropogenic sources to the balance of the cycle via wet and dry precipitation processes. The rate of movement of arsenic from the atmosphere is not known at present.

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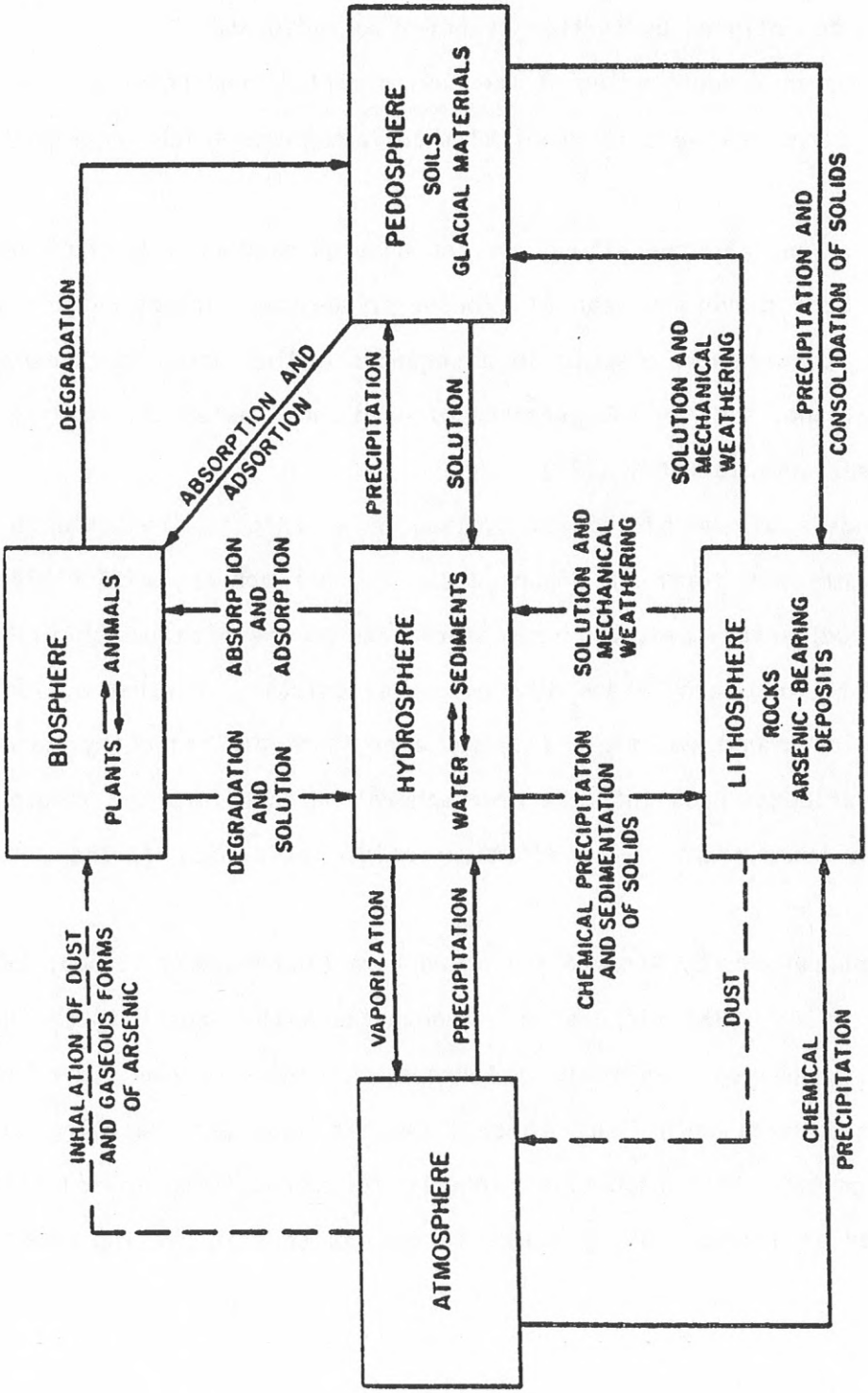

Figure 3-1. The generalized geochemical cycle for arsenic.

Source: Union Carbide (1977).

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Dry and wet fall onto soils may be followed by movement through soils either into ground water or surface water. Passage of arsenic into surface waters may then be followed by further transfer to sediments.

Complicating an understanding of the environmental cycling of arsenic is the existence of chemical and biochemical transformations which occur within the cycle.

Trivalent arsenic in the atmosphere can undergo oxidation to the pentavalent state. Such conversion can also occur in aerated surface waters. On the other hand, pentavalent arsenic in an aqueous medium which is somewhat acidic is an oxidant, and, in the presence of oxidizable material, it will react to form trivalent arsenic (NAS, 1977).

One hypothesis of the biological cycling of arsenic is presented in a generalized scheme set forth in Figure 3-2. In this scheme, Wood (1974) proposes that sedimentary bacteria reduce arsenate to arsenite, which in turn may be altered to form methyl- and dimethyloxy arsenicals. Further action of bacteria and molds transforms these intermediates to di-and tri-methyl arsine. These volatile products pass into the hydrosphere and then into the atmosphere, where oxidative transformation to dimethyl-arsinic acid and, further, to inorganic arsenic occurs.

More recent reports by Andreae and co-workers (Andreae and Klumpp, 1979; Andreae, 1979; 1980; 1983) dispute this hypothesis with respect to marine environments. In analyses performed by Andreae and other workers, no volatile organoarsenic compounds were found to be formed in seawater, negating the hypothesis suggesting that reductive biomethylation resulting in volatile compounds serves as a contributing source to the atmospheric cycling of arsenic.

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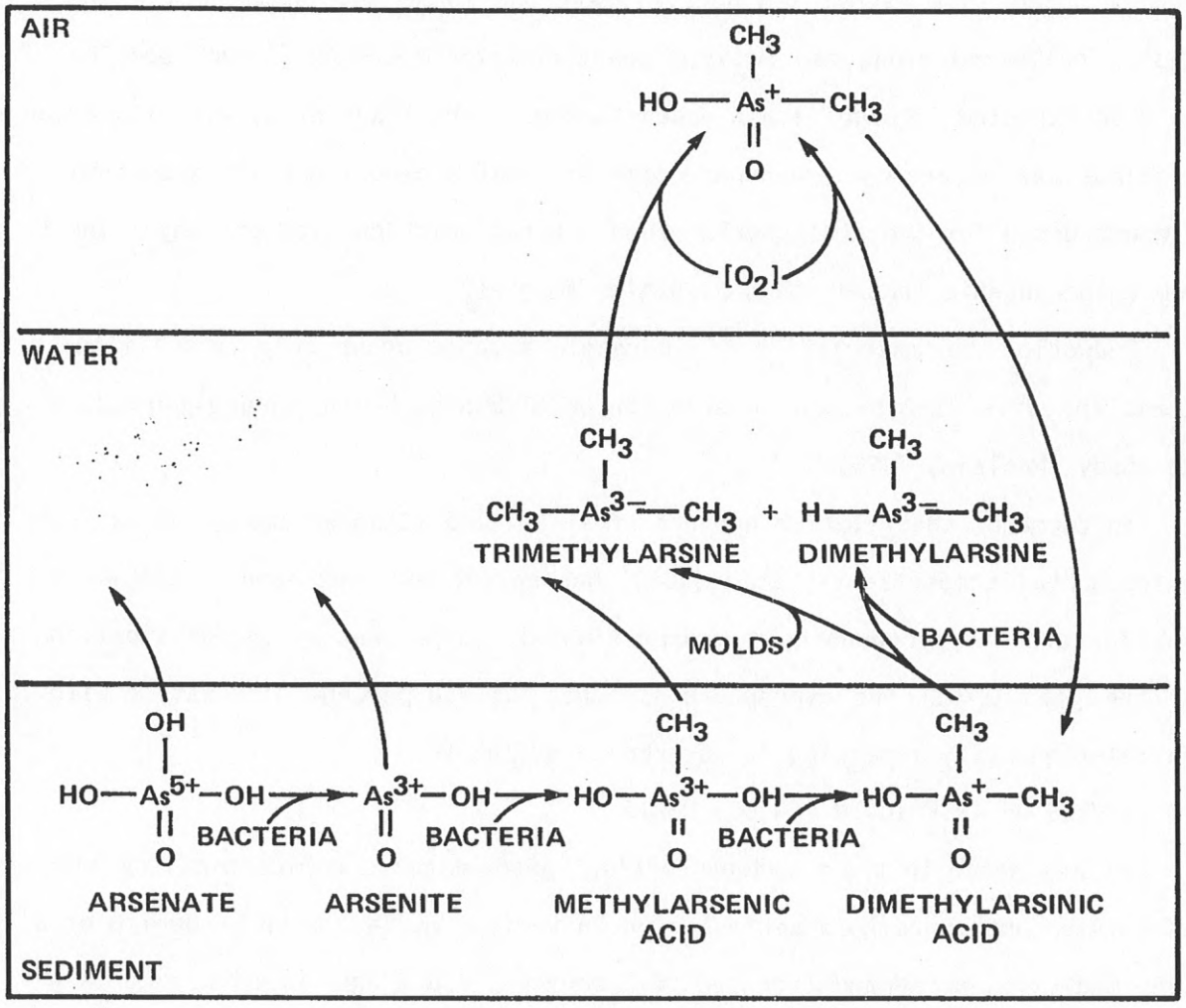

Figure 3-2. The proposed biological cycle for arsenic.

Source: Wood (1974)

While the authors did note the occurrence of biomethylation, the observed products were non-volatile, water-soluble methylated oxoacids of low toxicity. Further, the site of biotransformation was reported to be planktonic algae residing in the photic zone, rather than sedimentary bacteria. Similarly, the authors noted that methylated species were not found in a number of rain samples collected along the Pacific coast between 1976-1978. Such species would be expected if significant ocean-to-atmosphere transfer by biomethylation reactions was occurring. Andreae suggested that a global mass balance could be constructed for the atmospheric arsenic cycle which derived its major input from anthropogenic, rather than biogenic, sources.

Reduction and methylation of inorganic arsenic occur only to a limited extent in soils, 1-2 percent over a period of months having been reported in one study (Woolson, 1976).

In terms of the relative amounts of arsenic partitioned among the various environmental compartments, Suta (1980) has calculated that land is the major sink for arsenic, accounting for approximately 90 percent of the dissipation for the year 1974. The atmosphere accounts for 7-8 percent dissipation with the least quantity appearing in waterborne effluents.

3.3 LEVELS OF ARSENIC IN VARIOUS MEDIA

As was noted in the previous section, geochemical and biological cycling mechanisms contribute to arsenic burden in various media. Such burdening of a given medium is augmented from specific sources, e.g., agro chemicals containing arsenic applied to agricultural lands.

Available information on the arsenic content of media with which man interacts is generally in the form of total amounts of the element, with limited data available for assessing specific chemical forms. Since the toxicity of arsenicals varies with chemical form, any supporting data for determining chemical states will be discussed in this report, however fragmentary.

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3.3.1 Levels of Arsenic in Ambient Air

The most comprehensive data for ambient air levels of arsenic in the U.S. are those of the National Air Sampling Network conducted by the U.S. EPA. Measurements from this network are summarized in Table 3-2. All values were determined from nuclear activation analysis of individual 24-hour high volume particulate samples. As shown in Table 3-2, the number of observations available is considerably different from year to year. This is due to changes in the participation of state and local agencies operating the individual sites and, for the year 1981, only about half the samples collected have been analyzed and reported into the network data base at this time. Thus, direct comparison of the summary statistics from year to year may be of limited utility.

A closer examination of the NASN data by site indicates that in areas not influenced by copper smelters, maximum 24-hour concentrations do not exceed 0.1 $\mu g/m^3$. There are only two exceptions of approximately 600 site/years represented in the table where there were observations above 0.1 $\mu g/m^3$--Omaha, Nebraska, and Charleston, West Virginia. The site in Charleston ceased operation after 1978; therefore, it is difficult to interpret the single value above 0.1 $\mu g/m^3$. Repeated observations above 0.1 $\mu g/m^3$ have occurred at the site in Omaha, Nebraska.

Using the NASN data base, U.S. annual arithmetic mean arsenic concentrations are plotted in Figure 3-3. The plot suggests considerable variability over the five-year period with no clear direction of trend. Perhaps the most striking feature in the data is the relatively low annual arsenic level observed in 1980. A partial explanation for this observation may be the strike which idled most of the nation's copper smelters from June through September of 1980 (Eldred et al., 1983).

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TABLE 3-2. CUMULATIVE FREQUENCY DISTRIBUTION OF NASN INDIVIDUAL 24-HOUR AMBIENT AIR ARSENIC LEVELS

Year	Minimum Detection Limit	Number of Observations	Percentile[a]				Arithmetic Mean	(SD)
			30	50	70	99		
1977	.004	5385	0	0	.004	.048	.0049	.0165
1978	.006	1679	.006	.006	.008	.075	.0109	.0253
1979	.005	1263	.005	.005	.005	.077	.0091	.0192
1980	.007	2934	0	0	0	.037	.0026	.0113
1981	.007	688	0	0	0	.058	.0059	.0275

[a]Percentile values indicate the percentage of stations below the given air level. Values in $\mu g/m^3$.

Source: National Arsenic Data Base, OAQPS/OANR, U.S. Environmental Protection Agency (Akland, 1983).

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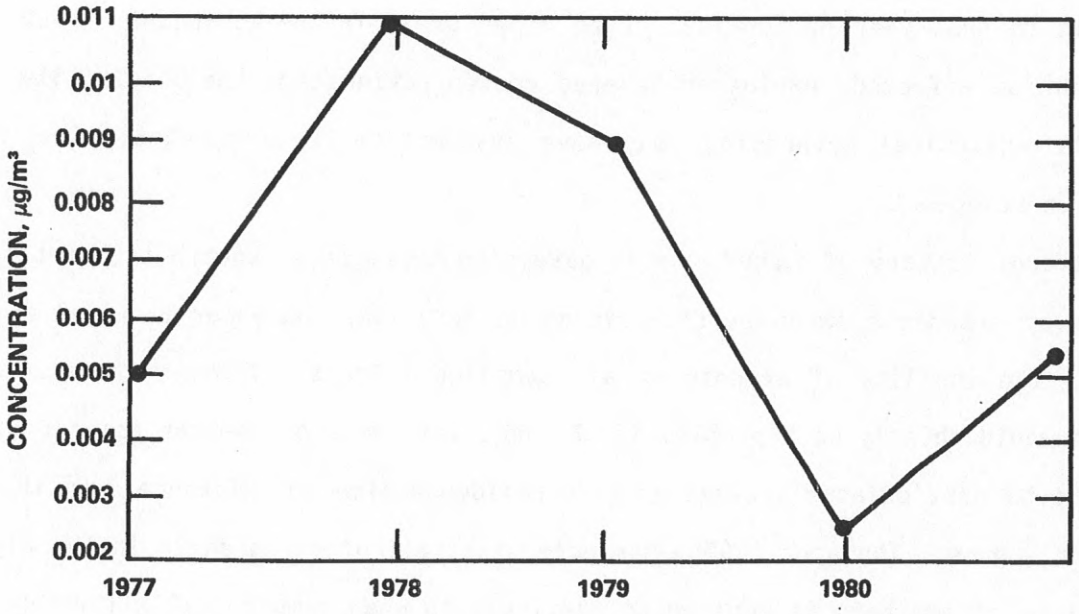

Figure 3-3. NASN annual average arsenic concentrations.

Source: National Atmospheric Data Base, OAQPS/OANR, U.S. Environmental Protection Agency (Akland, 1983).

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The locations of these primary copper smelters in the U.S. are listed in Table 3-3. Examination of the NASN data by individual sites shows that the highest arsenic levels are consistently recorded in areas of Arizona, Montana, Tennessee, Texas, and Washington, which are impacted by the copper smelting industry. Thus, the closure of many of these plants for a substantial period in 1980 may have had the effect of depressing the nationwide average concentration of arsenic in ambient air for that year. Unfortunately, the possible effect of the 1980 copper smelter strike cannot explain the low arsenic levels observed in that year nationwide. Even urban areas in the Northeast, which would not be affected, exhibited lowered concentrations and the possibility that the analytical methodology may have systematically affected results cannot be ruled out.

Several factors of importance in assessing these data concern the partitioning of arsenic between particulate-bound fractions and vapor material as well as the lability of arsenic on air sampling filters. Non-particulate arsenic would chiefly be a problem in the immediate area of smelter emissions, adhesion to particulates increasing with residence time and distance from the emission source. Thompson (1976) has noted that all of the arsenic in the air in regions of smelters is adhered to particulates when sampled 2-3 kilometers from the operation. Lao et al. (1974) have cautioned about the hazard of arsenic loss, chiefly as the trioxide, from samplers at levels of 1.0 microgram or less. Walsh et al. (1977a), however, could not remobilize particulate arsenic once trapped in samplers. Whatever the hazard, the NASN values are internally consistent, remote areas having the lowest values and regions of smelter operations having the highest levels.

An important consideration in assessing the significance of air exposure of arsenic to health risk is the chemical form or forms of arsenic in the

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TABLE 3-3. PRIMARY COPPER SMELTERS IN THE UNITED STATES

	Location	Company
1.	Anaconda, Montana	Anaconda Company
2.	Tacoma, Washington	Asarco, Inc.
3.	Garfield, Utah	Kennecott Copper Corp.
4.	El Paso, Texas	Asarco, Inc.
5.	McGill, Nevada	Kennecott Copper Corp.
6.	Hidalgo, New Mexico	Phelps Dodge Corp.
7.	Hurley, New Mexico	Kennecott Copper Corp.
8.	Hayden, Arizona	Kennecott Copper Corp.
9.	Hayden, Arizona	Asarco, Inc.
10.	Miami, Arizona	Inspiration Consolidated Copper Corp.
11.	Morenci, Arizona	Phelps Dodge Corp.
12.	Ajo, Arizona	Phelps Dodge Corp.
13.	Douglas, Arizona	Phelps Dodge Corp.
14.	San Manuel, Arizona	Magma Copper Company
15.	Copper Hill, Tennessee	Cities Services Company
16.	White Pine, Michigan	Copper Range Company

Source: National Arsenic Data Base, OAQPS/OANR, U.S. Environmental Protection Agency (Akland, 1983).

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ambient air of the United States. Work by Johnson and Braman (1975), as well as that of Attrep and Anirudhan (1977), indicates that methylated arsenic, possibly in significant amounts, has been found in air samples, but its presence can likely be ascribed to either biotic activity or the use of methylated arsenics as herbicides. This is not in total agreement with Andreae (1983), who suggests that methylated atmospheric arsenic is due predominantly to anthropogenic sources, based upon his studies of marine environments. Methylated forms become a minor factor in suburban and urban areas.

It is not clear from the available data what forms of inorganic arsenic are in most air samples: trivalent, pentavalent or mixtures of these two oxidation forms. Crecelius (1974) found that rain water samples for an urban area of the western U.S. contained only about one-third (35 percent) trivalent arsenic. In a study conducted at various sites along the Pacific coast, Andreae (1980) observed wide variations in the ratio of arsenite to arsenate in rain. He attributed this variability to emissions of predominantly pentavalent arsenic from the sea surface and trivalent arsenic from industrial emissions (particularly those from a copper smelter in the Northwest), and by redox reactions during the residence of arsenic in atmospheric particulates and hydrometeors. Caution should be exercised, however, in interpreting any extrapolations from washout samples to original air composition, given the lability of inorganic arsenic to oxidize or reduce depending on aeration, acidity of the rain sample, and presence of oxidizable matter.

In summary, then, one can assume that methylated arsenic is of minor concern in suburban and urban/industrial air samples, and that the major inorganic portion is a variable mixture of the trivalent and pentavalent forms.

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3.3.2 Levels of Arsenic in Drinking Water

The National Interim Primary Drinking Water Regulations, promulgated under the Safe Drinking Water Act, set the Maximum Contaminant Level (MCL) for arsenic in U.S. public water supplies at 50 µg/l (40 CFR Part 141). EPA is currently reviewing the arsenic MCL as part of its program to promulgate National Revised Primary Drinking Water Regulations (EPA, 1983).

In general, arsenic is not found in drinking water at levels exceeding the MCL. The Community Water Supply Survey conducted in 1969 found only 2 of the 969 supplies examined (0.2 percent) with levels exceeding 50 µg/l (McCabe et al., 1970). More recently, the Rural Water Survey conducted in 1978 reported that 0.8 percent of rural households exceeded the 50 µg/l level. Small rural communities showed a much higher population (6.6 percent) of households exceeding 50 µg/l than large rural communities (0.0 percent) and other rural areas (0.4 percent). The proportion of households exceeding 50 µg/l was greatest in the West (2.1 percent) and North Central (1.8 percent); none were found to exceed 50 µg/l in the Northeast or South (Francis et al., 1982). Compliance monitoring of public water supplies as required by the current drinking water regulations has revealed that approximately 100 of the nation's 60,000 public water supplies (0.2 percent) have levels exceeding the current MCL (Wentworth, 1983).

Notable exceptions to the generally favorable picture for U.S. population exposure to drinking water arsenic are isolated well water sources associated with geochemical enrichment by arsenic found mainly in the western U.S. and Alaska (Arsenic. NAS, 1977; Whanger et al., 1977; Harrington et al., 1978; Southwick et al., 1981). Whanger et al. (1977) have noted that well water arsenic levels in Lane County, Oregon, have ranged up to 2.2 ppm (one well) with levels generally increasing with well depth. Harrington et al. (1978) also noted that an area of Fairbanks, Alaska, had well water levels

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ranging as high as 10 ppm, representing geochemical input as well as contamination by residues from prior gold-mining activity. Southwick et al. (1981) reported levels ranging from 0.18-0.27 ppm in desert communities in Utah.

As with arsenic in air, it is important to take into account available information regarding the chemical forms of arsenic in the potable water supplies. It is reasonable to assume that the chief form of arsenic in most municipal water supplies, particularly surface reservoirs, would be pentavalent arsenic due to aeration and chlorination. Similarly, the major forms of arsenic in well waters relatively enriched in arsenic have been analyzed and also appear to be predominantly in the pentavalent inorganic state (Whanger et al., 1977; Harrington et al., 1978; Southwick et al., 1981). The chemical character of arsenic-rich well water in the U.S. versus other regions of the world will be taken up elsewhere.

3.3.3 Arsenic in Food

Perhaps the most useful body of data for assessment of the contribution of food arsenic to the total exposure picture in the U.S. is the recent survey carried out from August 1975 to July 1976 by the U.S. Food and Drug Administration (Johnson et al., 1981a,b). In Table 3-4 are summarized the average arsenic levels in various adult food classes for the period noted above; values are expressed analytically as arsenic trioxide. Corresponding average arsenic levels in food classes of 6-month-old infants and 2-year-old toddlers are summarized in Table 3-5.

In comparing the mean levels in comparable food categories, it appears that for children and adults, meat, fish, and poultry constitute the greatest dietary source of arsenic. Within this category, shellfish and other marine foods contain the highest levels of arsenic (Jelenik and Corneliussen, 1977). For infants, grain and cereal products constitute the only known source of arsenic intake from the categories measured.

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TABLE 3-4. LEVELS OF ARSENIC (As_2O_3) BY FOOD CLASS IN ADULT FOOD COMPOSITES FROM 20 U.S. CITIES (AUGUST, 1975 - JULY, 1976)

Food Class Composite	No. of Positive Composites	As, ppm Mean (Range)
Dairy products	1	0.004(0.08)[a]
Meat, fish and poultry	17	0.19(0.03-0.46)
Grain and cereal products	8	0.02(0.03-0.10)
Potatoes	ND[b]	----
Leafy vegetables	ND	----
Legume vegetables	1	0.004(0.07)
Root vegetables	1	0.004(0.07)
Garden fruits	1	0.005(0.10)
Fruits	ND	----
Oils, fats and shortening	1	0.002(0.04)
Sugar and adjuncts	ND	----
Beverages (including drinking water)	1	0.008(0.15)

[a]Mean values are based on 20 composites for every food class.

[b]ND = not detected

Source: Adapted from Johnson et al. (1981a).

TABLE 3-5. LEVELS OF ARSENIC (As_2O_3) BY FOOD CLASS IN INFANT AND TODDLER FOOD COMPOSITES FROM 10 U.S. CITIES (AUGUST, 1975 - JULY, 1976)

Food Class Composite	No. of Positive Composites	As, ppm Mean (Range)	
		Infant	Toddler
Water	ND[a]	----	----
Whole milk, fresh	ND	----	----
Other dairy and substitutions	ND	----	----
Meat, fish and poultry	ND(I) 7(T)	----	0.092 (0.06-0.29)[b]
Grain and cereal products	3(I) 2(T)	0.018(0.04-0.09)	0.008(0.03-0.05)
Potatoes	ND	----	----
Vegetables	ND	----	----
Fruits and fruit juices	ND	----	----
Oils and fats	ND(I) 1(T)	----	0.003(0.03)
Sugar and adjuncts	ND(I) 1(T)	----	0.004(0.04)
Beverages	ND	----	----

[a]ND = not detected

[b]Mean values are based on 10 composites for every food class.

Source: Adapted from Johnson et al. (1981a).

Johnson et al. (1981a) have calculated that the total adult daily intake of arsenic (as As_2O_3) for August 1975 to July 1976 was approximately 65 µg. (Corresponding elemental content can be obtained by multiplying by 0.75. Thus, the intake of elemental arsenic would be 50 µg.) This represents an increase over the 1974 value of 21 µg reported by Jelenik and Corneliussen (1977). Differences in the two years can primarily be accounted for by increases in the arsenic content of meat, fish, and poultry; grains and cereal products; beverages; and dairy products. Johnson et al. (1981a) did not discuss whether the apparent increase in arsenic levels in certain categories represented a trend or merely reflected analytical variation from year to year. It should be noted, however, that arsenic mean levels in all food categories generally declined over the years 1967-1974. Therefore, data collected over the past few years (1977-present) but, as yet, unanalyzed, should be closely examined in order to determine whether the increases seen in 1975-1976 have actually constituted the beginning of a new trend.

In no other medium is the issue of chemical forms of arsenic more complex and simultaneously more important than in food, given the fact that the diet is a major, if not the main, source of arsenic for most of the U.S. population. As will be pointed out in a later section, arsenic in crustaceans and other marine life is present in the form of various chemically complex organoarsenicals, which appear to be not only resistant to metabolism but are rapidly excreted intact. Comparatively speaking, then, these forms are regarded as being toxicologically inert.

3.3.4 Arsenic in Soils

Soil arsenic levels are mainly of concern in this section to the extent that arsenic mobility and transformation in this medium allow for passage of the element to ground water, air and the food chain (via plant uptake). This

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area has been reviewed in some detail (Arsenic. NAS, 1977; Woolson, 1977; Walsh et al., 1977b).

Background levels of arsenic in soils range from less than 1 ppm to above 40 ppm, and the relative enrichment of this background level with agricultural practices is secondary to fallout from air in the regions of industrial activity and can be of the order of 100 times. In Table 3-6 are listed some comparative values for uncontaminated soils versus soils contaminated by the repeated use of defoliants and insecticides containing arsenic (Walsh and Keeney, 1975).

Arsenic in soils is usually bound to clay surfaces containing amorphous aluminum or iron oxides, the degree of immobilization (adsorption) being a function of soil type, soil pH, phosphate levels, levels of iron or aluminum as well as residence in soil. Soil-adsorbed arsenic is rather inert to transformation or movement and it is the soluble fraction which is of interest, usually in the pentavalent form. Pentavalent arsenic arises from both soil aeration and degradation of methylated arsenic herbicides. Little reductive methylation of arsenic occurs in typical soils compared to sediments, Woolson (1976) observing that only 1-2 percent conversion of arsenate occurred over a period of months.

Transfer of soil arsenic to plants entails the soluble, labile fraction of arsenic and the site of uptake is the root system where highest levels are found. Edible portions of most food plant classes are low. This is also the case for terrestrial flora, but marine plant life such as algae accumulates considerable levels of arsenic (Irgolic et al., 1977).

3.3.5 Other Sources of Arsenic

Small and McCants (1962) found an average of 1.5 ppm arsenic in tobacco residues taken from U.S. tobacco grown in soils having average arsenic levels

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TABLE 3-6. A COMPARISON OF ARSENIC LEVELS IN ARSENIC-TREATED AND UNCONTAMINATED SOILS IN NORTH AMERICA

Sampling site	Total As content, ppm: uncontaminated soil	Total As content, ppm: treated soil[a]	Crop
Colorado	1.3 - 2.3	13 - 69	Orchard
Florida	8	18 - 28	Potato
Idaho	0 - 10	138-204	Orchard
Indiana	2 - 4	56 - 250	Orchard
Maine	9	10 - 40	Blueberry
Maryland	19 - 41	21 - 238	Orchard
New Jersey	10.0	92 - 270	Orchard
New York	3 - 12	90 - 625	Orchard
North Carolina	4	1 - 5	Tobacco
Nova Scotia	0 - 7.9	10 - 124	Orchard
Ontario	1.1 - 8.6	10 - 121	Orchard
Oregon	2.9 - 14.0	17 - 439	Orchard
	3 - 32	4 - 103	Orchard
Washington	6 - 13	106 - 830	Orchard
	8 - 80	106 - 2553	Orchard
	4 - 13	48	Orchard
Wisconsin	2.2	6 - 26	Potato

[a]These are results from soils that had been repeatedly treated with an As pesticide or defoliant. Soils treated experimentally are not included.

Source: Walsh and Keeney (1975).

REC 4961

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of 3 ppm. Of the total arsenic content of cigarette tobacco, 10-15 percent is in mainstream smoke (Thomas and Collier, 1945) in an unidentified form. In the past, levels of up to 40 ppm arsenic were detected in U.S. cigarettes (Holland and Acevedo, 1966) owing to arsenical use as pesticides. Lower current levels probably reflect curtailed use of arsenic as a pesticide in tobacco growing.

While current levels of arsenic may be lower in tobacco than had been the case, past exposure of cigarette smokers remains a health factor in considering respiratory cancer risk, given the long clinical induction period (decades) for this health effect (see Chapter 7).

REC 4962

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4. ARSENIC METABOLISM

4.1 ROUTES OF ARSENIC ABSORPTION

The significance of various routes of arsenical intake for man and various other animal species is dependent upon the physical and chemical form of the arsenical, the mode of exposure, and the animal species under study. The major routes that are of significance to general public health are inhalation and ingestion, either via direct intake of food and water or secondary intake via the inhalation of arsenic in a form and size where it is eventually swallowed. Inhalation is probably of more significance in occupational settings, while oral intake is the major exposure route for the population at large.

Percutaneous absorption of arsenic, while poorly studied, appears to be a relatively minor route of exposure except under certain occupational exposure conditions.

4.1.1 Respiratory Absorption

Some quantitative and qualitative information about the respiratory deposition and absorption of arsenic by human subjects has been reported. Holland and co-workers (1959) used a group of hospital patients (lung cancer) to assess the deposition and absorption of inhaled arsenic using arsenite-containing cigarettes labeled with arsenic-74 as well as arsenite-containing aerosols. Deposition amounted to approximately 40 percent and more than three-fourths (75 to 85 percent) of the deposited arsenic was absorbed from the lungs within 4 days. While it may be argued that the health status of these subjects may have influenced the extent of absorption, it is nevertheless reasonable to infer that relatively rapid and extensive absorption of arsenic from the human lung likely occurs.

REC 4963

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A study of a group of workers (Pinto et al., 1976) exposed to airborne arsenic in a copper smelter in 5-day test periods demonstrated average urinary arsenic excretion values ranging from 38 to 539 μg/liter to be associated with averages of air levels of arsenic ranging from 3 to 295 $\mu g/m^3$ (overall 53 μg As/m^3). Urinary arsenic was correlated with workplace air exposure (0.53, $p < 0.01$). Either direct pulmonary absorption or swallowing of larger particulate matter was evident as seen from elevations of urinary arsenic within 24 hours.

In a later study of copper smelter workers in which urinary excretion of arsenic was determined as total levels and chemically variant forms, Smith et al. (1977) studied control subjects and individuals from low, medium, and high arsenic exposure groups. In that study, the variations in concentrations of all arsenic forms isolated in urine--trivalent, pentavalent, methyl, and dimethylarsenic--were directly correlated with levels of airborne exposure (the relevant issue of arsenic biotransformation in vivo being discussed elsewhere in this chapter). An important feature of the Smith et al. (1977) report was the observation of a difference in the tightness of the correlation between excretion and exposure as a function of particle size. Both smaller, clearly respirable (<5 μm) and larger, less respirable (>5 μm) arsenic particles correlated well with excretion levels, but the less respirable arsenic-excretion relationship was seen to be much stronger than that for the finer mode particles. According to the authors, this is due to the swallowing of the large particle fraction and significant absorption from the GI tract.

Some animal data have also been reported on arsenic absorption via the respiratory tract. Bencko and Symon (1970) observed that hairless mice breathing a solid aerosol of fly ash containing 180 μg As/m^3 for several weeks had

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increases in tissue arsenic values. Since the particle size was determined to be only less than 10 μm, part of this intake may have occurred via the GI tract. Increases in tissue arsenic in two exposure groups also occurred when rats were exposed to arsenic trioxide (condensation aerosols: 1.0, 3.7, and 46 $\mu g/m^3$) for 90 days (Rozenshtein, 1970).

Relatively rapid absorption of pentavalent arsenic (arsenate solution) was noted by Dutkiewicz (1977) when rats were exposed intratracheally (arsenate solution labeled with arsenic-74; 0.1 and 4.0 mg/kg). Arsenic tissue distribution dynamics were similar for intratracheal and companion intravenous exposure studies, indicating that the rate of intratracheal arsenic uptake more closely resembles that from parenteral administration than do oral or percutaneous exposures.

The pulmonary retention of arsenic compounds with different solubilities has recently been studied by two research groups.

Inamasu et al. (1982) gave 61 male Wistar rats single intratracheal instillations of arsenic trioxide or calcium arsenate suspended in phosphate buffer (pH 6.9). Controls (19) were given instillations of the phosphate buffer solution. The total dose of arsenic administered to each animal was about 2 mg in 0.2 ml suspensions.

Four to five of the arsenic-exposed animals were killed at intervals from 15 minutes to 168 hours after instillation. The average amounts of arsenic recovered in lungs of rats at 15 minutes after the instillation of calcium arsenate and arsenic trioxide were 1146 μg and 620 μg, respectively. After 24 hours, almost all of the deposited arsenic trioxide had disappeared from the lungs, whereas only about 50 percent of the calcium arsenate had been cleared as shown in Figure 4-1.

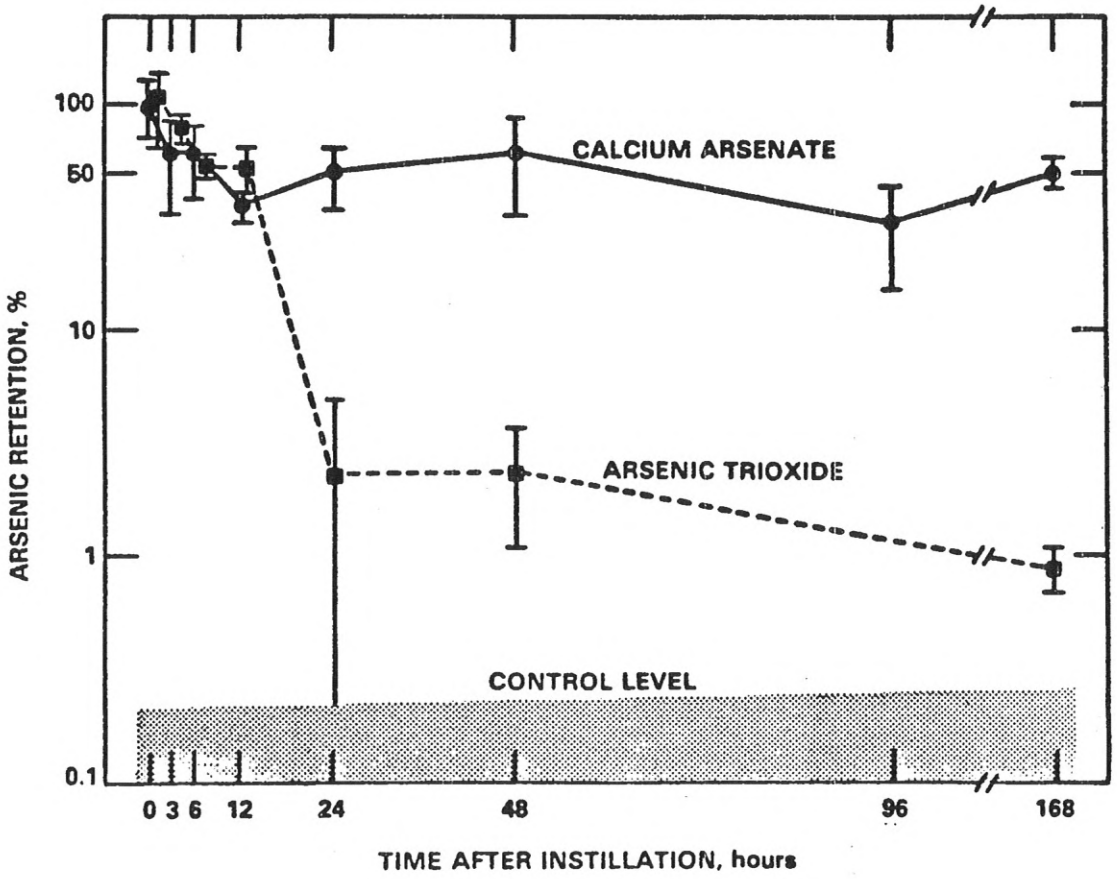

Figure 4-1. Arsenic retention in rat lungs following intratracheal instillation of a single dose. Percentage values are based on the average amount of arsenic present in rat lungs at 15 minutes after instillation of arsenic trioxide (- ■ -) or calcium arsenate (—●—). Vertical bars: means ± S.D.

Source: Inamasu et al. (1982).

Of the small remaining amount of arsenic trioxide, most gradually disappeared over the next several days, declining to a level of 5.6 µg at 168 hours after instillation, a level slightly higher than that seen in the controls (1.3 µg). In contrast, calcium arsenate remained at about the same level 168 hours after instillation as was observed after 24 hours (768 µg), clearly demonstrating a much higher level of retention compared to arsenic trioxide.

In the study by Pershagen et al. (1982), male Syrian golden hamsters were given four weekly intratracheal instillations of suspensions of arsenic trioxide, arsenic trisulfide and calcium arsenate in doses of 0.3, 0.5 and 0.5 mg arsenic, respectively. The suspensions were made in 0.9 percent NaCl, and sulfuric acid was added accordingly to equalize the acidity of the three different suspensions. Twenty animals were assigned to each treatment group. Five animals in each group were killed immediately after the first instillation. Two to five animals were then killed one week after two or four instillations and two weeks after four instillations.

The mortality was highest among the animals exposed to arsenic trioxide. In this group, 9 of the remaining 11 animals not sacrificed for tissue analysis had died by the week following the third instillation. In contrast, at the second instillation, two animals died in the group receiving arsenic trisulfide but no further deaths occurred in this group. A total of three animals receiving calcium arsenate died during the first week following the fourth instillation. Aside from those animals specifically sacrificed for tissue analysis, no other deaths occurred in this group either.

In the lungs, the amounts of arsenic were 386, 755 and 866 mg/kg wet weight immediately following instillation of arsenic trioxide, arsenic sulfide and calcium arsenate, respectively. One week after the second instillation

the amounts were 0.81, 9.2 and 579 mg/kg, respectively. In Figure 4-2 it can be seen that after the fourth instillation the differences between arsenate-exposed animals and the other groups were even more pronounced. Examination of the lungs revealed severe lung damage only among animals exposed to calcium arsenate. In all groups, areas with epithelial hyperplasia and metaplasia were seen.

Although different species and different time intervals were used in the above studies, the results were very consistent, i.e. arsenic trioxide was rapidly cleared from the lungs, whereas calcium arsenate was very slowly eliminated. The differences appear to be related to the relative solubility of the compounds, calcium arsenate having the lowest solubility. The doses in these two experiments were of the same magnitude, but the lung damage reported by Pershagen et al. among the arsenate-exposed animals might have influenced the clearance mechanisms. In addition, the possibility of higher acidity in the suspensions used by Pershagen et al. may also have had an influence.

The large differences in retention of arsenic compounds demonstrated in these two studies are of great interest in relation to the association between airborne arsenic and lung cancer. These differences in retention might explain the relatively high concentration of arsenic found in deceased smelter workers whose last exposure to arsenic occurred many years prior to death (Brune et al., 1980) (see Section 4.4). These workers were thought to be exposed to arsenic trioxide, but it may be that the retained fraction noted in the lungs was another arsenic compound of less solubility.

4.1.2 Gastrointestinal Absorption

In both man and experimental animals, factors which govern the absorption of arsenic from the gastrointestinal tract include the chemical form of the element, its physical characteristics, and dosing level. It can be stated

REC 4968

TR 1653

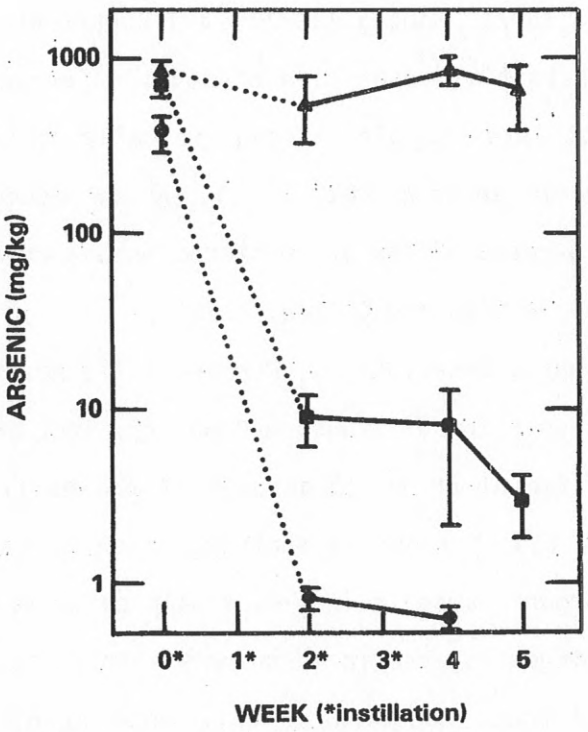

Figure 4-2. Lung concentrations of arsenic in hamsters given weekly intratracheal instillations of arsenic trioxide (●), arsenic trisulfide (■), or calcium arsenate (▲) (bars indicate ±1 S.D.). Animals at Week 0 were killed immediately following the first instillation; other animals were killed either 1 or 2 weeks after an instillation.

Source: Pershagen et al. (1982).

that soluble arsenicals will be generally more extensively absorbed than the insoluble forms. On the other hand, one should be cautious in extending correlations of simple water solubility to the chemical milieu existing in the GI tracts of various species.

Taken collectively, the reports of Coulson et al. (1935), Ray-Bettley and O'Shea (1975), Crecelius (1977), Mappes (1977), and Buchet et al. (1981a,b) demonstrate that very substantial absorption of soluble inorganic trivalent arsenic from the GI tract into the bloodstream typically occurs. Greater than 95 percent of inorganic arsenic taken orally by man appears to be absorbed, with less than 5 percent of the administered amount appearing in feces (Coulson et al., 1935; Ray-Bettley and O'Shea, 1975).

Consistent with the above observations, Mappes (1977) observed that daily oral intake of an aqueous solution of around 0.8 mg trivalent arsenic resulted in a daily urinary excretion of 69 to 72 percent of the daily dose in one subject. Also, Crecelius (1977) reported that ingestion of 50 µg trivalent and 13 µg pentavalent inorganic arsenic in a wine sample led to the appearance of 80 percent of all the ingested arsenic in urine within 61 hours. Crecelius (1977), however, reported that ingestion of well water mainly containing identified pentavalent inorganic arsenic led to urinary clearance of half the intake within approximately 3 days.

More recently, Buchet et al. (1981b) found that daily arsenic excretion via urine in human volunteers exposed to the dose range 125-1000 µg/day amounted to 60 percent of the dose. Steady state was achieved within 5 days after arsenic dosing began.

In contrast to the relatively high absorptive rate for soluble inorganic arsenic, Mappes (1977) reported that insoluble arsenic triselenide (As_2Se_3), when taken orally, passes through the GI tract with negligible absorption.

REC 4970

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Arsenic intake via the diet of non-occupationally exposed populations requires that one consider the issue of bioavailability. Arsenic in foodstuffs is probably incorporated into the matrix of these commodities in a variety of ways.

The "shrimp" arsenic present in crustaceans and other fish appears to represent a complex organic form of the element which has prompted considerable recent study (LeBlanc and Jackson, 1973; Westöö and Rydälv, 1972; Munro, 1976; Edmonds et al., 1977; Penrose et al., 1977; Crecelius, 1977; Edmonds and Francesconi, 1977). In brief, the results of such studies indicate that the arsenic present in shellfish and other marine foods appears to be extensively absorbed and rapidly excreted intact as a complex organoarsenical by man and animals, and, as such, does not appear to pose a particular health threat to man.

Studies of the oral intake and absorption of arsenicals in experimental animals have also been conducted and generally confirm the findings derived from the above human studies. More specifically, soluble inorganic arsenic, delivered as either trivalent or pentavalent solutions, is almost completely absorbed from the GI tract of rats (Coulson et al., 1935), with 88 percent absorption being observed for arsenic trioxide solution (Urakabo et al., 1975; Dutkiewicz, 1977) and 70 to 90 percent for arsenate solution. Similar observations have been made for pigs (Munro et al., 1974), with 90 percent of arsenic trioxide solution being absorbed, and monkeys (Charbonneau et al., 1978a), with 98 percent of arsenic trioxide being absorbed. Also, Charbonneau et al. (1978b) fed arsenic-containing fish (Atlantic grey sole) to adult female monkeys as a homogenate (1 mg fish arsenic/kg body weight) and noted that about 90 percent of the intake was absorbed, of which about 75 percent appeared in urine after 14 days. In a related study, swine and adolescent

monkeys were seen to absorb approximately 70 and 50 percent, respectively. On the other hand, arsenic trioxide in suspension given orally to rabbits and rats was reported to result in only about 40 and 30 percent absorption, respectively (Ariyoshi and Ikeda, 1974).

4.1.3 Transplacental Passage

Potential fetal exposure to toxic elements via the mother is a matter of major importance given the potential sensitivity of *in utero* development to deleterious impacts of exogenous toxic agents.

In an arsenic-detection study of maternal-newborn blood groups, Kagey et al. (1977) reported that cord blood levels approximated those of mothers in 101 subject sets. Tissue analysis (Kadowaki, 1960) of fetus arsenic in a presumably healthy Japanese population indicated measurable element levels by at least month four of gestation which increased to month seven. Of importance in this study was the observation that brain levels, as well as those of bone, liver, and skin, were the highest of all tissue tested.

Complicating the issue is the chemical nature of the tissue arsenic assayed in either of the two studies noted above, inasmuch as precise chemical speciation was not attempted. Also, the Japanese study presumably did not select material in a manner such that dietary histories could be discerned. Thus, questions can be raised regarding implications of these data for fetotoxicity.

Transplacental transfer of arsenic has also been demonstrated in experimental animals. Transplacental transfer of arsenate administered parenterally in hamsters has been demonstrated by Ferm's laboratory (Ferm, 1977; Hanlon and Ferm, 1977). The movement was rapid, with embryonic tissues showing levels close to those in maternal blood 24 hours after dosing. Trivalent arsenic exposure results in transplacental passage in pregnant rats. Arsenic was detected in newborn rats when the dams received arsenic trioxide in their diets.

4.2 BIOTRANSFORMATION PROCESSES IN VIVO

An understanding of the metabolism of inorganic arsenic by man and a number of other species is substantially complicated by a series of newly-revealed biotransformations, including methylation of inorganic arsenic. It is thus appropriate to discuss *in vivo* transformation processes at this point, since many of the data dealing with blood transport, tissue distribution and subsequent excretion are much better understood in light of these findings.

A major factor in the determination of transformation processes for arsenic in man and other animals was the evolution of appropriate analytical methods within the decade which permit chemical speciation of chemically variant forms of arsenic with reference to both oxidation-state lability and inorganic versus organo-substituted arsenic.

These procedures involve different analytical approaches and include selective reduction of various arsenic forms to the hydride, and subsequent analysis by colorimetry (Lakso et al., 1979), emission spectrometry (Braman and Foreback, 1973; Crecelius, 1977), atomic absorption spectrometry (Edmonds and Francesconi, 1977; Buchet et al., 1980), and gas-liquid chromatography (Andreae, 1977; Talmi and Bostick, 1975). Alternatively, inorganic arsenic (III) or (V) and methylated forms can be directly measured by ion-exchange chromatographic techniques (Tam et al., 1978; Henry and Thorpe, 1980).

There are a number of points germane to consideration of *in vivo* transformations of arsenic: 1) biomethylation of inorganic arsenic; 2) oxidation-reduction of inorganic arsenic *in vivo*; 3) the relative chemical stability of inorganic arsenic to oxidation-reduction as it affects experimental dosing and chemical speciation in biological media.

4.2.1 Biomethylation of Inorganic Arsenic in Humans and Experimental Animals

An extensive literature has recently appeared documenting the *in vivo* methylation of inorganic arsenic to monomethyl and dimethyl arsenic (the latter

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being the major methylated metabolite) in every mammalian system studied to date, including man.

While the quantitative features of this phenomenon may vary among species, one can generally state that: 1) dimethyl arsenic is the major transformation product in both humans and animals, with higher amounts of monomethyl arsenic, when formed, found in humans; 2) methylation is assumed to be a route of detoxification of the more toxic inorganic forms; 3) dimethyl arsenic appears to be a terminal metabolite, formed relatively rapidly and rapidly excreted; 4) while the in vivo methylating capacity of a given system may persist over a range of inorganic arsenic exposure, at some point the body burden of the unmethylated fraction is enough to induce toxic effects, evidenced by the extensive literature dealing with inorganic arsenic toxicity; 5) retrospective assessment of earlier data dealing with arsenic metabolism, including distribution and excretion, must be viewed in light of current knowledge about biomethylation in different species; and 6) biomethylation appears to be a reductive process involving step-wise arsenic reduction and methyl transfer steps.

4.2.1.1 Human Studies--Using a method that permits the determination of tri- and pentavalent inorganic arsenic as well as mono- and dimethylarsenic acids via selective reduction, volatilization, and helium-arc emission detection, Braman and Foreback (1973) analyzed the urinary excretion of arsenic in four human subjects. About 66 percent of the total urine arsenic concentration (22.5 ppb) was present as dimethylarsinic acid and 17 percent as pentavalent inorganic arsenic. Trivalent inorganic arsenic and methylarsonic acid were present in equal amount, approximately eight percent each.

Crecelius (1977) reported the urinary excretion of form-variable arsenic when a human subject ingested arsenic-rich wine (50 µg trivalent and 13 µg pentavalent). About 80 percent of the arsenic ingested with the wine was

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excreted within 61 hours. Of the total excreted, 63 percent was in the form of dimethylarsenic acid, 18 percent was monomethyl arsenic acid, and approximately 9 percent each was in the two inorganic forms.

Consumption of well water containing 200 µg of arsenate by a subject in the same study showed urinary trivalent arsenic at near background levels with an elevation in pentavalent form as well as significant excretion of dimethylarsenic. Of the total amount ingested, about 50 percent was recovered in urine by 3 days. Arsenic as contained in canned crab tissue was also studied in this experiment. It has been established that arsenic is present in marine foods in an organic form which is excreted intact.

The study of Smith et al. (1977), using basically the same speciation/analysis techniques noted in the previous study and involving urinary profiles for a group of copper smelter workers, also confirmed transformation processes in vivo. In controls, as well as in three study groups that varied as to intensity of airborne trivalent arsenic oxide exposure, dimethyl arsenic was the dominant species in urine, followed by methyl arsenic, trivalent arsenic and pentavalent arsenic, in descending order.

In another smelter worker study, Buchet et al. (1980) assessed the distribution of arsenic and metabolites in urine samples in different groups according to the degree of inorganic arsenic exposure. Total urinary arsenic in exposure groups ranged from 74 to 934 µg/liter, of which 75 percent represented methylated forms (mono- and dimethyl), with dimethyl arsenic predominating. Control subjects showed a somewhat higher level of methylated arsenic in urine, approximately 90 percent, suggesting some dependency of the extent of methylation on the level of exposure.

A number of recent studies have described in more detail the biomethylation of inorganic arsenic using human volunteers.

Buchet et al. (1981a) followed the urinary excretion of inorganic and methylated arsenic in 3-5 volunteers ingesting single amounts of arsenic at a dose of 500 µg, in the form of either arsenite, monomethyl or dimethyl arsenic. After 96 hours, 46 percent of the dose in subjects given arsenite (trivalent arsenic) was excreted, 25 percent in the inorganic form and 75 percent as methylated metabolites. Of the latter, one-third was monomethyl arsenic and two-thirds was the dimethylated form. Dimethyl arsenic was excreted intact, 75 percent of the ingested amount appearing in urine by 96 hours. With monomethyl arsenic, excretion reached 80 percent by 96 hours, with around 13 percent of the urine level representing conversion to the dimethyl form.

In a follow-up report, these workers (Buchet et al., 1981b) monitored the urinary excretion of various arsenical forms in 4 human subjects undergoing repeated ingestion (5 days) of trivalent inorganic arsenic as a meta arsenite salt at 4 levels--125, 250, 500 or 1000 µg As. By 14 days, the percent of methylated forms of total forms ranged from 74-93 percent over the intake range. From this study, it would appear that the methylating capacity of the human subject was unaffected up to the 500-µg As level, at which point some decrease in methylated arsenic as a percentage of total was observed.

Yamauchi and Yamamura (1979) reported their results with 3 volunteer subjects who ingested an arsenic-rich extract (prepared from a particular kind of seaweed) containing 2.88 ppm total arsenic. Of the total amount, 86 percent was pentavalent inorganic arsenic, 7 percent was trivalent inorganic arsenic and 7 percent was dimethyl arsenic. These volunteers ingested the preparation as a single dose at a level of 10 µg/kg body weight, for total amounts of 650, 680, and 760 µg in the three subjects. By 48 hours, urine levels of total arsenic amounted to 36 percent of the dose. Of the excreted amount, dimethyl and monomethyl arsenic accounted for 47.4 and 25.3 percent, respectively.

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4.2.1.2 Animal Studies--To date, biomethylation processes involving inorganic arsenic and experimental animals have been documented in dogs (Lakso and Peoples, 1975; Charbonneau et al., 1978a; Tam et al., 1979a), mice (Vahter, 1981), rabbits (Marafante et al., 1980; Bertolero et al., 1981), the bovine (Lakso and Peoples, 1975), and the rat (Odanaka et al., 1978). While the level of methylated forms of arsenic in most experimental species resembles that in man, approximately 80 percent, there is a greater amount of the dimethyl and a lesser amount of monomethyl arsenic.

Vahter (1981) has shown: (1) that the degree of biomethylation is dose-dependent, at least in mice, falling off in relative percentage with increasing level of dosing; (2) that this dependency probably accounts for the observation of dose-dependent retention in mice; and (3) methylation occurs to a greater extent with trivalent arsenic than with the pentavalent form, although retention, relative to total dose, is greater with the trivalent form.

Recently, Vahter et al. (1982) have reported that the Marmoset monkey, alone among all mammalian experimental species studied thus far, does not methylate inorganic arsenic.

4.2.2 In Vivo Oxidation/Reduction of Inorganic Arsenic In Mammalian Systems

From all available evidence, the biochemical mechanism of *in vivo* methylation of inorganic arsenic appears to be a reductive process, and sequential arsenic reduction and transmethylation steps in the pathway have been documented in microbial systems (Challenger, 1978; McBride et al., 1978). In mammalian systems, recent studies support a similar reduction/methylation sequence as observed in microflora.

Oxidation of trivalent inorganic arsenic to the pentavalent state has been claimed in dogs (Ginsberg, 1965), rats (Winkler, 1962), mice (Bencko et al., 1976), and humans (Mealey et al., 1959). An important factor in considering these studies critically is the fact that none of the reports considered

the presence of methylated arsenic, which may well have affected the analytical techniques employed and the analytical data obtained. Secondly, except for the Bencko et al. (1976) study, it is not clear that careful attention was paid to the oxidation state composition of dosing media or the effect of sample handling on oxidation state stability. In the Mealey et al. (1959) report, the analytical method involved acidification of urine with hydrochloric acid and extraction of the presumed "trivalent" arsenic into benzene, leaving the presumed "pentavalent" form in the aqueous phase. Since Mushak et al. (1977) have shown that methylarsonic and dimethylarsinic (cacodylic) acid behave like the pentavalent inorganic form in this extraction procedure, it is probable that the "arsenate" fraction was mainly methylated arsenic.

In the study of Crecelius (1977), where chemical speciation techniques were employed, it does not appear that ingestion of a sample containing mainly arsenite (trivalent form) is associated with excretion of pentavalent inorganic arsenic as the chief inorganic form. After 61 hours, 80 percent of the ingested amount appeared in urine, with the two inorganic forms each constituting minor fractions, mono- and dimethyl arsenic being the main forms.

Evidence for the in vivo reduction of pentavalent to trivalent inorganic arsenic has been claimed in several early reports. Lanz et al. (1950) reported some reductive conversion (10-15 percent) of arsenate to arsenite in rats, using as a method the precipitation from urine of arsenate as a mixed salt and analysis of the supernatant for arsenic (III). The accuracy of this method for partitioning trace arsenic levels is questionable. Furthermore, at the time of this study, the presence of methylated arsenic was not known. Therefore, it is not possible to accept the authors' conclusions since unprecipitated arsenic could also have consisted of methylated forms.

Ginsberg (1965) reported that 14 percent of urinary and 6 percent of plasma arsenic in dogs receiving intravenous infusion of arsenate was in the

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form of trivalent arsenic. In this study, trivalent was presumably separated from pentavalent arsenic by chelation-extraction using ethyl xanthate. Based on current knowledge that methylated arsenic was present, it is difficult to accept the data without knowledge of the behavior of mono- and dimethyl arsenic in this analytical method.

In the recent report of Tam et al. (1979b) using dogs dosed with arsenate, a small amount of trivalent inorganic arsenic was detected in urine, using ion-exchange and thin-layer chromatographic techniques. These authors did not independently determine the extent of artifactive interconversion between the two forms using these techniques.

In a recent study by Vahter (1981), in which mice and rats were administered ^{74}As-labeled trivalent or pentavalent arsenic, the author reported that increases in retention with dose were less pronounced for the pentavalent form than for the trivalent form due to the fact that elimination of pentavalent arsenic seemed to be less dependent on methylation. Nevertheless, increases in retention with pentavalent arsenic were observed. Vahter discussed the possibility that the observed dose-related increase in retention after exposure to pentavalent arsenic may have been partly due to *in vivo* reduction of the pentavalent to trivalent form. Noting the work of McBride et al. (1978), whose studies indicated that certain microorganisms required reduction of pentavalent arsenic to trivalent before methylation could proceed, Vahter suggested that a similar mechanism might have been functioning in both the mice and rats. Evidence to support this hypothesis was presented in the author's observation that trivalent arsenic seemed more readily methylated than pentavalent.

Two recent studies, carefully designed for the specific purpose of addressing the oxidation/reduction issue for inorganic arsenic *in vivo*, have demonstrated that pentavalent arsenic (arsenate) undergoes reduction *in vivo* to

the trivalent state in the rat (Rowland and Davies, 1982) as well as in mice and rabbits (Vahter and Envall, 1983). In both of these investigations, the issue of artifactual interconversion of these two valence states was carefully addressed.

In the rat (Rowland and Davies, 1982), administration of moderate doses of pentavalent arsenic led to rapid reduction to the trivalent form. In mice and rabbits, the rate of conversion was somewhat slower than in the rat, but still occurred at a significant rate. Trivalent arsenic was measured in arsenate-dosed mice plasma by 1 hour post-dosing.

In a summary report, Peoples (1983) reported, without experimental detail, that the feeding of sawdust containing chromated copper arsenate did not result in measurable urinary levels of trivalent arsenic. Since these animals were exposed to copper as well as chromium (VI), in addition to arsenate, it is difficult to differentiate any influence these agents may have had on the results. Peoples (1983) also noted that renal perfusion of dogs with a very dilute solution of arsenate did not lead to renal reduction of pentavalent to trivalent arsenic. In the absence of experimental details, it is not possible to determine what steps were taken to avoid artifactual conversion of trivalent back to pentavalent arsenic, if the lower valence form was indeed formed.

Studies by Lerman and Clarkson (1983) of penta- and trivalent arsenic in the rat are fully consistent with a reductive methylation process. Using in vivo and in vitro techniques, the authors showed that the isolated rat liver hepatocyte readily methylates trivalent arsenic, while virtually no conversion occurs with the pentavalent form, although it is known that pentavalent arsenic is also extensively methylated in vivo. These data suggest that arsenate must first be converted to arsenite elsewhere in the organism.

Two recent studies using human subjects and identical chemical speciation techniques for arsenic appear to offer conflicting data regarding pentavalent arsenic reduction.

Crecelius (1977) noted that ingestion, by a single subject, of a sample of well water tested as having 200 µg As only in the pentavalent form resulted in a urinary level of trivalent arsenic which was virtually the same as background concentration before taking the arsenic sample. Although urine was collected for approximately 3 days, a significant amount of the total dose was unaccounted for, making it difficult to draw any conclusions from the study.

Yamauchi and Yamamura (1979) fed a preparation of seaweed containing 86 percent pentavalent arsenic and 7 percent each of trivalent inorganic and dimethyl arsenic to 3 human subjects as one dose at a total dosing of 650, 680, and 760 µg total arsenic. By 48 hours, based on their method which was the Braman et al. (1977) procedure, 36 percent of the original dose appeared in urine, with 75 percent present as methylated forms and about 17 percent present as trivalent arsenic (6.3 percent of the total amount ingested). The authors calculated that the amount of trivalent inorganic arsenic was greater than could be ascribed to the small amount ingested originally and they stated that the fraction represented in vivo reduction of pentavalent arsenic. Since the mean intake was approximately 700 µg, the 7 percent present as trivalent inorganic arsenic amounted to 49 µg, of which 36 percent or 18 µg would have been expected to appear in urine in some form. Using 75 percent methylation, only approximately 4-5 µg would have been present as the trivalent form, when in fact a mean value of 43.4 was found (range: 36-51 µg). Since the Braman et al. (1977) method is a reasonably accurate speciating technique and there is little evidence that samples were handled in a way to promote artifactive formation of trivalent arsenic after excretion, the data cannot be readily questioned on this basis.

4.2.3 Chemical Stability of Trivalent and Pentavalent Inorganic Arsenic to Oxidation-Reduction

In aerated water, trivalent inorganic arsenic will undergo extensive oxidation to the pentavalent form, particularly when present at low levels (Feldman, 1979).

The pH of aqueous solutions appears to be the major factor in the relative stability of either valency form. Buchet et al. (1980) found that trivalent arsenic in solutions at pH of 7.0 or 9.6 were oxidized to the extent of 70-90 percent within one week, compared to 25 percent conversion at pH 4.8.

Vahter and Norin (1980) also noted rapid oxidation of As (III) in aqueous solution at room temperature, while storage at 4°C showed little conversion.

Pentavalent inorganic arsenic, on the other hand, is stable at neutral or alkaline pH but undergoes reduction with decreasing pH (Durrant and Durrant, 1966).

In studies directed to *in vivo* transformations of inorganic arsenic, urine levels are commonly used and some data exist regarding valency stability of arsenic in urine.

Buchet et al. (1980) found that trivalent inorganic arsenic in urine at pH 7.0 or less was relatively stable, with only 10 percent oxidation occurring by 7 days. At pH 9.5, 50 percent of oxidation occurred within one day.

4.3 DISTRIBUTION OF ARSENIC IN MAN AND ANIMALS

Blood is the main vehicle for transport of arsenicals from absorption sites to the tissues, with the hemokinetic character of arsenic being dependent on the animal species studied.

It is readily apparent from the literature that the rat constitutes an anomalous model for studies of the fate of inorganic arsenicals *in vivo* and this includes the clearance behavior of rat blood-borne arsenic (Hunter et al., 1942; Ducoff et al., 1948; Lanz et al., 1950; Ariyoshi and Ikeda, 1974;

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Klaassen, 1974; Tsutsumi and Kato, 1975; Dutkiewicz, 1977). In the case of the rat, arsenic in blood is only slowly cleared following exposure, with about 80 percent of the total blood arsenic content localized in the erythrocyte. The half-times of blood clearance for inorganic arsenic in the rat (trivalent or pentavalent) is on the order of 60 to 90 days (Lanz et al., 1950; Ariyoshi and Ikeda, 1974).

Arsenic in the blood of other species--man (Ducoff et al., 1948; Mealey et al., 1959; Tam et al., 1979b), mice (Lanz et al., 1950; Crema, 1955), rabbit (Hunter et al., 1942; Ducoff, 1948; Klaassen, 1974), dog (Lanz et al., 1950; Hunter et al., 1942), and primates (Hunter et al., 1942; Klaassen, 1974)--whether given as the pentavalent form or as the trivalent form, is rapidly cleared. Normal blood arsenic values for individuals in the U.S. and Europe are in the range of 1-5 µg total arsenic/liter whole blood (Bergstromn and Wester, 1969; Damsgaard et al., 1973; Kagey et al., 1977; and Valentine et al., 1979). According to Kagey et al. (1977), cigarette smokers showed mean blood arsenic levels approximately 50 percent higher than nonsmokers. It is reasonable to assume that human background blood levels reflect mainly dietary arsenic, much of which would likely be in various organo-arsenical forms that are extensively absorbed and rapidly cleared.

Clearance of arsenic in dog and man was found to fit a three-compartment model by Charbonneau et al. (1978a) and Tam et al. (1979b) with half-times of 1, 5, and 35 hours, respectively. When contrasted with the work of Tam et al. (1978), which reported the time-dependent in vivo methylation of arsenic and excretion in dogs, the various components presumably relate to initial excretion of inorganic arsenic, followed by clearance of dimethyl arsenic.

The tissue partitioning of arsenic in man has been studied using both autopsy and dosing data. Kadowaki (1960) found (measurements in ppm, wet

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weight) that nails (0.89), hair (0.18), bone (0.07-0.12), teeth (0.08) and skin (0.06) generally housed the highest absolute amounts of arsenic, while heart, kidney, liver and lung contained somewhat lower levels (0.04-0.05). Brain tissue (0.03) had an arsenic level only slightly lower than other soft tissues. Liebscher and Smith (1968), analyzing tissue samples (ppm dry weight) from non-exposed sources in Scotland, observed lung to have the highest levels (0.09), with liver and kidney levels (0.03) not materially different from other soft tissue. Like the Kadowaki study, hair (0.46), nails (0.28) and skin (0.08) had the highest absolute values; however, bone and teeth (0.05) did not contain levels appreciably different from some other tissues (pectoral muscles, 0.06; ovary, 0.05; and pancreas, 0.05).

In addition to the autopsy studies by Kadowaki (1960) and Liebscher and Smith (1968), Larsen et al. (1979) have recently reported on a detailed study of the topographical distribution of arsenic in normal human brain tissue. Arsenic is distributed throughout all brain regions, with white matter showing higher levels than gray matter.

In looking at tissue distribution of arsenic in experimental animals, exposure of various species to either tri -or pentavalent arsenic leads to the initial accumulation of the element in liver, kidney, lung, spleen, aorta, and skin (Hunter et al., 1942; Ducoff et al., 1948; Lanz et al., 1950; Peoples, 1964; Ariyoshi and Ikeda, 1974; Cikrt and Bencko, 1974; Klaassen, 1974; Tsutsumi and Kato, 1975; Urakabo et al., 1975; Dutkiewicz, 1977; Sabbioni et al., 1979; Marafante et al., 1980). With the exception of the rat, a species in which metabolism of arsenic is only a very limited model for study of this element (vide supra), clearance from soft tissue is rather rapid except for the skin, where the high sulfhydryl group content may promote tight trivalent arsenical binding. As also seen with human tissue, arsenic is apparently lodged in

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brain of experimental animals exposed to arsenic, with slow clearance reported (Crema, 1955).

Recently, Vahter and Norin (1980) compared the dependency of dose and valency form of inorganic arsenic on tissue compartmentalization of arsenic in mice. Unlike most of the earlier reports, these workers used chemical speciation techniques (ion-exchange chromatography) to verify that their dosing media contained purely tri- or pentavalent arsenic. Using single oral dosing at 0.4 or 4.0 mg/kg levels and radioisotopic tri- or pentavalent arsenic, levels of arsenic in kidney, liver, bile, brain, skeleton, skin and blood were always greater (2-10 fold) in terms of percent total dose for the trivalent form than for the pentavalent form, and most pronounced at the higher dose. These workers ascribe much of this difference to relative methylating efficiency as a function of exposure level and valence form.

In a similar study using Golden Hamsters exposed to injected tri- or pentavalent radioisotopic arsenic, with care taken to assure valence purity, Ckirt et al. (1980) found that levels of arsenic in liver, kidneys, gut wall and bile were always greater, 2 to 25-fold, with trivalent arsenic exposure.

4.4 ARSENIC ACCUMULATION

The long-held view of arsenic as an element that accumulates in the body was mainly based on the behavior of arsenic in the rat, an animal model which in retrospect was the least helpful in understanding the fate of the toxicant *in vivo* for other mammalian species and man.

Based on current arsenic elimination data for all mammalian species studied other than the rat (*vide supra*), one concludes that marked long-term accumulation of arsenic generally does not occur in physiologically vital components of the body. This is in contrast to, say, long-term lead accumulation in bone or cadmium accumulation in renal cortex. Autopsy tissue data for

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human subjects of different ages are not conclusive regarding possible long-term tissue accumulation. Kadowaki (1960) did observe higher mean levels of arsenic in skin and kidney samples of subjects approximately 50 years of age versus infant values, but dietary histories of the subjects were not available to allow for differentiation of increases in arsenic levels due to current versus past exposures for the older subjects. Deposition in hair is really excretory in nature, not accumulative.

Brune et al. (1980) have reported that lung tissue from retired smelter workers from the Rönnskär smelter in Sweden, on autopsy, had median values for arsenic which were about 8 times higher than that for a control group. Kidney and liver values, however, were not significantly different between smelter worker groups and controls. Arsenic accumulation in the lung of smelter workers even after several years of retirement and removal from workplace exposure (interval of 2-19 years) suggests that a very insoluble form of arsenic exists in smelter ambient air and is inhaled by these workers.

Lindh et al. (1980) measured the arsenic in autopsy femur samples of 7 occupationally exposed workers. The time between retirement and death ranged from 0-21 years. A control sampling from 5 autopsy cases was included. Using both neutron activation analysis and proton-induced X-ray emission (PIXIE) techniques, no clear evidence of significant arsenic accumulation in bone was seen. The scatter of levels was wide in the worker group, 0.006-0.21 ppm, with a median of 0.014 ppm, versus a range of 0.005-0.007 ppm in the control samples.

4.5 ARSENIC EXCRETION IN MAN AND ANIMALS

Renal clearance appears to be the major route of excretion of absorbed arsenic in man and animals, biliary transport of the element leading to enteric reabsorption with little carriage in feces.

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Recent data for normal or background levels of arsenic in urine of human subjects in the U.S. reveal values of less than 20 µg/liter (20 ppb). If seafood has been consumed, such values can rise considerably to levels of 1,000 µg/liter or higher (Westöö and Rydälv, 1972; Pinto, 1976).

In a study designed to assess the utility of urine arsenic measurement in occupational exposure settings, Mappes (1977) reported excretion data for both single and multiple daily dosing for a human subject ingesting an arsenite solution. By 3 hours, renal excretion was maximal, with about one-quarter of the single dose appearing in the urine by day 1 post-exposure. With successive arsenite ingestion (0.8 mg As), daily urinary clearance after 5 days was about two-thirds of daily intake.

Buchet et al. (1981b), in their study of human subjects ingesting arsenite in amounts ranging from 125-1000 µg/day for 5 days, calculated a steady state occurring within 5 days. With steady state, 60 percent of daily intake is excreted daily. This figure is in good agreement with that of Mappes (1977) cited above.

Crecelius (1977) noted that following ingestion of arsenic in wine [50 µg As (III), 13 µg As (V)], approximately 80 percent of the dose was excreted within 61 hours. Oral ingestion of arsenic (V) in well water (200 µg), however, led to about 50 percent urinary excretion by 3 days post-ingestion. Mealey et al. (1959) measured urine arsenic in patients given trivalent arsenic by intravenous administration, with approximately 60 percent of the dose amount appearing in the urine within 24 hours. Hunter et al. (1942) noted that a group of human subjects given arsenic via parenteral administration exhibited considerable variance in the urinary clearance of arsenic, ranging from 30 to 80 percent after 4 to 5 days.

As might be predicted from the in vivo behavior of arsenicals in the rat, urinary excretion of arsenic in this species is very slow (due to erythrocyte

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retention) on the order of two to five percent of the arsenic intake by several days post-dosing (Coulson et al., 1935; Ariyoshi and Ikeda, 1974). Urakabo et al. (1975) calculated a half-time of 84 days for arsenic in the rat.

Slow clearance of arsenic from the rat gave rise to the widely-held assumption for many years that arsenic was one of the elements that accumulated in the body. Other species excrete arsenic rapidly. Mice, rabbits, swine, dogs, and monkeys clear the majority of injected trivalent arsenic within 24 hours, with excretion usually being $\geq$70 percent within that time period (Ducoff et al., 1948; Crema, 1955; Munro et al., 1974; Lakso and Peoples, 1975; Tam et al., 1978; Charbonneau et al., 1978a). Other studies also indicate rapid urinary clearance of arsenic given in the pentavalent form to species other than the rat (DuPont et al., 1942; Ginsberg and Lotspeich, 1963; Peoples, 1964; Lakso and Peoples, 1975).

Several studies have compared the relative rates of elimination of radiolabeled (^{74}As) trivalent and pentavalent inorganic arsenic (Vahter and Norin, 1980; Vahter, 1981) where precautions were taken to assure the purity of the respective dosing solutions as to valency state. Whole-body retention of trivalent inorganic arsenic in mice was 2-3 times greater than that of arsenate while retention times for both forms were dose-dependent, increasing with increasing exposure. In these studies, the animals received single oral doses of either form at levels of 0.04 to 4.0 mg As/kg. Differences in elimination rates appeared to relate to the relative degree of methylation of inorganic arsenic to the rapidly excreted methylated forms, chiefly dimethyl arsenic. Furthermore, differences in excretion rates were dose-dependent. At 0.04 mg As/kg, there was no difference between tri- and pentavalent arsenic elimination (Vahter, 1981).

Biliary transport of arsenic has been reported for a number of species. Bile-excreted arsenic is reabsorbed. Cikrt and Bencko (1974) noted that the

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rat had a higher biliary excretion rate for the trivalent than for the pentavalent form (approximately 10:1). Klaassen (1974) noted that the biliary excretion rate was much greater for the rat than for either the rabbit or the dog.

Cikrt et al. (1980) monitored biliary exretion in the Golden Hamster using penta- or trivalent inorganic arsenic. Significant differences in biliary excretion rates and cumulative excretion were seen between the two forms, being much greater for the trivalent form. However, fecal and urine arsenic content were greater with pentavalent arsenic administration. Biliary transport data for man are not available.

Deposition of arsenic in such organs as hair and nails can be considered an excretory mechanism for arsenic. Although hair analysis has had a long history in the chemical and forensic arsenic literature, for reasons of both analytical convenience and the possibility of establishing an exposure history from sectional analysis, many questions remain unanswered. The relationship between arsenic deposition in hair and various exposure parameters has not been well defined on a quantitative basis, nor are the physiological mechanisms well understood. The chemical nature of hair arsenic is also largely unknown.

5. ARSENIC TOXICOLOGY

The acute and chronic toxicity of arsenic will largely depend on the chemical form and physical state of the compound involved. Inorganic trivalent arsenic is generally regarded as being more acutely toxic than inorganic pentavalent arsenic, which in turn is more toxic than methylated forms of arsenic (NAS, 1977; Pershagen and Vahter, 1979; WHO, 1981). The previously noted (Chapter 3) "fish arsenic" is regarded as nontoxic. It is thus necessary to always specify, if possible, arsenic compounds when discussing effects and constructing dose-effect and dose-response relationships. In addition, factors like particle size and solubility must be taken into account. Trivalent compounds with low solubility, e.g., arsenic sulfide, will have low oral toxicity but may be retained in the lung (Pershagen et al., 1982).

The following chapter discusses the non-mutagenic/non-carcinogenic effects of exposure to inorganic arsenic. Because of the large volume of information available regarding the mutagenic and carcinogenic effects of inorganic arsenic, these topics have been discussed in the following chapters.

5.1 ACUTE TOXICITY OF ARSENIC IN MAN AND ANIMALS

In animal experiments the oral LD_{50} has been found to vary from 15 to 293 mg/kg body weight in rats and from 10-150 mg/kg in other animals (Dieke and Richter, 1946; Harrison et al., 1958). The lower values refer to experiments with soluble arsenic compounds. Franke and Moxon (1936) found that the LD_{75} 48 hours after i.p. administration was 4-5 mg As/kg body weight for sodium arsenite and 14-18 mg/kg for sodium arsenate.

Acute effects seen in animals after oral exposure are similar to effects seen in human beings and include gastroenteritis, diarrhea and cardiovascular effects (Nelson et al., 1971; Selby et al., 1977).

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A large number of acute arsenic poisonings are described in the literature, but few data exist on actual doses and type of compound. Vallee et al. (1960) estimated the lethal dose to be on the order of 70 to 180 mg for arsenic trioxide. Acute symptoms are due to severe gastrointestinal damage, resulting in vomiting and diarrhea and general vascular injury which may lead to shock, coma or even death. Other acute symptoms are muscular cramps, facial edema, and cardiovascular reactions (Holland, 1904; Done and Peart, 1971).

Acute symptoms have also been seen after airborne exposure to high concentrations of arsenic trioxide, causing severe irritation of nasal mucosa, larynx, and bronchi (Holmqvist, 1951; Pinto and McGill, 1953).

Reversible effects on the hematopoietic and cardiovascular systems and peripheral nervous disturbances with slow recovery have also been noted (Ohta, 1970; Heyman et al., 1956; Jenkins, 1966; Nagamatsu and Igata, 1975: O'Shaughnessy and Kraft, 1976; Hamamoto, 1955; Chhuttani et al., 1967; LeQuesne and McLeod, 1977).

Over the years, a number of large-scale poisonings have occurred due to contamination of beer (Kelynack et al., 1900), soy sauce (Mizuta et al., 1956), dried infant milk (Tokanehara et al., 1956), and well water (Yoshikawa et al., 1960). These episodes mainly caused subacute and chronic symptoms and will be discussed in the following sections.

5.2 CHRONIC TOXICITY OF ARSENIC IN MAN AND ANIMALS

5.2.1 Neurotoxic Effects

Arsenic neurotoxicity, including both peripheral and central nervous system injury, has long been recognized as being associated with acute, subacute, and chronic exposures to relatively high levels of inorganic arsenic. These have been well characterized as to their major pathophysiological features, clinical course, sequelae and associated histopathology.

Reynolds (1901) provided one of the earliest detailed descriptions of arsenic-induced neurotoxic effects in his report on the clinical assessment of more than 500 patients who had consumed arsenic-contaminated beer.

Neurological involvement started with sensory changes, e.g., paresthesias, hyperesthesias, and neuralgias, accompanied by considerable muscle tenderness. Varying degrees of motor weakness, progressing from distal to proximal muscle groups, also occurred and culminated at times in paralysis of affected muscle groups or extremities. Certain indications of central nervous system (CNS) damage, e.g., loss of memory and general mental confusion, were also observed but were discounted by Reynolds (1901) as being less likely due to arsenic than chronic alcoholism or concurrent excessive selenium intake.

Peripheral nervous system (PNS) effects similar to those described by Reynolds (1901) have since been observed in numerous other cases of acute, subacute, and chronic arsenic exposures (Silver and Wainman, 1952; Mizuta et al., 1956; Heyman et al., 1956; Jenkins, 1966; Hara et al., 1968; Chhuttani et al., 1967; Ishinishi et al., 1973; Nakamura et al., 1973; Nagamatsu and Igata, 1975; O'Shaughnessy and Kraft, 1976; Frank, 1976; Garb and Hine, 1977; LeQuesne and McLeod, 1977) and are now recognized as classic clinical symptoms of arsenic poisoning. Such symptoms include peripheral sensory effects characterized by the appearance of numbness, tingling, or "pins and needles" sensations in the hands and feet, as well as decreases in touch, pain, and temperature sensations in a symmetrical distribution. These symptoms are often variously accompanied by burning sensations, sharp or shooting pains, and marked muscle tenderness in the extremities. Peripheral neuritis symptoms originate distally and, over the course of a few weeks, often progressively become more widespread in both lower and upper extremities, usually appearing first in the feet and later in the hands.

Collectively, the above components of the classical clinical syndrome associated with excessive arsenic exposure are highly indicative of progressive peripheral polyneuropathy, involving both sensory and motor nerves, and most intensively affecting long-axon neurons. In addition, biopsy and autopsy studies have provided histopathological evidence verifying peripheral nerve damage, especially Wallerian degeneration of long-axon myelinated nerve fibers in cases of human arsenic exposure where frank neurological signs and symptoms were manifested (Heyman et al., 1956; Jenkins, 1966; Chhuttani et al., 1967; Ohta, 1970; LeQuesne and McLeod, 1977).

The pattern of development of peripheral neuropathic effects is closely associated with the type of exposure. Acute exposure to a single high dose of arsenic can produce a fairly rapid onset of both motor dysfunctions and paresthesias. In one report, the onset was within 10 days (LeQuesne and McLeod, 1977) after exposure. Slow, incomplete recovery is usually seen in these cases.

Under more chronic occupational exposure conditions to lower levels of arsenic compounds, the development of neuropathy symptoms can be more gradual and insidious, and not only bilateral, but unilateral polyneuropathies without motor paralysis have been reported (Ishinishi et al., 1973; Nakamura et al., 1973). Again, the time course for recovery from the neuropathies, once induced, tends to be slow and on the order of years. Gradual onsets of peripheral neuropathies and slow recoveries have also been reported with subacute or chronic exposures to arsenic via ingestion of contaminated soy sauce (Mizuta et al., 1956) or anti-asthmatic herbal preparations containing arsenic trioxide or arsenic sulfide (Tay and Seah, 1975).

It is difficult to determine the levels of arsenic associated with the induction of peripheral neuropathies. For subacute or chronic poisoning situations, information has been provided in only a few studies by which

effective exposure parameters can be estimated. Mizuta et al. (1956), for example, reported that peripheral neuropathies occurred in 20 percent of 220 patients of all age groups poisoned by ingestion of arsenic-contaminated soy sauce, with approximately 3 mg arsenic (likely as calcium arsenate) estimated to be ingested daily for 2-3 weeks, resulting in total effective doses up to approximately 60 mg. Also, Tay and Seah (1975) reported polyneuropathies in approximately 50 percent of 74 patients poisoned by daily ingestion of 3.3 or 10.3 mg/day of arsenic trioxide or arsenic sulfide in anti-asthmatic medicinal pills.

More subtle peripheral neurotoxic effects arising from chronic exposure to lower levels of arsenic in occupational or non-occupational groups are more difficult to establish, particularly as indexed by abnormal electromyographic or nerve conduction velocity findings. In one such study, Landau et al. (1977) reported relationships between length and intensity of occupational arsenic exposure (mainly to arsenic trioxide via inhalation) of smelter workers and alterations in peripheral nerve functioning. The manner in which the data were reported, however, precludes precise characterization of dose-effect/dose-response relationships.

In their study of arsenic in the drinking water of residents from Millard County, Utah, Southwick et al. (1981) conducted neurological examinations on all study participants 47 years of age and younger (see Section 7.1.2.2 for discussion of the total study population). Neurological examination revealed that conduction velocities for nerves studied (ulnar motor, median motor, ulnar sensory, median sensory, peroneal, sural) did not vary significantly with respect to age or community. In those individuals that exhibited below-normal conduction velocities, a slightly greater proportion was seen in exposed participants--12 percent of 67 controls versus 16 percent of 83 exposed. The

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sural nerve seemed most often to be affected even after adjusting by a correction factor of 1.8 m/s/degree in individuals who had nerve temperatures below 30° C. (Velocities below 37 m/s at 30° C or above were considered abnormal). Slowing of sural nerve conduction was reported equally in exposed and control participants. Nerve conduction velocities regressed against annual arsenic dose and the log of the dose showed no significant associations.

Similar difficulties have been encountered in attempts to characterize dose-effect/dose-response relationships for arsenic-induced peripheral nerve functional deficits (as demonstrated by electromyographic recording techniques) in studies of two other populations chronically exposed to arsenic: (1) a population of Yellowknife Canadian Indians exposed via occupational contact with arsenic in a gold mining and smelting facility, or, in the case of the families of such workers, via arsenic emissions from the facility into the ambient environment (Canadian Public Health Assoc., 1978); and (2) a Nova Scotia population exposed, via geological arsenic contamination of wells, to levels >0.05 ppm arsenic in drinking water (Hindmarsh et al., 1977).

Several of the clinical reports discussed above not only document peripheral nerve damage but also contain descriptions of arsenic-induced central nervous system (CNS) disturbances or encephalopathy effects ranging in severity from memory losses and general mental confusion to convulsions, stupor, coma and even death (Heyman et al., 1956; Jenkins, 1966: Frank, 1976; Nagamatsu and Igata, 1975; O'Shaughnessy and Kraft, 1976; Garb and Hine, 1977). The onset and courses of such CNS effects have not been well defined, but they appear to closely parallel the development of peripheral neuropathy effects. Cases of prolonged encephalopathy indexed by electroencephalogram (EEG) recordings of abnormal brain wave patterns up to a year after cessation of exposure have been reported (Freeman and Couch, 1978; Bental et al., 1961). Such effects

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appear to be a much less constant feature of arsenic-induced neurotoxic effects in adults than are peripheral neuropathies.

Certain studies suggest, in contrast, that children may be more susceptible to arsenic-induced CNS damage. For example, severe CNS deficits have been observed in children exposed for several months as babies to arsenic-contaminated powdered milk formulas in Morinaga, Japan (Hamamoto, 1955; Okamura et al., 1956; Yamashita et al., 1972; Masahiki and Hideyasu, 1973; Japanese Pediatric Society, 1973). Follow-up studies on the children exposed to arsenic as infants have revealed: (1) increased incidence of severe hearing loss (>30 dB) in 18 percent of 415 children examined compared to less than 1 percent incidence of hearing loss in corresponding age-group children; (2) increased incidence of abnormal electroencephalographic (EEG) brain wave patterns in 14 percent of the exposed children, more than double the expected rate for comparable normal pediatric populations; and (3) observations of increased incidences of persisting mental retardation, epilepsy, and other indications of severe brain damage.

In another study (Bencko and Syman, 1977), hearing losses in children were reported to be associated with arsenic exposure derived from emissions from a nearby coal-fired power plant combusting high-arsenic-content coal. Both air and bone conduction hearing losses were observed, suggesting inner ear damage. Failure to find analogous hearing losses in children exposed to atmospheric arsenic emitted from a copper smelter in the United States (Milham, 1977) has raised questions regarding arsenic-induced damage to the inner ear in children.

Very few animal toxicology studies have focused on investigation of neurotoxic effects of arsenic on the CNS. Rozenshtein (1970), for example, reported evidence of CNS functional deficits, as indexed by altered conditioned reflexes, as well as histopathologic evidence of CNS structural damage,

e.g,. pericellular edema and neuronal cytolysis in the brain, in rats exposed for three months to an arsenic trioxide aerosol resulting in an arsenic concentration of 46 μg/m^3. Similar but less severe effects were also obtained with exposure of other rats to a 3.7 μg As/m^3 aerosol. CNS deficits, indexed by impaired avoidance conditioning in the absence of demonstrable histopathologic changes in brain tissue, were also reported (Osato, 1977) for suckling rats administered 2 or 10 mg arsenic trioxide via stomach intubation over a 40-day period.

5.2.2 Cardiovascular Effects

A specific cardiovascular effect is "Blackfoot" disease, a peripheral vascular disease leading to gangrene of the toes, feet, legs and fingers. This disease has been reported in an area of Taiwan, where exposure to inorganic arsenic via drinking water is known to occur. In their skin cancer study of the Taiwanese population (see Section 7.1.2.2 for complete discussion of the total study population), Tseng and co-workers (1968, 1977) also investigated the occurrence of Blackfoot disease. The total prevalence of Blackfoot disease was lower than the prevalence of skin cancer, but higher in the younger age groups (Table 5-1). The overall prevalence rate for Blackfoot disease was 0.9-1.2 percent for males and 0.7 percent for females after age 39.

A group of 1108 patients with Blackfoot disease from the endemic area was identified during 1958 to 1975 (Tseng, 1977). There were 669 males and 439 females. Patients were included in the series if they had: 1) objective signs of ischemia, and 2) subjective symptoms of ischemia. Follow-up was attempted using a variety of methods to trace the subjects. At the end of follow-up, 528 patients had died, a fatality rate of 47.7 percent.

A history of typical ischemic symptoms such as numbness was used to estimate the date of onset of Blackfoot disease. Duration of intake of arsenic

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TABLE 5-1. PREVALENCE OF BLACKFOOT DISEASE (per 1000) BY AGE AND ARSENIC EXPOSURE (ppm)

Arsenic content of drinking water (ppm)	Age 20-39	40-59	>60
<0.3	4.5	10.5	20.3
0.3 - 0.6	13.2	32.0	32.2
>0.6	14.2	46.9	61.4

Source: Adapted from Tseng, 1977.

water at the time of onset represents the period of time between first use of such intake and the time of onset of the disease. Duration of intake of arsenical water represents the duration of time during which the patient started drinking artesian well water up to the time of survey or up to the time of change of source of drinking water. For native patients, the duration is estimated to be equivalent to their ages, but for patients who came from areas without artesian wells the duration was counted as starting from the year of arrival.

A classification system of percentage of permanent disability was created and each patient was assigned to the appropriate category.

It was determined (determination not specified) that all patients with Blackfoot disease had consumed artesian well water before the onset of disease, and none of the residents of the endemic area who had consumed surface water or water from shallow wells developed Blackfoot disease.

In some parts of the arsenic endemic area, a new source of drinking water was provided in 1956. The incidence of Blackfoot disease was therefore examined in year of onset periods (1955 and before, 1956-1965, and 1966-1975). There were no cases of Blackfoot disease among area residents who were born after

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the tap water supply was instituted in 1956. Furthermore, as the duration of intake of arsenical water increased (across all 3 exposure levels) the incidence of Blackfoot disease increased. In addition, the degree of permanent disability of patients was significantly correlated with duration of intake of arsenical water at time of onset of the disease.

There are also data indicating that other substances may be involved in the etiology of Blackfoot disease. Lu et al. (1977, 1978) found fluorescent compounds in water samples from an area with endemic Blackfoot disease. Of the compounds discovered, tentative identifications of D-lysergic acid and/or ergometrine, ergotamine and calciferol have been made (Irgolic, 1982). These substances may have been at least contributing factors to this disease, since some of them, or similar compounds, are known vasoactive agents.

Vascular changes were also noted among persons living in Antofagasta, Chile (see Section 7.1.2.2 for discussion of study groups). Raynauds syndrome and acrocyanosis were reported to occur in 30 and 27 percent, respectively, in a group of 100 persons studied by Borgono and Greiber (1972).

Raynauds syndrome has also been reported to occur among German vintners. Butzengeiger (1940) studied 180 persons and found that 22.8 percent had evidence of vascular disorders of the extremities. Butzengeiger (1949) studied 192 vinegrowers and found that 28.7 percent had ECG changes. There was, however, no control group.

In epidemiological studies of smelters (see Section 7.1.2.1 for complete discussion of studies), peripheral vascular disease has generally not been found. However, mortality studies indicate that there might be some cardiovascular effects, although study results have been conflicting. Thus, Axelson et al. (1978) found a higher mortality in cardiovascular disease, but analysis of the data indicate that if such an effect occurred it probably needed higher

exposure levels than those causing lung cancer. A study by Ott et al. (1974) indicated, on the other hand, that the arsenic-exposed workers had less mortality than expected.

In studies on workers at the Anaconda Copper Smelter in Montana, both Lee and Fraumeni (1969) and Lee-Feldstein (1983) reported that cardiovascular mortality was significantly elevated in the workers--SMR=118 and SMR=129, respectively ($p < 0.01$)--but not related to duration of arsenic exposure. In a study cohort of these same workers, Higgins et al. (1982) reported that cardiovascular mortality increased with increasing ceiling arsenic exposure among smokers, but not among nonsmokers--at 500-4999 ug/m^3, SMR=165 for smokers ($p < 0.01$), SMR=100 for nonsmokers; at >5000 ug/m^3, SMR=182 for smokers ($p < 0.01$), SMR=166 for nonsmokers. In contrast, Lubin et al. (1981) did not find an excess in cardiovascular disease mortality (SMR=108) in their study cohort of workers from the same smelter. The cohorts in all four of these studies were slightly different.

The conflicting findings of these reports suggest that the relationship between arsenic exposure and cardiovascular disease is quite complex and in need of additional research.

5.2.3 Teratogenesis and Developmental Effects

5.2.3.1 Animal Studies--In a recent review of the toxicological effects of prenatal exposure to arsenic, Hood (1983) discussed the number of variables that influence effects on offspring of maternal arsenic exposure during pregnancy. Included in the variables are the forms of arsenic administered, species and individual differences in susceptibility, dose level and exposure route, peak level attained in the conceptus, maternal metabolism and excretion, and timing of exposure during gestation; the length of the list being indicative of the complex nature of arsenic toxicity induced during prenatal exposure.

Teratogenic effects of arsenic compounds, at least at relatively high exposure levels, have been demonstrated in a number of animal species. Studies by Ridgeway and Karnofsky (1952), for example, demonstrated no gross abnormalities in chick embryos following injection of sodium arsenate into embryonate eggs at 0.20 mg As/egg on day 4 of gestation. Retardation in body weight gain and feather growth, as well as certain other abnormalities, were, however, observed in chickens hatched from arsenic-treated eggs.

Later experimental studies on mammalian species have demonstrated teratogenic effects of arsenic in hamsters, rats and mice.

Ferm and Carpenter (1968) produced malformations in 15-day hamster fetuses via intravenous (I.V.) injections of sodium arsenate into pregnant dams on day 8 of gestation at dose levels of 15, 17.5 or 20 mg/kg body weight. The variety of malformations obtained with prenatal arsenic exposure of hamsters--including exencephaly, encephaloceles, skeletal defects and genitourinary system defects and the effects of other related experimental manipulations, e.g., protective effects of co-treatment with selenium--were reviewed in a later report by Ferm (1977).

Willhite (1981) injected arsenate (20 mg/kg) or arsenite (2-10 mg/kg) into pregnant golden hamsters at day 8 of gestation and observed axial skeletal disorders in offspring--cranioschisis aperta with exencephaly and cranioschisis occulta--while 10 hours after dosing, embryos showed a delay in neural fold elevation and neural tube closure with arsenate exposure.

Teratogenic and embryotoxic effects of prenatal arsenic exposure of mice have also been reported (Hood and Bishop, 1972; Hood and Pike, 1972; Hood et al., 1977). Increased fetal resorption, decreased fetal weights and various malformations (such as exencephaly, micrognathia, agnathia, exophthalmos, anophthalmia, hydroencephaly, cleft lip, ectrodactyly, micromelia, fused vertebrae and forked ribs) were observed following single intraperitoneal (I.P.)

injections of sodium arsenate (45 mg As/kg body weight) in Swiss-Webster mice (the single injection occurring on one day between days 6 and 12 of gestation) (Hood and Bishop, 1972). Co-treatment with 2,3-dimercaptopropanol (BAL) reduced arsenic-associated malformations (Hood and Pike, 1972; Hood et al., 1977).

Many similar embryotoxic and fetal teratogenic effects, along with other effects (renal and gonadal agenesis), have also been observed following I.P. injections of sodium arsenate in pregnant rats (Beaudoin, 1974; Burk and Beaudoin, 1977), again at relatively high dose levels (e.g., 30 mg/kg body weight).

Compared to pentavalent arsenic, trivalent arsenic as the arsenite salt appears to be proportionally more embryotoxic. For example, the fetotoxic effects seen by Baxley et al. (1981) in mice exposed to 40-45 mg/kg As as arsenite were comparable to effects observed by Hood et al. (1978), in which a much higher level of arsenate (120 mg/kg As) was administered.

The above studies are suggestive of significant effects on reproduction and development of mammalian species being induced by prenatal arsenic exposure. However, only very minimal effects, or none at all on fetal development, have been observed in studies on chronic oral exposure of pregnant rat or mice dams to relatively low levels of arsenic via drinking water (Schroeder and Mitchener, 1971). Nadeyenko et al. (1978) reported that intubation of rats with arsenic solution at a dose level of 0.0025 mg/kg for a period of 7 months, including pregnancy, produced no significant embryotoxic effects and only very infrequent slight expansion of ventricles of the cerebrum, renal pelvises and urinary bladder. Also, Hood et al. (1977) reported that very high single oral doses of arsenate solutions (120 mg/kg) to pregnant mice were necessary to cause prenatal fetal toxicity, while multiple doses of 60 mg/kg on 3 days had little effect. This report suggests that the higher doses required with oral versus

parenteral exposure relate to the more rapid methylation to less toxic forms of oral arsenic owing to its initial passage through the liver, where methylation may occur. Similar results were obtained with mice in a later study (Hood et al., 1978).

Given the presence of biomethylation in mammalian species exposed to arsenic, the question arises as to whether fetotoxicity resides only in the untransformed inorganic arsenic or is due to some of the metabolites formed in vivo. Hood et al. (1982a) have demonstrated that methylated metabolites cross the placental barrier in mice given arsenite and that these methylated forms are actually the major form of arsenic in fetuses by 12 hours post-dosing.

Recently, three groups of investigators have reported their results on the comparative teratogenicity of methylated arsenicals, administered as such, to different species.

Willhite (1981) found no teratogenic response when pregnant golden hamsters were given methylated arsenic at single doses up to a level of 100 mg As/kg. Rogers et al. (1981) administered dimethylarsenic to pregnant CD rats and CD-1 mice on days 7-16 of gestation via oral gavage. Dosing was from 7.5 to 60 mg/kg/day for rats and 200 to 600 mg/kg/day for mice. Fetal and maternal toxicity was observed in both species. A teratogenic response in mice was confined to cleft palate in the 400- and 600-mg regimens. In the rat, there was a dose-dependent incidence of irregular palatine rugae.

Hood et al. (1982b) exposed pregnant golden hamsters to either dimethyl- or monomethyl arsenic at dosages of either 900 or 1000 mg/kg of the former agent and 500 mg/kg of the latter. The levels of dimethylarsenic administered were seen to be acutely toxic to dams and were associated with significant resorption rates and malformations in survivors. In the case of the monomethyl arsenic, the overall teratogenic potency was observed to be lower.

Harrison et al. (1980) exposed CD-1 mice to monomethyl arsenic by injection (1500 mg/kg salt, i.p.) on one of gestation days 8, 9, or 10. Treatment at days 9 and 10 of gestation resulted in increased resorption and mortality rates of 37 and 43 percent, respectively, while the day 8 group showed no such effects. Skeletal malformations were also seen at the 9 and 10 gestation day exposures. While details for dimethylarsenic were not provided, it was noted that such treatment also resulted in fetotoxicity and teratogenicity, with exencephaly the primary gross malformation observed.

The available data, in summary, indicate that while the methylated arsenicals are less teratogenic and fetotoxic on an equivalent dose basis, the nature of the effects is comparable. There also appears to be a species sensitivity difference for arsenical teratogenicity and fetotoxicity, the rat being more sensitive than mice or golden hamsters.

Animal studies on the effects of early postnatal administration of arsenic compounds on growth and development have generally failed to yield any significant positive results at sublethal arsenic dose levels. Tamura (1978), for example, reported no effects on the growth and development of postnatal rats fed arsenic trioxide in their diet from the 7th to 21st day following birth at a dose level of 1.5 mg/kg/day, in comparison to a 50 percent mortality rate at a 15.0 mg/kg body weight dose. Similarly, Ferslew and Edds (1979) observed no significant effects on growth or development of young swine fed arsanilic acid at 0.01 percent concentration for 31 days commencing at 3 weeks of age, despite observations of significant alterations by organo-arsenic of white blood cell counts, serum alkaline phosphatase activity, and other blood chemistry parameters and significant increases of arsenic in various soft tissues and urine. In another study (Heywood and Sortwell, 1979), both 3.75 and 7.5 mg/kg/day doses of an arsenic compound fed to adolescent or infant rhesus monkeys resulted in mortality in most of the exposed animals, but no notable

effects in growth or development of animals surviving the dosing period. Unfortunately, the lack of experimental data in the above studies on the effects of exposure across a range of dose levels, besides the ones employed, greatly limits their utility in terms of determining possible dose-effect or dose-response relationships between postnatal arsenic exposure and induced effects on growth and development.

It should be noted that, whereas some of the above animal studies provide highly suggestive evidence for arsenic effects on reproduction and development, at least at high exposure levels, one cannot confidently extrapolate the results to estimate the probability of occurrence of similar or analogous effects in man. Still, some suggestions of possible arsenic effects on human reproduction and development have been derived from certain epidemiology studies discussed below.

5.2.3.2 Human Studies--Available data are mainly from studies in Sweden on male and female smelter workers. These studies were not designed specifically to study effects of arsenic but rather to study the effects, in general, of the smelter work. While data from these studies suggest a low-level effect of smelter pollutants on neighboring (proximate) populations, the diverse agents involved preclude making conclusive statements about the specific effects of arsenic.

Congenital malformations were found to occur at about the same rate, 3.0 percent among women employed at the Rönnskär smelter, as among women living in six areas belonging to the hospital serving the Rönnskär area (Nordström et al., 1978c). However, mean birthweights were lower among offspring to female Rönnskär workers (Nordström et al., 1978a, 1978b).

The number of spontaneous abortions was also increased among women working in this smelter; the highest rate (17 percent) was found among women

employed during pregnancy or who had been employed prior to pregnancy and lived close to the smelter. Women working in close connection with smelting processes had a rate of 28 percent of spontaneous abortion compared with other female employees. When both parents were employed, the abortion rate was 19.4 percent compared to 13.5 percent when the father was not employed.

Studies on spontaneous abortion among women living in the vicinity of the smelter were also conducted (Nordström et al., 1978d). In four areas, the rate varied between 7.6 and 11.0 percent. The highest rate occurred in the area closest to the smelter, but many women employed at the smelter live in that area.

5.2.4 Hematological Effects

The hematopoietic system in man has been shown to be affected by arsenic exposure in cases of acute, subacute or chronic intake, taking the form of anemia, leukopenia, granulocytopenia and eosinophilia. Such effects appear to be reversible, the system recovering in a matter of weeks after exposure ends.

Hamamoto (1955), in his report of infant poisoning by arsenic-contaminated milk in Japan, described marked anemia and leukopenia with lymphocytosis in most of a group of 59 infant patients. Erythropoiesis was disturbed in bone marrow of 19 children studied. Within a month, the hematology appeared to show normal values. Similarly, Mizuta et al. (1956) found blood disturbances, including anemia with leukopenia and lymphocytosis, in subjects surveyed for ingestion of soy sauce contaminated with arsenic.

Two recent studies dealing with acute and subacute arsenic poisoning (Feussner et al., 1979; Lerman et al., 1980) have demonstrated arsenic-induced megaloblastic anemia. Feussner et al. (1979) demonstrated that arsenic was present in bone marrow by using electron-probe microanalysis.

Chronic exposure to arsenic occasions hematological effects which resemble those seen with subacute exposure. Terada (1960), in his survey of patients exposed to arsenic in well water contaminated by industrial activity in Niigata, Japan, saw anemia as a common feature, with the anemia being either normochromic (50 percent) or hyperchromic (30 percent). In their study on individuals living in communities in Utah where arsenic was present in drinking water, Southwick et al. (1981) also reported the presence of anemia in certain individuals; however, anemia was not significantly more prevalent in exposed populations. Anemia has been reported in subjects exposed to arsenic occupationally or in medicinals (Kyle and Pease, 1965; Westhoff et al., 1975).

In animals, decreased hemoglobin production has been seen in rats fed both arsenate (Mahaffey and Fowler, 1977) and arsenite (Byron et al., 1967) and in cats given either form orally (Massmann and Opitz, 1954). The study of Woods and Fowler (1977), in which arsenate was given orally to rats and mice at 20, 40 or 85 ppm in drinking water, showed that the sites of disturbance of the heme biosynthetic pathway by arsenate mainly involved depression of ALA-synthetase and heme-synthetase activity, with elevation in the urinary levels of chiefly uroporphyrin and also coproporphyrin. The increase in uroporphyrin appears to be specific to arsenic.

5.2.5 Hepatic Effects

In the reports of Hamamoto (1955) and Mizuta et al. (1956), dealing with arsenic contamination in infant milk and soy sauce, respectively, swollen livers appeared to be a common clinical feature. Of the children exposed to milk arsenic, all subjects presented with this feature (61/61). In the autopsies of fatal outcome cases, hemorrhagic necrosis and fatty degeneration of the liver were seen. In the survivors, liver function tests were not very revealing, being within normal limits in most cases. In both of the above episodes, liver size returned to normal after exposure ceased.

Over the years, chronic intake of arsenic has been reported to be associated with hepatic damage in the form of portal hypertension, malignant liver disease and cirrhosis. In the Manchester beer poisoning episode, Reynolds (1901) noted widespread liver disease in drinkers of such beer, with the extent of the disease being related to the amount of arsenic in the beverage.

The incidence of hepatic cirrhosis among German vintners has been reviewed by Luchtrath (1972), who noted that the frequency of liver cirrhosis decreased with the banning of arsenical pesticides. The use of arsenic as an anti-syphilitic is also known to be associated with hepatic cirrhosis (Baldridge, 1934).

Non-cirrhotic portal hypertension has been infrequently noted in the literature (Morris et al., 1974; Szuler et al., 1979). Szuler described one case report of presinusoidal portal hypertension in a patient taking an arsenic antiasthmatic for 55 years. Cirrhosis was absent and liver function was not disturbed.

In the smelter study by Axelson et al. (1978) there was a tendency towards an increased mortality in liver cirrhosis among arsenic-exposed workers.

5.2.6 Renal Effects

Functional and/or biochemical impairment of the human renal system is mainly seen in acute poisoning by arsine, AsH_3 (Uldall et al., 1970; Fowler, 1977). Oligouria and anuria progressing to renal failure are common acute responses. Persistent renal sequelae in subjects surviving the acute stage of arsine poisoning include chronic renal insufficiency and hypertension. Histologically, the injury is mainly tubular and interstitial.

Acute or chronic renal effects associated with arsenate or arsenite exposure are less well characterized. Gerhardt et al. (1978) have recently described a case of acute arsenic poisoning from contaminated illicit liquor.

Acute renal bilateral cortical necrosis was diagnosed in the patient who survived the acute stage to eventually develop reduced renal size and cortical calcification.

In the clinical survey of Hamamoto (1955) of Japanese infants poisoned with arsenic-contaminated milk, possible renal injury was diagnosed by the presence of hematuria, leukocyturia and glycosuria (23.7 percent, 42.3 percent and 13.5 percent, respectively). Reversibility of these indices was apparent, with only three percent of the patients still showing pathological changes after one month. Terada (1960) also noted proteinuria in cases of arsenic poisoning in Niigata, Japan, arising from ground water contamination from an arsenic plant.

5.2.7 Respiratory Effects Other Than Cancer

Nasal septum perforation is a rapid tissue response in workers encountering high airborne arsenic levels (NAS, 1977; Hine et al., 1977; Lundgren, 1954).

In the detailed smelter worker study of Lundgren (1954), 1,276 subjects in a worksite with levels up to 7 mg As/m^3 showed two types of respiratory disturbances relating to the nature of the processing and presumably the form of the arsenic. Refined arsenic handling was associated with septal perforation and rhinopharyngolaryngitis, while workers in the roaster, furnace, and connector areas showed tracheobronchitis and signs of pulmonary insufficiency. In the latter group, exposure was mixed, including both arsenic and sulfur dioxide. A recent report has suggested, furthermore, that workplace arsenic may also be present as the sulfide (Smith et al., 1976).

Chilean children exposed to arsenic in drinking water (Borgono et al., 1977) showed a chronic cough and bronchitic history.

5.2.8 Immunosuppressant Effects

The role of inorganic arsenic as an immunosuppressant in man is mainly inferred from indirect data accumulated over the years (Arsenic. NAS, 1977).

First, the therapeutic utility of arsenicals, such as arsenite-based Fowler's solution in the treatment of steroid-responding disorders and as a lymphocytostatic agent, suggests action as an immunosuppressant.

Secondly, certain manifestations indicative of likely immune system disorders have been observed with arsenic exposure, (e.g., the occurrence of herpes simplex and chronic pulmonary infections) and suggest a role of arsenic as an immunosuppressant (Arsenic. NAS, 1977). Histories of chronic cough and bronchitis in Chilean children exposed to arsenic in drinking water (Borgono et al., 1977) would tend to support such a role.

5.3 FACTORS AFFECTING ARSENIC TOXICITY

The most widely recognized and studied arsenic interactive behavior is with selenium, and much of the early data has been reviewed by Levander (1977).

The known antagonistic relationship of arsenic and selenium in a number of animal species was first described by Moxon and co-workers (Moxon and Dubois, 1939; Dubois et al., 1940), who also demonstrated the utility of dietary arsenic supplementation in protecting livestock from the toxic levels of selenium in certain fodders. Both penta- and trivalent arsenic are equally effective in protecting against selenium toxicity, and do so regardless of the chemical form by which selenium exposure occurs.

An understanding of the <u>in vivo</u> mechanisms by which arsenic imparts a protective effect on selenium toxicity has only recently been gained.

The ability of arsenic to retard the formation of volatile selenium in the form of dimethyl selenide (Kanstra and Bonhorst, 1953) apparently involves inhibition of microsomal methyl transferase, an enzyme sensitive to arsenite (Ganther and Hsieh, 1974). An overall protective effect still exists, however, since arsenic promotes the biliary excretion of selenium (Levander and Baumann, 1966; Ganther and Baumann, 1962). According to Levander (1977), enhanced biliary

clearance of selenium in the presence of arsenic probably involves an excretory conjugate of both, since selenium likewise enhances the biliary excretion of arsenic.

Rössner et al. (1977) showed a protective effect for arsenite against the cytotoxicity of selenite, using suspension cultures of mouse fibroblasts exposed to these agents at 10^{-5} to 10^{-11} M. Interestingly, selenite, in turn, had only a low protective effect against arsenite cytotoxicity.

Few data exist for interactive relationships between arsenic and other elements. In one of the few pertinent studies bearing on this issue, the effects of concomitant oral exposure to cadmium, lead and arsenic versus single-agent exposure effects have been reported by Mahaffey and Fowler (1977). Cadmium and arsenic together retarded weight gain in young adult rats to a greater extent than either element alone.

6. ARSENIC MUTAGENICITY

Various inorganic compounds of arsenic have been tested for mutagenicity in a variety of test systems ranging in complexity from bacteria to peripheral lymphocytes of exposed human beings. Information on these tests has been reviewed herein and elsewhere (Flessel, 1978; NAS, 1977; Leonard and Lauwerys, 1980; WHO, 1981). The following chapter is divided into five major sections discussing studies indicative of mutagenic damage, as well as interactions of arsenic with other mutagens and possible mechanisms of mutagenic action.

6.1 GENE MUTATION STUDIES

6.1.1 Prokaryotic Test Systems (Bacteria)

Arsenic does not appear to induce gene mutations in bacteria (Table 6-1). Sodium arsenite ($NaAsO_2$) was tested for its ability to induce reverse mutations in E. coli (Nishioka, 1975). Three bacterial strains auxotrophic for tryptophan were tested for growth in the absence of tryptophan after arsenic treatment. Nishioka reported that arsenic induced mutations in wild type cells and in cells deficient in excision repair ($uvrA^-$) but not in cells deficient in recombinational repair ($recA^-$). This suggested that the rec function is necessary for arsenic-induced mutagenesis in E. coli.

The observations by Nishioka were not reproducible in subsequent studies by Rossman et al. (1980). In these latter studies, the authors examined sodium arsenite-induced mutagenesis in five strains of E. coli, all auxotrophic for tryptophan and carrying different mutations for DNA repair capacities. In addition, Rossman et al. used three protocols for quantifying the presence of mutant cells: the spot test, the plate test and the fluctuation test. Arsenite did not increase the mutation frequency in any E. coli strain using any of the

TABLE 6-1. SUMMARY OF MUTAGENICITY OF ARSENIC: GENE MUTATIONS

Reference	Test system	Chemical Information	Results	Comments
Nishioka, 1975	Reverse mutation in E. coli Strains: WP2 (trp^-) WP2 uvrA ($uvrA^-$, trp^-) CM571 ($recA^-$, trp^-)	$NaAsO_2$ 8.0×10^{-4} M in WP2 1.6×10^{-4} M in WP2 uvrA 1.6×10^{-4} M in CM571 Source: Nakarai Chemical LTD (reagent grade) Solvent: H_2O	$NaAsO_2$ positive for mutations in WP2 and WP2 uvrA but not in CM571. Increases were approximately 10x background.	1. Doses of arsenite were selected to kill 60-70% of cells. 2. Lack of mutagenesis in CM571 suggests that a rec function is required for mutagenesis in E. coli. 3. Rossman et al. (1981) were unable to reproduce these mutation studies. They claimed (a) that the induced mutation frequencies observed by Nishioka were within the normal range of background, (b) that they observed a 31-fold difference in cytotoxicity studies compared to Nishioka, and (c) that Nishioka used an incorrect method for determining mutation frequency.

TABLE 6-1. (continued)

Reference	Test system	Chemical Information	Results	Comments
Rossman et al., 1980	Induction of reverse mutations in E. coli at the trp locus. Assays: Spot test, Plate test, Fluctuation test Strains: WP2 (trp^-); $WP2_S$ (trp^-, uvrA-); WP6 (trp^-, $polA1^-$); WP10 (trp^-, $recA1^-$); $WP44_S$-NF (trp^-, $uvrA^-$, tif-1/sti^-). tif-1 mutation confers a thermally inducible SOS repair system resulting in normal mutation at 30°C and a 20-fold increase in mutation at 42°C.	$NaAsO_2$: 50 µl of 0.1 M in spot tests with $WP44_S$-NF (30°C), WP2, WP6, and WP10. $NaAsO_2$: 10 µl of 0.01 M in spot test $WP44_S$-NF, 10 µl of 0.1 M in spot test $WP44_S$-NF. $NaAsO_2$: 25 mM in plate tests WP2. $NaAsO_2$: 0.4, 1, 2, mM in fluctuation test WP2.	Arsenic did not increase the mutation frequency in any of the assays. Arsenic showed a dose-dependent decrease in mutations in $WP44_S$-NF at 42°C.	1. Results indicate that arsenic may inhibit SOS repair.
Lofroth and Ames, 1978 (abstract only)	Salmonella microsome assay	Arsenite and arsenate	Negative	1. No data available since information comes from an abstract.

TABLE 6-1. (continued)

Reference	Test system	Chemical Information	Results	Comments
Singh, 1983	Gene conversion at the trp locus and reverse mutation at the ilv locus in S. cerevisiae. Strain D7 = $\frac{\text{a ade 2-40 trp-5-12 ilv 1-92}}{\alpha \text{ ade 2-119 trp 5-27 ilv 1-92}}$	$NaAsO_2$ (0.1 M added to well, volume not indicated) Solvent: H_2O	Negative for conversion. Weak positive for mutation.	1. Study lacking sufficient experimental details.
Amacher and Paillet, 1980	Forward gene mutation at the thymidine kinase (TK) locus in mouse L5178Y cells.	Na_2HAsO_4 Doses tested: (0.83×10^{-4}, 1.1×10^{-4}, 1.47×10^{-4}, 1.96×10^{-4}, 2.26×10^{-4} M) Source: Fisher Solvent: Normal saline	Negative	1. Exposed 3 hrs at 37°C. 2. Survival ranged from 66% at the low dose to 35% at the high dose. 3. Other metals such as cadmium, nickel, and trans-platinum were positive.
Rossman et al., 1980	Induction of forward mutations in Chinese hamster cells in vitro at HGPRT locus and the sodium-potassium ATPase locus.	$NaAsO_2$ (0.5×10^{-6} M, 2 days) ouabain resistance (5.0×10^{-6} M, 1 hour) ouabain resistance (20×10^{-6} M, 1.5 hours) thioguanine resistance (100×10^{-6} M, 25 min) thioguanine resistance	No increased mutation	1. UVC and MNNG used as positive controls. 2. Doses of arsenite used varied from slightly inhibitory to cell growth to fairly toxic.

TABLE 6-1. (continued)

Reference	Test system	Chemical Information	Results	Comments
Oberly et al., 1982	Forward gene mutation at the thymidine kinase (TK) locus in mouse L5178Y cells.	$NaAsO_2$ (3.8×10^{-6}, 7.7×10^{-6}, 11.5×10^{-6}, 15.4×10^{-6}, 19.2×10^{-6} M) Na_2HAsO_4 (7.5×10^{-5}, 9.7×10^{-5}, 11.8×10^{-5}, 14.0×10^{-5} M) Source: Mallinckrodt	$NaAsO_2$ was negative in the presence of Aroclor-induced rat S-9 mix; $NaAsO_2$ was positive for the three highest doses tested in the absence of S-9 mix; Na_2HAsO_4 was negative in the absence of an Aroclor-induced rat S-9 mix; Na_2HAsO_4 was positive at the three highest doses tested in the presence of an S-9 mix.	1. Chemical exposure was for 4 hours. 2. Only positive data were shown; negative results were only mentioned in the text. 3. The spontaneous mutation rate varied a great deal between experiments; between 2.5 and 17.9 mutants per 10^5 survivors. Most of the arsenic-induced mutant frequencies were between or just slightly above this spontaneous range. 4. The increases in mutant frequencies occurred at very low survival levels for both compounds; the highest doses caused 97% lethality. 5. At survivals above 10% none of the mutant frequencies exceeded the limits of the control mutant frequency range.

test protocols. Indeed, arsenic showed a dose-dependent suppression of mutations in strain $WP44_S$-NF. This strain carries a mutation (tif-1) which confers a thermally inducible SOS repair system (error-prone repair) resulting in normal spontaneous mutation at 30°C and a 20-fold increase in mutation at 42°C. The presence of sodium arsenite in the medium was sufficient to suppress this temperature-induced increase in the mutation frequency by one-half. This observation suggests that arsenic may inhibit SOS repair, a pathway which is highly important in bacterial mutagenesis. Such a repair pathway has not been detected in mammalian cells.

Rossman et al. (1980) offered explanations for the discrepancies between their results and those of Nishioka. First, they pointed out that the arsenic-induced mutation frequencies reported by Nishioka were all within the normal range of background. Second, they observed a 31-fold difference in cytotoxicity in the same bacterial strains. Third, they noted that Nishioka used an incorrect method for determining mutation frequency, basing his calculations on the initial size of the cell inoculum instead of on the final size of the plated population.

Arsenite and arsenate have also been found to be negative in the Ames Salmonella microsome assay (Lofroth and Ames, 1978). Although this work is reported only in abstract form, it may be assumed the assay was performed properly as Ames is a cited author.

Consideration of the above results alone, however, should not be taken as proof that inorganic arsenic is non-mutagenic. Bacterial systems are generally insensitive for the detection of metal mutagens because of the large amount of magnesium salts, citrate and phosphate in the minimal medium which prevent the entry of metal mutagens into bacterial cells (McCann et al., 1975).

6.1.2 Eukaryotic Microorganisms (Yeast, Fungi)

Sodium arsenite was tested for its activity in inducing reverse mutation and mitotic gene conversion in the yeast Saccharomyces cerevisiae (Singh, 1983). The diploid strain used in this study (D7) is auxotrophic for tryptophan, isoleucine, and valine, and measures gene conversion at the trp locus and reverse mutation at the ilv locus. Arsenite was inactive for gene conversion and weakly positive for mutation. This study was generally lacking in details and raw data were not shown.

6.1.3 Mammalian Cells In Vitro

Sodium arsenate was tested for the induction of forward mutations at the thymidine kinase locus in mouse L5178Y cells (Amacher and Paillet, 1980). Doses of arsenate were selected such that between 66 percent to 35 percent of cells survived a three-hour treatment. Arsenate was found not to increase the spontaneous mutation rate in these cells, while other known or suspected mutagenic metals (cadmium, nickel, and trans-platinum) were positive.

Using the same system, Oberly et al. (1982) tested sodium arsenate and sodium arsenite in the presence and in the absence of an Aroclor-induced rat S-9 mix. Sodium arsenite gave positive results at the three highest doses when tested in the absence of S-9 mix. In the presence of S-9 mix, the results were reported to be negative, although no data were presented. Sodium arsenate gave positive results at the three highest doses tested in the presence of S-9 mix. Again, without presenting data, the outcome in the absence of metabolic activation was reported to be negative. The authors concluded that these two arsenic compounds were weak mutagens. There are, however, several problems with this interpretation. First, the spontaneous mutation rate varied a great deal in these studies: between 2.5 and 17.9 mutants per 10^5 survivors. Most of the arsenic-induced mutant frequencies fell between or just slightly above

this spontaneous range. Second, the increases in mutant frequencies occurred at very low survival levels for both compounds; the highest doses used caused 97 percent lethality. Thus, at survivals exceeding 10 percent none of the mutant frequencies exceeded the limits of the range of control mutant frequencies. Taking these observations into consideration, the authors' conclusions do not seem well supported.

Sodium arsenite was also tested for the induction of forward mutations at two loci in V79 cells (Chinese hamster lung fibroblasts) (Rossman et al., 1980). The two genes studied were hypoxanthine guanine phosphoribosyl transferase (HGPRT) and membrane-bound sodium potassium ATPase. Mutations in these two enzymes were enumerated through the observation of cell clones resistant to thioguanine or ouabain, respectively. Both the concentration of the chemical as well as the incubation times were varied; there was, however, no increase in the mutation frequency at either locus. The positive controls, UVC (ultraviolet light 254 mm) and methylnitronitrosoguanidine (MNNG) were effective in elevating the mutant frequency.

6.2 CHROMOSOMAL ABERRATION STUDIES

6.2.1 Chromosomal Aberrations In Vitro

A large number of studies indicate that both trivalent and pentavalent arsenic compounds are capable of breaking chromosomes in vitro (Table 6-2). One of the earliest reports on the clastogenic potential of arsenic was from a study performed with mitogenically stimulated human peripheral lymphocytes (Petres and Hundeiker, 1968). Although the test compound was reported to be Na_2HAsO_3, it is assumed the authors meant Na_2HAsO_4. Positive results were reported, although no actual raw data were presented.

Paton and Allison (1972) tested both sodium arsenite and sodium arsenate for the induction of chromosomal aberrations in human diploid fibroblasts and

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TABLE 6-2. SUMMARY OF MUTAGENICITY OF ARSENIC: CHROMOSOME ABERRATIONS

Reference	Test System	Chemical Information	Results	Comments
Petres and Hundeiker, 1968 (paper in German, English summary)	Chromosome aberrations induced in human peripheral lymphocytes exposed in vitro.	Na_2HAsO_3 0.5×10^{-6} and 10^{-6} g/ml of medium (assume Na_2HAsO_4 is meant) 1.6×10^{-6} M and 3.2×10^{-6} M	Positive at both doses.	1. No raw data were presented in this paper.
Paton and Allison, 1972	Chromosomal aberrations in human fibroblasts and human peripheral lymphocyte (HPL) cultures exposed in vitro.	$NaAsO_2$ (2.9×10^{-9} to 1.8×10^{-8} M) HPL. Na_2HAsO_4 (5.8×10^{-8} M) HPL. $NaAsO_2$ (2.9×10^{-9} to 5.8×10^{-8} M) fibroblasts. Source: British Drug House Chemical LTD. Solvent: H_2O	Positive for $NaAsO_2$ in HPL. Positive for $NaAsO_2$ in fibroblasts. Negative for Na_2HAsO_4 in HPL.	1. Incubation with chemical was for 48 hrs and 24 hrs for HPL and fibroblasts, respectively. 2. "Subtoxic" doses were used.
Larramendy et al., 1981	Induction of chromosomal aberrations in Syrian hamster embryo (SHE) cells and human peripheral lymphocytes (HPL) in vitro.	$NaAsO_2$ (7.7×10^{-6} M) in HPL and SHE. Na_2HAsO_4 (3.2×10^{-5} M) in HPL and SHE. Source: Chemical Services Inc. "100% pure" Solvent: Cell culture medium	Highly significant increase in the aberration frequency with both compounds in HPL and SHE.	1. Arsenite was about an order of magnitude more genotoxic than arsenate. 2. Both compounds induced mainly chromatid type aberrations. 3. Doses tested were generally non-cytotoxic. 4. Exposure to arsenic was for 24 and 48 hrs. in SHE and HPL, respectively.

TABLE 6-2. (continued)

Reference	Test System	Chemical Information	Results	Comments
Nakamuro and Sayato, 1981.	Chromosomal aberrations in cultured human peripheral lymphocytes (HPL) and fibroblasts.	As_2O_3 (3×10^{-7}, 12×10^{-7}, 36×10^{-7}M). $AsCl_3$ (6×10^{-7}, 24×10^{-7}, 72×10^{-7}M). $NaAsO_2$ (6×10^{-7}, 24×10^{-7}, 72×10^{-7}M). Na_2HAsO_4 (24×10^{-7}, 72×10^{-7}, 240×10^{-7}M). H_3AsO_4 (6×10^{-7}, 24×10^{-7}, 72×10^{-7}M). As_2O_5 (3×10^{-7}, 12×10^{-7}, 36×10^{-7}M). Source: Wako Pure Chemical Co. Solvent: H_2O	1. All arsenic compounds were clastogenic, all gave linear dose-response functions in lymphocytes. $NaAsO_2$ and H_3AsO_4 were positive with linear dose-response functions in fibroblasts. 2. Trivalent compounds were more potent than pentavalent compounds. The observed order for decreasing potency was: As_2O_3 > $AsCl_3$; Na AsO_2 >> Na_2HAsO_4 > H_3AsO_4; As_2O_5.	1. Treatment of lymphocytes was for the last 24 hours of culture. 2. Fibroblasts were exposed for 48 hrs. 3. All compounds induced more chromatid-type aberrations.

TABLE 6-2. (continued)

Reference	Test System	Chemical Information	Results	Comments
Nordenson et al., 1981	Chromosomal aberrations in peripheral lymphocytes of 3 normal volunteers - *in vitro* exposure.	$NaAsO_2$ (77×10^{-8}, 150×10^{-8}, 230×10^{-8}, 310×10^{-8} M). Na_2HAsO_4 (77×10^{-8}, 150×10^{-8}, 230×10^{-8}, 310×10^{-8} M). Source: Merck Solvent: Normal saline	$NaAsO_2$ caused a dose-related increase in gaps and chromatid breaks. Na_2HAsO_4 was negative.	1. Arsenic added 24 hours after initiation of culture, harvested at 72 hours. 2. Only scored gaps, chromatid and chromosome breaks. 3. Also examined G_0 effects: 24 hr. exposure without PHA, remove arsenic, add PHA, harvest after 48 hours; examined "$NaAsO_4$" - do not know what compound was really tested. 4. Reason for negative result with arsenate is that a sufficiently high dose was not tested. Should have increased concentration by an order of magnitude.

TABLE 6-2. (continued)

Reference	Test System	Chemical Information	Results	Comments
Wan et al., 1982	Induction of chromosome aberrations in vitro in CHO cells and human peripheral lymphocytes (HPL).	$NaAsO_2$ (10^{-6}, 5×10^{-6}, 10^{-5} M) CHO; (0.5×10^{-6}, 10^{-6}, 5×10^{-6} M) HPL Na_2HAsO_4 (5×10^{-5}, 8×10^{-5}, 10^{-4} M) CHO. Purity: Analytical grade Source: Fisher Scientific Co. Solvent: H_2O	Dose-related increase for both compounds in CHO. $NaAsO_2$ gave dose-related increase in HPL.	1. Trivalent was 5 to 10 x more potent than pentavalent. 2. All doses tested were inhibitory to CHO cell growth. 3. Arsenic present for entire culture period (22 hrs.) in CHO cells, and final 48 hrs of culture in HPL.
Poma et al., 1981b	Induction of chromosomal aberrations in mouse bone marrow and spermatogonia in vivo.	As_2O_3, single I.P. injection (4, 8 and 12 mg As/kg). Solvent: H_2O	Negative in bone marrow. Negative in spermatogonia.	1. Mouse strain: Swiss Albino 2. Sex: male. 3. Age: 12 weeks 4. Number of animals per dose group: 4-8. 5. Cells per animal: 100. 6. Sacrifice times: 12, 24, 36, 48 hrs post injection.

mitogenically stimulated human peripheral lymphocytes. Sodium arsenite gave positive results in both cell types while sodium arsenate was tested only in lymphocytes and was reported to be negative. Since arsenate (which most investigators find to be considerably less potent than arsenite) was tested at a lower concentration, the negative result is not surprising.

In a more recent study, the effects of sodium arsenite and sodium arsenate on chromosomal aberration frequencies were examined in cultured human peripheral lymphocytes and in Syrian hamster embryo cells (Larramendy et al., 1981). Both compounds gave highly significant increases in chromosomal aberrations in both cell types. Arsenite was more potent by approximately an order of magnitude, and both compounds induced mainly chromatid-type aberrations.

Nakamuro and Sayato (1981) tested six arsenic compounds for the induction of chromosomal aberrations in cultured human peripheral lymphocytes and in human skin fibroblasts. All arsenic compounds tested were clastogenic and all gave linear dose-response functions in lymphocytes. Trivalent compounds were more potent than pentavalent compounds. The observed order for decreasing potency was As_2O_3 > $AsCl_3$; $NaAsO_2$ >> Na_2HAsO_4 > H_3AsO_4; As_2O_5 (Figure 6-1). $NaAsO_2$ and H_3AsO_4 were positive, showing linear dose-response functions in fibroblasts. All compounds induced predominantly chromatid-type aberrations.

In another study, the effects of sodium arsenite and sodium arsenate on the induction of chromosomal aberrations in human peripheral lymphocytes exposed <u>in vitro</u> were examined using two protocols (Nordenson et al., 1981). In the first protocol, cells were mitogenically stimulated with PHA, arsenic was added after 24 hours and cells were harvested after 72 hours (48-hour arsenic exposure). Using this method, sodium arsenite was found to increase the frequency of chromatid breaks and gaps in a dose-dependent fashion. Sodium arsenate was reported to be negative, but these investigators employed

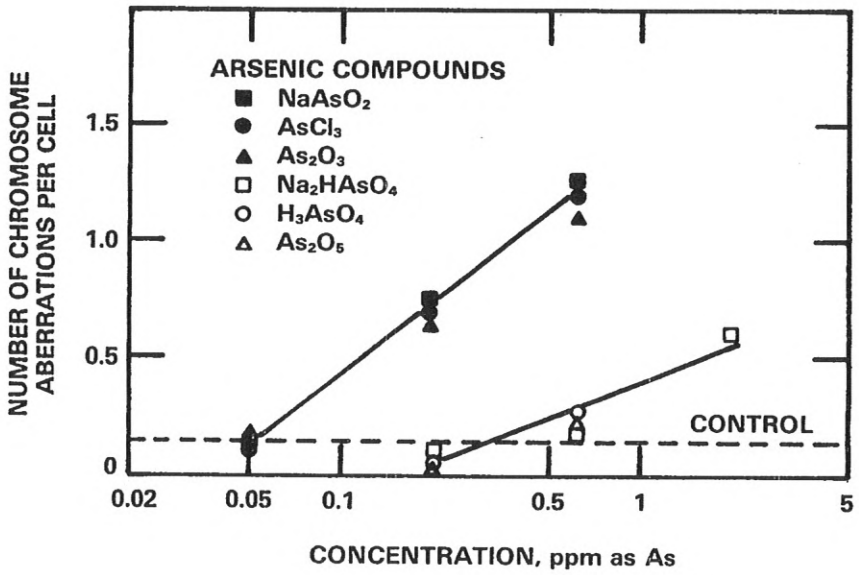

Figure 6-1. The induction of chromosome aberrations in cultured human peripheral lymphocytes by six arsenic compounds.

Source: Nakamuro and Sayato (1981).

the same concentrations of arsenate as were tested for arsenite. It is possible that higher doses of arsenate would also have yielded positive results. In the second protocol, G_0 (unstimulated) lymphocytes were exposed to arsenic for 24 hours, and the cells were washed, stimulated with PHA and harvested after 48 additional hours. Using this protocol the authors reported that "$NaAsO_4$" was negative. One may assume that the authors meant $NaAsO_2$, since having observed a lack of activity for arsenate in the first protocol, it would seem unwarranted to test it in the second. If the test compound was indeed arsenite, these observations suggest that arsenic has its effect through some influence on DNA synthesis and not by directly damaging DNA.

In the most recent study on *in vitro* clastogenic effects of arsenic compounds, sodium arsenite and sodium arsenate were tested in CHO cells and human peripheral lymphocytes (Wan et al., 1982). Both compounds showed dose-dependent increases in aberrations in CHO cells; arsenite was also positive in lymphocytes. Again, trivalent arsenic was 5 to 10 times more potent than pentavalent arsenic.

6.2.2 Chromosomal Aberrations In Vivo

There is only one report in the literature (excluding abstracts) in which the clastogenic effects of arsenic were tested in a mammalian species *in vivo* (Poma et al., 1981b). These authors examined chromosomal aberration frequencies in mouse bone marrow cells and spermatogonia after administration of As_2O_3 (4, 8 and 12 mg of arsenic/kg). This trivalent form of arsenic was previously shown to be the most potent form *in vitro* (Nakamuro and Sayato, 1981). Four to 8 animals were included in each dose group; animals were killed at 12, 24, 36 and 48 hours after exposure and 100 metaphase cells per animal were scored. This represents an acceptable protocol, and the study appears to have been properly performed. There was no significant increase in aberrations in either

bone marrow or spermatogonia following arsenic treatment. An important question in this study is whether sufficiently high doses were tested. The LD_{50} for arsenic trioxide in rats is 104 mg As/kg; thus, the highest dose used in this mouse study is only 13 percent of the rat LD_{50}. One can crudely compare the doses of arsenic trioxide which were effective in vitro to those used in this study by simply equating the test animal to an equivalent volume of water. Such a comparison indicates the mice were "1.6×10^{-4} M" effective for arsenic while the same compound was effective for inducing aberrations in vitro at approximately 0.7 to 7.0×10^{-4} M arsenic. Clearly this represents a very crude comparison since intact animals can bind, compartmentalize and excrete a toxicant while cells in culture cannot. Thus, it is not clear whether higher doses should have been tested in this study.

6.2.3 Chromosomal Aberrations and SCE in Cells of Arsenic-Exposed Human Beings

The majority of studies indicate that people exposed to arsenic due to occupation or pharmaceutical treatment display increased levels of chromosomal aberrations and SCE in peripheral lymphocytes (Table 6-3). It should be noted that most of the studies which have examined aberrations and SCE are poor in quality due either to errors in experimental protocol, misclassification of aberrations, poor choice in controls and/or not performing studies in a blind fashion.

Beckman et al. (1977) examined the frequency of chromosomal aberrations in peripheral lymphocytes of nine smelter workers who were exposed to arsenic. The levels and the forms of arsenic to which the workers were exposed were not indicated. A statistically significant increase in aberrations was found in the exposed population. There are several problems with this study. First, the authors use an incorrect definition of gaps. They state: "Gaps are commonly defined as achromatic regions exceeding the width of a chromosome." This, in

TABLE 6-3. SUMMARY OF MUTAGENICITY OF ARSENIC: CHROMOSOMAL ABERRATIONS AND SCE IN CELLS OF EXPOSED HUMANS

Reference	Test System	Chemical Information	Results	Comments
Beckman et al., 1977	Chromosomal aberrations in lymphocytes of 9 smelter workers exposed to arsenic.	Arsenic from smelter	Positive, six-fold increase in percent aberrant cells; eight-fold increase in aberrations per cell.	1. Authors used an incorrect definition of gaps. 2. Cells cultured too long (72 hours). 3. Cells scored per individual were unknown. 4. Number of control individuals and cells per control individual were not specified. 5. Some workers were also exposed to lead and selenium.
Nordenson et al., 1978	Chromosomal aberrations in lymphocytes of 33 smelter workers.	Arsenic from smelter	Positive	1. Divided workers into high exposure (18 individuals), medium exposure (11), low exposure (4) and new employees (6). 2. The controls were an unspecified number of apparently historical controls. 3. No dose effect. 4. Wrong definition of gaps. 5. Cell culture time too long. 6. Large difference between controls and new employees.

TABLE 6-3. (continued)

Reference	Test System	Chemical Information	Results	Comments
Burgdorf et al., 1977	Compared SCE and chromosomal aberrations in lymphocytes of 6 patients treated with arsenic, with results from 44 control individuals.	All treated with Fowler's solution (1% $KAsO_2$ in H_2O), for time periods between 4 and 27 years. Five of these individuals had not been treated for at least 24 years.	No difference in frequencies of chromosomal aberrations. SCE frequencies were increased more than 2-fold in arsenic-treated patients.	1. Cultured cells for 72 hours - too long for examination of aberrations. 2. No indication that study was scored blind. 3. Patients exposed to other agents (e.g. 4000 rad x-irradiation, 5000 rad x-irradiation, fluoroscopy twice weekly while receiving arsenic, 4 had asthma).
Petres et al., 1977	Chromosome aberrations in lymphocytes of 31 individuals exposed to arsenic.	Arsenic exposure related to treatment for psoriasis or associated with vine-growing.	Positive, nine-fold increase in aberrations among arsenic-exposed individuals.	1. 31 exposed individuals, 31 controls. 2. Cell culture time too long (72 hours). 3. Scored both gaps and achromatic lesions - same aberration. 4. Scored secondary constrictions - not generally considered an aberration. 5. No indication of the number of cells per person scored. 6. Saw a 5-fold increase in aneuploidy among arsenic-exposed individuals, always hypodiploidy, which suggests an artifact.

TABLE 6-3. (continued)

Reference	Test System	Chemical Information	Results	Comments
Nordenson et al., 1979	Chromosome aberrations and SCE in peripheral lymphocytes of 8 psoriatic patients treated with arsenic.	Total arsenic dose per individual varied from a low of 300 mg up to 1200 mg. Most had not been treated for 15 years.	Psoriatic patients treated with arsenic showed significantly higher (three-fold) levels of aberrations compared to control psoriatics. Psoriatic patients treated with arsenic had the same levels of SCE as controls.	1. Slides were scored blind. 2. Investigators controlled for age and sex but not for ethanol use, smoking, drug use, or infection. 3. The increases in aberrations were not dose-related. 4. Cultured cells for 72 hours: too long for aberrations. 5. Scored too few cells for SCE in control patients; provided total number of cells scored, but number of cells per individual was unknown.

TABLE 6-3. (continued)

Reference	Test System	Chemical Information	Results	Comments
Wen et al., 1981	SCE in peripheral lymphocytes of 13 Blackfoot disease patients (arsenic-exposed) and 13 controls.	Exposure to arsenic from well water; years of use ranged from 15 to 58. Most had not consumed contaminated water for 12 years.	Arsenic-exposed individuals showed small but statistically higher SCE level. Ranges for arsenic-exposed (9.1 to 17.5 SCE/cell) and controls (7.8 to 12.0 SCE/cell) showed considerable overlap.	1. Patients exposed to a large number of other drugs, including pantopan, scopolamine, promethazine hydrochloride, meperidine, ketamine hydrochloride, Pyrabital, Valium, ampicillin, Kanamycin, Sedes, diphenhydramine hydrochloride, Kolantyl, Complamin, Venostatin, Ulcerin, metoclopramide, Sulpyrin, chloramphenicol, reserpine, Bartropine, dextromethorphan, furosemide, and Hustazol. 2. All patients had undergone leg or foot amputation.

fact, is a definition for a break. A gap is commonly defined as an achromatic lesion not exceeding the width of a chromatid arm. Second, the total number of cells examined are given but the cells per individual worker, cells per individual control, and total number of control individuals are not listed. Third, these investigators cultured the lymphocytes for 72 hours, a duration 24 hours longer than optimum, since most chromosome aberrations are cytotoxic, and cells with such lesions generally do not survive more than a single cell cycle. After 72 hours of culture, the majority of cells have divided three times, eliminating many damaged cells. Clearly, however, this type of error tends to underestimate the frequency of aberrations. Finally, workers were also exposed to other potentially clastogenic agents such as lead and selenium.

A report one year later by the same group (Nordenson et al., 1978) extended this study to a total of 33 smelter workers. In this study individuals were grouped into high exposure (18 people), medium exposure (11), low exposure (4) and new employees (6). The groupings were based on the nature of the job; quantitative measurements of exposure were not performed. The workers were reported to have a higher level of chromosome aberrations than did the controls. However, the controls were of an unspecified number and, apparently, historical, the definition of gaps was incorrect, cells were cultured for 72 hours, and large differences were found between historical controls and new employees. Due to these problems, the positive findings reported are questionable.

Burgdorf et al. (1977) compared SCE and chromosomal aberration frequencies in lymphocytes of six patients treated with arsenic (for asthma, psoriasis or anxiety) to results from 44 control individuals. All patients had been treated with Fowler's solution (1% $KAsO_2$ in water) for time periods varying between 4 and 27 years. Five of these individuals had not been treated for at least 24 years. The authors found no difference in frequencies of chromosomal aberrations, but reported a more than 2-fold higher SCE frequency in arsenic-treated

patients. Each of the patients had an SCE level which was significantly higher than the mean level for controls. Problems with this study included a 72-hour culture period for aberrations, no indication that slides were scored "blind," and the fact that patients were exposed to other agents (4000 rad x-irradiation, 5000 rad x-irradiation, fluoroscopy twice weekly concomitant to arsenic exposure).

In a similar study, Petres et al. (1977) compared chromosome aberrations in lymphocytes of 31 arsenic-exposed people to 31 controls. Arsenic exposure resulted from treatment for psoriasis or was associated with vine-growing. The levels and forms of arsenic exposure were not indicated. A statistically significant increase in aberrations was found in the exposed group. These authors also reported a five-fold increase in aneuploidy among arsenic-exposed individuals. Problems in this study include: (1) a 72-hour cell culture period; (2) no indication of the number of cells per person scored; (3) scoring both gaps and achromatic lesions, identical endpoints; (4) scoring secondary constrictions, which are generally not considered to be aberrations; and (5) all aneuploid cells were hypodiploid, which suggests an artifact.

Nordenson et al. (1979) compared chromosome aberrations and SCE in peripheral lymphocytes of 8 arsenic-treated psoriatic patients to 8 untreated psoriatic controls. Total arsenic dose per individual varied from a low of 300 mg up to 1200 mg. Most had not been treated for 15 years. Psoriatic patients treated with arsenic showed significantly higher levels of aberrations compared to controls, but showed similar frequencies of SCE. The increase in aberrations was not related to the total arsenic dose. Although these authors controlled for age and sex, there was no apparent control for smoking, drug use or ethanol consumption. An average of 15 cells per individual were scored for SCE; generally, 20 cells per individual is considered the acceptable minimum. As in the other studies, the cells were cultured for 72 hours.

Frequencies of SCE were compared in 13 patients exposed to arsenic in drinking water to SCE frequencies in 13 control individuals (Wen et al., 1981). All patients displayed symptoms of Blackfoot disease, a peripheral vascular disease resulting from chronic arsenic intoxication. Patients had used contaminated water for 15 to 58 years; most had switched to uncontaminated tap water 12 years before this study. Arsenic-exposed individuals showed a small but statistically higher SCE level. Ranges for arsenic-exposed (9.1 to 17.5 SCE/cell) and controls (7.8 to 12.0 SCE/cell) showed considerable overlap. Sources of error in this study are large since the arsenic-exposed group had also been exposed to over 20 different pharmaceuticals.

6.3 OTHER STUDIES INDICATIVE OF MUTAGENIC DAMAGE

6.3.1 Preferential Killing of Repair-Deficient Bacterial Strains

Arsenic compounds have generally been found to preferentially kill bacteria that carry particular mutations in DNA repair pathways (Table 6-4). Both sodium arsenite and sodium arsenate gave positive results in the B. subtilus "rec assay" (Nishioka, 1975). In this assay, test chemicals are spotted onto filter discs and the discs are placed at the centers of a bacterial lawn composed of rec^+ cells (H17) or rec^- cells (M45, deficient in recombinational DNA repair). The size of the zone of growth inhibition is measured for both strains, with a differential response (more killing of M45) indicative of a DNA-damaging agent. Sodium arsenite was reported to give a moderately positive response while sodium arsenate was reported to give a weakly positive response.

The results for sodium arsenate were reproduced in the B. subtilus rec assay and positive responses for four other arsenic compounds (As_2O_5, As_2O_3, $AsCl_3$, $3AsO_5$) have been reported (Kanematsu et al., 1980). These authors indicated that all arsenic compounds gave "strongly positive" responses (greater than 6 mm growth difference).

TABLE 6-4. MUTAGENICITY OF ARSENIC: ASSAYS INDICATIVE OF DNA DAMAGE OR REPAIR

Reference	Test System	Chemical Information	Results	Comments
Nishioka, 1975	Rec assay in B. subtilus. Strains: H_{17} (rec^+, arg^-, trp^-) M45 (rec^-, arg^-, trp^-	$NaAsO_2$ (0.05 M) Na_2HAsO_4 (0.05 M) 0.05 ml aliquot spotted onto filter disc. Source: Nakarai Chemical LTD. Solvent: H_2O	$NaAsO_2$ moderate positive response in rec assay. Na_2HAsO_4 weak positive response in rec assay.	
Kanematsu et al., 1980	Implication of DNA damage through the measurement of growth of normal (rec+) and recombination-repair-deficient (rec^-) B. subtilis, "rec assay." Strains: H_{17} (rec^+, agr^-, trp^-) M45 (rec^-, arg^-, try^-).	As_2O_5 (0.05 M) As_2O_3 (0.05 M) $AsCl_3$(0.03 ml) $3AsO_5$ (0.05 M) Na_2HAsO_4 (0.1 M) 0.05-ml portions of aqueous solutions at the indicated concentration are applied to the paper disc. Source: Marvichi Chemical LTD. Solvent: H_2O	All arsenic compounds gave strong positive responses. (Greater than 6-mm difference in growth).	1. Plates kept at 4°C for 24 hrs. prior to incubation at 37°C. This "cold incubation" increases the sensitivity of the assay 20 to 50 times.

TABLE 6-4. (continued)

Reference	Test System	Chemical Information	Results	Comments
McCarroll et al., 1981	E. coli micro-suspension assay. Measures preferential killing of repair-deficient strains. Strains WP2 (wild type) WP2 UVRA ($uvrA^-$) CM611 ($lexA^-$, $uvrA^-$) WP67 ($polA^-$, ($uvrA^-$) WP100 ($recA^-$, $uvrA^-$) WP3110 (thy^-) P3478 ($polA^-$, thy^-)	Na_2HAsO_4 500, 250, 125, 62.5, 31.3, 15.6, 7.8, 3.9, 1.9, 0.98, 0.5, 0.2 (µg/well). $NaAsO_2$ Same	Na_2HAsO_4 was positive at 130 µg/well in strain WP100. $NaAsO_2$ was positive at 63 µg/well in strain CM 611. Results in all other strains were negative.	1. The total volume per well is not clearly stated, thus the molarity of the arsenic solutions can not be calculated 2. Strain WP100 is deficient in excision repair and in postreplicational repair (both SOS error-prone and recombinational). 3. Strain CM611 is deficient in excision repair and in post-replicational error-prone (SOS) repair.
Nordenson et al., 1981	SCE in peripheral lymphocyes, in vitro exposure.	Source: Merck Solvent: Normal saline $NaAsO_2$ (390×10^{-8} M)	Positive SCE response (1.5-fold increase).	1. Added arsenic to cultures 24 hours after initiation of culture, harvested at 72 hours.

TABLE 6-4. (continued)

Reference	Test System	Chemical Information	Results	Comments
Larramendy et al., 1981	Induction of SCE in Syrian hamster embryo (SHE) cells and human peripheral lymphocytes (HPL) in vitro.	$NaAsO_2$ (7.7×10^{-7}, 1.9×10^{-6} M) in HPL. Na_2HAsO_4 (1.6×10^{-5}, 3.2×10^{-5} M) in HPL. $NaAsO_2$ (3.8×10^{-7}, 3.8×10^{-6}, 7.7×10^{-6} M) SHE. Na_2HAsO_4 (3.2×10^{-6}, 8×10^{-6}, 1.6×10^{-5}, 3.2×10^{-5} M) SHE. Source: Chemical Services Inc. "100% pure" Solvent: Cell culture medium	Dose-related increases in SCE with both compounds in both HPL and SHE (two-fold increases).	1. Arsenite was about an order of magnitude more genotoxic than arsenate. 2. Doses tested were generally non-cytotoxic. 3. Both compounds were less efficient in inducing SCE in human whole blood cultures than in purified lymphocyte cultures. 4. Exposure to arsenic was for 24 and 48 hrs. in SHE and HPL, respectively.
Andersen, 1983	Sister chromatid exchange in cultured human lymphocytes (3 donors); and in P388D cells (continuous line of macrophage cells derived from DBA/2 mouse).	$NaAsO_2$ (10^{-6}, 10^{-7}, 10^{-8} M) P388D cells. Na_2HAsO_4 (10^{-5}, 10^{-6}, 10^{-7} M) P388D cells. $NaAsO_2$ (10^{-6} M) human lymphocytes. Solvent: H_2O	Both compounds negative in P388D cells. $NaAsO_2$ positive in lymphocytes from all three donors.	1. Chemical exposure was 48 hrs. in P388D cells. 2. Chemical exposure 24, 48, and 72 hrs. in lymphocytes. 3. Results in lymphocytes variable between donors, ranging from 30% to 117% increases in SCE frequencies for the three individuals.

TABLE 6-4. (continued)

Reference	Test System	Chemical Information	Results	Comments
Crossen, 1983	Sister chromatid exchange in cultured peripheral lymphocytes from 4 normal human volunteers.	Na_2HAsO_4 (1.34×10^{-5}, 2.68×10^{-5} M) $NaAsO_2$ (7.69×10^{-7}, 1.54×10^{-6} M) Source: BDH Chemicals Solvent: H_2O	Na_2HAsO_4 - 1 donor increased SCE, 2 donors unchanged SCE, 1 donor decreased SCE. $NaAsO_2$ - 2 donors increased SCE, 2 donors unchanged. Both compounds negative when cells treated during G_o and <u>not</u> present during replication.	1. Results suggest that arsenic does not damage DNA but may interfere with DNA replication. 2. Even positive responses were generally not dose-related. 3. Large variation in baseline SCE levels between individuals. 4. Both compounds present during final 48 hrs of culture.

TABLE 6-4. (continued)

Reference	Test System	Chemical Information	Results	Comments
Ohno et al., 1982	SCE induction in DON Chinese hamster cells in vitro.	$NaAsO_2$ ($7.7 \times 10.^{-6}$ M) As_2O_5 (1.4×10^{-5} M) Na_2HAsO_4 (5.4×10^{-6} M)	All compounds gave a significant increase in the SCE frequency (1.5-fold, 1.6-fold and 1.5-fold, respectively).	1. Chemical exposure was for 28 hrs. 2. Doses tested caused a 50% inhibition in cell growth.
Wan et al., 1982	Induction of SCE in CHO cells in vitro.	$NaAsO_2$ (10^{-6}, 10^{-5} M) Purity: analytical grade. Source: Fisher Scientific Co. Solvent: H_2O	Dose-related increase in SCE (2.4-fold increase).	1. Arsenic present for entire culture period (24 hrs).

TABLE 6-4. (continued)

Reference	Test System	Chemical Information	Results	Comments
Tkeshelashvili et al., 1980	Fidelity of DNA synthesis components: 1. E. coli DNA polymerase. 2. Artificial DNA template poly-[d(A-T)]. 3. Radiolabeled nucleotide triphosphates	Na_2HAsO_4 (0.1, 0.5, 1.0., 5.0 mM) As_2O_5 (0.1, 0.5, 2.5, 10.0 mM) Source: Either ICN Corp. or J.T. Baker Purity: 99.9%	Neither arsenic compound affected the "natural" error rate.	1. Other metals such as chromium increase the error rate in this system. 2. This is a very artificial system, i.e., the polymerase is a bacterial-repair enzyme, the DNA is an artificial template containing only two nucleotide bases and the system is carried out entirely in vitro.
Fornace and Little, 1979	Induction of DNA-protein crosslinking and single-strand DNA breaks in mouse C3H/10T 1/2 cells (alkaline elution).	$NaAsO_2$ (1 mM) Solvent: Cell culture medium	No crosslinks detected. Positive for single-strand breaks (equivalent to 120 rad of X-ray)	1. Cells were treated for 1 hour; only 2.2% of cells survived this treatment.

Sodium arsenate and sodium arsenite were also found positive in the E. coli microsuspension test (McCarroll et al., 1981). In this assay, a variety of E. coli strains carrying mutations for DNA repair are incubated in multiwell microplates with a serially-diluted test compound. The highest dose at which growth is evident is compared in wild type and DNA repair-deficient strains. Again, a differential sensitivity to growth inhibition is indicative of DNA damage. Sodium arsenate was found to preferentially inhibit the growth of strain WP100 ($recA^-$, $uvrA^-$) compared to wild type cells. This strain is deficient in excision as well as recombinational repair. Sodium arsenite was positive in strains WP100 and CM611 ($lexA^-$, $uvrA^-$). This latter strain is deficient in excision repair and is not inducible for post-replicational error-prone (SOS) repair. Negative results were seen in strains which are only deficient in excision repair, implying that arsenic-induced damage is not repaired by this pathway or that arsenic has no effect on enzymes which repair spontaneous damage through excision repair.

6.3.2 DNA Damage in Mammalian Cells In Vitro

Fornace and Little (1979) examined the effects of sodium arsenite on the induction of DNA-protein crosslinks and single-strand DNA breaks in mouse C3H/10T 1/2 cells using alkaline elution (Table 6-4). This technique measures the rate at which radiolabeled DNA passes through a polyvinyl chloride filter having a defined pore size. Treatment of cells for one hour did not induce DNA-protein crosslinks but did cause a significant increase in single-strand breaks. The level of breakage observed was equivalent to treating the cells with 120 rad of x-ray. It should be noted that the treatment protocol was highly toxic with only 2.2 percent of cells surviving the treatment.

6.3.3 Fidelity of DNA Synthesis

Some metals, such as chromium, are thought to be mutagenic by interfering with a DNA polymerase-editing function. As a result they increase the rate at

which "errors" are made in DNA replication. Loeb and co-workers have designed an *in vitro* system that measures the rate at which particular nucleotides are inappropriately incorporated into DNA (Sirover and Loeb, 1976; Tkeshelashvili et al., 1980) (Table 6-4). In this system, the DNA template is a repeating sequence of adenine and thymidine (poly[d(A - T]) which is incubated with *E. coli* DNA polymerase I, and ^{32}P-labelled dTTP and ^{3}H-dGTP. By monitoring the ratio of the two isotopes in acid precipitable material one can quantify the frequency with which an error in incorporation is made. Neither sodium arsenate nor arsenic pentoxide (As_2O_5) affected the "natural" error rate. Chromium was shown to be positive in this assay. It should be cautioned that this is a very artificial system, i.e., the polymerase is a bacterial-repair enzyme, the DNA is an artificial template containing only two nucleotide bases, and the system is carried out entirely *in vitro*.

6.3.4. Induction of Sister Chromatid Exchanges (SCE) In Vitro

Arsenic compounds have been extensively tested for the induction of SCE in a variety of cell types *in vitro*. Almost without exception the results are positive (Table 6-4). Significant increases in SCE frequencies were shown in human peripheral lymphocytes treated with sodium arsenite (Nordenson et al, 1981; Larramendy et al., 1981; Anderson, 1983; Crossen, 1983) and sodium arsenate (Larramendy et al., 1981; Crossen, 1983). The studies by Crossen, however, suggested that individuals may vary significantly in their susceptibility to arsenic-induced SCE. Crossen noted that arsenite increased the SCE frequency in cells from two donors but had no effect in cells from two other donors. Arsenate increased the SCE frequency in one donor, had no effect in two other donors and slightly decreased the SCE frequency in a fourth donor. Crossen also used a protocol in which cells were exposed to arsenic in G_o (unstimulated), washed and then cultured for SCE analysis. The results were

similar to those seen for chromosomal aberrations (Nordenson et al., 1981), i.e., neither arsenite nor arsenate increased SCE levels when treatment occurred during a nonreplicative phase. Again, these results indicate that arsenic must be present during DNA synthesis (SCE occur during S phase) to have an effect.

Arsenic has also been tested for SCE induction in Chinese hamster lines *in vitro*. Wan et al. (1982) reported a dose-related increase in SCE in CHO cells exposed to sodium arsenite, while Ohno et al. (1982) reported significant increases in the SCE frequency in DON cells exposed to single doses of sodium arsenite, sodium arsenate, and arsenic pentoxide.

6.4 INTERACTIONS OF ARSENIC WITH OTHER MUTAGENS

6.4.1. Bacterial Studies

The effects of sodium arsenite (1 mM) on the frequencies of UVC-induced mutations were measured in *E. coli* strain WWP_2 (trp^-, $uvrA^-$), a strain deficient in excision repair (Rossman et al., 1977). Arsenite was found to reduce the number of UVC-induced mutations by 30 to 40 percent. This observation suggests that arsenic may interfere with SOS (error prone) DNA repair, and may, therefore, be a bacterial antimutagen (Table 6-5).

In a later study, Rossman (1981) further examined the effect of sodium arsenate and sodium arsenite on frequencies of UVC-induced mutations. In *E. coli* WP2, which is proficient in all repair pathways, arsenite increased UVC mutagenesis at doses up to 0.25 mM and then decreased the mutation frequency at higher doses. The increase in mutation was seen only in excision repair-proficient strains. These observations suggest that arsenic interferes with excision repair at low doses and interferes with SOS repair at higher doses.

Fong et al. (1980) examined the effect of sodium arsenate on the frequency of UVC-induced single-strand DNA breaks in *E. coli* (Table 6-5). The presence

TABLE 6-5. SUMMARY OF MUTAGENICITY OF ARSENIC: INTERACTIONS WITH MUTAGENS

Reference	Test System	Chemical Information	Results	Comments
Rossman et al., 1977	Interaction of UVC and arsenic in E. coli for mutation. Strain WWP_2 (trp^-, $uvrA^-$).	$NaAsO_2$ (1 mM) plus 1.25, 5.0, and 10 J/m^2 UVC	$NaAsO_2$ reduced the number of UVC-induced mutants by 30 to 40 %.	1. Suggests that arsenic interferes with SOS repair. 2. May not be relevant to mammals since this type of repair has not been found.
Rossman, 1981	Interaction of arsenic and UVC in the induction of mutations of E. coli. Strains: WP2 (trp^-) $WP2_s$ (trp^-, $uvrA^-$) WP6 (trp^-, $polA1^-$) WP5 (trp^-, $lexA^-$) WP10 (trp^-, $recA^-$)	$NaAsO_2$ (0.1, 0.25, 0.5, 0.75 mM) plus 5.6 J/m^2 in WP2. Na_2HAsO_4 (0.1, 0.3, 0.5 mM) plus 5.6 J/m^2 in WP2. $NaAsO_2$ (0.2 mM) plus 5.6 J/m^2 in WP2, 0.6 J/m^2 in $WP2_s$, 1.2 J/m^2 in WP6, 0.6 J/m^2 in WP5, 0.6 J/m^2 in WP10 Source: Fisher Chemical Co.	Arsenite increased UVC mutagenesis in WP2 at doses up to 0.25 mM and then decreased mutation frequency at higher doses. This increase was not seen with arsenate. The effect with arsenite was seen only in excision repair-proficient strains.	1. Observations indicate that arsenic may interfere with excision repair at lower doses and with SOS repair at higher doses.

TABLE 6-5. (continued)

Reference	Test System	Chemical Information	Results	Comments
Fong et al., 1980	Induction of single-strand (S.S) DNA breaks in E. coli after exposure to UVC light (alkaline sucrose sedimentation). Strains used: WP2-wild type WP6-(polA), lacks DNA polymerase used in repair WP2-(uvrA), deficient in excision repair.	$NaAsO_2$ (1,2,3,4, 5 mM)	1 mM arsenic inhibited the induction of S.S. breaks in WP2 and WP6 after exposure to UVC (40 J/m^2 and 10 J/m^2, respectively). 3 mM arsenic prevented the rejoining of S.S. breaks after UVC (5 J/m^2) in WP2 (uvrA) cells.	1. Arsenic prevents enzymatic incision in DNA after exposure to ultraviolet light. 2. Authors speculate this may result from arsenic-induced depletion of cellular ATP. 3. Arsenic may inhibit post-replicational repair since it prevented rejoining of S.S. breaks in cells deficient in excision repair.
Jung et al., 1969	Inhibition of unscheduled DNA synthesis (UDS) in human epidermal cells seen in biopsies derived from seven normal volunteers after UV irradiation.	Na_2HAsO_4 (10^{-5}, 10^{-6} M)	Arsenic inhibited UVC-induced UDS.	1. Tissue biopsies were incubated with arsenic for either 1 hr or 4 hrs prior to UVC exposure. 2. There were no dose- or incubation time-related effects on inhibition of UVC-induced UDS. 3. Actual numbers were not shown.

TABLE 6-5. (continued)

Reference	Test System	Chemical Information	Results	Comments
Rossman, 1983 (progress report)	Mutation in V79 cells. Interaction of UVC and arsenite.	Arsenite	No interaction	1. No data provided.
Poma et al., 1981a (abstract)	Interaction between arsenic and ethyl methanesulfonate in the induction of chromosome aberrations in vivo in Swiss-albino mice: bone marrow, and spermatogonia.	Arsenic (12 mg As/kg) EMS (200 mg/kg) pre- or post-treatment.	No interaction	1. No experimental details, work described in an abstract.
Sram, 1976	Chromosomal aberrations in bone marrow cells of ICR mice. Each dose group consisted of 5 female mice. Animals sacrificed 24 hours after a single dose of TEPA, scored 250 metaphases/group (assume 50/animal).	$NaAsO_2$ in drinking water for 8 weeks. 10 mg/l (7.7×10^{-5} M) 100 mg/l (7.7×10^{-4} M) TEPA 2 mg/kg	$NaAsO_2$ alone did not appear to induce aberrations although the spontaneous rate was not clearly indicated. The lower dose of arsenic in drinking water did not affect the frequency of TEPA-induced aberrations. The higher dose of arsenic resulted in a synergistic increase in the aberration rate.	1. This study was lacking in experimental details.

TABLE 6-5. (continued)

Reference	Test System	Chemical Information	Results	Comments
Sram, 1976	Interaction of $NaAsO_2$ and TEPA for dominant lethals in ICR mice; each treated and control group consisted of 20 males and 40 females/week. Mating continued for 3 to 8 weeks after the application of TEPA.	$NaAsO_2$ in drinking water for 8 weeks/ generation, males were exposed for 4 generations prior to mating. 10 mg/l (7.7×10^{-5} M) 100 mg/l (7.7×10^{-4} M) TEPA 2 mg/kg	$NaAsO_2$ alone did not appear to induce dominant lethals, although it is not clear what the spontaneous rate was. There appeared to be a positive interaction between TEPA and the higher exposure to arsenic.	1. This study was badly lacking in experimental details. 2. It was not indicated at what time after TEPA administration the increase in dominant lethals was seen, thus it is not known which germ cell stage was affected.

of strand breaks in DNA was measured by alkaline sucrose sedimentation. One mM arsenite was found to inhibit the induction of strand breaks in WP2 (wild type) and WP6 polA (lacks DNA polymerase I) after exposure to UVC. The presence of 3 mM arsenate in growth medium prevented the rejoining of strand breaks after UVC exposure in WP2 uvrA cells (excision repair-deficient). The authors interpreted these observations to suggest: (1) that arsenic prevents enzymatic incision of DNA after UVC exposure (UVC alone does not cause strand breaks), and (2) that arsenic may inhibit post-replicational repair since it prevented rejoining of breaks in cells deficient in excision repair. The authors further speculated that the inhibition of enzymatic incision may result from arsenic-induced cellular depletion of ATP.

6.4.2 Mammalian Cells In Vitro

The interaction of sodium arsenate and UVC on levels of unscheduled DNA synthesis (UDS) was measured in cells from human skin biopsies taken from seven volunteers (Jung et al., 1969; Table 6-5). Arsenate was tested at two concentrations (10^{-5}, 10^{-6}M) and for two preincubation periods (1 and 4 hrs). Arsenic was reported to inhibit the level of UVC-induced UDS, although there were no dose- or time-related effects. The actual numbers were not reported in the paper.

Rossman (1983) examined the effect of arsenite on UVC-induced HGPRT mutations in V79 cells. Although no data were provided in this report, the outcome was reported to be negative.

6.4.3 Mammalian Cells In Vivo

The interaction of arsenic and ethylmethanesulfonate (EMS) on levels of chromosome aberrations *in vivo* was examined in bone marrow and spermatogonial cells of Swiss-albino mice (Poma et al., 1981a). The arsenic dose was 12 mg As/kg combined with either pre- or post-treatment with 200 mg/kg of EMS. No

interactions were reported. It should be cautioned that this information has only been reported in abstract form.

Sram (1976) examined the effects of including sodium arsenite in drinking water (7.7×10^{-5}, 7.7×10^{-4} M) on frequencies of tris (1-aziridinyl) phosphine oxide (TEPA)-induced (2 mg/kg) chromosomal aberrations in ICR mouse bone marrow cells. Animals were given arsenic-laced water for 8 weeks, were injected with TEPA, and killed after 24 hours. A total of 250 cells per dose group (5 animals per dose) were scored. Sodium arsenite alone did not appear to induce aberrations, although the spontaneous rate was not clearly indicated. The lower dose of arsenic in drinking water did not affect the frequency of TEPA-induced aberrations. The higher concentration of arsenic resulted in a synergistic increase in the aberration rate. This study was, unfortunately, lacking in experimental details.

Sram (1976) did essentially the same study for the examination of dominant lethality in ICR mice. Animals were maintained for 4 generations prior to mating on arsenic-laced drinking water (7.7×10^{-5}, 7.7×10^{-4} M). TEPA was again given as a single dose of 2 mg/kg. Each treated animal and a control group of 20 males was mated with 40 females per week. The matings continued for 3 to 8 weeks after mutagen application. Sodium arsenite alone did not appear to induce dominant lethals, although the spontaneous rate was not clearly indicated. The lower dose of arsenic in drinking water did not affect the frequency of TEPA-induced dominant lethals. The higher concentration of arsenic resulted in a synergistic increase in the dominant lethal rate. It was not indicated at what time after TEPA administration the increase in dominant lethals occurred; thus, it is not known which germ cell stage was affected. This study also failed to provide experimental details.

6.5 POSSIBLE MECHANISMS OF ACTION

Arsenic is unusual in several respects. First, unlike the overwhelming majority of clastogenic agents, arsenic does not appear to directly damage DNA. Rather, it seems to have its effect through some interference with DNA synthesis. This contention is supported by the observations that arsenic induces chromosomal aberrations and SCE only when it is present during DNA replication. Incubation and removal of arsenic before DNA synthesis has no effect (Nordenson et al., 1981; Crossen, 1983).

Second, arsenic is highly unusual in that it induces chromosomal aberrations and SCE while it fails to induce gene mutations. In this regard, it is like diethylstibesterol, which is another highly unusual carcinogen. X-irradiation, although capable of producing chromosome aberrations as well as gene mutations, is much more potent for the former endpoint. There is a small possibility, however, that the discrepancy for arsenic may be founded on an artifact. Protocols for gene mutation assays generally involve cellular incubation with the test agent for relatively short time periods (2 to 3 hours), while protocols for aberrations often involve the presence of the test agent for one or two entire cell cycles (12 to 48 hours). Thus, in the latter protocol, arsenic would be present for at least an entire S phase for all cells, whereas, when tested for gene mutations, arsenic would be present for only a small fraction of the S phase in approximately one-third to one-half of the cells. Since the evidence available suggests that arsenic has its effect only during DNA replication, this may account for the discrepancy.

Arsenic has long been known to be a sulfhydryl reagent capable of inhibiting a number of thiol-dependent enzyme systems, trivalent forms being much more potent than pentavalent forms (Leonard and Lauwerys, 1980). Thus, one possible mechanism of action for arsenic would be the inhibition of DNA repair enzymes. The work of Rossman (1981) in bacteria and Jung (1969) in human

skin cells *in vitro* lends support to this hypothesis. Also, the observations of Sram (1976) on the interactions of arsenic with TEPA for the induction of chromosomal aberrations and dominant lethals support such a contention. The potencies of trivalent and pentavalent arsenicals as sulfhydryl reagents are similar to their potencies as clastogens and SCE-inducing agents. Observations which counter this hypothesis are the reports by Rossman that arsenic has no effect on the frequency of UVC-induced mutations in mammalian cells *in vitro* and the fact that arsenic does not affect the frequency of EMS-induced aberrations *in vivo* (Poma et al., 1981a).

Another possible mechanism for the action of arsenic may be through its occasional incorporation into the DNA backbone in place of phosphorus. There are several lines of evidence to support this mechanism. First, for this to occur, arsenic would have to be present during DNA synthesis and would have no effect on non-dividing cells. Second, such a mechanism could explain why arsenic is clastogenic (such a bond would be weaker than the normal phosphodiester bond) but does not induce gene mutation. Third, arsenic has been shown to cause strand breaks in DNA (Fornace and Little, 1979). X-irradiation, a potent clastogen and poor inducer of gene mutations, also predominantly causes strand breaks as its major DNA lesion. An argument against such a mechanism is the observation that the trivalent forms are more potent than pentavalent forms, while pentavalent arsenic should be more likely to substitute for phosphorus in DNA. Therefore at present, there is no single, unambiguous explanation for the mechanisms by which arsenic breaks chromosomes or induces SCE.

7. ARSENIC CARCINOGENICITY

The case for the association of inorganic arsenic with skin and lung cancer as well as other visceral carcinomas has been extensively reviewed (Arsenic NAS, 1977; IARC, 1973 and 1980; NIOSH, 1975; Hernberg, 1977; Sunderman, 1976, Pelfrene, 1976; Kraybill, 1978; Wildenberg, 1978; Pershagen and Vahter, 1979; WHO, 1981). The following chapter is divided into three major sections discussing human studies, animal studies and quantitative carcinogenic risk estimates.

7.1 HUMAN STUDIES

The literature on arsenic carcinogenicity in humans is summarized in Table 7-1. This subsection on human studies will first focus on clinical pathophysiological aspects of arsenic carcinogenesis, followed by pertinent epidemiological studies of arsenic-induced carcinogenesis.

7.1.1 Clinical Aspects of Human Arsenic Carcinogenesis

In man, chronic exposure to arsenic induces a characteristic sequence of changes in skin epithelium, proceeding from hyperpigmentation to hyperkeratosis which may be histologically described as showing keratin proliferation of a verrucose nature with derangement of the squamous portions of the epithelium or may even be described in some cases as squamous cell carcinomas.

Late onset skin cancers, associated with arsenic exposure, appear to be of two histopathological types: squamous carcinomas in the keratotic areas and basal cell carcinomas. In one study dealing with skin cancer after prolonged use of Fowler's solution (Neubauer, 1947), the ratio of types was approximately 1:1.

Arsenic-associated skin cancers differ from those of ultraviolet light etiology by occurring on areas generally not exposed to sunlight, e.g. palms and soles, and occurring as multiple lesions (Arsenic. NAS, 1977; Pershagen

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TABLE 7-1. SUMMARY OF CASE REPORTS AND EPIDEMIOLOGIC STUDIES OF CANCER OR PRECANCEROUS LESIONS IN PERSONS EXPOSED TO ARSENIC

Media	Study Population	Author(s)	Type of Study	Results	Highlights and Deficiencies
Air	Smelter workers-Tacoma, Washington (Analysis of deaths for 1946-1960)	Pinto and Bennett (1963)	Proportionate mortality	No difference in lung cancer proportionate mortality between exposed and unexposed workers.	Workers leaving the plant before retirement were not included. In the classification of workers by exposure, the "non-exposed" group apparently were exposed since they also had high levels of arsenic in the urine.
	Smelter workers-Tacoma, Washington (follow-up from 1950-1971)	Milham and Strong (1974)	Cohort	40 observed lung cancer deaths versus 18 expected ($P < 0.001$).	Urinary arsenic levels of persons living around the smelter decreased with distance from the smelter.
	Smelter workers-Tacoma, Washington (follow-up from 1949-1973)	Pinto et al. (1977)	Cohort	32 observed respiratory cancer deaths, versus 10.5 expected ($P < 0.05$). Dose response seen by urinary arsenic levels and by duration and intensity of exposure.	Study consisted of only pensioners.
	Smelter workers-Tacoma, Washington (Follow-up from 1941-1976)	Enterline and Marsh (1982)	Cohort	104 respiratory cancer deaths observed versus 52.5 expected ($P < 0.01$). Dose response found by intensity and duration of exposure.	Short-term high-intensity arsenic exposures appeared to have a greater effect than did long-term low-intensity exposures; SO_2 exposure was found to have little or no effect.
	Smelter workers-Anaconda, Montana (Follow-up from 1938 to 1963)	Lee and Fraumeni (1969)	Cohort	147 respiratory cancer deaths observed versus 44.7 expected ($P < 0.01$). Dose response found by intensity and duration of exposure.	A dose response was found between exposure to sulfur dioxide and respiratory cancer mortality. Exposure to sulfur dioxide could not be separated from exposure to arsenic, however.
	Smelter workers-Anaconda, Montana (Follow-up from 1964 to 1977)	Lubin et al. (1981)	Cohort	146 respiratory cancer deaths versus 88.7 expected ($P < 0.01$).	Exposure to sulfur dioxide was not found to have an independent effect on cancer risk.
	Sample of 1800 of the smelter workers-Anaconda, Montana (Follow-up from 1938-1977)	Welch et al. (1982); Higgins et al. (1982)	Cohort	24 respiratory cancer deaths versus 4.6 expected ($P < 0.01$) in the heavy exposure category. Dose response found by intensity (both time-weighted average and ceiling level categories) of exposure.	Analysis of lung cancer mortality by SO_2 exposure found that SO_2 did not play an important role in the respiratory cancer process.

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TABLE 7-1. (continued)

Media	Study Population	Author(s)	Type of Study	Results	Highlights and Deficiencies
Air	Smelter workers-Anaconda, Montana (Follow-up from 1938 to 1977)	Lee-Feldstein (1983)	Cohort	302 respiratory cancer deaths observed versus 105.8 expected ($P < 0.01$). Dose response found by duration and exposure.	
	Lung cancer from the parish where the Ronnskar smelter is located	Axelson et al. (1978)	Case-control	For smelter workers, the lung cancer mortality odds ratio was 4.6; there also was a significantly ($P < 0.02$) elevated risk of leukemia and myeloma among smelter workers.	Exposure to sulfur dioxide did not appear to be associated with lung cancer.
	Lung cancer deaths in the city of Saganoseki-machi, Japan	Kuratsune et al. (1974)	Case-control	58% of lung cancer cases were found to be former smelter workers versus 15.8% in controls.	The cause of death listed on the death certificate was validated using detailed pathologic analysis.
	Copper smelters in Sagnoseki-machi, Japan	Tokudome and Kuratsune (1976)	Cohort	29 trachea, lung, and bronchus cancer deaths versus 2.44 expected ($P < 0.01$); 3 observed colon cancer deaths versus 0.59 expected ($P < 0.05$). A lung cancer dose response was seen by length of employment and level of exposure.	The latent period ranged from 13 to 50 years, with an average of 37.6 years.
	Smelter workers in Magna, Utah	Rencher et al. (1977)	Proportionate mortality and cohort	7 percent of the deaths were lung cancer deaths compared to 0 to 2.2 percent for other factory workers and 2.7 percent for the State; the lung cancer death rate was found to be 10.1 per 10,000 versus 2.1 and 3.3 per 10,000 for mine workers and the State, respectively.	
	Residents living near a smelter in El Paso. Texas	Rom et al. (1982)	Case-control	No association was found between lung cancer and distance from the plant.	Effects of migration, smoking and occupation were not considered.

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TABLE 7-1. (continued)

Media	Study Population	Author(s)	Type of Study	Results	Highlights and Deficiencies
Air	Residents of Deer Lodge and Silver Bow Counties, Montana	Newman et al. (1976)	Ecological correlation	There was an increase found in the incidence of lung cancer among men. In one of the cities there was also an increase in lung cancer among women.	No adjustment was made for cancer cases which may be occupational.
	All counties in the United States with smelters	Blot and Fraumeni (1975)	Ecological correlation	Average lung cancer mortality rates were significantly elevated for both males and females in 36 counties with smelters processing copper, lead, or zinc ores.	
	Residents near a smelter in Utah	Lyon et al. (1977)	Case-control	No association between cancer and distance from the smelter was found.	Lymphoma cases which may have an association with arsenic exposure were used as controls. Effects of smoking, migration, and occupation were not considered.
	Residents near Ronnskarverken smelter in northern Sweden	Pershagen et al. (1977)	Ecological correlation	A significantly higher mortality rate for lung cancer was noted for men in the exposed area. The increase was no longer significant when occupational cases were excluded, however.	When excluding occupational cases of lung cancer from the study population, lung cancer cases for a comparable occupational group were not excluded from the comparison population.
	Population surrounding an arsenical pesticide facility	Matanoski et al. (1976, 1981)	Ecological correlation	The lung cancer mortality for males in the census tract in which the plant was located was 3-4 times higher than the control tracts ($P < 0.05$).	The difference in the lung cancer mortality rate in the index tract could not be explained by occupation.
	Arsenical sheep dip manufacturing workers	Hill and Faning (1948)	Proportionate mortality	29.3 percent of deaths were due to lung cancer versus 12.9 percent of deaths among workers in the same geographic area who were not exposed to arsenic ($P < 0.05$). The excess in cancer deaths was mainly due to an excess in lung cancer and skin cancer.	

TABLE 7-1. (continued)

Media	Study Population	Author(s)	Type of Study	Results	Highlights and Deficiencies
Air	Arsenical pesticide manufacturing workers	Ott et al. (1974)	Proportionate mortality and cohort	16.2% and 3.5% of deaths in the exposed group were from cancer of the respiratory system and from lymphatic and hematopoietic cancers, except leukemia, respectively, versus 5.7 and 1.4% in the controls; the cohort mortality study found 20 respiratory cancer deaths and 5 deaths of the lymphatic and hematopoietic tissues versus 5.8 and 1.3 expected, respectively (both significant at $P < 0.01$).	A respiratory cancer mortality dose response was not found below an average dosage of 3890 mg of arsenic, but above that dosage there was a good dose response. It should be noted, however, that all of the respiratory cancer at or below 3890 mg had less than one year of exposure. Thus, it is unlikely that those deaths were due to arsenic exposure.
	Retirees of an arsenical pesticide plant in Baltimore, Maryland (follow-up from 1960 to 1972)	Baetjer et al. (1975)	Proportionate mortality and cohort	The proportionate mortality ratio (PMR) was 6.58 for respiratory cancer ($P < 0.05$); for cause-specific mortality the observed-to-expected ratios were 16.67 for respiratory cancer and 50 for lymphatic cancer (both with $P < 0.05$).	The cohort study was limited to pensioners only.
	Retirees of an arsenical pesticide plant in Baltimore Maryland (follow-up 1946 to 1977)	Mabuchi et al. (1979)	Cohort	12 observed lung cancer deaths versus 3.6 expected ($P < 0.05$); a dose response by duration of employment was seen for those with exposure of high intensity.	
	Wenatchee Valley orchard workers in the state of Washington	Nelson et al. (1973)	Cohort	No difference was found between the cohort and the state of Washington for overall cancer mortality or for lung cancer mortality.	
	German vintners	Roth (1958)	Proportionate mortality	Of 47 autopsies among vintners with chronic arsenic intoxication, 64% of the deaths were due to cancer, 60% to lung cancer; 6 of the 47 and 13 of the 47 were reported to have liver and skin tumors, respectively.	No controls were used. There was no indication of how the autopsy cases were selected.

TABLE 7-1. (continued)

Media	Study Population	Author(s)	Type of Study	Results	Highlights and Deficiencies
Water	Residents of a section of Taiwan with high levels of arsenic in the drinking water	Tseng et al. (1968); Tseng (1977)	Cross-sectional	A skin cancer prevalence rate of 10.6/1000 for those drinking well water was found compared to 0/1000 for a control area. The skin cancer rate followed a dose response by arsenic concentration in the water.	
	Sample of inhabitants of Antofagasta, Chile	Borgono and Greiber (1972)	Cross-sectional	Abnormal skin pigmentation and hyperkeratosis were found in Antofagasta where high arsenic levels in the water were reported. No skin cancers were reported, however.	
	Residents of certain departments in the province of Cordoba, Argentina, exposed to high levels of arsenic in the water	Bergoglio (1964)	Proportionate mortality	The proportion of cancer deaths was higher than for the province as a whole (23.84% versus 15.3%, $P < 0.05$). Of the cancer deaths, respiratory cancer was reported to be 35% and skin cancer 2.3%.	The data were apparently not age-adjusted. No comparison was made of the percentage of respiratory and skin cancer deaths in the affected departments with the respective proportion for Cordoba Province.
	Patients at a dermatology clinic in eastern Argentina	Arguello et al. (1938)	Case reports	The largest proportion of cases in the clinic (82%) came from areas with the highest incidence of chronic endemic regional arsenical intoxication.	The study was not population-based.
	Residents in an area of Lane County, Oregon	Morton et al. (1976)	Cross-sectional	The prevalence of skin cancer was not found to be associated with arsenic concentrations in the water.	The sample size was relatively small.
	Residents of Hinckley and Deseret, Utah, where relatively high arsenic contamination of the drinking water supplies existed and Delta, Utah, which had very little arsenic contamination of the water supply	Southwick et al. (1981)	Cross-sectional; mortality comparison	There was no dermatological evidence of arsenic ingestion in Hinckley or Deseret. No evidence of unusual cancer mortality patterns in Hinckley was found.	Sample size was very small-only 145 in the exposed group, 105 in the controls. The town of Hinckley is rather small for a mortality analysis. The population was only 400 in 1970.

TABLE 7-1. (continued)

Media	Study Population	Author(s)	Type of Study	Results	Highlights and Deficiencies
Water	353 cases of Blackfoot disease and 353 controls matched for sex and age in an area of Taiwan with an endemic arsenic contamination of the water supply	Ch'i and Blackwell (1968)	Case-control	Significantly ($P < 0.01$) more cases than controls were found to consume deep well water (known to be contaminated with arsenic) and population had a low socioeconomic status.	
	Two persons living in an area of Taiwan with endemic high levels of arsenic in the water supply	Astrup (1968)	Case report	Both individuals had developed Blackfoot disease.	
Water, soil, dust	One female child	Falk et al. (1981b)	Case report	Child, with a history of pica, developed hepatic angiosarcoma with associated congenital dysplasia of the liver and an infantile benign hemangioendothelioma suggesting pre-natal as well as post-natal etiological factors.	
Milk	A group of children in Japan	Yamashita et al. (1972)	Cohort	Hyperpigmentation and depigmentation were found to be prevalent in about 15 percent of the survivors approximately 15 years after exposure.	There was no comparison group.
Arsenical medicinals	Patients being treated with arsenical medicinals	Hutchinson (1888)	Case reports	Six patients treated with arsenical medicinals exhibited the keratotic lesions associated with arsenical poisoning.	
Arsenical medicinals	Patients being treated for skin diseases and various internal disorders with arsenical medicinals.	Neubauer (1947)	Case reports	143 individuals with epitheliomas and who had taken arsenical medicinals.	

TABLE 7-1. (continued)

Media	Study Population	Author(s)	Type of Study	Results	Highlights and Deficiencies
Arsenical medicinal	Patients treated with Fowler's solution (an arsenical medicinal) by a private practitioner	Fierz (1965)	Cohort	106 of the 262 patients reporting for physical examination reported hyperkeratosis; 21 cases of skin cancer were also found. The response increased with increasing dose.	Less than 45% of the cohort presented themselves for physical examination, and the author himself reported that the patients reporting for examination were not a representative sample. Furthermore, no controls were used.
Arsenical medicinal	Patients treated with arsenical medicinals	Reymann et al. (1978)	Cohort	Of 389 persons treated with arsenical medicinals, 41 internal malignant neoplasms were found to occur versus 44.6 expected. No increase in internal malignant neoplasms was found by dose.	There was no control group. Internal organs presumably include the lung, and there was no control for smoking, a major confounder with regard to lung cancer.
Arsenical medicinal (Fowler's Solution)	Patients treated with Fowler's solution	Cuzick et al. (1982)	Cohort	A statistically significant association of ingestion of Fowler's solution with deaths from internal malignancies was not found. A subset of 142 of the 487 in the cohort was examined and 49% were found to show dermal signs of arsenicism including skin cancer (11%).	In the subset of 142, deaths from internal malignancies occurred only in those who had previously demonstrated dermal signs of arsenicism, leading the authors to conclude that perhaps persons who show signs of arsenicism are at a greater risk of death from internal malignancies.
Arsenical medicinal (Fowler's Solution)	Male patient	Regelson et al. (1968)	Case report	Hemangioendothelial sarcoma of the liver.	
Arsenical medicinals (Fowler's Solution)	27 cases exposed to arsenic either via arsenical drugs or via occupation	Sommers and McManus (1953)	Case reports	Skin carcinomas were reported in all cases; visceral cancers were reported for some of the cases.	
Arsenical medicinal	Male patient	Nurse (1978)	Case report	Adenocarcinoma of the kidney	Patient treated with a variety of other drugs before developing kidney cancer.

TABLE 7-1. (continued)

Media	Study Population	Author(s)	Type of Study	Results	Highlights and Deficiencies
Arsenical medicinal	2 male patients 1 female patient	Knoth (1966)	Case reports	Female developed mammary carcinoma and skin cancer; 1 male patient developed a reticulosarcoma of the glans penis; 1 male developed skin cancer.	
Arsenical medicinals, occupational exposure, and air (occupational) exposure	16 vintners who were arsenical pesticide users; patient who took arsenical medicinals	Braun (1958)	Case reports	Skin and visceral cancers were reported among the vintners; skin and lung cancers were reported for one patient taking an arsenical medicinal; skin cancer was reported for the other patient who took an arsenical medicinal.	
Arsenical medicinals (Fowler's Solution)	2 male patients	Morris et al. (1974)	Case reports	One patient developed skin pigmentation, skin tumors, carcinoma of the larynx, and a probable bronchial carcinoma; the other developed skin pigmentation and keratosis. Both developed noncirrhotic portal hypertension.	
Arsenical medicinal (Fowler's Solution)	Female patient	Prystowsky (1978)	Case report	Woman developed nasopharyngeal cancer; also developed palmar and plantar keratosis.	
Arsenical medicinals (Fowler's (Solution)	4 male patients and 1 female patient	Popper et al. (1978)	Case reports	The cases developed angiosarcoma of the liver.	
Arsenical medicinal (Fowler's Solution)	1 male patient	Lander et al. (1975)	Case report	The patient developed angiosarcoma.	

TABLE 7-1. (continued)

Media	Study Population	Author(s)	Type of Study	Results	Highlights and Deficiencies
Arsenical medicinal (Fowler's Solution)	1 male patient	Roat et al. (1982)	Case report	The patient developed both angiosarcoma and skin cancer.	
Arsenical medicinal (Fowler's Solution)	7 male patients and 1 female patient	Falk et al. (1981a)	Case reports	The cases developed angiosarcoma.	
Wood preservative	Wood treaters in Hawaii	Gilbert et al. (1983)	Cross-sectional and cohort	No association of arsenic exposure with cancer mortality or morbidity was found.	The sample size was small (only 88 in the study cohort and 61 in the controls in the cross-sectional study; 125 in the mortality study; 182 in the morbidity study).

and Vahter, 1979; WHO, 1981; Tseng, 1977; Sunderman, 1976). This appears to be the case for medicinal (Neubauer, 1947), environmental (Tseng et al., 1968), and occupational (Roth, 1958; Braun, 1958) exposure. The time lag between initiation of exposure and occurrence of skin cancer has been reported to range from 6 to 50 years for arsenical medicinally-induced skin cancer. The minimal latency period for skin cancer in the most reliable epidemiologic study of arsenic-contaminated drinking water was reported to be 24 years.

The amount of data on the histological classification of lung tumors associated with occupational arsenic exposure is limited. Newman et al. (1976) report that arsenic-associated lung cancers are usually the poorly differentiated type of epidermoid bronchogenic carcinoma. These investigators studied worker groups with diagnosed lung cancer in copper-mining and smelting communities in Montana. Of 25 smelter workers, 4 had well-differentiated epidermoid carcinoma, 10 poorly differentiated epidermoid carcinoma, 7 small-cell undifferentiated epidermoid carcinoma and 3 acinar-type adenocarcinoma. Copper miners and "non-copper" control individuals had lung cancer profiles which were similar to each other.

The time period between initiation of exposure and the occurrence of arsenic-associated lung cancer was found in a couple of studies to be on the order of 35-45 years (Lee and Fraumeni, 1969). Recently, a latency period of <20 years was reported by Enterline and Marsh (1980; 1982) based upon their studies of copper smelter workers in Tacoma, Washington. Tokudome and Kuratsune (1976) found that the latent period for lung cancer ranged from 13 to 50 years.

The association of other visceral cancers with arsenic exposure has been noted in a number of reports and has been reviewed elsewhere (WHO, 1981; Arsenic. NAS, 1977; NIOSH, 1976; IARC, 1973). For example, hemangiosarcoma of

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the liver, a rare form of cancer, has been diagnosed in workers exposed to arsenic and in non-occupationally arsenic-exposed individuals (Roth, 1958; Regelson et al., 1968; Lander et al., 1975; Falk et al., 1981a and b; Roat et al., 1982). Morris et al. (1974) have postulated that the peculiar hepatic fibrosis associated with arsenic-induced portal hypertension is a precursor state for subsequent progression to hepatic angiosarcoma. Popper et al. (1978) have noted that the hepatic fibrosis and hypertension seen in humans with Thorotrast, vinyl chloride or arsenic exposure are also induced by agents which presumably also have a role in hepatic angiosarcoma.

Other cancers noted in arsenic-exposed subjects include: lymphomas and leukemia (NIOSH, 1976; Ott et al., 1974); renal adenocarcinoma (Sommers and McManus, 1953; Nurse, 1978); and nasopharyngeal carcinoma (Prystowsky et al., 1978).

Pelfrene (1976) has criticized the reports of internal malignant neoplasms associated with arsenic exposure on the basis of the relative rarity of their detection in large-scale studies of chronic arsenic exposure such as that of Tseng (1968, 1977). More recently, Reymann et al. (1978) reported on a study of a group of 389 patients who took arsenic medicinally in the 1930s. An excess of internal cancers was not observed in the total cohort when compared with the expected incidence of malignant internal neoplasms based on the Danish Cancer Registry. The size of the cohort was probably too small to have detected an increase, however.

7.1.2 Epidemiological Aspects of Human Arsenic Carcinogenesis

7.1.2.1 Cancer of the Lung--A large number of reports are available on possible associations between occupational exposure to arsenic and cancer of the respiratory system. As is common in studies of this type, exposure data are very uncertain and the arsenic exposure is not always clearly defined regarding the physicochemical properties of the arsenic compounds. The picture is often

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confused by simultaneous exposure to other agents, especially sulfur dioxide and metals. Data on smoking are often lacking or incomplete.

An excess mortality in respiratory cancer has especially been noted among workers engaged in the production and usage of pesticides, and among smelter workers.

In 1948, Hill and Faning presented data on proportional mortality rates among British workers exposed to a mixture of ingredients--including sodium arsenite, powdered sulfur and soda ash--used in the manufacture of a sheep-dip powder. Between 1910 and 1943, 75 deaths had occurred among workers in the sodium arsenite factory and 1,216 deaths had occurred among workers in the same area but without known exposure to arsenic. Proportionate mortality analysis showed that of the deaths among factory workers, 29.3 percent had died from cancer, whereas the corresponding figure for the other workers was 12.9 percent. The excess in cancer deaths among the factory workers was mainly due to an excess in lung cancer, 31.8 percent of all cancer deaths compared with 15.9 percent; and in skin cancer, 13.6 percent compared with 1.3 percent.

Among the factory workers, chemical workers, who were the workers most closely associated with arsenite production, had a higher proportion of cancer deaths than did the factory workers as a group. Furthermore, all lung cancer deaths had occurred among the chemical workers.

Arsenic in the air of the sodium arsenite factory was determined in 1945-46 (Perry et al., 1948) and concentrations up to 4 mg As/m^3 were found by sampling for 10 minutes. No data were given on the age of the deceased, and smoking habits were not recorded. The data do not allow any conclusions about exposure before 1943. Nevertheless, this study indicated that there might be an increased risk for respiratory cancer in the manufacture of arsenic-containing pesticides, and studies in two United States plants have given further support.

Ott et al. (1974) studied the mortality of workers in one of these two chemical plants. From 1919 to 1956 one unit formulated and packaged insecticides containing arsenic in the form of lead arsenate, calcium arsenate, copper acetoarsenite, and magnesium arsenate. During this period, the proportions of the different compounds varied. The main product was lead arsenate. The size of the workforce was about 30 in 1928 and 100 in 1948. Turnover was high with less than 25 percent of the men remaining with the unit for more than one year. Arsenic concentrations in air in 1943 were between 0.18 and 19 mg As/m^3 in the packaging area; in 1952 concentrations were 1.7-40.8 mg As/m^3 and 0.26-7.5 mg/m^3 in the drum dryer area and packaging area, respectively. By combining job classifications and air arsenic data, four exposure classifications were obtained with estimated arsenic exposures (8-hr TWA) of 5, 3, 1, and 0.1 mg/m^3. The total dosage was then calculated for each individual by multiplying air levels with the number of days at work and assuming that 4 m^3 were inhaled during a working day.

Mortality was studied by analysis of proportionate mortality and by a retrospective cohort analysis. Nearly 2,000 employees in the factory had died between 1940 and 1972. One hundred seventy-three were identified as having worked one or more days in the arsenical production unit and who then either worked for the company until death or died after retirement.

Ott et al. (1974), after adjusting for age and year of death, compared the differences in proportionate mortality between the study group and the controls. Among the exposed, respiratory cancer accounted for 16.2 percent of the deaths compared with 5.7 percent in the controls ($p < 0.001$). There was also a significant increase ($p < 0.05$) in deaths from lymphatic and hematopoietic cancers, except for leukemia. Table 7-2 shows the observed-to-expected ratios for respiratory cancer in relation to exposure. (In the original table, dosage estimates were based on 4 m^3 inhaled per 8 hr and expressed as the natural logarithms.

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TABLE 7-2. OBSERVED AND EXPECTED DEATHS DUE TO RESPIRATORY MALIGNANCIES, BY EXPOSURE CATEGORY

TWA Concentration x months of exposure	Average dosage mg	No. of total deaths†	Respiratory Malignancy Deaths			
			Observed*	Expected	Ratio	Observed / Expected
<1	105	26	1 (1)	1.77		.6
1-1.9	316	17	2 (2)	1.01		2.0
2-3.9	630	24	4 (4)	1.38		2.9
4-5.9	1050	22	3 (3)	1.36		2.2
6-11.9	1991	27	3 (3)	1.70		1.8
12-23.9	3890	18	2 (2)	.97		2.1
24-59.9	8833	13	3 (1)	.77		3.9
60-95.9	16257	13	5 (0)	.79		6.3
96+	74332	13	5 (0)	.72		7.0

†n = 173, 138 workers had less than one year of exposure.

*Number in brackets shows respiratory cancer deaths in workers exposed less than one year.

Source: Modified from Ott et al. (1974), and Blejer and Wagner (1976).

In the present table, dosage is expressed in mg and is based on 10 m^3 inhaled air.) There is no tendency towards a dose-response relationship at total exposures from 105 to 3890 mg, but a sharp increase is noted at higher dosages. Furthermore, Blejer and Wagner (1976) reported that of the 173 deaths, 138 had occurred among workers with less than one year of exposure. In that group, 16 deaths were due to respiratory cancer. As seen in Table 7-2, 15 of those deaths occurred in the six groups with average total exposures estimated to be from 105 to 3890 mg. There are no quantitative data on other compounds that these workers might have been exposed to during their total time with the company; however, it is known that in addition to the arsenic-containing insecticides, the plant processed and packaged several other products, the most important of which were powdered sulfur and dry lime sulfur.

The retrospective cohort analysis was based on a roster of 603 workers who had worked for at least one month in the actual unit between 1940 and 1973. Workers leaving the company before retirement as well as workers who had been exposed to asbestos were not included in the analysis. It was stated that virtually all men with at least one year of exposure had been identified. Person-years, by 10-year age groups, for five calendar year groups were calculated and expected number of deaths were calculated by using United States white male mortality data. Table 7-3 shows that by this analysis a significant increase ($p < 0.01$) in deaths due to respiratory cancer was found among exposed workers. There was also a significant increase ($p < 0.01$) in the number of deaths due to malignant neoplasms in lymphatic and hematopoietic tissues, except leukemia.

A chemical plant in Baltimore was the subject of two studies concerning the working environment and one study concerning the outer environment. This plant started producing arsenic acid in the early 1900s and in the early

TABLE 7-3. OBSERVED AND EXPECTED DEATHS FOR SELECTED CAUSES IN RETROSPECTIVE COHORT ANALYSIS (1940-1973)

	Observed deaths	Expected deaths (U.S. white males)	Ratio of observed to expected deaths
All causes	95	113.5	.84
Malignant neoplasms, total	35	19.4	1.80
Respiratory system	20	5.8	3.45†
Digestive organs & peritoneum	7	6.3	1.11
Lymphatic & hematopoietic tissues except leukemia	5	1.3	3.85†
All other sites	3	6.0	.50
Diseases of cardiovascular system	41	58.5	.70
Emphysema, chronic bronchitis, & asthma	4	2.8	1.43
All external causes	9	12.7	.71
All other causes	6	20.1	.30

† $p < 0.01$

Source: Ott et al. (1974).

1950s production of arsenical pesticides started. Lead arsenate, calcium arsenate and sodium arsenate were among the compounds produced. Production terminated in 1974 (Matanoski et al., 1976). The plant also produced chlorinated hydrocarbons and organic phosphates. Data on air concentrations of arsenic are lacking.

In the first study, Baetjer et al. (1975) reported on both the proportionate mortality and age-specific death rates of workers who had retired between 1960 and 1972 and generally had at least 15 years' employment. Seventeen of 22 deaths among male white workers and two of five among female workers were due to malignant neoplasms. The female deaths did not appear to be related to occupational exposure, whereas, the male deaths did. Of the 17 malignant neoplasms in males, 10 were in the respiratory tract, 3 were lymphosarcomas, and the remaining 4 were of other tissues. The proportionate mortality analysis, based on mortality data for the city of Baltimore, showed an observed/expected ratio of 6.58 for respiratory cancer ($p < .05$) and 15.79 for cancer of the lymphatic and hematopoietic system ($0.1 < p < 0.05$). The age-specific death rate analysis showed that deaths from respiratory cancer were 16.67 times the expected, and, that for lymphosarcomas, the observed number was 50 times that of the expected number. The authors reported that observed and expected rates for non-cancer deaths did not differ significantly ($p < 0.05$).

In a second study (Mabuchi et al., 1979), a follow-up was made of workers employed from 1946 to 1974. Since exposure data were lacking, an attempt was made to classify workers according to exposure to arsenicals and non-arsenicals. A roster of 3,141 workers was obtained. Since 2,189 workers had been employed for less than 4 months, a 20 percent random sample was drawn from that population and together with the remaining 952 workers constituted the study popula-

tion: 1,050 males and 343 females, mainly white. Exposure assessments were made, and the workers were categorized into one of six exposure groups.

Of the study population, 240 had died: 197 males and 43 females. Expected deaths were calculated from the city of Baltimore statistics. The observed/expected ratios for lung cancer were analyzed by exposure, year of first employment, and duration of employment. A statistically significant increase in lung cancer mortality (SMR = 336, $p < 0.05$) was found among "predominantly arsenical production" workers. There was a clear lung cancer mortality dose response among these workers by duration of exposure. Those employed 15-24 years and 25+ years both had statistically significant ($p < 0.05$) lung cancer SMRs (1365 and 2750, respectively). Interestingly, statistically significantly elevated SMRs were only found in "predominantly arsenical production" workers, but not in workers engaged entirely in arsenical production. Further analysis revealed that the proportion of workers engaged entirely in arsenical production for 5 years or more was relatively low (1 percent), while the proportion of workers exposed predominantly, but not entirely, to arsenic for 5 years or more was much higher (29 percent). This difference in duration of exposure may have accounted for the absence of excess lung cancer mortality among the workers engaged entirely in arsenical production. Data on smoking were not obtained.

Occupational exposure to arsenical pesticides has been common among vintners and agricultural workers. Exposure has mainly been to lead arsenate. In a study of orchard workers who used lead arsenate in the Wenatchee Valley in the state of Washington, Nelson et al. (1973) found a deficit of lung cancer mortality for the period 1938-68 when compared with mortality for the state of Washington.

Because the results of this study were at variance with previous evidence on the long-term effects of arsenic exposure, NIOSH reviewed data from other

sources and used alternative procedures in an attempt to verify the findings. Analysis of respiratory cancer mortality data by occupational category for the state of Washington for the period 1950-71 found that orchardists had 19 percent more deaths from respiratory cancer than expected. An analysis of cancer mortality rates for 1950-69 for the counties comprising the locale from which the orchardist sample was drawn by Nelson et al. found that males had a 7 percent higher respiratory cancer rate than expected among males. The county from which most of the orchardists were drawn had a 31 percent excess ($P < 0.01$) of lung cancer mortality. Thus, it was NIOSH's (1975) conclusion that the Nelson et al. report did not accurately depict the cancer experience of persons exposed to lead arsenate spray in the Wenatchee Valley.

Several studies in Germany indicate that workers exposed to arsenic trioxide when spraying vineyards had a high mortality in cancer, especially lung cancer. In one report (Roth, 1958), it was stated that of 47 autopsies among vintners with chronic arsenic intoxication, 30 (64 percent) were due to cancer, and 18 to lung cancer (60 percent of all cancer deaths). The author did not state how the cases were selected, nor were controls used in the study.

Gilbert et al. (1983) studied a group of 182 workers in Hawaii exposed for at least 3 months during the period 1960-1981 to the wood-treating chemicals chromated-copper-arsenate (CCA), pentachlorophenol (penta), tributyl tin oxide (TBTO) and lindane. The study was divided into two parts: (1) a cohort comparison study of 88 workers and 61 controls and (2) a historic prospective study which consisted of a morbidity and a mortality analysis of the entire cohort.

In the cohort comparison study, 61 controls were matched on the basis of age, sex, race, level of physical activity, and weight to 88 wood treatment

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workers who were "qualified and agreed to participate in the study." Controls were recruited from among the membership of carpenters', ironworkers', masons', plumbers', and stevedores' unions and from the names of friends and relatives referred to the study by participating members of the occupational cohort. Fourteen of the controls were reported to be carpenters and 13 of them had had exposure to either CCA or penta or both. Their urine arsenic levels, however, were reported not to differ significantly from those of other controls. The exposed group and the control group were each given a comprehensive health examination consisting of a questionnaire and clinical and laboratory tests including analysis of a urine sample for penta, arsenic, copper, chromium, and tin levels. Only penta was found to be significantly elevated in the urine of the exposed group over that of the controls. The authors reported that there were no "clinically significant" differences between the exposed group and the controls. No significant differences were found between the wood treaters and controls with respect to educational level, smoking history, or alcohol consumption.

The historical prospective study identified three cases of cancer, one by means of the questionnaire in the cross-sectional study and the other two by means of the Hawaii Tumor Registry. One of the cancer cases was a bladder cancer case; the other two were colorectal cancer cases. For the mortality analysis, the vital status of 125 of the 182 workers (69 percent) was able to be determined. Of these 125, six deaths occurred, five from cardiovascular disease, the other from an unknown cause. The authors calculated that eight deaths would have been expected in this group, three of which would have been from cancer. The authors did not state the basis of the expected number of cancer deaths.

There are limitations in the study design and sample size of this study which make the results with regard to the evaluation of a cancer risk among

the wood treaters inconclusive. A cohort comparison study on the basis of a single medical examination is an inappropriate approach to determine if a cancer risk exists in the wood treater group, particularly when the group consists primarily of persons who are currently employed as wood treaters (60 of 88 were current employees). Most persons who have developed cancer will either have died or left the work force. In addition, the sample size (88 current or former wood treaters and 61 controls) would have been too small to detect an excess cancer risk. Also, it should be noted that the inclusion in the controls of 13 carpenters who had been exposed to arsenic-treated wood certainly presents a potential bias, despite the fact that the authors claimed that the levels of arsenic in the urine of these 13 were not significantly different from those in other controls. In this regard it should be noted that no effort had apparently been made to restrict the intake of seafood or other foods or liquids, which might have elevated urine arsenic levels, prior to collection of the urine samples. The mean level of urinary arsenic in both the study group and in the controls was significantly ($P < 0.01$) higher than what the authors reported would be a normal level.

The historic prospective study also had limitations. Again, the sample size was too small to adequately determine whether an excess risk of cancer existed in the study cohort. Only 125 were included in the mortality study and only 182 were included in the morbidity study. Arsenic exposure via inhalation and ingestion is known to be associated with lung and nonmelanoma skin cancer, respectively. Nonmelanoma skin cancer is rarely fatal and thus, an excess risk of skin cancer would not have been detected in such a small mortality study. The Hawaii Tumor Registry, which was one of the primary sources of information used to identify cancer cases for the morbidity study, does not even report nonmelanoma skin cancer.

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There is also a question of whether the authors had sufficiently allowed for a cancer latency period in their study. The authors did not indicate the length of follow-up of the cohort members. Some indication is provided, however, in the data reported by the authors on the length of employment of the 88 workers in the study cohort of the cohort comparison study. These workers were part of the population in the incidence and mortality studies. Of the 88 workers, 60 had worked 10 years or less and 80 had worked 15 years or less at the time of the physical examination in 1981. Twenty-two of the study cohort in the cohort comparison study were former employees. At the minimum, assuming that the workers had had no breaks in employment, 58 of 125 (46 percent) in the mortality study would have been followed for only 15 years or less and 38 of 125 (30 percent) would have been followed for only 10 years or less. In the morbidity study, if, again, no breaks in employment of the workers are assumed, 58 of 182 (32 percent) would have been followed for only 15 years or less and 38 of 182 (21 percent) would have been followed for only 10 years or less. In conclusion, this study is inadequate to conclude whether an excess risk of cancer exists in the wood treater population in Hawaii.

Occupational exposure to arsenic also occurs in smelters where exposure is predominantly to arsenic trioxide. Several studies have been done on mortality among workers at the copper smelter in Tacoma, Washington. Pinto and Bennett (1963) reported on the proportionate mortality of 229 workers from 1946 to 1960. Workers leaving the plant before retirement were not included. The proportionate mortality of the smelter workers was compared with that of males in the state of Washington in 1958. Of all cancer deaths, the respective proportions of lung cancer were 41.9 and 23.7 percent, respectively. The authors then classified the smelter workers according to arsenic exposure and did not find any difference between exposed and non-exposed. However, the "non-exposed" had elevated arsenic levels in urine, suggesting possible exposure.

More extensive studies have since been published, showing an increase in lung cancer among arsenic-exposed workers (Milham and Strong, 1974; Pinto et al., 1977; Pinto et al., 1978; Enterline and Marsh, 1980; Enterline and Marsh, 1982).

Milham and Strong (1974) examined county records from 1950 to 1971 to find the number of deaths due to respiratory cancer among county residents employed at the smelter. Expected number of cases were calculated for the smelter population by using the 1960 age-cause specific mortality statistics for white males in the United States. Forty deaths were observed and 18 were expected.

The two papers by Pinto et al. (1977, 1978) refer to the same study and the following is based on the 1978 paper. The cohort studied consisted of 527 men who were living pensioners on January 1, 1949 or who became pensioners before January 1, 1973. Complete job histories were obtained for 525 men. The average duration of employment was 28 years, ranging from 7 to 54 years and beginning in 1910. Death certificates were obtained for all 324 men who had died during the observation period (1949-1973). Expected numbers of deaths were calculated from statistics of the state of Washington.

An exposure index was constructed by using data on urinary levels of arsenic obtained in 1973. Mean urinary concentrations were calculated for 32 departments, and the individual exposure index was obtained by multiplying urinary arsenic level with years of work in a department. If an individual had worked in more than one department, the index values were added. By dividing the exposure index by the total number of years in the smelter, an index of intensity of exposure was obtained, i.e., the average urinary arsenic level. These indices were created to enable interdepartmental comparisons and did not reflect past exposure since air analysis in the 1930s to 1940s indicated

that exposure might have been 5-10 times higher at that time. It may have been still higher in 1910.

Data were also obtained on smoking habits from all men still alive and from relatives of men who had died since January, 1961. Table 7-4 (Pinto et al., 1978) shows that there was a significant increase ($p < 0.05$) in deaths from all causes, in cancer deaths in general, and, specifically, in deaths from respiratory cancer. Almost all of the excess mortality could be explained by the increase in lung cancers which could not be explained by smoking.

Table 7-5 shows respiratory cancer deaths in relation to exposure index (a value which reflects both the duration and intensity of exposure). An increase in SMR with exposure is seen. Table 7-6 shows that both duration and intensity of exposure contributed to the excess in respiratory cancer. As stated above, the urine values are relative and do not reflect the actual exposure.

It was also shown that the main excess occurred in ages 65-74 years, whereas at higher ages the lung cancer rate was closer to expected rates.

More recently, Enterline and Marsh (1980, 1982) conducted additional studies on workers at this same copper smelter in Tacoma. A cohort of 2802 males who worked a year or more during the period 1940-1964 was identified. Since a one-year work exposure was required for eligibility into the cohort, actual follow-up did not start until 1941 and extended through 1976. In the cohort, the vital status of 51 could not be verified, leaving 2751 persons. In that group, 1061 deaths had occurred. There was a significant increase in total cancer mortality which wholly depended on an increase in deaths from lung cancer. Arsenic exposure was estimated for each man on the basis of a representative average urinary arsenic level for workers in a given department. Using this representative value, an individual value was calculated for each

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TABLE 7-4. OBSERVED AND EXPECTED DEATHS AND STANDARDIZED MORTALITY RATIOS FOR SELECTED CAUSES OF DEATH OF 527 MALES OF COHORT UNDER STUDY*

Cause of death	Disease Classification†	Observed	Expected	SMR
All Causes		324	288.7	112.2‡
Cancer	140-205	69	46.5	148.4‡
Digestive	150-159	20	16.4	122.0
Respiratory	160-164	32	10.5	304.8‡
Lymph, etc.	200-203, 205	2	2.1	95.2
Urinary	180,181	3	3.3	90.9
All Other Cancers		12	14.2	84.5
Stroke	330-334	43	38.0	113.2
Heart Disease	400-443	144	132.3	108.8
Coronary Heart Disease	420	120	110.2	108.9
All Other Heart Disease		24	22.1	108.6
Respiratory Disease	480-493, 500-502	11	10.8	101.8
All Other Causes		57	61.8	92.2

*Cohort consisted of living male pensioners from a copper-smelting plant who were living January 1, 1949, and whose causes of death were noted through December 31, 1973.

†Numbers from rubrics of 7th Revision of International Classification of Diseases.

‡P<.05

Source: Pinto et al. (1978).

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TABLE 7-5. OBSERVED AND EXPECTED RESPIRATORY CANCER DEATHS AND STANDARDIZED MORTALITY RATIOS BY ARSENIC EXPOSURE INDEX

Exposure index	Mean index	No. of men	Respiratory Cancer Deaths		
			Observed	Expected	SMR
Under 2,000	1,514	36	1	0.9	111.1
2,000-2,999	2,513	109	4	2.1	190.5
3,000-5,999	4,317	205	11	3.9	282.0*
6,000-8,999	7,473	109	7	2.3	304.3*
9,000-11,999	10,135	38	4	0.7	571.4*
12,000 and over	14,712	29	5	0.6	833.3*

*p <.05

Source: Pinto et al. (1978).

TABLE 7-6. OBSERVED AND EXPECTED RESPIRATORY CANCER DEATHS AND STANDARDIZED MORTALITY RATIOS BY INTENSITY AND DURATION OF EXPOSURE TO ARSENIC

Intensity of exposure (µg/liter urine)	Duration of exposure					
	less than 25 years			25 years and more		
	Observed	Expected	SMR	Observed	Expected	SMR
50-199	2	2.1	95.2	10	3.6	277.8*
200-349	4	1.5	266.7	8	2.2	363.6*
350 and over	3	0.5	600.0*	5	0.6	833.3*

*P<.05

Source: Pinto et al. (1978).

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man for each year of employment in a given department, and a total exposure estimate per individual was made by summing values across all jobs and all years of employment.

This method of estimating exposure differed from earlier methods employed by Enterline and co-workers (Pinto et al., 1977, 1978) in that estimates of historic exposure, based upon simple linear interpolations and extrapolations of actual data from 1948-52 and 1973-75, were used to characterize exposure by department, rather than by 1973 urinary measurements. Use of this new method of analysis partially helped to eliminate exposure underestimates of workers employed in the early years of the smelter operation. However, the present method did not totally eliminate this bias because urinary arsenic levels were only determined for workers starting in 1948. For workers exposed prior to 1948 (approximately 80 percent of the present study cohort), urinary arsenic values for 1948-52 were assumed to apply. Furthermore, the average urinary arsenic level for some departments may have been based on only a few samples, thereby limiting the usefulness of the departmental average as a representative measure of any given worker's urinary arsenic level. The authors did note that in areas of the smelter where arsenic levels were reported to be high, workers tended to be measured more often for urinary arsenic. Thus, averages for those areas were, in fact, more representative.

Using this time-weighted measure of exposure, a life table method for accumulative dose, a 10-year lag period and a standard population of mortality rates in the state of Washington, the authors reported that SMRs for respiratory cancer ranged from 155 in the lowest exposure category to 246 in the highest category. Table 7-7 shows the relationship between the time-weighted estimates of arsenic exposure lagged 0 and 10 years and respiratory cancer. This relationship was much weaker than that previously reported by Pinto et al. (1977, 1978). Enterline and Marsh noted that results from the two sets of

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TABLE 7-7. RESPIRATORY CANCER DEATHS AND SMRs BY CUMULATIVE ARSENIC EXPOSURE LAGGED 0 AND 10 YEARS, TACOMA SMELTER WORKERS

Cumulative Exposure (μg/As/1) (urine-years)	Lag			
	0 Lag		10-Year Lag	
	Observed Deaths	SMR	Observed Deaths	SMR
<500 (302)	8	202.0	10	155.4
500-1500 (866)	18	158.4	22	176.6*
1500-3000 (2173)	21	203.2**	26	226.4**
3000-5000 (4543)	26	184.1**	22	177.6*
7000+ (13457)	31	243.4**	24	246.2**

* $p<0.05$

**$p<0.01$

()Mean of class interval

Source: Enterline and Marsh (1982).

studies were not totally comparable due not only to the differences in the exposure estimates noted above, but also to differences in follow-up periods. In earlier reports, the follow-up started after exposure stopped at retirement, whereas in the present study, follow-up started at various points in the work experience of the workers, allowing for follow-up and dose accumulation to proceed concurrently. When the authors analyzed a subsample of the present study cohort, consisting of 582 workers retired at age 65 and over (paralleling the experimental design of the earlier studies), a stronger dose-response relationship was, in fact, observed.

Table 7-8 shows the respiratory cancer deaths and SMRs by duration of exposure and time since first exposure. From Table 7-8, it appears that neither duration of exposure nor long latent periods made strong contributions to excess respiratory cancer. The authors suggested that this may have been due to the high SMRs observed shortly after termination of employment but not noted thereafter; thus, for workers with less than 10 years of exposure the

TABLE 7-8. RESPIRATORY CANCER DEATHS AND SMRs BY DURATION OF EXPOSURE AND LATENCY, TACOMA SMELTER WORKERS

Duration (years)	Latency (Years) <10 Observed Deaths	<10 SMR	10-19 Observed Deaths	10-19 SMR	20-29 Observed Deaths	20-29 SMR	30+ Observed Deaths	30+ SMR	Total Observed Deaths	Total SMR
<10	1	55.6	10	265.4*	17	210.1**	12	137.9	40	178.9**
10-19	-	-	6	156.4	8	278.0*	4	137.9	18	187.2*
20-29	-	-	-	-	13	197.0*	13	265.3**	26**	226.1*
30+	-	-	-	-	-	-	20	221.3**	20	221.3**
Total	1	55.6	16	210.4*	38	216.3**	49	191.8**	104	198.1**

* $p < 0.05$

** $p < 0.01$

Source: Enterline and Marsh (1982).

SMR is highest 10-19 years after date of hire; for workers employed 10-19 years, the SMR is highest 20-29 years after date of hire, etc. This high relative risk of lung cancer mortality in the decade following termination of employment, which essentially disappears in the following 20 years, prompted the authors to suggest that arsenic may be a promoter rather than an initiator. However, when the authors reanalyzed the data according to a method which followed workers only from the point of termination or retirement, both duration of exposure and intensity of exposure contributed more strongly to respiratory cancer mortality (Table 7-9). The difference in the two analyses led the authors to suggest that the weak dose-response relationship observed in the first analysis may have resulted from a tendency for workers in high-exposure jobs to leave employment more quickly than those in low-exposure jobs.

In studying the interactive effects of sulfur dioxide, the authors did not find significant differences in respiratory cancer incidence in two departments which both had high arsenic exposures (7500 $\mu g/m^3$) but differing SO_2 exposures, one having low to moderate exposures (520 ppm) and the other having essentially none. Because the respiratory cancer SMRs were quite similar in the two departments, the authors suggested that SO_2 exposure did not play an important role in respiratory cancer excess at that particular smelter.

In discussing their overall study results, Enterline and Marsh noted that, in this particular case, a dose response was not observed when dose was measured in terms of cumulative dose. The results seen in Table 7-8 suggest that short exposures seemed to have a disproportionately greater effect than long exposures and that effects of early exposure tended to diminish with time. Table 7-9 suggests that short high-intensity exposures may have a greater effect than longer-term, more low-level exposures. The fact that different results are obtained when different exposure/follow-up methods are

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TABLE 7-9. RESPIRATORY CANCER DEATHS AND SMRs BY DURATION AND INTENSITY OF EXPOSURES, TACOMA SMELTER WORKERS

Duration of exposure (years)	Intensity estimate: Low† No. at risk	Observed deaths	Expected§ deaths	SMR	High++ No. at risk	Observed deaths	Expected§ deaths	SMR
<10	687	15	8.83	169.9	824	25	12.26	203.9**
10-19	149	7	2.61	268.2*	168	11	3.42	321.6**
20-29	225	10	3.59	278.6**	171	16	2.77	577.6**
30+	159	9	2.98	302.0**	165	11	3.17	347.0**
Total	1220	41	18.01	227.7**	1328	63	21.62	291.4**

* $p < 0.05$.

** $p < 0.01$.

† low = <290 µg/As/ℓ urine (mean 163).

++ high = ≥290 µg/As/ℓ urine (mean 477).

§ Based on Washington State white males.

Source: Enterline and Marsh (1982).

employed suggests that choice of experimental design has a possible influence on results. The possibility that some workers may have simply been more susceptible than others may also have accounted for the dose-response relationships observed in this study.

Because the authors suggested that the role of arsenic in the carcinogenesis process may have been as a promoter rather than an initiator, the significance of cumulative exposure to arsenic as a measure of dose would be questionable in regard to the induction of respiratory cancer as observed in this study. The role of arsenic as an initiator as well as a promoter cannot be ruled out, however. Until further research is done, the authors' conclusions from this study remain speculative.

Mortality of workers in a smelter in Magna, Utah, was studied by Rencher et al. (1977). Average hourly air concentrations of arsenic in 12 work areas were between zero and 22 mg/m^3 in 1975 (NIOSH, 1975). However, exposure before 1959 had likely been higher, since a processing of ore with a relatively low arsenic content began in that year. In the period 1959 to 1969, 965 deaths had occurred among all current or former employees, and death certificates were obtained for virtually all deceased. The proportionate mortality for smelter workers was compared with that for mine workers, concentrator workers, refinery workers, and office workers, and for the population above 20 years of age for the entire state of Utah in 1968. Among the smelter workers, 7 percent of the deaths were due to respiratory cancer, whereas the percentage for the other factory employees varied from 0 to 2.2 percent and was 2.7 percent for the state. Data on smoking were obtained for all smelter workers and for subsamples of the other employee groups and indicated that nonsmoking smelter workers had the same percentage of deaths from lung cancer as mine and concentrator workers who smoked. By applying lifetable methods, age-adjusted

death rates were obtained. For smelter workers, a death rate for lung cancer of 10.1 per 10,000 was obtained compared with 2.1 and 3.3 per 10,000 for mine workers and the state population, respectively. Causes of death were compared with a cumulative exposure index obtained by multiplying the number of days spent in each department by the average exposure level and then summing. The average exposure to arsenic as well as sulfur dioxide, sulfates, lead, and copper was found to be higher for the lung cancer cases than for other causes of death.

In addition to these studies, a large study by Lee and Fraumeni (1969) involving 8,047 white males was conducted at the Anaconda Copper Smelter in Montana from 1938 to 1956.* Data were obtained on time, place, and duration of employment for each individual, all subjects having worked at least 12 months in the smelter during the indicated study period. Follow-up was from 1938 to 1964. Death certificates were obtained, and the lifetable method was used to compute the expected number of deaths, using mortality rates of the state of Montana. The smelter workers were classified into 5 cohorts, based on total years of smelter work and the time period in which the years were worked: (1) 15 or more years worked before 1938; (2) 15 or more years worked between 1938 and 1963; (3) 10-14 years; (4) 5-9 years; and (5) 1-4 years. An attempt was also made to classify the workers according to exposure to arsenic and sulphur dioxide. Exposure to arsenic for more than 12 months had occurred among 5,185 men. These workers were divided into three groups; heavy, medium, and light exposures. This division was based on exposure times and place at work. Arsenic concentrations in air were primarily determined from a

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*While the original Lee and Fraumeni study reported on the mortality experience of male smelter workers in unidentified states, subsequent analyses of these workers indicate that they were employed solely at the Anaconda smelter in Montana.

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1965 survey by Public Health Service officials (NIOSH, 1975). These air data are shown in Table 7-10.

According to a former public health official associated with this survey, actual measurements were collected during two different periods--one in 1965 and one "about five to six years earlier"--and at several locations within given departments (Archer, 1983; personal communication). It is impossible, however, to determine how the values listed in Table 7-10 are distributed over these different time periods and locations. Further, it is also impossible to determine the number of hours sampled at a given location. Therefore, the arithmetic means used by Lee and Fraumeni to characterize heavy, medium and light exposures can only be viewed as very rough estimates of arsenic exposure, their primary value being in their relative scale of measurement.

In Table 7-11 it is seen that heavy and medium exposures resulted in significant increases in SMR for respiratory cancer. The SMR was highest (800) in workers belonging to cohort 1 (more than 15 years of smelter work before 1938), and then decreased to 263 among workers with 1-14 years of smelter work. Among the workers with light exposure, the SMR was 250, 310, and 214 in cohorts 1, 2, and 3-5, respectively. Among the smelter workers with less than 12 months' exposure to arsenic, the SMR was 286.

Lee and Fraumeni also looked at factors that possibly had confounding effects on their study results. Smoking histories were not recorded; however, based upon information obtained from other studies, Lee and Fraumeni concluded that smoking alone could not have accounted for the excess respiratory cancer mortality of the magnitude observed in their study.

In contrast to smoking, the authors did note a positive relationship between exposure to sulfur dioxide and respiratory cancer mortality; however, they found it difficult to separate the relationship of arsenic from sulfur

REC 5087

TABLE 7-10. 1965 SMELTER SURVEY ATMOSPHERIC ARSENIC CONCENTRATIONS (mg As/m^3)

"Heavy exposure area" as classified by Lee and Fraumeni

Arsenic Roaster Area		Mean:	1.47
0.10	0.20	Median:	0.185
0.10	0.22		
0.10	0.25		
0.10	0.35		
0.10	1.18		
0.10	5.00		
0.17	12.66		

"Medium exposure area" as classified by Lee and Fraumeni

Reverberatory Area		Mean:	1.56
0.03	0.93	Median:	0.88
0.22	1.00		
0.23	1.27		
0.36	1.60		
0.56	1.66		
0.63	1.84		
0.66	1.94		
0.76	2.06		
0.78	2.76		
0.78	3.40		
0.80	4.14		
0.83	8.20		
Treater Building and Arsenic Loading		Mean:	1.50
0.10	0.48	Median:	0.295
0.10	0.62		
0.10	3.26		
0.11	7.20		

"Light exposure areas" as classified by Lee and Fraumeni

Copper Concentrate Transfer System		Mean:	0.70
0.25		Median:	0.65
0.65			
1.20			
Samples from Flue Station		Mean:	0.17
0.10		Median:	0.17
0.24			
Reactor Building		Mean:	0.004
0.001	0.003	Median:	0.002
0.002	0.009		
0.002	0.010		
0.002			

Source: National Institute of Occupational Safety and Health (1975).

REC 5088

TR 1773

TABLE 7-11. OBSERVED AND EXPECTED DEATHS FROM RESPIRATORY CANCER, WITH STANDARDIZED MORTALITY RATIOS (SMR), BY COHORT AND DEGREE OF ARSENIC EXPOSURE, 1938-63

Cohort	Respiratory cancer mortality	Maximum exposure to arsenic (12 or more months)* Heavy	Medium	Light
All cohorts combined	Observed	18	44	45
	Expected	2.7	9.2	18.8
	SMR	667†	478†	239†
1	Observed	8	22	14
	Expected	1.0	3.3	5.6
	SMR	800†	667†	250†
2	Observed	6	12	9
	Expected	0.9	2.2	2.9
	SMR	667†	545.†	310†
3-5‡‡	Observed	4	10	22
	Expected	0.9	3.8	10.3
	SMR	444§	263§	214†
Number of persons in arsenic category*		402	1,526	3,257

*The remaining 2,862 men in the study worked less than 12 months in their category of maximum arsenic exposure and had an SMR of 286†.

†Significant at the 1% level.

‡‡Cohorts 3, 4, and 5 were combined, since observed and expected deaths were small for each cohort alone.

§Significant at the 5% level.

Source: Lee and Fraumeni (1969).

dioxide. Most of the work areas having heavy arsenic exposure were also areas having medium sulfur dioxide exposure; conversely, all work areas with heavy sulfur dioxide exposure were areas of medium arsenic exposure. The authors did note, however, that persons with the heaviest exposure to arsenic and moderate or heavy exposure to sulfur dioxide were those most likely to die of respiratory cancer in this particular instance.

Since the Lee and Fraumeni study, additional research has been conducted on the employees of the Anaconda smelter. Lubin et al. (1981) studied 5403 of these employees. These workers had all been employed for 12 months or more between January 1, 1938, and December 31, 1956, and were known to be alive as of December 31, 1963. Essentially, this cohort was equivalent to the surviving members from the Lee and Fraumeni cohort.

Exposure was from date hired to December 31, 1963; follow-up was from 1964 to 1977. Classification of exposure categories was similar to that of Lee and Fraumeni. However, unlike the study of Lee and Fraumeni, a cumulative arsenic exposure index was calculated for each worker. This index was derived by, first, weighting the three exposure categories and then multiplying the number of years an individual worked in a given category by this weight and summing over categories. The weights were derived from mean airborne dust concentrations taken during 1943 to 1958, which averaged 11.3, 0.58 and 0.29 mg As/m^3 in the respective heavy, medium and light categories. These values differed from those used by Lee and Fraumeni to group departments (Table 7-9). It should be noted that the exposure estimates used by Lee and Fraumeni were based upon more recent monitoring data primarily collected in 1965. Lubin et al. reduced weights in the heavy category by a factor of 10 in order to account for the wearing of respirators as was observed "at least in recent years." SMRs were calculated by comparisons to U.S. white males.

REC 5090

The mortality experience of workers during the years 1964 to 1977 was similar to that of the workers studied by Lee and Fraumeni during the period 1938-1963. Excess deaths from respiratory cancer corresponded to areas of highest arsenic levels. The authors noted an overall strong gradient in risk associated with the indices of cumulative arsenic exposure. However, the authors also noted that this gradient was less clear when weighting of the high-exposure category was reduced ten-fold to account for respirator usage. According to Welch et al. (1982), however, respirator usage was not common prior to 1964.

Some study differences were noted by Lubin et al. between their respective study and that of Lee and Fraumeni. Differences in excess respiratory cancer--65 percent in the more recent period versus a three-fold excess in the earlier period--were partially attributed to differences in respiratory cancer rates observed between the two comparison populations. Respiratory cancer rates in the general populace have increased in recent years; therefore, comparisons to recent populations will produce lower relative risks than comparisons to past general populations in which the rates of respiratory cancer were lower. The authors also noted that the comparison populations differed in composition. Lee and Fraumeni used white males in the state of Montana as their standard population, whereas Lubin et al. used U.S. white males. As noted in this study, as well as elsewhere (Welch et al., 1982; Higgins et al., 1982), death rates for specific causes of death (inclusive of respiratory cancer) have been reported to be lower in Montana. Finally, the authors suggested the possibility that individuals most susceptible to lung cancer contracted the disease in the earlier period and were, thus, lost to the study follow-up due to death.

In looking at SO_2 exposures, the authors were unable to totally separate the possible interactive effects of SO_2 with arsenic. However, they did note

that after controlling for arsenic, no significant increase in mortality could be associated with heavy or medium SO_2 exposures, whereas the association with arsenic exposure persisted after controlling for SO_2. This finding is consistent with that of other researchers studying smelter populations (Enterline and Marsh, 1982; Welch et al., 1982; Higgins et al., 1982).

In an update of the earlier study co-authored with Fraumeni, Lee-Feldstein (1983) observed the mortality experience of the same Anaconda workers (with the exception of two women) from 1938 to 1977. The workers (8045) were assigned to one of five cohorts on the basis of total years of employment. Cohort 1 worked 25+ years; cohort 2, 15-24 years; cohort 3, 10-14 years; cohort 4, 5-9 years, and cohort 5, 1-4 years. SMRs were calculated by comparison to the combined white male populations in the states of Idaho, Wyoming and Montana.

Of the thirteen specific causes of death considered, tuberculosis, digestive and respiratory cancer, vascular lesions of the CNS, diseases of the heart, emphysema, and cirrhosis of the liver showed a significant excess of observed deaths over that expected; however, only excesses in respiratory cancer showed a positive gradient with length of employment when comparing cohorts 1 through 5. The ratio of observed to expected mortality from respiratory cancer was approximately 5.1, 4.5 and 2.3 in the heavy, medium and light arsenic-exposure groups, respectively. This was in accord with the earlier results of Lee and Fraumeni, except that the ratio of observed respiratory cancer deaths to that expected in the heavy exposure category in the earlier study was 7.

Brown and Chu (1983c) discussed the Lee-Feldstein (1983) data with regard to its implications on the multistage theory of cancer. They indicated that analysis of the data suggests that arsenic acts as a late-stage carcinogen

because: (1) there was an increasing excess lung cancer mortality risk with increasing age at initial exposure, and (2) the excess mortality was independent of time after exposure stopped.

Higgins et al. (1982) and Welch et al. (1982) reported on a sample of 1800 workers at the Anaconda smelter. Compared to the 8047 workers studied by Lee and Fraumeni, this cohort of 1800 workers included all the workers originally designated in Lee and Fraumeni's heavy exposure category (277) and a random sample (20 percent) of the remaining known workers. The date of entry into the study cohort ranged from 1938 to 1956, providing the individual had one year of work experience. Unlike other studies on these workers, smoking histories on the 1800 workers were obtained either by direct questioning or by proxy respondent. SMRs were based on comparisons to white males both in the state of Montana and the United States.

From industrial hygiene records for the period 1943 to 1965, estimates of airborne arsenic concentrations within 35 smelter departments were provided. A total of 818 samples were collected from 18 departments and departmental averages were calculated from these measurements. The remaining 17 departments were estimated by analogy with those that were known. The departments were then grouped into four categories in which arsenic exposure was characterized as low ($<100\ \mu g/m^3$), medium ($100\text{-}499\ \mu g/m^3$), high ($500\text{-}4999\ \mu g/m^3$) or very high ($>5000\ \mu g/m^3$).

Workers were assigned to these categories based upon estimations of both time-weighted average (TWA) arsenic exposure levels and ceiling levels. TWA values were individually calculated based upon the time that a worker spent in a given department and the average arsenic concentration estimated for that department. This quantity was summed across all departments the individual worked in and was divided by total time worked to yield a TWA. TWA arsenic

exposures were calculated at entry into the study cohort and at the beginning of January, 1964, corresponding to the end of the follow-up period used by Lee and Fraumeni. TWA differences between these two periods could have increased, decreased, or remained the same depending on the work history of an individual worker. In contrast, ceiling levels were defined as the highest level to which an employee was exposed for a period of 30 days or more. Ceiling levels were calculated at entry into cohort, at the beginning of 1964 and at the beginning of 1978. Unlike a TWA value, a worker's ceiling level could only increase or remain the same from point of entry into the cohort.

Data were analyzed according to five different exposure/follow-up methods which varied in the amount of overlap allowed between exposure and follow-up periods. Method I, the primary method used by the authors, included each worker's arsenic exposure up to the date he entered the cohort. Follow-up was from entry to 1978; thus, there was no overlap of the two periods. Method IV--exposure from date hired to 1964, follow-up from 1964 to 1978--also had no overlap. Methods II and V had complete overlap--exposure from date hired to 1964, follow-up from 1938 to 1964 and exposure from date hired till termination, follow-up from 1938 to 1978, respectively. Method III had partial overlap--exposure from date hired to 1964, follow-up from 1938 to 1978. Except where specifically noted, results were given according to Method I.

The results of the study supported the thesis that exposure to arsenic was strongly related to respiratory cancer mortality in workers at the Anaconda smelter. SMRs for the total cohort for all causes of death were identical when compared to either the state of Montana or U.S. white males (both SMRs = 133, significant at 0.01 level); however, SMRs for specific causes were somewhat higher when compared to Montana males than when compared to U.S. males. Exposure to arsenic appeared to be the principal factor in the observed

increased risk for respiratory cancer, the study cohort having 3 times the expected death rate for white men living in Montana. Exposure to other occupational contaminants, such as sulfur dioxide and asbestos, did not appear to account for respiratory cancer excess, while smoking explained only a small fraction of the excess.

Of particular note were the differing respiratory cancer results obtained under the two categories of arsenic exposure (Tables 7-12 and 7-13). The SMR for men in the lowest TWA category was elevated, although not significantly so, whereas the SMRs in the other TWA categories were significantly elevated. Mortality for respiratory cancer by ceiling arsenic exposure showed that SMRs were only signficantly elevated in the high and very high categories, whereas they were close to expectation in the two lower exposure categories. Date of hire showed a definite relationship to mortality from respiratory cancer. Workers who were employed in the early years of the smelter operation--from 1884 to 1938, but particularly prior to 1923, when a selective floatation process which markedly improved fume and dust recovery was introduced--had higher SMRs, indicating that the overall higher arsenic exposures in the early years were associated with higher death rates from respiratory cancer. Age at hire did not seem to have a confounding effect, although the authors did note that the SMRs for respiratory cancer showed more fluctuation with age than did all causes of death.

Tables 7-14 and 7-15 show comparisons of TWA and ceiling respiratory cancer mortality as analyzed by the different exposure/follow-up methods. The authors noted that, while there was some variation in the SMRs derived from the different methods, the same basic pattern of increasing respiratory cancer SMRs with increasing TWA and ceiling arsenic exposures could be seen for each method. The authors indicated that none of the exposure/follow-up methods found a significantly ($P < 0.05$) increased respiratory cancer risk for ceiling level

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TABLE 7-12. MORTALITY FOR ALL CAUSES AND RESPIRATORY CANCER FROM 1938 TO 1978 BY TIME-WEIGHTED AVERAGE (TWA) ARSENIC EXPOSURE AS OF ENTRANCE INTO COHORT

TWA Arsenic ($\mu g/m^3$)	N	Person-Years	All Causes Obs	All Causes Exp	All Causes SMR	Respiratory Cancer Obs	Respiratory Cancer Exp	Respiratory Cancer SMR
<100	547	13152	219	196.7	111*	11	7.9	138
100-	542	14157	216	178.0	121**	22	7.3	303**
500-	565	13460	292	184.7	158**	29	7.7	375**
5000-	146	3552	89	56.1	159**	18	2.6	704**

* Significant at 0.05 level

** Significant at 0.01 level

Source: Higgins et al. (1982).

TABLE 7-13. MORTALITY FOR ALL CAUSES AND RESPIRATORY CANCER BY CEILING ARSENIC EXPOSURE AS OF ENTRANCE INTO COHORT

Ceiling Arsenic ($\mu g/m^3$)	N	Person-Years	All Causes Obs	All Causes Exp	All Causes SMR	Respiratory Cancer Obs	Respiratory Cancer Exp	Respiratory Cancer SMR
<100	445	10591	165	152.1	108	8	6.2	129
100-	276	7083	80	80.5	99	4	3.4	116
500-	833	20757	416	288.5	144**	41	11.8	348**
>5000	246	5889	155	94.4	164**	27	4.1	662**

* Significant at 0.05 level

** Significant at 0.01 level

Source: Higgins et al. (1982).

REC 5096

TABLE 7-14. RESPIRATORY CANCER MORTALITY BY METHOD OF ANALYSIS AND TWA ARSENIC CATEGORY

TWA Arsenic ($\mu g/m^3$)	METHOD OF ANALYSIS I[a]				III[b]				IV[c]			
	N	Obs	Exp	SMR	N	Obs	Exp	SMR	N	Obs	Exp	SMR
<100	547	11	7.9	138	522	5	7.9	63	354	4	4.8	84
100-	542	22	7.3	303**	580	28	7.8	359**	410	16	5.1	313**
500-	565	29	7.7	375**	515	29	7.1	408**	313	9	4.2	216*
≥5000	146	18	2.6	704**	183	18	2.7	673**	111	9	1.6	573**

*Significant at 0.05 level

**Significant at 0.01 level

[a]Exposure from date hired to cohort entry. Follow-up from cohort entry to 1978.

[b]Exposure from date hired to 1964. Follow-up from cohort entry to 1978.

[c]Exposure from date hired to 1964. Follow-up from 1964 to 1978.

Source: Higgins et al. (1982).

TABLE 7-15. RESPIRATORY CANCER MORTALITY BY METHOD OF ANALYSIS AND CEILING ARSENIC CATEGORY

Ceiling Arsenic ($\mu g/m^3$)	METHOD OF ANALYSIS															
	I[a]				III[b]				IV[c]				V[d]			
	N	Obs	Exp	SMR	N	Obs	Exp	SMR	N	Obs	Exp	SMR	N	Obs	Exp	SMR
<100	445	8	6.2	129	275	3	4.0	75	178	3	2.3	130	267	3	3.9	77
100-	276	4	3.4	116	218	2	2.5	79	152	0	1.6	-	210	2	2.4	83
500-	833	41	11.8	348**	970	41	13.8	298**	656	20	8.7	230**	969	41	13.7	300**
≥5000	246	27	4.1	662**	337	34	5.2	652**	202	15	3.0	496**	354	34	5.5	617**

*Significant at 0.05 level

**Significant at 0.01 level

[a]Exposure from date hired to cohort entry. Follow-up from cohort entry to 1978.

[b]Exposure from date hired to 1964. Follow-up from cohort entry to 1978.

[c]Exposure from date hired to 1964. Follow-up from 1964 to 1978.

[d]Exposure from date hired to 1978. Follow-up from cohort entry to 1978.

Source: Higgins et al. (1982).

categories less than 500 $\mu g/m^3$ of arsenic (Table 7-15). For the respiratory cancer SMR analysis by TWA exposure, a significantly ($P < 0.05$) elevated SMR was not found in the lowest dose category. In the 100-499 $\mu g/m^3$ TWA exposure category, there was a significantly ($P < 0.05$) elevated respiratory cancer SMR (Table 7-14). The respiratory cancer SMR in this category would not have been significant, however, if those respiratory cancer deaths with <500 $\mu g/m^3$ ceiling arsenic exposure had been excluded from the analysis. The authors concluded that if a worker in the study had not been exposed to <500 $\mu g/m^3$ ceiling level, he would have had little, if any, excess cancer risk.

A number of criticisms have been made of this study (48 FR 1864), a few of which bear mentioning at this point. The representativeness of the exposure estimates as they relate to overall exposure conditions in the smelter and specifically to the cohort's TWA and ceiling exposures has been criticized. The authors noted that individual worker exposure estimates, based upon area measurements rather than personal samples, would not likely have great precision. Furthermore, estimates of analogy--as in 17 of the departments--weaken the reliability of overall exposure estimates, although areas that were thought to be "problem" areas of high exposure were areas that were generally measured. The extent to which respirator usage was an effective protective measure is also unknown. In interviews with former workers, however, indications were that the use of respirators was not widespread or regular during the period prior to 1964. Collectively, the authors stated that exposure estimates probably tended to affect results such that exposure values were underestimated from 1884 to 1938, were reasonable for 1938 to 1964, and were overestimated for the period after 1964.

The authors found that workers who had not experienced a ceiling level of 500 $\mu g/m^3$ of arsenic did not have an elevated risk of lung cancer. However, the number of lung cancer deaths that could be predicted using a linear dose-

response model (see Section 7.3.1) in the group of workers with <500 $\mu g/m^3$ arsenic ceiling exposure would not be significantly different than the number of lung cancer deaths actually found. This was determined using the linear risk model (Section 7.3.1) and data obtained from Higgins and made available by Consultants in Epidemiology and Occupational Health (1982) on the cross-tabulation of the number of workers in cumulative and ceiling exposure categories. Higgins et al. are presently undertaking a study of the entire Anaconda cohort; however, results of this study will not be forthcoming until late 1984.

In foreign smelters, an excess in lung cancer mortality has also been found. The Rönnskär smelter in Sweden, which has been processing arsenic-rich ores since the 1920s, has been the subject of several studies. Axelson et al. (1978) conducted a case-control study of mortality from respiratory cancer in relation to employment at that smelter. In the parish surrounding the smelter, 369 deaths have been recorded in the registers for men aged 30-74 years during the years 1960 to 1976. Causes of death were obtained in all cases. Smoking habits were obtained from medical files. Cases were defined as subjects who died of malignant tumors of the lung, other cancers, cardiovascular disease, cerebrovascular disease, and cirrhosis of the liver. The control group was made up of persons from the same parish who died from causes other than the above, excluding 44 persons with diabetes, mental deficiency and unclear diagnoses. Attempts were made to assess exposure and four exposure groups were constructed, based on intensity and duration of exposure and time between initiation of exposure and death. It was found that occupational exposure to arsenic was associated with a significant increase in deaths from lung cancer. For the three exposure groups with at least 3 months of exposure occurring 5 years

prior to death, the lung cancer mortality ratio was 4.6. In these groups, there was an increase with exposure intensity. For the fourth group in which either persons were not exposed or the first exposure was for a period less than 3 months and/or death occurred within 5 years of this first exposure, a risk of respiratory cancer was not found.

Other agents, including sulfur dioxide, did not seem to be associated with lung cancer in this study. In 83 percent of the exposed lung cancer cases there was a history of smoking. A study of smoking habits by Pershagen (1978) showed that the excess lung cancer mortality could not be explained by smoking habits.

Because a high lung cancer mortality rate was noted among males in Saganoseki-machi, Japan, for the period 1967-69, Kuratsune et al. (1974) did a case-control study of lung cancer cases in that town. The nineteen cases of lung cancer for the period 1967-69 were compared with nineteen controls randomly selected from deaths of diseases other than cancer of the lung, skin, or bladder for the 1967-69 period. Smoking and drinking habits, residential and occupational histories, and exposure to atomic bomb radiation were the factors compared. Fifty-eight percent of lung cancer cases were found to be former smelter workers vs. 15.8 percent in the controls ($p < 0.01$). The relative risk was reported to be 9.0 (confidence limits not reported). No difference was found between the cases and controls for smoking habits, residential history, drinking habits, or atomic bomb radiation.

Tokudome and Kuratsune (1976) did a cohort study of 2765 male workers, including 839 copper smelter workers at the metal refinery in Saganoseki-machi, Japan. Deaths which occurred between 1949 and 1971 were analyzed in the

study. The expected number of deaths was calculated using mortality data for Japanese males. A significantly increased mortality was noted for lung cancer (SMR = 1189; observed = 29; expected = 2.44; $p < 0.01$) and colon cancer (SMR = 508; observed = 3; expected = 0.59; $p < 0.05$). A dose response was demonstrated between lung cancer mortality and the degree of exposure measured by length of employment and level of exposure. A very high excess mortality from lung cancer (SMR = 2500; 10 observed; 0.4 expected; $p < 0.01$) was found among smelter workers who had worked in the heaviest exposure category and who had been employed over 15 years before 1949. The latent period in this study ranged from 13 to 50 years.

Studies have also been performed to see if there is any increase in lung cancer among residents in areas surrounding smelters. Lyon et al. (1977) compared the incidence of lung cancer and lymphoma in Utah residents from 1970-1975 in relation to the distance of these residents from a smelter and found no association. It should be noted that distance from the smelter was based on address at the time of diagnosis; nothing regarding the length of time lived near the smelter was factored into the analysis. Furthermore, use of lymphoma cases as controls is questionable since lymphomas may also be associated with arsenic (Ott et al., 1974). Thus, the conclusion of the study that there was no association between lung cancer and distance from the smelter is questionable.

In a more recent study, Rom et al. (1982) compared lung cancer with breast and prostate cancer in residents living near a non-ferrous smelter in El Paso, Texas. The study period ranged from 1944-1973. Similar to methods used by Lyon et al. (1977), comparisons were made in relation to distance from the smelter. Breast and prostate cancer were chosen as control cancers because they have no known association with arsenic exposure. The authors reported

that the distribution of lung cancer cases (575) and control cancer cases (1490) was roughly the same for the different distances studied. No association between lung cancer and distance from the smelter was found, nor were there any associations for race, age or sex. However, the authors did note that they were unable to control for such factors as smoking, occupation and migration and were unable to obtain environmental exposure measurements over most of the years studied.

In Montana, the studies by Newman et al. (1976) showed that there was an increase in the incidence of lung cancer among men in cities where copper smelters are located. In one of the cities there was also an increased incidence of lung cancer among women. It was not stated to what extent occupational exposure had caused the increase, and there was no control for smoking.

In the Blot and Fraumeni study (1975), the cancer mortality in 71 counties with smelters and refineries was studied from 1950 to 1969. Comparisons were made with the remaining 2,985 counties in 48 states. In 36 counties with smelters processing copper, lead, or zinc ores, lung cancer mortality was significantly higher both among males ($p < 0.01$) and females ($p < 0.05$). For all 36 counties with these industries the median SMR was 112 for males and 110 for females. Although occupational cancers were included in the analyses and, therefore, contributed to some of the excess risk, the number of workers in the smelter industry generally comprised a small fraction of the total population (less than 1 to 3 percent); thus, it was unlikely that occupational exposures alone accounted for the observed excess mortality in males or the increased risk for females. Although this study is suggestive of a lung cancer effect in populations surrounding smelters, it is unknown if the lung cancer cases were even exposed to arsenic. Thus, the results, although suggestive, are inconclusive.

In the Baltimore, Maryland area, Matanoski et al. (1976, 1981) studied cancer mortality in areas near the earlier mentioned pesticide facility. They found an excess of all cancers and respiratory cancers among males in the area nearest to the factory but not among females. Soil arsenic levels generally corresponded to lung cancer and all cancer incidences, with the highest average of arsenic in the soil (63 ppm) reported in the area with the greatest cancer risk. The authors were unable to account for the differences noted between males and females, but suggested that smoking may have contributed to these differences. Other environmental factors and/or occupational exposure may have also influenced cancer mortality excess. Further environmental sampling of arsenic and conducting of community surveys were recommended to address these unknown factors.

Pershagen et al. (1977) studied cancer deaths in the area surrounding the Rönnskär smelter in Sweden. From 1961 to 1975 there was a significant excess of respiratory cancers in the male population (SMR = 250) compared to residents in an area without known emissions of arsenic but in which the same age distribution and occupational profiles applied. When the occupationally exposed cases were excluded, significant increases in respiratory cancers were no longer detected (SMR 173); however, the male population still showed a tendency to excess lung cancers. No similar occupational group was excluded from the comparison population, however. There was no tendency to an increase in lung cancer among women.

7.1.2.2 Cancer of the Skin and Precancerous Skin Lesions--An elevation in the proportionate mortality of skin cancer was reported by Hill and Faning (1948) for factory workers manufacturing sodium arsenite and by Roth (1957, 1958) for German vintners. In addition, an increased incidence of skin cancer has been reported after long-term oral exposure to arsenic.

In Taiwan a large population had long-term exposures to inorganic arsenic in drinking water. Exposure started in 1910-20 when water was obtained from deep wells, 100-200 m. below the surface. Already in the 1920s, vascular changes began to appear, and in the 1950s, the first epidemiological studies were conducted. The arsenic content of the water varied from 0.01 to 1.82 mg/l (Ch'i and Blackwell, 1968; Astrup, 1968; Tseng et al., 1968; Tseng, 1977), generally being 0.4 - 0.6 mg/l, whereas water from shallow wells or other surface waters generally contained from near zero to 0.15 mg As/l.

Tseng et al. (1968) and Tseng (1977) have reported the results from a large-scale epidemiologic survey of arsenic-related diseases in an area with high arsenic concentrations in drinking water. The population at risk was 103,514 persons. Thirty-seven villages with a population of 40,421 were surveyed house-to-house. Examinations were made with special attention to pigmentation, hyperkeratosis, and cancer of the skin. Four hundred twenty-eight cases of arsenical skin cancer were found, resulting in a rate of 10.6/1000. No cases were under 20 years of age. The prevalence rate increased markedly with age except for females >70. Over 10 percent of the people >59 were affected by skin cancer. The overall male/female ratio was 2.9:1, with males having a higher rate in all age groups >29.

The villages were divided into 4 exposure levels: <0.3, 0.3-0.6, $\geq$0.6, and undetermined, based on their water arsenic content. There was a clear cut ascending gradient of prevalence from low to high in each of 3 age groups (Table 7-16).

Hyperpigmentation (melanosis) was found in 18.4 percent of the total population: 19.2 percent for males and 17.6 percent for females. Usually the prevalence was higher for males than females. The rates increased steadily with age for males and did likewise for females until a peak was reached at 50-59, followed by a gradual decline.

TABLE 7-16. PREVALENCE OF SKIN CANCER (per 1000) BY AGE AND ARSENIC EXPOSURE (ppm)

Arsenic content of drinking water (ppm)	Age 20-39	40-59	>60
<.3	1.3	4.9	27.1
0.3 - 0.6	2.2	32.6	106.2
>0.6	11.5	72.0	192.0

Source: Adapted from Tseng et al. (1968).

The overall prevalence rate for keratosis was 7.1 percent - 7.5 percent for males and 6.8 percent for females. Males had higher rates in the greater than-49-year group. The prevalence increased for both males and females up to age 70 and then declined.

As was the case for skin cancer, the prevalence rates for hyperpigmentation and keratosis suggested that positive correlations existed between these conditions and the arsenic content of the water in the artesian wells; the greater the arsenic content, the higher the prevalence.

In the total survey of 40,421 people, 7418 cases of hyperpigmentation, 2868 of keratosis, 428 of skin cancer, and 360 of Blackfoot disease (see Section 5.2.2) were found. Many of these occurred in combination in the same individual.

The data were examined by comparing expected (based on overall rates) and observed rates for various combinations of the 4 end points. The obtained ratios indicated quite strongly that a common underlying cause existed for the 4 conditions, presumably chronic arsenicism.

A control population of 7500 persons from nonendemic areas was examined in the same way as the arsenic-exposed persons. Four thousand, nine hundred

and seventy-eight people lived on Matsu Island; its water supply was from shallow wells and no arsenic was detectable by the analytic methods used in the main series. The remaining portion of control population members came from 5 villages on Taiwan whose water source was shallow wells with arsenic levels between 0.001-0.017 mg/ℓ (ppm). No cases of melanosis, keratosis, or skin cancer were observed in the entire control population.

Although age at onset of the conditions was difficult to assess, some information on latency was obtained. "We know from the study that the youngest cancer patient was 24, the youngest with hyperpigmentation was 3, and the youngest with keratoses was 4." This meant that hyperpigmentation could occur in patients who were exposed from birth for at least 3 years, keratosis for 4 years, and cancer for 24 years (Tseng et al., 1968).

While the Taiwanese data collected in the late 1960's strongly implicated arsenic as the etiological source of the observed diseases, recent findings have called to question the hypothesis of arsenicism as sole causative source in the induction of cardiovascular effects. The discovery by Lu et al. (1977b, 1978) of fluorescent compounds identified as alkaloids--either lysergic acid, dihydrolysergic acid or a derivative of ergotamine tartfate--has opened the possibility that other toxic mechanisms may have been involved. Ergotamine-like compounds in combination with high alkalinity, characteristic of these waters, have been shown to cause gangrene (Lu et al., 1977a,b; 1978). Whether these compounds have a confounding effect on skin cancer is presently unknown.

In addition, recent analyses by Irgolic (1982) on a limited number of samples have shown the water samples to contain predominantly pentavalent arsenic and no organic arsenicals. Samples taken from two wells in the Yenshei Province of Taiwan were collected in plastic cubitainers. Two samples each of unpreserved water and water preserved either by addition of 0.1 weight percent

of ascorbic acid or by acidification of 0.1 M HNO_3 were sent to the U.S. for analysis a few days after collection. Treatment of samples by HNO_3 or ascorbic acid was done immediately upon collection (Irgolic, 1983; personal communication). Samples were analyzed during a two-week period after arrival in the U.S., the total time lapse between collection and analyses ranging from one to three weeks. The results of the analyses can be seen in Table 7-17. Additional water samples collected from other parts of Taiwan also contained pentavalent arsenic. However, these samples were less reliable in that the collection period was unknown, and, upon arrival in the U.S., these samples had a yellowish hue with some flocculated matter present (Irgolic, 1982).

Several questions still remain to be answered in regard to water-usage patterns of the Taiwanese. For instance, it is not clear how quickly the water drawn from the wells was consumed; nor is it clear how much of the water was consumed in tea or other beverages where cooking preparations, such as boiling, would have altered the chemical form of the arsenic. These questions need to be answered in light of the possible effect these answers might have on interpreting the observed skin cancer incidence.

Ch'i and Blackwell (1968) conducted a case-control study in the area of Taiwan studied by Tseng et al. The authors compared a variety of factors between 353 cases of Blackfoot disease and 353 controls matched for sex and age. Socioeconomic status, occupation, cigarette smoking, diet, and consumption of deep well water which was arsenic-contaminated were the factors compared. Two factors were found to be significantly different between the cases and controls. Significantly ($P < 0.01$) more cases than controls were found to consume deep well water and to have a lower socioeconomic status. Though the author concluded that the primary contributing cause of Blackfoot disease was consumption of deep well water, the socioeconomic differences cannot be completely discounted.

TABLE 7-17. RESULTS OF TOTAL ARSENIC ANALYSES AND ARSENITE AND ARSENATE DETERMINATIONS IN THE YENSHEI WATER SAMPLES*

Sample	TOTAL ARSENIC, ppm: Ascorbic Acid 0.1%	0.1 M HNO_3	Unpreserved	HG[a]	ICP[b]	Arsenite, ppm by HG	Arsenate, ppm by HG
Well I	-	+	-	0.84±0.02	0.73±0.01	-	-
	+	-	-	0.88±0.01	0.72±0.01	0.024±0.001	0.85±0.01
	-	-	+	0.85±0.01	0.73±0.01	0.022±0.001	0.83±0.08
Well II	-	+	-	1.05±0.08	0.95±0.01	-	-
	+	-	-	1.16±0.03	0.96±0.01	-	-
	-	-	+	1.11±0.02	0.98±0.01	0.024±0.01	1.08±0.02

*Average ± average deviation of at least three determinations per sample.

[a]HG = Hydride generation technique.

[b]ICP = Inductively coupled argon plasma emission spectrometry.

Source: Irgolic (1982).

Other studies have also explored the relationship of arsenic to skin cancer and various skin lesions. Similar chronic effects as seen in Taiwan have been reported in other countries.

In Antofagasta, Chile, a new water supply was put into service in 1958. In the 1960s, physicians began noticing dermatological manifestations and even deaths, especially among children. In an investigation of skin pigmentation in 27,088 school children from the province of Antofagasta, an overall incidence of 12 percent was reported (Borgono and Greiber, 1972). It was discovered that the drinking water contained 0.8 mg As/l. Borgono and Greiber compared 180 inhabitants of Antofagasta with a community without exposure to arsenic via drinking water. Abnormal skin pigmentation was reported to be present in 80 percent and hyperkeratosis in 36 percent of the Antofagasta inhabitants, whereas none was found in the control group ($p \leq 0.05$).

In 1970, a water treatment plant was installed and there was a considerable drop in arsenic. According to Borgono et al. (1977), there were no skin lesions in children born since the water treatment began. However, it should be noted that in this more recent study the sample size of children born since the water treatment plant began was small (306) and no comparison population was studied. Therefore, any conclusions associating the lack of dermatological manifestations with the decrease in arsenic must take into account the small sample size. In regard to skin cancer, the follow-up may not have been long enough to detect a difference.

In addition to the work of Borgono and co-workers, Zaldivar and Guillier published a series of papers on the Antofagasta situation (Zaldivar, 1974; Zaldivar, 1977; Zaldivar and Guillier, 1977). The first of these (Zaldivar, 1974) describes a study on a total of 457 patients (208 males and 249 females) bearing cutaneous lesions (leukoderma, melanoderma, hyperkeratosis, and squamous cell carcinoma). The cases were collected both by the author and the

local hospital during the period 1968 to 1971. Children 0 to 15 years of age accounted for 69.2 percent of the male cases and 77.5 percent of the female cases. The average incidence/100,000 for cases with cutaneous lesions in 1968 to 1969 were 145.5 and 168.0 for males and females, respectively. By 1971 the incidence rates had dropped to 9.1 and 10.0 for males and females, respectively. The decline in morbidity was so rapid that a conclusion that arsenic was the cause of the skin lesions would have to be considered suspect.

The existence of arsenical waters in an eastern area of the province of Cordoba, Argentina, has been known for many decades (Arguello et al., 1938; Bergoglio, 1964). Effects noted on the population from this area include hyperpigmentation, keratosis, and skin and respiratory cancer. A large area of the province, mainly in the east and somewhat to the south, is the focal point for chronic endemic regional arsenical intoxication (CERAI) (Arguello et al., 1938). This CERAI is due to the ingestion of well water coming from the uppermost sheet of underground water--the principal source of arsenic--as well as to the ingestion of arsenic from the wells, which varies among wells throughout the region. The concentration also varies with rainfall. Vanadium is also elevated in areas with high arsenic content. A later report (Bergoglio, 1964) indicates that progress had been made in improving the hygienic condition of the drinking water.

Arguello et al. (1938) summarized the early history of investigations (1913 to mid-1938) into the health outcomes associated with the ingestion of arsenic-contaminated water. They also reported the results of an investigation of a large series of epitheliomas collected from mid-1932 to September 1938 at the dermatosyphilology clinic of a medical school in the arsenic-contaminated area. The series consisted of 323 cases of epithelioma of which 39 or 12.1 percent were cases with clinical evidence of CERAI.

Patients exhibiting CERAI had characteristic cutaneous lesions, represented by the symmetrical palmo-plantar keratoderma and melanoderma, although the latter symptom was seen less frequently. Foot and hand keratoderma were seen in 100 percent of the CERAI patients. Appearance usually occurred 2 to 3 years after the onset of intoxication. A prodrome of the keratosis is the appearance of an erythema in the same location, and a subjective crawling sensation and local fever. Otherwise, it is a state of dryness which precedes the keratosis.

Arguello et al. (1938) also reported that most patients also had hyperhidrosis and abnormalities of pigmentation. The melanoderma appeared early in the process and was variable among patients. It was described as small dark spots ranging in diameter from 1 to 10 mm. They had a tendency to coalesce and appeared predominantly on the trunk in the areas not exposed to the sun. Atropy was associated with telangiectasia and loss of color, or leukoderma, between the hyperpigmented areas (the "raindrop" appearance cited by Reynolds, 1901).

Geographically, the largest proportion of cases in the clinic came from the areas with the highest incidence of CERAI. Because the authors' data are not population-based, however, it cannot be stated that the incidence of skin cancer is significantly increased in these areas. The authors reported that the hands and feet were the locations of choice for the arsenical epitheliomas (38.5 percent vs 3.9 percent) compared to the nonarsenical epitheliomas. An example of this was seen in the head where 81.6 percent of the nonarsenical epitheliomas occurred versus 15.4 percent for arsenical epitheliomas.

Bergoglio (1964) did a proportionate mortality study of residents of certain departments (counties) in the Province of Cordoba, Argentina, where endemic arsenic levels in the water supply are reported to be very high. The

proportion of cancer deaths was higher in those departments than for the province as a whole (23.84 percent versus 15.3 percent; $P < 0.05$). Of the cancer deaths, respiratory cancer constituted 35 percent and skin cancer 2.3 percent. From the description by the author, it can probably be inferred that these data are not age-adjusted. No comparison is made of the percentage of respiratory and skin cancer deaths in the affected departments with the respective proportion for Cordoba Province.

Morton et al. (1976) investigated the relationship of skin cancer morbidity and the ingestion of arsenic-contaminated drinking water in Lane County, Oregon. The southcentral region of Lane County is underlaid by an arsenic-rich stratum called the Fisher formation, which is known to produce high arsenic levels in waters from wells drilled into the land. An extensive search of the pathology records of medical providers in Lane County, Oregon, was conducted in 1972 for the occurrence of skin cancer during the years 1958 to 1971. Cases were thoroughly screened to eliminate duplications and were then coded to 1970 census tract numbers according to the residential address at the time of diagnosis. Water samples were obtained in all census tracts at selected points in all municipalities and water districts in the county, as well as from single-family water sources. The single-family water sources were neither randomly nor uniformly distributed throughout the county but instead were heavily concentrated in the regions believed to have water arsenic problems. Water samples collected during 1968 to 1974 were compiled into mean concentrations for each census tract and census tract region. The authors stated that it seemed reasonable to assume that the samples were representative of the earlier time periods as well.

The skin cancer data were expressed in four sets of rates because of the availability of 4 sets of population estimates. Overall mean annual incidence

rates for the entire 1958 to 1971 period used mean population estimates based on all four sets of denominators. Census tract regions were devised to simplify analysis and presentation. Table 7-18 presents the water arsenic level obtained. As can be readily seen, the South rural area had a much greater arsenic exposure than any of the other sections of the county. Figure 7-1 contrasts the parts of the county underlaid by the Fisher formation, and subsequent higher arsenic levels, with the parts of the county experiencing higher squamous cell skin cancer. Relatively little concordance is noted. A multiple regression analysis performed by the authors demonstrated essentially no relation between skin cancer and water arsenic. It should be noted that water arsenic levels in this study varied from 0 to 2150 ppb. The authors point out that the Lane County water arsenic levels were much lower than those reported for Taiwan and Antofagasta. In particular, only 5 percent of the Lane County samples contained 100 or more ppb of arsenic in contrast to 48 percent of the samples in that range in the Taiwan data.

Similar findings were reported by Southwick et al. (1981) in a study conducted on residents of West Millard County, Utah. As an area in which naturally occurring arsenic in public drinking water had been reported, West Millard provided an "excellent opportunity to study the effects of arsenic exposure on a homogeneous, stable population with a predominantly 'Mormon lifestyle'" (Southwick et al., 1981). The exposed communities of Hinckley and Deseret had average arsenic concentrations of 0.18 mg/l and 0.27 mg/l, respectively (based upon monthly water samples taken between May 1976 to May 1977). The control community of Delta had average arsenic concentrations of 0.02 mg/l. All drinking water in the study communities came from wells and the predominant species of arsenic was reported as the pentavalent form (85 percent).

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TABLE 7-18. LANE COUNTY WATER ARSENIC LEVELS 1974-1978

Geographic region	Arsenic, ppb			1970 Population served by water districts	
	mean*	range	no. of samples	number	% of area residents
Rural	16.5+	0-2150	491	29,470	44
North	7.6	0-24	29	3,644	39
East	11.8	0-70	80	7,383	49
South	33.0	0-2150	186	12,713	59
Midwest	9.7	0-107	159	1,260	10
Coast	4.7	<1-13	37	4,470	54
Urban	4.8	0-860	67	135,260	91
NE Springfield	3.9	0-8	14	16,235	92
SW Springfield	6.0	0-30	4	18,460	96
S Eugene	5.3	0-750	10	29.230	88
W Eugene	6.5-	0-860	20	16,470	96
NW Eugene	3.8	<1-8	6	20,730	85
N Eugene	3.8	0-8	8	11,690	81
Core Eugene	4.0	<1-8	5	22,445	100
Lane County	8.6	0-2150	558	164,730	76

*Values with terminal digit of 5 indicate direction from which rounded, e.g., 0.51 - 0.5+, 0.49 - 0.5.

Source: Morton et al. (1976).

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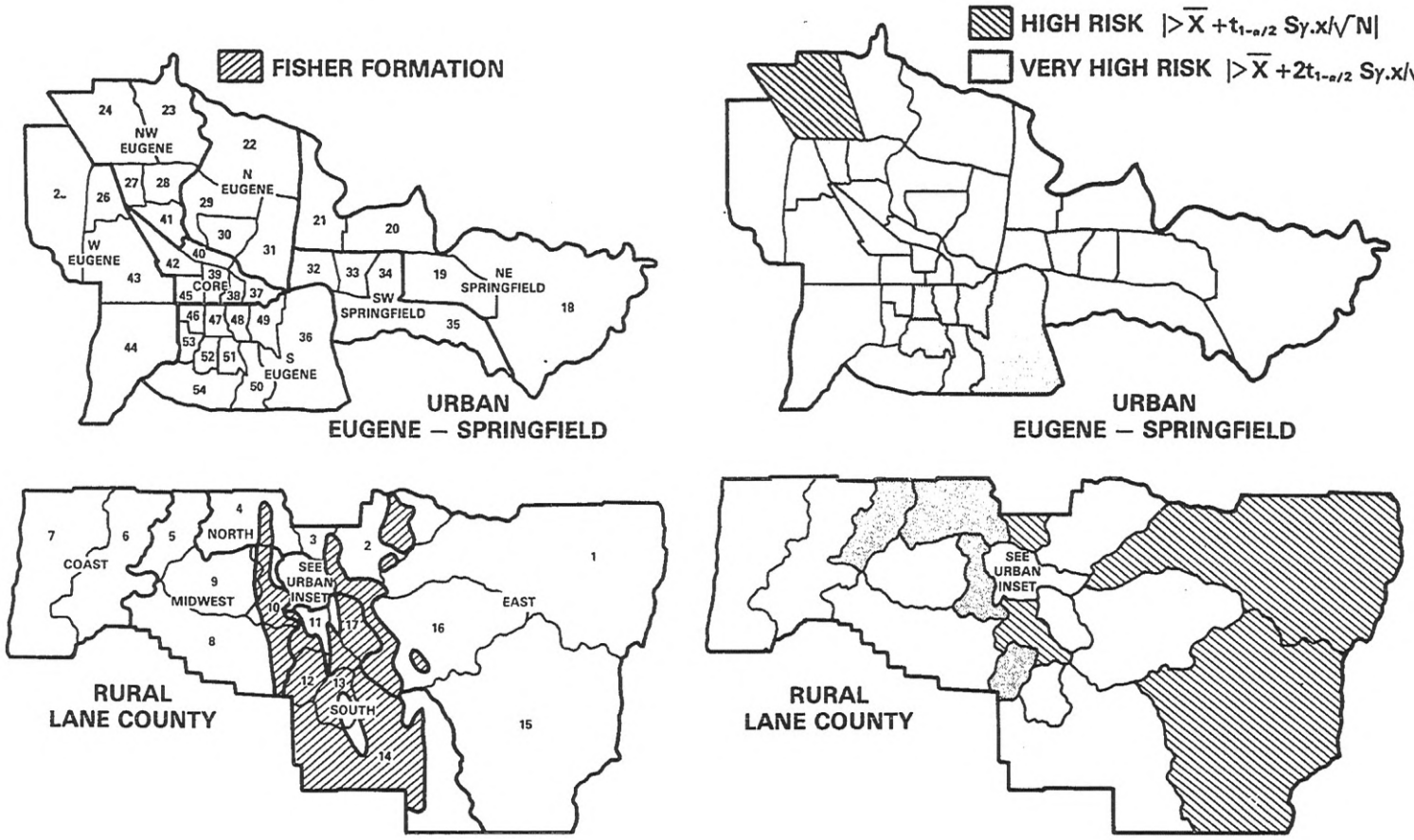

Figure 7-1. Comparison of census tracts experiencing exposure to the Fisher formation and exhibiting high skin cancer occurrence.

Source: Morton et al. (1975).

All study participants from the exposed communities were required to be five years of age or older and to have been residents of Hinckley or Deseret for at least the previous five years. Control participants were selected at random from age and sex categories matched to the exposed participants. Control participants were required to have lived their entire lives either in Delta or communities where arsenic in drinking water did not exceed the national standard of 0.05 mg/l.

Physical examinations were conducted to detect signs and symptoms associated with chronic arsenic poisoning. A total of 250 people participated in these examinations (145 exposed, 105 control); not all of these participated in each part of the examination, however. No explanation was provided by the authors as to the differences in participation rate for different parts of the examination. Urine and hair samples were collected from 94 and 74 percent of the participants, respectively. Dermatological examinations were conducted on 249 individuals. Neurological and hematological examinations were also conducted and are discussed in Sections 5.2.1 and 5.2.4, respectively. In addition, the incidence of cancer and vascular diseases in the study population was compared to other counties in the state of Utah.

The study results showed a clear relationship between the amount of arsenic consumed in drinking water and the amount measured in hair and urine. Differences between exposed and control populations were statistically significant.

Of the 249 participants examined for dermatological signs of arsenic toxicity (palmar and plantar keratosis and hyperkeratosis, tumors, diffuse pigmentation, arterial insufficiency), only 12 showed such signs and no participant had more than one sign. The 12 individuals were not clustered among the more heavily exposed, and when the dermatological signs were regressed

against annual arsenic dose and the log of the dose, no significant associations were found.

Age-adjusted cancer incidence rates showed Hinckley to have a somewhat lower cancer incidence than Delta. Cancer death rates, 1956 to 1976, showed Hinckley to have the highest rate (138 per 100,000) when compared to 42 other Utah communities. Table 7-19 shows age-specific death rates for Utah and three Millard County communities. (Fillmore is the County seat; comparisons to Deseret were not made due to the community's small population). Between 1956 and 1976, 14 cancer deaths were reported for Hinckley. All of these deaths occurred in individuals 45 years or older and the cancers were types most frequently reported for Utah: lung, breast, large intestine, prostate, stomach, leukemia, kidney, uterus, bone and connective tissue. Hinckley had generally lower death rates for cardiac and vascular diseases than did the control community of Delta. The authors noted that no unusual death patterns likely to be associated with arsenic exposure were seen in Hinckley.

Certain weaknesses exist with this study, most notably, that of a small study population from which to derive meaningful statistical analyses. Furthermore, children and adults were not treated separately. In regard to sample size, the authors felt that the small sample size was somewhat compensated by the homogeneity and stability of the predominantly nonsmoking population. Data on food consumption were also missing which might have influenced urinary arsenic levels. This, in turn, may have resulted in overstating the strength of the dose-response relationship for urinary arsenic and arsenic in drinking water. It should also be noted that some participants were reported to have an average daily water consumption greater than 8ℓ, which seems very high, even

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TABLE 7-19. AGE-SPECIFIC DEATH RATES FOR UTAH AND THREE MILLARD COUNTY COMMUNITIES (DEATHS/100,000/YEAR)

Community Characteristics	Age Groups and (Number of Deaths)					
	0-4	5-14	15-24	25-44	45-64	65+
CANCER						
State	7 (158)	6 (274)	6 (223)	19 (875)	149 (4749)	558 (7680)
Fillmore	0	14 (1)	0	17 (1)	196 (13)	706 (25)
Delta	0	0	22 (1)	61 (4)	189 (11)	986 (29)
Hinckley	0	0	0	0	390 (6)	1053 (8)
CARDIOVASCULAR						
State	1 (25)	0.4 (18)	1 (34)	18 (840)	275 (8788)	2079 (28587)
Fillmore	0	0	0	17 (1)	392 (26)	1638 (58)
Delta	0	0	0	30 (2)	344 (20)	1599 (47)
Hinckley	0	0	0	0	325 (5)	1316 (10)
CEREBROVASCULAR						
State	1 (24)	0.5 (23)	1 (36)	4 (201)	52 (1651)	797 (10965)
Fillmore	0	0	0	0	60 (4)	1017 (36)
Delta	0	0	0	0	34 (2)	1088 (32)
Hinckley	0	0	0	0	0	789 (6)
ARTERIOSCLEROSIS						
State	0	0.07 (3)	0.2 (7)	0.5 (21)	13 (406)	202 (2781)
Fillmore	0	0	0	0	15 (1)	311 (11)
Delta	0	0	0	0	17 (1)	272 (8)
Hinckley	0	0	0	0	65 (1)	395 (3)
AGE GROUP SIZE						
State	119,004	224,417	175,607	227,502	159,613	68,759
Fillmore	157	347	202	293	332	177
Delta	202	400	224	330	291	147
Hinckley	40	108	57	79	77	38

Death rates from 1956-1975 for cancer, cardiovascular disease, cerebrovascular disease, and arteriosclerosis, showing numbers of deaths and the average size of the age group.

Source: Southwick et al. (1981).

taking into account the hot summers. In reporting on the lack of arsenic-related effects in this study population compared to others (Tseng et al., 1968; Borgono and Greiber, 1972; Borgono et al., 1977; Zaldivar, 1977; Zaldivar and Guiller, 1977), the authors did note that populations in Taiwan and Antofagasta were exposed to considerably higher concentrations of arsenic in their drinking water.

Interestingly, the importance attached to the fact that no adverse effects were seen in this group of individuals exposed to drinking water arsenic levels four times that allowed by the Interim Primary Drinking Water Regulations (0.05 mg As/l) is somewhat compromised by the very characteristics of the population that make it useful for epidemiological study. The fact that this study population is so homogeneous and stable and, therefore, lends itself to a relatively well controlled statistical analysis, also makes it less useful in terms of being representative of the overall population of the U.S. For this reason, any generalizations that might be drawn from this study population are subject to limitations.

In addition to exposures via drinking water, food exposures and therapeutic exposures have also caused skin lesions and cancers. Hyperpigmentation and depigmentation of the skin were found to be common among the survivors of the Morinaga milk poisoning in 1955. A follow-up study conducted on the exposed children when they were 17-20 years of age showed the prevalence of lesions to be 15 percent (Yamashita et al., 1972). It is not known if any skin cancers have developed.

Hutchinson (1888) first reported on a possible association of skin cancer with the use of arsenical medicines. Prior to that, the association between these arsenical agents and keratotic lesions had been recognized. In his classic paper, Hutchinson reported on 6 patients with case histories who

exhibited the keratotic lesions associated with arsenical poisoning. He felt that the clinical series supported two principal conclusions:

1. Prolonged internal use of arsenic may seriously affect the nutrition of the skin and that use may produce warty or corn-like indurations.

2. Continued use of arsenic may result in a tendency for these "arsenic corns" to grow downward and pass into epithelial cancer.

Neubauer (1947) later compiled a series of reports on 143 cases of medicinal arsenical epitheliomas. He excluded five categories of cases reported in the literature to keep the series consistent with regard to diagnosis of case and history of arsenical use. Seventy-one percent of the patients being treated with arsenical medicine were patients suffering from skin diseases, especially psoriasis (54 percent). In contrast, only a small percentage of the cases reported came from patients treated with arsenic for various internal disorders. In nearly all cases the drugs used were inorganic and almost all were trivalent. The most commonly used arsenical was potassium arsenite. No externally applied arsenic-related skin cancer case was reported in the series.

The elapsed time from the beginning of administration of the arsenical drug to the beginning of the epitheliomatous growth was variable, but averaged 18 years regardless of the type of lesion. In cases with keratosis, the latent period to the onset of keratosis was about half the latent period to the onset of the epithelioma, i.e., about 9 years. Thirty-three percent of the patients were 40 or younger. Of the 143 patients, 13 had or developed miscellaneous cancers at other sites, but such cases were not reported systematically.

Fierz (1965) reported a follow-up study of patients treated with arsenic by a private practitioner. An accurate assessment of the total arsenic intake

in terms of the amount of Fowler's Solution administered was available to the investigator from patient records. The follow-up examination was conducted under the auspices of a local polyclinic. Fourteen hundred fifty patients were identified as having received arsenic treatment, and invitations were mailed for them to come for a free follow-up medical examination. During the period March 1963 to April 1964, 262 patients presented themselves for examination. Two hundred eighty patients were not located while 100 patients actively refused to participate. Only patients under 65 years of age were invited to participate in the study. The author admits that the patients reporting for examination were not a representative sample. In fact, he categorizes them into three groups which range the spectrum of likely biases. There were patients satisfied with the results of the arsenic treatment and wishing to express thanks, patients in whom disturbing side effects were occurring, and finally patients who were still suffering from the initial disease and who were eager to get a consultation.

Arsenic treatment was prescribed for individuals suffering primarily from three main skin diseases: psoriasis (64 patients), neurodermatitis (62), and chronic eczema (72). In addition, treatment was also prescribed for 64 patients suffering from assorted skin diseases other than those listed above.

Fierz noted that the arsenic treatment showed good success. Of the 64 cases of psoriasis, 55 reported a favorable effect while taking the drops. Forty-eight of 62 patients with neurodermatitis reported a favorable effect. This effectiveness was the cause for the patients' reliance on the drug.

Upon examination, 106 of 262 patients (40.4 percent) reported hyperkeratoses, although frequently a detailed examination was necessary to find the changes. Hyperkeratoses were round, superficially verrucose papules, 1 to 3 mm in diameter. The number and the exact presentation of the hyperkeratoses varied from case to case.

In the series, 21 cases of skin cancer were found comprising 8 percent of the total subjects. As was in the case of hyperkeratosis, some variability was observed in the expression of the skin cancers. Multiple basal cell carcinoma was the most frequent histologic type observed, occurring in 48 percent of the cancer patients. The basal cell carcinomas appeared morphologically as polycyclic, sharply bounded erythemas with slight infiltration. In 13 of the 21 cancer cases, multiple carcinomas were observed, a much higher proportion than had been observed with other causes of skin cancer. Of the 21 patients with carcinomas, 16 showed distinctly developed arsenic warts on the palms and soles simultaneously with the skin tumors.

Both hyperkeratosis and skin cancer were found to vary with increasing arsenic intake. Above 400 ml of Fowler's solution, more than 50 percent of the patients studied showed hyperkeratosis. As the dose increased there was a corresponding increase in the simultaneous occurrence of hyperkeratosis of the palms and soles. Only 2/15 cases of hyperkeratosis with intakes of up to 250 ml had a simultaneous presentation, while 16/27 had a simultaneous presentation with intake of 250 to 500 ml.

As with the hyperkeratosis, skin cancer increased with increasing arsenic doses. Below 500 ml only basal cell carcinomas were found; spindle cell carcinomas were only found above that dose. The latency period for hyperkeratosis was at a minimum 2.5 years; skin cancer, however, had a minimum latency period of 6 years with a mean latency period of 14 years.

Cuzick et al. (1982) conducted a mortality analysis of a cohort of 478 patients given Fowler's solution to determine if persons taking the solution were at an increased risk of internal malignancies. The cohort consisted of 213 males (45 percent) and 265 females (55 percent) who took Fowler's solution for various lenghts of time ranging from 2 weeks to 12 years (mean duration,

8.92 months) during the period of 1945-1969. Follow-up was until January 1, 1980; the mean follow-up time for the entire cohort was 20.3 years. The median cumulative dose of arsenic was reported as 448 mg, with most patients consuming arsenic at a rate of about 250 mg/month.

Within the defined risk period, 139 patients died, 265 patients were known to be alive and at risk, 29 had passed 85 years of age, 19 had emigrated, and 26 could not be traced. Because of the unreliability of the expected values in the open-ended group beyond 85 years of age, deaths and person-years at risk after age 85 were ignored. Persons who emigrated were censored as of the date of emigration.

A subset of 142 of the cohort were physically examined during 1969-70, and the presence of arsenical keratoses, hyperpigmentation, and skin cancer was recorded. No signs of internal malignancy were clinically apparent at the time of examination. This subset was chosen because the individuals were known to be alive and were able to be traced.

The results showed that risk ratios were similar for both males and females. No signs of internal malignancy were clinically apparent in the patients given physical examinations, and mortality was not found to be significantly increased for any internal malignancies in the cohort, although it was somewhat elevated for death from bladder cancer (observed = 3, expected = 1.19, $P = 0.12$). The ratio of observed-to-expected deaths from all neoplasms, from cancer of the digestive organs, from cancer of the respiratory organs, and from all causes was analyzed by cumulative dose level. No trend by cumulative dose level was found; however, the risk ratios were low for deaths from all neoplasms, digestive cancers, and respiratory cancers in the lowest dose group, with the risks for deaths from all neoplasms being significantly ($p < 0.05$) lower than expected. A significant positive trend in the ratio of

observed-to-expected mortality for all neoplasms was found for dose in the period 5-9 years from first exposure, but this trend was not found in other time intervals since first exposure.

Of the subset of 142 patients examined for skin manifestation of arsenicism, their overall mortality was consistent with the remainder of the cohort. Within this group, 45 percent had keratosis, 14 percent had hyperpigmentation, and 11 percent were found to have skin cancer. The authors did not indicate what the expected proportions of patients with these signs would be. Some patients showed 2 or all 3 signs of arsenicism, and 49 percent showed at least one of the signs. The appearance of signs was dose- and age-related. Patients with signs had higher median doses (672 mg) than those without any signs (448 mg), and this was significant ($P < 0.001$) by the Wilcoxon rank-sum test. Forty percent of patients with signs had cumulative doses above 1000 mg, whereas only 22 percent of the patients without arsenical signs had cumulative doses above 1000 mg. On the average, patients with signs were 7 years older and had received their first exposure 6 calendar years earlier than those without signs. Within the group with exposures > 1000 mg, those with signs were, again, an average of 7 years older, and they had their first exposure 3 years earlier. It is interesting to note that all seven of the subsequent deaths from internal malignancy in this subgroup had been identified as showing signs of arsenicism. No deaths from cancer occurred in the group without physical signs.

In summary, this study provided little evidence that ingestion of arsenic is related to a risk of mortality from internal malignancies. Non-fatal skin cancer was found, however, to be related as a function of dose to ingestion of Fowler's solution. The authors indicated that perhaps persons who demonstrate signs of arsenicism following arsenic exposure retain arsenic longer than those

who do not show signs, which may suggest that persons who demonstrate signs of arsenicism are at a greater risk of internal malignancies. This was suggested by the fact that all of the deaths from internal malignancies in the subset of individuals that was examined for signs of arsenicism occurred in individuals who demonstrated such signs.

Knoth (1966) also reported on two patients treated with arsenical medicinals and who developed skin cancer. Roth (1958) reported that of 47 autopsy cases of vintners with chronic arsenic intoxication, 13 had skin tumors.

Gilbert et al. (1983) conducted a study on wood treaters in Hawaii who were occupationally exposed to arsenic (see Section 7.1.2.1 for complete discussion of study). The authors found no evidence of risk of skin cancer, but inadequacies in the study design and the small sample size limit the ability to draw valid conclusions from the data.

7.1.2.3 Other Cancers--Whereas there are many studies suggesting that there is an association between inhalation exposure and respiratory cancer and oral exposure and skin cancer, respectively, there are no consistent data with regai to cancer in internal organs.

Reymann et al. (1978) have investigated the relationship between the intake of arsenic for medicinal purposes and subsequent internal neoplasms. Study subjects were identified by examining the files of a dermatology clinic in Denmark for the years 1930 to 1939. Two rosters of study subjects were generated: 1) persons treated with arsenic for multiple basal cell carcinoma, Bowen's disease, psoriasis, verruca planus, and lichen planus, and 2) persons with keratoses from the first roster plus 30 other persons identified as having keratoses. The first roster of 413 persons comprised the basic study population; 24 persons were excluded for various reasons, resulting in a final study population of 389 persons. The malignancy histories of both populations

were traced through the years 1943-1974 in the Danish Cancer Registry. For each person a length-of-observation period was determined and an expected number of internal malignant neoplasms was determined using the former data.

In the main study population, 41 cases were observed versus 44.6 cases expected. Therefore, no increased incidence of internal malignancies was noted in the arsenic-treated patients. However, examination of the data by individual skin disease categories showed that women with multiple basal cell carcinoma had a significantly higher incidence of internal cancer. The same trend, although not significant, was observed in female patients exhibiting verruca planus. Next, an analysis was made of a possible dose-response relationship using duration of treatment as the exposure variable. The categories were low, medium and high, based on <1 month, 1-3 month, and >3 month duration of standard dose administration (6-8 mg As_2O_3). No relationship between dose and internal organ cancer was noted for the total population or by sex. In addition, the form of arsenic administered did not seem to affect the incidence of internal cancer, nor was any effect noted due to period of observation. Reymann et al. did not provide a definition of the term "internal cancer." It is presumed that the authors included lung cancer in their definition. If so, the authors did not provide any adjustment for smoking. Regardless, the sample size of 389 persons is probably too small to detect an excess in the incidence of internal cancer, even if lung cancers were excluded.

The keratosis group was not analyzed in the same way. Eight of the 19 men with keratosis died before 1974. Four of these were due to cancer of the internal organs. Expected deaths were 1.9. Similarly, 5 deaths due to cancer of the internal organs were observed in the 34 women with keratosis compared with 3.3 expected. Together there were 9 deaths due to cancer of the internal organs compared to 5.2 expected. Although the figure is almost doubled, it is

still not significant. On the average, the patients with keratosis received higher doses of arsenic than the other patients.

Hemangioendothelioma and reticulosarcoma of the liver has been reported by Roth (1958) to occur among German vintners exposed occupationally to arsenic. The same type of malignancy occurrence has also been reported in isolated cases by other authors (Pershagen and Vahter, 1979). Higgins et al. (1982) reported increased mortality for cirrhosis of the liver and urinary cancer in workers at the Anaconda Montana smelter.

More recently, Falk and coworkers (1981a) described a nationwide (U.S.) review of deaths from hepatic angiosarcoma during the years 1964-1974. Of 168 confirmed cases included for survey, a group of seven cases with a history of prolonged use of Fowler's solution was found. Taken with the data of Roth, chronic arsenic exposure, mainly via ingestion, appears to be associated with this very rare liver cancer.

In a review of four cases of hepatic angiosarcoma, Falk et al. (1981b) determined that one case, that of a child, involved environmental arsenic exposure in a copper-smelting community in Arizona. Since this child had a history of pica, the usual exposure routes were augmented by further arsenic intake.

Roat et al. (1982) reported a case of hepatic angiosarcoma in a subject who, 33 years earlier, had ingested Fowler's solution for the relatively short period of 6 months. The pre-existence of skin cancer in this subject, from age 25, of the type associated with arsenic exposure, was further support of an arsenic association.

Knoth (1966) reported on two patients who had been treated with arsenical medicinals and developed tumors at sites other than the skin or lung. One of the patients was a 61-year old woman who had been treated with an arsenical

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medicinal and developed mammary carcinoma. The other case was that of a 53-year old male who had been treated with an arsenical medicinal for cirrhosis vulgaris and developed a reticulosarcoma of the glans penis.

In the studies by Ott et al. (1974), an increased proportionate mortality due to malignant neoplasms of lymphatic and hematopoietic tissues was found. Axelson et al. (1978) found an increased risk of leukemia and myeloma in a case-control study of workers exposed at a smelter.

7.2 ANIMAL STUDIES

While arsenic carcinogenicity in test animals has not been observed in most studies, some recent reports have noted positive results. The literature on experimental inorganic arsenic carcinogenesis, as summarized in Table 7-20 and as reviewed by scientific bodies (NAS, 1977; NIOSH, 1975; IARC, 1973 and 1980) and individuals (Sunderman, 1976; Wildenberg, 1978; Pershagen and Vahter, 1979) supports this conclusion.

In light of the presently recognized anomalous metabolizing of inorganic arsenic by rats, studies which used rats as the experimental subjects should be viewed cautiously. Studies on other animal models have generally resulted in negative findings. A few of these studies are discussed below, but most have been summarized in Table 7-20.

In a study by Baroni et al. (1963), Swiss mice were given either arsenic trioxide dissolved in drinking water (concentration of 100 mg/ℓ) ad libitum for the duration of the 70-week experiment; or, sodium arsenate in a concentration of 15.8 gm/ℓ in a 2.5 percent solution of Tween 60 in water, applied twice weekly for the duration of the experiment. Each compound was tested alone, in combination with skin applications of croton oil (to test for initiating action), and after initiation with a single skin application of 7,12-dimethylbenz(a)anthracene or with administration of urethan by stomach tube

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TABLE 7-20. SUMMARY TABLE OF EXPERIMENTAL STUDIES OF ARSENIC CARCINOGENESIS

Route	Species (Strain)	Compound	Vehicle	Results*	Reference	Remarks
Oral	Mice (C57B16)	As_2O_3	Tap water or 12% aqueous ethanol	-	Hueper and Payne, 1962	Shortened life span of treated (aq. ethanol) vs. control.
Oral	Mice (Swiss)	As_2O_3	Drinking water	-	Baroni et al., 1963	
Oral	Mice (Swiss)	$NaAsO_2$	Drinking water	-	Kanisawa and Schroeder, 1967	Shortened life span, low dose.
Oral	Mice (NMRI)	As_2O_3	Drug (Psor-Intern) or Fowler's solution	+(?)	Knoth, 1966	Significance cannot be determined, uncomplete reporting by author.
Oral	Mice (C3H/St, female)	$NaAsO_2$	Drinking water	-	Schrauzer and Ishmael, 1974	
Oral	Rats (not specified)	$Pb_3(AsO_4)_2$ $Ca_3(AsO_4)_2$	Not specified	-	Fairhall and Miller 1941	Poor survival in treated. As reviewed by IARC (Vol. 23, 1980)
Oral	Rats (Bethesda Blacks)	As_2O_3	Tap water or aqueous ethanol (12%)	-	Hueper and Payne, 1962	
Oral	Rats (Osborne-Mendel)	$NaAsO_2$ Na_3AsO_4	Diet	-	Byron et al., 1967	Reduced survival at highest dose.
Oral	Rats (Long Evans)	$NaAsO_2$	Drinking water	-	Kanisawa and Schroeder, 1969	Low dose.
Oral	Rats (Wistar)	$Pb_3(AsO_4)_2$ Na_3AsO_4 $Pb_3(AsO_4)_2$ + NDEA Na_3AsO_4 + NDEA	Diet Diet Diet Diet	- - - -	Kroes et al., 1974	High mortality and 2 tumors (incidence not reported observed in lead arsenate group).

TABLE 7-20. (continued)

Route	Species (Strain)	Compound	Vehicle	Results*	Reference	Remarks
Oral	Dog	$NaAsO_2$ or Na_3AsO_4	Diet	-	Byron et al., 1967	Weight loss, early mortality, short duration of experiment.
Inhalation	Mice (not specified)	$NaAsO_2$	Aqueous aerosol	-	Berteau et al., 1978	Reported in an abstract form, high incidence in controls.
Intratracheal instillation	Rats (Wistar King) male	(1) As_2O_3 (2) Copper ore (3.95% Arsenic) (3) Flue dust	Not specified	- - -	Ishinishi et al., 1977	One tumor observed in treated, not significant.
Intratracheal instillation	Rats (Wistar King) male	As_2O_3	Aqueous solution	-	Ishinishi et al., 1976	One tumor observed in treated, not significant.
Intratracheal instillation	Rats (BDIX)	$Ca_3(AsO_4)_2$	Bordeaux mixture (contains $CuSO_4$ and $Ca(OH)_2$)	+	Ivankovic et al., 1979	Results cannot be attributed to arsenic alone.
Intratracheal instillation	Golden Hamsters (males)	As_2O_3 ± BP	Carbon carrier + dilute H_2SO_4	+	Pershagen et al., 1983	Adenomas significantly greater than controls ($p < 0.01$). Carcinomas in 3 treated animals vs. 0 in controls.
Intratracheal instillation	Golden Hamsters (female)	As_2O_3	Phosphate buffer	+	Ishinishi and Yamamoto, 1983	As_2O_3 was tumorigenic in a dose-response fashion.

TABLE 7-20. (continued)

Route	Species (Strain)	Compound	Vehicle	Results*	Reference	Remarks
Intratracheal instillation	Rats	Ore dust containing As at two levels of content	Not specified	+	Chung and Liu, 1982	Possible confounding effects of other elements present, unknown. No apparent differences in lung cancer with different As levels in dust.
Skin painting (application)	Mice (not specified)	$KAsO_2$ and As_2O_3	Ethanol	-	Leitch and Kennaway, 1922	Neubauer (1947) failed to confirm this observation.
Skin painting (application)	Mice (S)	$KAsO_2$ followed by croton oil in acetone	Methanol	-	Salaman and Roe, 1956	As reviewed by IARC (Vol. 23, 1980).
Skin painting (application)	Mice (Rockland all-purpose)	(1) $KAsO_2$ followed by croton oil in benzene	80% ethanol	-	Boutwell, 1963	As reviewed by IARC (Vol. 23, 1980).
Skin painting (application)	Mice (Rockland all-purpose)	(2) DMBA followed by $KAsO_2$ in 80% ethanol	acetone	Not carcinogenic	Boutwell, 1963	
Skin painting (application)	Mice (Swiss)	(1) Na_3AsO_4	Water containing Tween 60	-	Baroni et al., 1963	
		(2) Na_3AsO_4 followed by croton oil and DMBA	Water containing Tween 60	No promotional activity observed		
Subcutaneous injection	Mice (Swiss) female Progeny	Na_3AsO_4 Na_3AsO_4	Water Water	+ +	Osswald and Goerttler, 1971	

TABLE 7-20. (continued)

Route	Species (Strain)	Compound	Vehicle	Results*	Reference	Remarks
Subcutaneous implant	Rats (random-bred) male albino	$Ca_3(AsO_4)_2$	Paraffin pellets	-	Arkhipov, 1968	As reviewed by IARC (Vol. 23, 1980).
Subcutaneous injection	Rats (random-bred) male albino	$Ca_3(AsO_4)_2$	Sunflower oil	-	Arkhipov, 1968	
Subcutaneous injection (pre-natal + post-natal)	Mice (CFLP)	As_2O_3	Aqueous solution	+	Rudnai and Borzsony, 1981	Histological description of tumors poor.
Intravenous injection	Mice (Swiss) female	Na_3AsO_4	Water	+	Osswald and Goerttler, 1971	
Intramuscullary injection	Rats (Osborne-Mendel)	Arsenic	Metallic	-	Hueper, 1954	
Intramuscullary injection	Rabbits	Arsenic	Metallic	-	Hueper, 1954	
Oral	Mice (Swiss)	As_2O_3 and croton oil, DMBA or urethan	Drinking water	-	Baroni et al., 1963	
Oral	Mice (STS)	Arsanilic acid or $KAsO_2$ followed by DMBA (skin) then croton oil (skin) in benzene	Diet	-	Boutwell, 1963	As reviewed by IARC (Vol. 23, 1980).

(*) + statistically significant excess tumors observed over controls

\- no statistically significant excess tumors of treated vs. control or no tumors observed

(to test for promoting action). All tests failed to show any carcinogenic activity of the two compounds under the given experimental conditions.

Kanisawa and Schroeder (1969) treated Swiss mice with sodium arsenite (equivalent to 5 µg/ml As) in drinking water for the 30-month duration of their study. In the treated animals, the authors noted 6 malignant and 11 combined malignant and benign tumors out of 103 animals versus 15 malignant and 50 combined malignant and benign tumors out of 170 control animals; thus, the results were negative for showing any carcinogenic effect of sodium arsenite in this study.

In a study of Leitch and Kennaway (1922; as reported in IARC, 1980), 100 mice were given skin applications of a solution of potassium arsenite in ethanol containing 1.8 percent arsenic trioxide (later reduced to 0.12 percent due to a high death rate), thrice weekly for 3 months. Of the 33 mice that lived for 3 months, only one developed a metastasizing squamous cell carcinoma.

In certain animal systems, positive carcinogenic responses have been reported, however. For example, Osswald and Goerttler (1971) exposed pregnant Swiss mice to daily parenteral dosing of sodium arsenate (0.5 mg/kg, solution of 0.005 percent arsenate salt) for a total of 20 injections. Part of the offspring groups received 20 injections of the same level subcutaneously at weekly intervals. Leukemia or lymphoma was seen in 46 percent of the mothers (11/24) at the end of 2 years versus none in the controls. Of the treated offspring, 41 percent (17/41) of the males and about half of the females (24/50) developed leukemia versus only 3 of 55 male and female control offspring (approximately 6 percent). IARC (1973) has criticized this study for the absence of exposure of controls to the appropriate vehicle solution.

Knoth (1966) noted a significant frequency of tumors in 30 mice exposed to Fowler's solution orally (one drop/week, 20 weeks, approximately 5.3 mg As

total),including adenocarcinomas of the skin, lung, and lymph nodes. The absence of experimental details makes critical assessment of this study difficult.

Some recent animal studies have employed different exposure conditions than have been employed in the past. Berteau et al. (1978) have exposed a tumor-susceptible strain of female mice to a respirable aerosol of inorganic arsenic (1 percent aqueous solution of sodium meta-arsenite, 20 to 40 minutes daily, 5 days/week, 55 weeks total). The 30 exposed mice showed neither gross nor histological evidence of neoplasia.

In a two-part study, Ishinishi et al. (1977) examined the carcinogenic and co-carcinogenic effects of various arsenic compounds on male Wistar-King rats. In the first part of the study, arsenic trioxide, an arsenic-containing copper ore (containing 3.95 percent arsenic) or metal refinery flue dust (containing 10.5 percent arsenic) were administered to 51 rats via 15 weekly intratracheal instillations. The rats were observed over their lifespan. Of the 25 surviving rats, one adenocarcinoma was seen in the group receiving flue dust. One lung metastasis from osteosarcoma of the femur and one adenoma was reported in the group exposed to the copper ore. No malignant tumors were reported in the group receiving arsenic trioxide; however, one adenoma was reported for this group. All groups displayed squamous cell metaplasia in the airway and osteometaplasia in the alveolus of the lung.

In the second part of the study, 87 rats were instilled with each of the above compounds suspended in a saline solution containing benzo[a]pyrene (B[a]P) or with B[a]P, alone. Control rats (23) were instilled with the saline solution. Of the 34 surviving exposed rats, one adenocarcinoma was seen in the group receiving B[a]P plus copper ore. All exposed groups had squamous cell carcinomas of the lung. Of particular interest to the authors, was the noted co-carcinogenic effect of arsenic trioxide with B[a]P; rats in

this group exhibited a 43 percent incidence rate (3/7) for squamous cell carcinomas. This compared with a 14 percent (1/7) incidence rate in animals given B[a]P, alone. No benign or malignant tumors were seen in the 7 surviving control rats. Again, squamous cell metaplasia or osteometaplasia were seen in all groups.

The results indicated a positive interaction between arsenic trioxide and B[a]P; however, the authors noted that the numbers of surviving animals were too small to permit drawing any firm conclusions from the study.

In another study, Ishinishi et al. (1980) gave 30 male adult Wistar rats intratracheal instillations of arsenic trioxide in suspension for 15 weeks. Of the 19 rats that survived, only one malignant squamous cell carcinoma was observed over lifetime. No tumors were found in the controls.

Ivankovic and co-workers (1979) exposed rats, via intratracheal instillation, to a pesticide mixture corresponding to that used in the past for vineyard treatment and consisting of a mixture of copper (II) sulfate, calcium hydroxide and calcium arsenate. Of 25 rats exposed to approximately 0.07 mg arsenic, 10 died from lung necrosis or pneumonia. In the survivors, 9 animals (60 percent) showed multi-focal bronchogenic adenocarcinomas and bronchiolar/alveolar cell carcinomas.

This study appears to offer experimental evidence that the vineyard pesticide mixture, employed as such, could have been carcinogenic to vine dressers working with the material. One difficulty with this study is an ambiguity regarding its full significance for the general issue of arsenic-inducing carcinogenic effects by itself. Clearly, the high mortality rate, 40 percent, and the known toxicity of Bordeau mixture (copper sulfate plus calcium hydroxide) to animals (Pimentel and Marques, 1969) and man (Villar, 1974, Pimentel and Marques, 1969) suggest carcinogenesis; however, it is impossible

to clearly ascribe such activity to arsenic alone given the presence of other compounds within the mixture. In their studies, Ivankovic et al. (1979) did not include animal groups exposed to calcium arsenate alone or to Bordeau mixture alone.

Pershagen et al. (1983, in press) have studied the pulmonary carcinogenicity of arsenic trioxide alone and in combination with benzo(a)pyrene in male golden hamsters given 15 weekly intratracheal instillations of 3 mg As/kg and/or 6 mg/kg B[a]P. In this study, a carbon dust carrier with dilute sulfuric acid was employed to enhance retention of arsenic. Carcinomas of larynx, trachea, bronchi and lungs were found in 3 animals given just arsenic versus a zero response in controls. The incidence of adenomas, papillomas and adenomatoid lesions was higher in arsenic versus control groups ($p < 0.01$). While the carcinomas in the arsenic group did not reach statistical significance, the significantly higher incidence of the adenomas, papillomas, and adenomatoid lesions support the authors' conclusion that the carcinomas were not a chance finding. The use of the carrier to enhance lung retention of arsenic appears to be the key to the results in this study. By itself, the oxide of arsenic is rather rapidly cleared from the lung (see below).

Rudnai and Borzsony (1981) reported that a combination of pre- and postnatal exposure of CFLP mice to injected arsenic trioxide (1.2 µg As/g, days 15-18 of gestation; 5 µg As/animal for 3 days post-birth) resulted in a 63 percent lung tumor incidence at 1 year of age versus approximately 18 percent in controls. In this study, a detailed histological description of the tumors was not given, but it can be assumed that both adenomas and adenocarcinomas were observed.

Chung and Liu (1982) reported that the repeated intratracheal instillation of ore dust containing arsenic in rats resulted in a lung cancer incidence

rate of approxiamtely 15 percent (6/41) over a period of 3 years, while controls (N=18) showed no lung tumors. There was extensive metastasis in one animal. In this study, two compositions of metal content in ores were used, with the arsenic varying by 8-fold. The lung cancer rate for the two forms of ore dust were comparable, despite the 8-fold difference in arsenic, i.e., there was no simple dose response. On the other hand, the ores contained variable amounts of iron and lead, which may have affected both the dose response and, possibly, the actual incidence of the lung cancers.

Ishinishi and Yamamoto (1983) exposed female golden hamsters to arsenic trioxide by intratracheal instillation of a suspension in phosphate buffer, 15 times weekly, for 4 months, at a total dose of 5.3 mg As. A second group was given a total dose of 3.8 mg As. All animals were followed over their entire life span. The incidence of lung tumors (adenomas) for the combined exposure groups was approximately 17 percent versus no tumors in surviving controls. While the sample size was small, there was the suggestion of a dose response across the two exposure levels (3/10 for the higher dose; 1/10 for the lower dose). These data suggest that arsenic trioxide is tumorigenic in the golden hamster and may be carcinogenic.

Recently, both Inamasu et al. (1982) and Pershagen et al. (1982) have studied the effects of intratracheal instillation of calcium arsenate (see Section 4.1.1 for complete discussion of studies). Inamasu et al. gave single intratracheal instillations of arsenic trioxide or calcium arsenate to male Wistar rats. Pershagen et al. instilled male Syrian golden hamsters with four weekly suspensions of arsenic trioxide, arsenic trisulfide and calcium arsenate. The results of both studies showed that arsenic trioxide was rapidly cleared from the lungs, whereas calcium arsenate was slowly eliminated. The differences in clearance appeared to be related to solubility, with the less soluble calcium arsenate exhibiting the slowest clearance.

These recent findings might help to explain the differences noted above in the earlier studies of Ishinishi et al. (1977; 1980) and Ivankovic et al. (1979). In regard to the Ivankovic study, it may be that the calcium arsenate, of itself, contributed to the high mortality rate observed in the exposed rats.

Schrauzer and co-workers (Schrauzer and Ishmael, 1974; Schrauzer et al., 1977; Schrauzer et al., 1978) have reported experimental results using oral arsenic and the tumorigenic effect of the agent on spontaneous mammary adenocarcinomas in an inbred strain of mice (C_3H/St Mice). These workers noted that while arsenic retards the overall incidence of tumor formation (10 or 80 ppm As), it stimulates the growth of tumors that otherwise occur. When these animals were exposed to only 2 ppm As (arsenite) in drinking water, compared to levels of 10 or 80 ppm, there was no effect on frequency of tumors, although the same enhanced tumor growth was seen as before with levels of 10 or 80 ppm As (Schrauzer et al., 1978). Furthermore, a higher incidence of multiple tumors of the mammary gland was observed, as was the abolishing of the anticarcinogenic effect of selenium in this system when both elements were given together.

In support of the positive responses noted in the above animal studies, Dipaolo and Casto (1979) reported the transformation of cultured Syrian hamster embryo cells by direct exposure to sodium arsenate (NA_2HAsO_4). In their assay, 300 cells from secondary cultures of Syrian hamster embryo cells (HEC) were plated in complete medium with 20 percent serum in 50-mm plastic Petri dishes along with 6×10^4 HEC cells which had been irradiated as confluent monolayer cultures. Sodium arsenate at concentrations of 0 µg/ml (control), 2.5 µg/ml and 5.0 µg/ml in complete medium (with a final concentration of acetone less than 0.02 percent) were added 24 hours later. Dishes were fixed and stained nine days after seeding. Colonies were scored blind by two observers.

For the two sodium arsenate concentrations, the authors reported that the number of transformations were 1.16 and 2.08/dish, respectively, or 1.74 and 4.13 percent, respectively, on the basis of transformed colonies relative to total colonies scored. The authors also reported that typical colonies scored as transformed after direct treatment with a metal carcinogen were identical to those obtained with other chemical carcinogens. In addition, the authors claimed (data not shown) that when 2.5 µg benz(a)pyrene per ml of medium were used, the transformation frequency, on a colony basis, was 4 to 6 percent.

7.3 QUANTITATIVE CARCINOGEN RISK ESTIMATES

7.3.1 Introduction

This quantitative section deals with the unit risk for arsenic in air and water and the potency of arsenic relative to other carcinogens that the Carcinogen Assessment Group (CAG) of the U.S. Environmental Protection Agency has evaluated. The unit risk estimate for an air pollutant is defined as the lifetime cancer risk occurring in a population in which all individuals are exposed continuously from birth throughout their lifetimes to a concentration of 1 $\mu g/m^3$ of the agent in the air they breathe. The unit risk estimate for water is defined similarly, but with a water concentration of 1 µg/ℓ. Unit risk estimates are used for two purposes: (1) to compare several agents with each other in terms of carcinogenic potency, and (2) to give a crude indication of the human health risks that might be associated with exposure to these agents, if the actual exposures are known.

The data used for quantitative estimates can be of two types: (1) lifetime animal studies, and (2) human studies where cancer risk has been associated with exposure to the agent. It is assumed, unless evidence exists to the contrary, that if a carcinogenic response occurs at the dose levels used in a study, then responses at all lower doses will occur with an incidence that can be determined by an appropriate extrapolation model.

There is no solid scientific basis for any mathematical extrapolation model that relates carcinogen exposure to cancer risks at the extremely low concentrations which must be dealt with in evaluating environmental hazards. For practical reasons, such low levels of risk cannot be measured directly either by animal experiments or by epidemiologic studies. It is necessary, therefore, to depend on current knowledge of the mechanisms of carcinogenesis for guidance as to the correct risk model to use.

At the present time, the dominant view is that most cancer-causing agents also cause irreversible damage to DNA--a position supported by the fact that a large proportion of agents that cause cancer are also mutagenic. There is reason to expect that the quantal type of biological response, which is characteristic of mutagenesis, is associated with a linear non-threshold dose-response relationship. Indeed, there is substantial evidence from mutagenesis studies with both ionizing radiation and a wide variety of chemicals that this type of dose-response model is the appropriate one to use in estimating cancer risks from environmental exposures. This is particularly true at the lower end of the dose-response curve. At higher doses, there can be an upward curvature, probably reflecting the effects of multistage processes on the mutagenic response. The linear non-threshold dose-response relationship is also consistent with the relatively few epidemiologic studies of cancer responses to specific agents that contain enough information to make the evaluation possible (e.g., radiation-induced leukemia, breast and thyroid cancer, skin cancer induced by arsenic in drinking water, liver cancer induced by aflatoxins in the diet). There is also some evidence from animal experiments that is consistent with the linear non-threshold model (e.g., the initiation stage of the two-stage carcinogenesis model in rat liver and mouse skin).

Because of these factors, the linear non-threshold model is considered to be a viable possibility for the true dose-response relationship and, unless

direct evidence to the contrary is presented, it is used as the primary basis for risk extrapolation at low levels of exposure.

The quantitative aspect of carcinogen risk assessment is included here because it may be of use in setting regulatory priorities, evaluating the adequacy of technology-based controls, and other aspects of the regulatory decision-making process. However, the imprecision of presently available technology for estimating cancer risks to humans at low levels of exposure should be recognized. At best, the linear extrapolation model used here provides a rough but plausible estimate of the upper limit of risk--that is, with this model it is not likely that the true risk would be much more than the estimated risk, but it could be considerably lower. The risk estimates presented below should not be regarded, therefore, as accurate representations of true cancer risks even when the exposures involved are accurately defined. The estimates presented may, however, be factored into regulatory decisions to the extent that the concept of upper-risk limits is found to be useful.

7.3.2 Unit Risk for Air

7.3.2.1 Methodology for Quantitative Risk Estimates--The methodologies used to arrive at quantitative estimates of risk must be capable of being implemented using the data available in existing epidemiologic studies of exposure to airborne arsenic. In order to extrapolate from the exposure levels and temporal exposure patterns in these studies to those for which risk estimates are required, it will be assumed that the age-specific mortality rate of respiratory cancer per year per 100,000 persons for a particular 5-year age interval, i, can be represented using either of two models:

$$a_i(D) = a_i[1 + a'D^k] \qquad (1)$$

(a relative or multiplicative risk model), or

$$a_i(D) = a_i + 100{,}000a'D^k \qquad (2)$$

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(an absolute or additive risk model). With either model, a_i is the age-specific mortality rate per year of respiratory cancer in a control population not exposed to arsenic, a' is a parameter representing the potential of airborne arsenic to cause respiratory cancer, and D is some measure of the exposure to arsenic up to the ith age interval. For example, D might be the cumulative dose in $\mu g/m^3$ years, the cumulative dose neglecting exposure during the last 10 years prior to the ith age interval, or the average dose in $\mu g/m^3$ over some time period prior to the ith age interval. The forms to be used for D will be constrained by the manner in which dose was treated in each individual epidemiologic study. The parameter k determines the shape of the dose-response curve. Attention will be given particularly to the values k = 1 and k = 2. If k = 1, the age-specific incidence rates vary linearly with the dose level (a linear model), and if k = 2 they vary quadratically. At low exposures the extra lifetime probability of respiratory cancer mortality will vary correspondingly (e.g., linearly for k = 1 and quadratically for k = 2).

The dose-response data available in the epidemiologic studies for estimating the parameters in these models consists primarily of a dose measure D_j for the jth exposure group, the person-years of observation Y_j, the observed number of respiratory cancer deaths O_j, and the number E_j of these deaths expected in a control population with the same sex and age distribution as the exposure group. The expected number E_j is calculated as

$$E_j = \sum_i Y_{ji} a_i / 100{,}000, \qquad (3)$$

where Y_{ji} is the number of person-years of observation in the ith age category and the jth exposure group ($Y_j = \sum_i Y_{ji}$). This is actually a simplified representation, because the calculation also takes account of the change in the

age-specific incidence rates with absolute time. The expected number of respiratory cancer deaths for the ith exposure group is

$$E(O_j) = \sum_i Y_{ji} a_i (1 + a' D_j^k)/100{,}000$$

$$= E_j (1 + a' D_j^k) \qquad (4)$$

under the relative risk model, and is

$$E(O_j) = \sum_i Y_{ji} (a_i + 100{,}000 a' D_j^k)/100{,}000$$

$$= E_j + a' Y_j D_j^k \qquad (5)$$

under the absolute risk model. Consequently, with either model, $E(O_j)$ can be expressed in terms of quantities typically available from the published epidemiologic studies. Note that person-years of observation are not required if the multiplicative model is used.

Making the reasonable assumption that O_j has a Poisson distribution, the parameters a' and k can be estimated from the above equations using the method of maximum likelihood. Once these parameters are estimated, the age-specific mortality rates for respiratory cancer can be estimated for any desired exposure pattern.

To estimate the corresponding additional lifetime probability of respiratory cancer mortality, let $b_1, \ldots, b_{18}$ be the mortality rates, in the absence of exposure, for all cases per year per 100,000 persons for the age intervals 0-4, 5-9,..., 80-84, and 85+, respectively; let $a_1, \ldots, a_{18}$ represent the corresponding rates for malignant neoplasms of the respiratory system. The probability of survival to the beginning of the ith 5-year age interval is estimated as

$$\prod_{j=1}^{i-1} [1 - 5b_j/100{,}000]. \qquad (6)$$

Given survival to the beginning of age interval i, the probability of dying of respiratory cancer during this 5-year interval is estimated as

$$5a_i/100{,}000. \qquad (7)$$

The probability of dying of respiratory cancer given survival to age 85 is estimated as a_{18}/b_{18}. Therefore, the probability of dying of respiratory cancer in the absence of exposure to arsenic is estimated as

$$P_0 = \sum_{i=1}^{17} [5a_i/100{,}000) \prod_{j=1}^{i-1} (1 - 5b_j/100{,}000)] + (a_{18}/b_{18}) \prod_{j=1}^{17} (1 - 5_{bj}/100{,}000) \qquad (8)$$

Here the mortality rates a_i apply to the target population for which risk estimates are desired, and consequently will be different from those in (1)-(5), which applied to the epidemiologic study cohort. If the 1976 U.S. mortality rates (male, female, white, and non-white combined) are used in this expression, then $P_0 = 0.0451$.

To estimate the probability P_{EP} of respiratory cancer mortality when exposed to a particular exposure pattern EP, the formula (8) is again used, but a_i and b_i are replaced by $a_i(D_i)$ and $b_i(D_i)$, where D_i is the exposure measure calculated for the ith age interval from the exposure pattern EP. For example, if the dose measure used in (1) is cumulative dose to the beginning of the ith age interval in $\mu g/m^3$-years, and the exposure pattern EP is a

lifetime exposure to a constant level of 10 μg/m^3, then $D_i = (i-1)(5)(10)$, where the 5 accounts for the fact that each age inverval has a width of 5 years. The additional risk of respiratory cancer mortality is estimated as

$$P_{EP} - P_0. \qquad (9)$$

If the exposure pattern EP is constant exposure to μg/m^3, then $P_{EP} - P_0$ is called the "unit risk."

This approach can easily be modified to estimate the extra probability of respiratory cancer mortality by a particular age due to any specified exposure pattern. It is also clear that the applications of the approach are not limited to respiratory cancer.

7.3.2.2 Risk Estimates from Epidemiologic Studies--Prospective studies of the relationship between mortality and exposure to airborne arsenic have been conducted for the Anaconda, Montana smelter (Lee and Fraumeni, 1969; Lee-Feldstein, 1983; Higgins et al., 1982; Brown and Chu, 1983 a, b, c); and the Tacoma, Washington smelter (Pinto et al., 1977; Enterline and Marsh, 1982).

The study of Lee-Feldstein (1983) reported on an additional 14 years of follow-up of the cohort of 8047 studied by Lee and Fraumeni (1969), and used essentially the same methods of analysis as the earlier study. Therefore, it will not be necessary to consider the Lee and Fraumeni study in any detail in this report. Higgins et al. (1982) followed for an additional 14 years a sample of 1800 men from the cohort studied by Lee and Fraumeni, but used different exposure classifications and different methods of analyses.

Brown and Chu (1983 a, b, c), in a series of papers, arranged the Anaconda smelter data in such a manner that a mathematical model could be derived from it to account for the effect of the timing of exposure as predicted by the multistage model.

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Whereas Pinto et al. (1977) studied a cohort from the Tacoma smelter consisting of 527 men followed only after retirement, the study by Enterline and Marsh (1982) involved 2802 men and included follow-up prior to retirement. Consequently, the Enterline and Marsh study appears to provide a stronger basis for quantitative risk assessment than the Pinto et al. study.

In addition to studies of copper smelter workers, there have also been studies of workers exposed to arsenicals in the production or use of pesticides. Ott et al. (1974) studied the mortality experience of workers exposed to lead arsenate and calcium arsenate.

7.3.2.2.1 The Lee-Feldstein (1983) study. This study included 8047 white males who were employed as smelter workers for 12 months or more before 1957, and whose mortality experience was observed from 1938 through 1977. Altogether, the study involved 192,476 person-years of follow-up and 3550 deaths, including 302 from respiratory cancer (Table 7-21). Expected numbers of cancer deaths were calculated on an age-adjusted basis using the combined mortality experience of the white male population of Idaho, Wyoming, and Montana. As Table 7-21 indicates, malignant neoplasms of the digestive and respiratory tracts had SMRs of 125 and 285, respectively, both of which were significant at the 1 percent level (SMR = [observed/expected][100]).

Workers were categorized both by duration of employment and level of exposure to airborne arsenic in order to determine the effect of these parameters upon mortality. For each year of the study period, workers were assigned to one of five groups on the basis of total years of smelter employment completed (Table 7-22). Work areas in the smelter were divided into heavy, medium, or light exposure areas. Based upon this division, workers were categorized into heavy, medium, or light exposure groups, as determined by their maximum exposure for 12 or more months. The results for respiratory cancer based upon these categorizations are given in Table 7-23.

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TABLE 7-21. OBSERVED AND EXPECTED DEATHS DUE TO SELECTED CAUSES, WITH STANDARDIZED MORTALITY RATIOS (SMRs) AMONG SMELTER WORKERS, 1938-77

Cause of Death	List No.[a]	Number of deaths		SMR[b]
		Observed	Expected	
Tuberculosis	001-019	53	27.93	190[c]
Respiratory	001-008	47	25.51	184[c]
Other	010-019	6	2.42	248
Malignant neoplasms	140-199	609	370.74	164[c]
Digestive	150-159	167	133.58	125[c]
Respiratory	160-164[d]	302	105.81	285[c]
Other	140-148, 165-170, 177-181, 190-199	140	131.35	107
Vascular lesions of central nervous system	330-334	262	211.56	124[c]
Diseases of heart	400-443	1366	1056.55	129[c]
Influenza and pneumonia	480-483, 490-493	88	76.05	116
Emphysema (1963-77 only)	527	90	34.58	260[c]
Cirrhosis of liver	581	76	36.53	208[c]
Accidents	800-962	288	280.27	103
Motor vehicle	810-825, 830-835	106	115.55	92
Other	800-802, 840-862	182	164.72	110
Suicide and homicide	963-964, 970-979, 980-985	83	86.08	98
All other causes	Residual	606[e]	548.50	
Total		3522	2728.79	129[c]

[a]Seventh revision of International Lists of Diseases and Causes of Death.

[b]SMR = (observed/expected) x 100.

[c]Significant at 1% level. Bailar and Ederer (1964)

[d]Among the 302 deaths from respiratory cancer, the site was lung and bronchus (162,163) in 289 cases, larynx (163) in 9, mediastinum (164) in 3 and (160) in 1.

[e]Includes 19 emphysema deaths occurring in the years preceding 1963, for which emphysema death rates are not available from individual states.

Source: Lee-Feldstein (1983).

TABLE 7-22. DESCRIPTION OF LENGTH OF EMPLOYMENT GROUPS, WITH NUMBERS OF SMELTER WORKERS, NUMBERS OF DEATHS, PERSON-YEARS AT RISK, AND DURATION OF SMELTER EMPLOYMENT (BASED ON TOTAL WORK EXPERIENCE THROUGH SEPT. 30, 1977)

Length of employment group[a]	Number of persons[b]	Number of deaths	Number of person-years of follow-up[c]
1 (25 or more years)	1899	1169	27,053
2 (15 to 24 years)	1138	586	26,556
3 (10 to 14 years)	678	328	19,734
4 (5 to 9 years)	1082	433	30,854
5 (1 to 4 years)	3248	1006	88,279
TOTAL	8045	3522	192,476

[a]Employees in all cohorts were living on Jan. 1, 1938.

[b]Group assignment of each person here was based on his status at the termination of employment or on September 30, 1977 (whichever date was earlier).

[c]Represents cumulative follow-up experience over the study period, 1938-77, with a total of 67,569 person-years of follow-up in the period 1964-77. Individuals were initially counted at risk upon completing 1 year of employment or on Jan. 1, 1938, if employed at least a full year before that date. In each calendar year of the study period, employees were counted in the group reflecting their cumulative work experience to date.

Source: Lee-Feldstein (1983).

Exposure to airborne arsenic was estimated from 702 samples collected at 56 sampling stations during the years 1943-1958 (Morris, 1975). Morris estimated that airborne levels averaged 11.27, 0.58, and 0.27 mg/m^3 in the heavy, medium, and light exposure areas, respectively. Respirators were used with varying degrees of faithfulness in the high exposure areas; consequently, average individual exposures in these areas were probably much less than 11.27 mg/m^3. A rough estimate is that use of respirators reduces the exposure levels by a factor of 10 (OSHA, 1978).

TABLE 7-23. OBSERVED AND EXPECTED DEATHS FROM RESPIRATORY CANCER, WITH PERSON-YEARS OF FOLLOW-UP, BY COHORT AND DEGREE OF ARSENIC EXPOSURE

	Maximum Exposure to Arsenic (12 or more months)[a]					
	Heavy		Medium		Light	
Years of Exposure	Obs/Exp[b]	P-Y[c]	Obs/Exp	P-Y	Obs/Exp	P-Y
25 years+	13/2.5	2400	49/7	6837	51/16.3	14573
15-24	9/1.3	2629	13/4.0	6509	16/8.6	12520
Less than 15 years	11/2.4	6520	31/9.3	24594	69/31	78245

[a]The 1562 men who worked less than 12 months in their category of maximum arsenic exposure were not included in this table.

[b]Observed/Expected.

[c]Person-years of follow-up furnished by Dr. Lee-Feldstein (personal communication).

Source: Adapted from Lee-Feldstein (1983).

The Lee-Feldstein (1983) study has a number of features which support its use in making quantitative estimates of respiratory cancer risk from airborne arsenic. It was a large study that involved observations of a considerable number of respiratory cancer deaths. A substantial amount of follow-up was conducted of persons who had been exposed for 15 years or more. Estimates of exposure levels and work histories are available for estimating individual exposures and for determining dose response.

It would have been more appropriate for making quantitative estimates of risk to have categorized workers by their individual cumulative or average exposures, rather than by their maximum exposures for 1 year or more. In developing the quantitative estimates, it will be assumed that a worker's average exposure during work hours was equal to the exposure for the category to which he was assigned. However, because these assignments were based upon

maximum exposures for at least a 12-month period, this approach tends to overestimate exposures, and consequently, to underestimate the carcinogenic potency of arsenic.

Because smoking is also an important risk factor for respiratory cancer, it would have been very useful to have smoking histories for the workers. Higgins et al. (1982) collected some limited smoking data for this cohort. Higgins and co-workers suggest that the smelter workers smoked somewhat more than the average U.S. white male population, but the difference was not enough to have a major effect upon the outcome of the study.

Development of risk estimates: The data from the Lee-Feldstein (1983) study used in the risk assessment are listed in Table 7-24. The relative risk (observed/expected) from this table are graphed in Figure 7-2, and the absolute risks ([observed-expected/person-years) in Figure 7-3. It is clear from these graphs that the risk for the high-exposure group exposed for greater than 25 years is not commensurate with the risks for the other groups. Because of this, and also because the exposures in the high exposure groups are much more uncertain than those of the other groups, it was decided to estimate risk using only the low and medium exposure groups. Results of applying chi-square goodness-of-fit tests of the relative and absolute risk models with $k = 1$ and $k = 2$ are recorded in Table 7-25. The maximum likelihood estimates of the carcinogenic potency parameter a' are also listed in this table. The maximum likelihood fits of these models are graphed in Figures 7-2 and 7-3. All of the fits are poor (p less than 0.0001) with the exception of that for the absolute-risk model; this latter fit is marginally acceptable ($p = 0.025$).

The unit risk (additional risk of respiratory cancer death from lifetime exposure to 1 $\mu g/m^3$ airborne arsenic) obtained from the absolute-risk model with $k = 1$ is also listed in Table 7-25. This risk was estimated by applying (2), (8), and (9) with D_i based upon a constant exposure of 1 $\mu g/m^3$.

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TABLE 7-24. DOSE-RESPONSE DATA FROM LEE-FELDSTEIN (1983) USED FOR RISK ASSESSMENT

Cohort	Maximum Exposure to Arsenic	Cumulative Exposure[a] ($\mu g/m^3$-years)	Person-Years of Observation[b]	Observed Deaths	Expected Deaths
1	Heavy	36064	2400	13	2.5
(25 + years	Medium	18560	6837	49	7.0
(of exposure)	Light	9280	14573	51	16.3
2					
(15-25	Heavy	22250	2629	9	1.3
years of	Medium	11600	6509	13	4.0
exposure)	Light	5800	12520	16	8.6
3					
(less than	Heavy	5973	6520	11	2.4
15 years of	Medium	3074	24594	31	9.3
exposure)	Light				

[a]Exposures are in $\mu g/m^3$-years estimated as (air concentration)(duration). For light, medium, and heavy exposures, air concentration was estimated as 290, 580, and 1127 $\mu g/m^3$, respectively (OSHA, 1978). Duration was estimated as follows (cf. Table 7-22):

Cohort 1: Persons in this cohort had at least 25 years' exposure. If all had worked continuously throughout follow-up, average duration would have been 25 + 27053/1899 = 39 years. Therefore the midpoint (39 + 25)/2 = 32 years was used.

Cohort 2: The midpoint of the employed interval, i.e., (15 + 25)/2 = 20 years was used.

Cohort 3: A weighted average of the midpoints of the employment intervals, i.e.,

$$\frac{(3)\ (88279) + (7.5)(30854) + (12.5)(19734)}{88279 + 30854 + 19734} = 5.3 \text{ years was used.}$$

[b]Furnished by Dr. Lee-Feldstein.

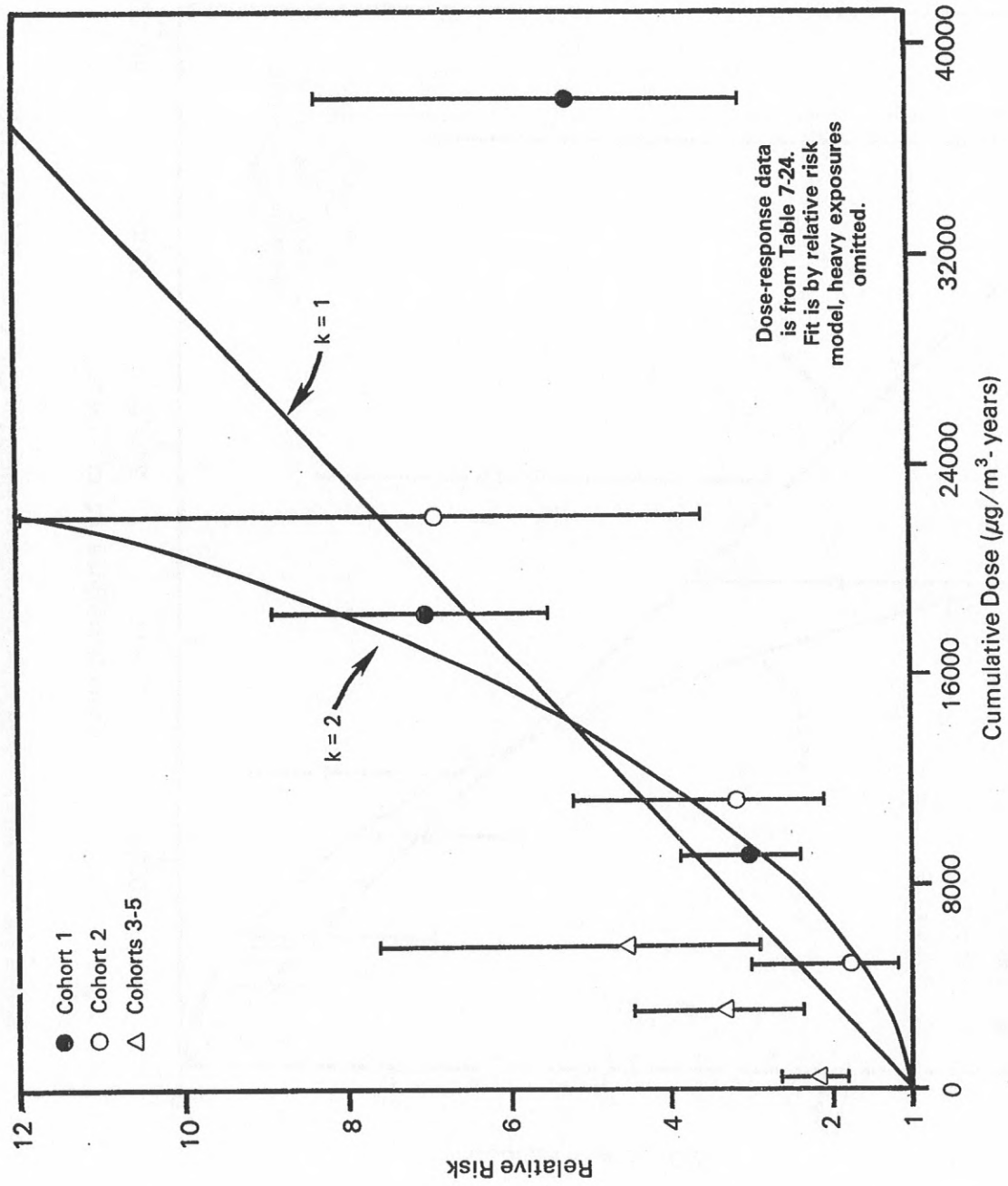

Figure 7-2. Relative risks and 90% confidence limits for data of Lee-Feldstein (1983).

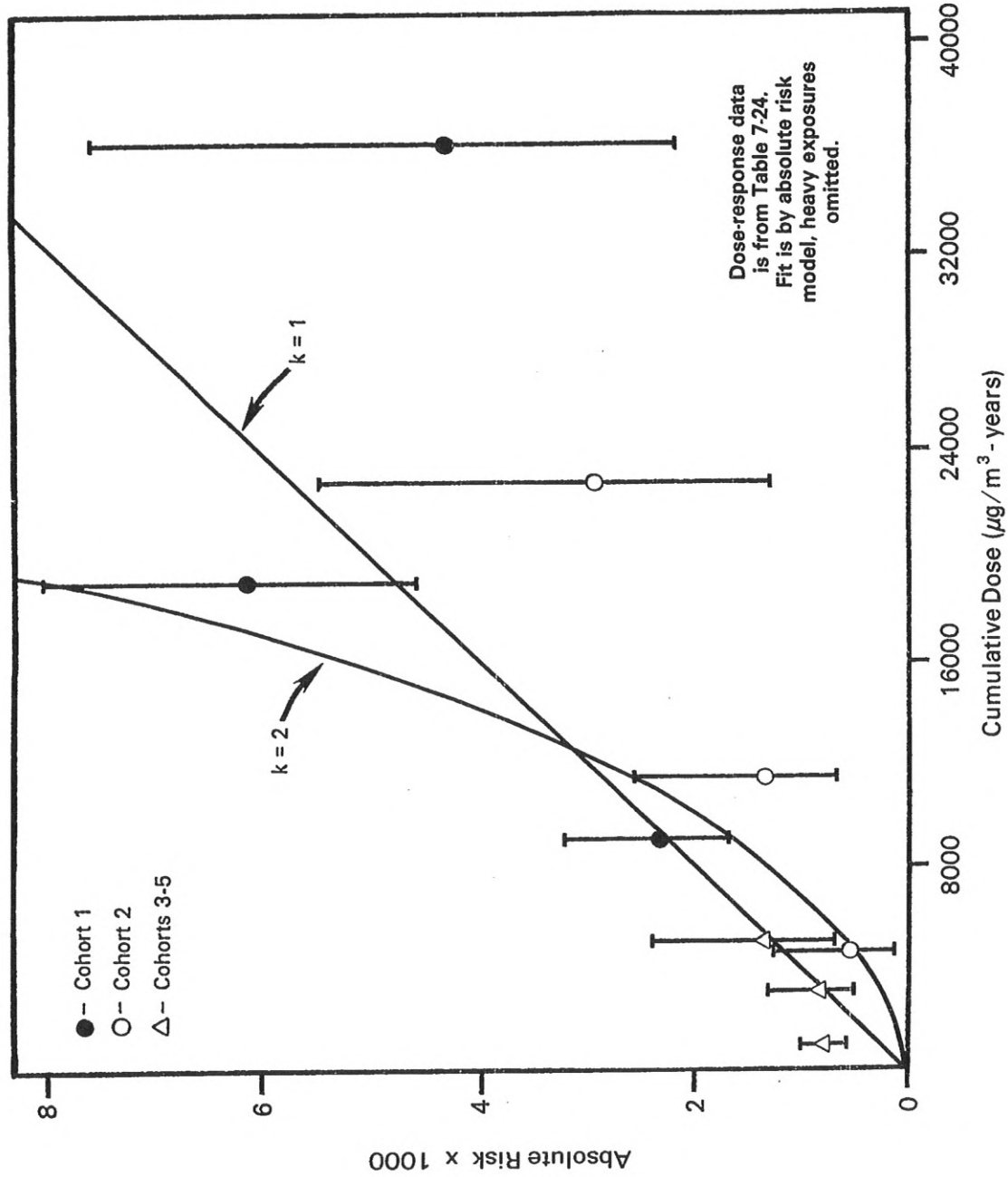

Figure 7-3. Absolute risks and 90% confidence limits for data of Lee-Feldstein (1983).

TABLE 7-25. SUMMARY OF QUANTITATIVE RISK ANALYSES

Exposed Population	Study and Data Source	Model	k	Results of Goodness-of-Fit Test: Carcinogenic Potency (a')[a]	x^2 (d.f.)	p-value	"unit" risk[b]
Anaconda smelter workers	Lee-Feldstein Table 7-24 (heavy exposure omitted)	absolute risk	1	2.48(-7)	12.7(5)	0.025	2.80(-3)
			2	2.09(-11)	60(5)	0.00001	lack of fit[d]
		relative risk	1	3.00(-4)	28(5)	0.00004	lack of fit
			2	2.09(-8)	79(5)	0.00001	lack of fit
	Higgins et al. Table 7-26	absolute risk	1	2.36(-7)	1.2(3)	0.75	4.90(-3)
			2	1.74(-11)	10.3(3)	0.017	1.05(-4)
		relative risk	1	3.17(-4)	2.57(3)	0.46	4.03(-3)
			2	2.18(-8)	15.4(3)	0.0015	lack of fit
	Brown & Chu Tables 7-27 and 7-29	absolute risk	1	9.45(-16)	7.01(7)	0.41	1.25(-3)
ASARCO smelter workers	Enterline & Marsh Table 7-33 (zero lag)	absolute risk	1	6.04(-7)[c]	5.5(4)	0.24	6.81(-3)
			2	1.43(-10)	20.7(4)	0.0003	lack of fit
		relative risk	1	4.6(-4)	11.6(4)	0.02	5.44(-3)
			2	1.01(-7)	23.4(4)	0.00011	lack of fit
	Enterline & Marsh Table 7-33 (10-year lag)	absolute risk	1	8.85(-7)	7.0(4)	0.14	7.60(-3)
			2	2.01(-10)	26.1(4)	0.00003	lack of fit
		relative risk	1	5.13(-4)	14.5(4)	0.006	lack of fit
			2	1.06(-4)	28.9(4)	0.00002	lack of fit
Dow pesticide manufacture workers	Ott et al. Table 7-34 (high exposure omitted)	relative risk	1	9.2(-4)	5.0(7)	0.66	1.36(-2)
			2	1.58(-7)	9.4(7)	0.23	7.68(-4)

[a] Potencies are in different units, depending upon model used (see text), and consequently are not comparable.

[b] Additional lifetime risk of respiratory cancer mortality from lifetime environmental exposure to 1 $\mu g/m^3$ arsenic.

[c] 6.04(E-7) means 6.04×10^{-7}.

[d] p-value of chi-square goodness-of-fit test is less than 0.01.

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Specifically,

$$D_i = 4.56[(i-1) + 2.5] \qquad (10)$$

was used, which represents the cumulative exposure in $\mu g/m^3$ resulting from a constant exposure to $\mu g/m^3$ from birth to the midpoint of the ith 5-year age interval. The factor 4.56 is needed to account for the fact that the workers in the occupational study used to estimate the carcinogenic potency of arsenic were only exposed during work hours. Assuming that workers were exposed for an average of 8 hours per day, 240 days per year, an environmental exposure to 1 $\mu g/m^3$ for 1 year is equivalent to an occupational exposure to

$$(1\ \mu g/m^3)(24\ \text{hours}/8\ \text{hours})(365\ \text{days}/240\ \text{days}) = 4.56\ \mu g/m^3 \qquad (11)$$

for 1 year.

7.3.2.2.2 The Higgins et al. (1982) study. Higgins et al. conducted additional independent follow-up through 1977 of a sample of 1800 men from the Anaconda smelter cohort studied by Lee and Fraumeni (1969). The sample included all of the men classified in the heavy exposure category by Lee and Fraumeni (1969), as well as a random sample of 20 percent of the remaining cohort. There were 80 deaths from respiratory cancer in the sample. Expected numbers were based upon the mortality rates of Montana white males, except for "all respiratory diseases"; U.S. white males were the referenced population for the latter category.

Higgins et al. also reviewed the industrial hygiene data and calculated average concentrations for the period 1943-1965 for 18 departments. No measurements were available for 17 departments, and average concentrations were estimated for these. These estimates were coupled with work histories

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updated through 1978 to obtain exposure measures for each individual in the study. Three types of individual exposure measures were considered: ceiling, time-weighted average (TWA), and cumulative. Ceiling exposures were estimates, in $\mu g/m^3$, of the highest exposure a man experienced for 30 days or more. TWA exposures were estimates, in units of $\mu g/m^3$, of the time-weighted average exposures during the period of employment. Cumulative exposures were estimates of total exposure in units of $\mu g/m^3$-years.

Higgins et al. investigated 5 combinations of follow-up and time period during which exposure was assessed: I. Exposure was assessed up to the date a worker entered the study and follow-up was from entry into the study through 1978; II. Exposure was assessed up to 1964 and follow-up was also through this date; III. Exposure was assessed through 1964 and follow-up was through 1978; IV. Exposure was assessed through 1964 and follow-up was from 1964 through 1978; V. Exposure was assessed through 1978 and follow-up was also through 1978. These different methods were considered principally because of the perceived difficulties of overlapping exposure and follow-up periods. Thus, with methods I and IV, exposure and follow-up periods were disjoint, whereas with methods II and V they coincided.

The analyses based upon ceiling exposures are not considered suitable for quantitative risk assessment because it seems extremely unlikely that respiratory cancer risk would be a function of peak exposures for any 30-day period, regardless of the other exposures that might have been experienced. This is also the case with the TWA analyses, because the exposures were averaged only over the period of employment, without regard to the duration of employment. If either of these dose measures were appropriate, it would mean, for example, that exposure to 500 $\mu g/m^3$ for 1 month would produce the same risk as exposure to 500 $\mu g/m^3$ for 30 years--which seems highly unlikely.

Thus, the analyses of Higgins et al. which appear to be most appropriate for developing quantitative estimates are those based upon cumulative exposure. This particular type of analysis was applied only to method V and applied only in Higgins (1982). The results of this analysis for lung cancer are listed in Table 7-26.

TABLE 7-26. RESPIRATORY CANCER MORTALITY 1938-1978 FROM CUMULATIVE EXPOSURE TO ARSENIC FOR 1800 MEN WORKING AT THE ANACONDA COPPER SMELTER[a]

Cumulative Exposure $\mu g/m^3$-years	Person-Years of Observation	Observed Deaths	Expected Deaths
0-500 (250)[b]	13845.9	4	5.8
500-2000 (1250)	10713.0	9	5.7
2000-12000 (7000)	11117.8	27**	6.8
≧ 12000 (16000)	9015.5	40**	7.3

[a]From Higgins (1982), Table 6.

[b]Numbers in parenthesis indicate assumed average exposures.

**Significant at 0.01 level.

Information on the smoking habits of 80.6 percent of the 1800 men was obtained from questionnaires administered directely to those still living and to close friends or relatives of those who were deceased. Sixteen percent of the smelter workers were "non-smokers" compared with 24-36 percent of U.S. males from 1955 through 1978. Thus, it appears that the smelter workers smoked somewhat more than the average U.S. male. However, no confounding was detected between arsenic exposure and smoking; 15.1 percent of those in the "heavy" exposure group were non-smokers, versus 16.3 percent in the other

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exposure groups. Significant increases in respiratory cancer were observed even among non-smokers exposed to high levels of arsenic.

Development of risk estimates: The relative risks (observed/expected) from Table 7-26 are graphed in Figure 7-4, and the absolute risks ([observed-expected]/person-years) in Figure 7-5. Results of applying chi-square goodness-of-fit tests of the relative- and absolute-risk models with $k = 1$ and $k = 2$ are recorded in Table 7-25. The maximum likelihood estimates of the carcinogenic potency parameter a' are also listed in Table 7-25. The maximum likelihood fits of those models are graphed in Figures 7-4 and 7-5. The fits for $k = 1$ are both excellent, with the absolute-risk model providing a slightly better fit than the relative-risk model ($p = 0.75$ vs. $p = 0.46$). The fits for $k = 2$ are much less adequate ($p = 0.017$ for the absolute-risk model and $p = 0.0015$ for the relative-risk model).

The unit risks (defined as the additional risk of respiratory cancer death from lifetime exposure to 1 $\mu g/m^3$ airborne arsenic) obtained from the absolute- and relative-risk models with $k = 1$ are also listed in Table 7-25.

These risks were estimated by applying (1) or (2), (8), and (9) with D_i based upon a constant exposure of 1 $\mu g/m^3$. Specifically,

$$D_i = (4.56)(72) \qquad (12)$$

was used, which represents the average lifetime cumulative exposure in $\mu g/m^3$ resulting from a constant exposure to 1 $\mu g/m^3$. Average lifetime exposure is used because it seems most commensurate with the treatment of exposure by Higgins et al.; in their analysis all of the person-years attributable to a single worker were placed into a single exposure category based upon total lifetime exposure, and consequently person-years of observation were placed into exposure categories according to exposures which had not yet occurred. It

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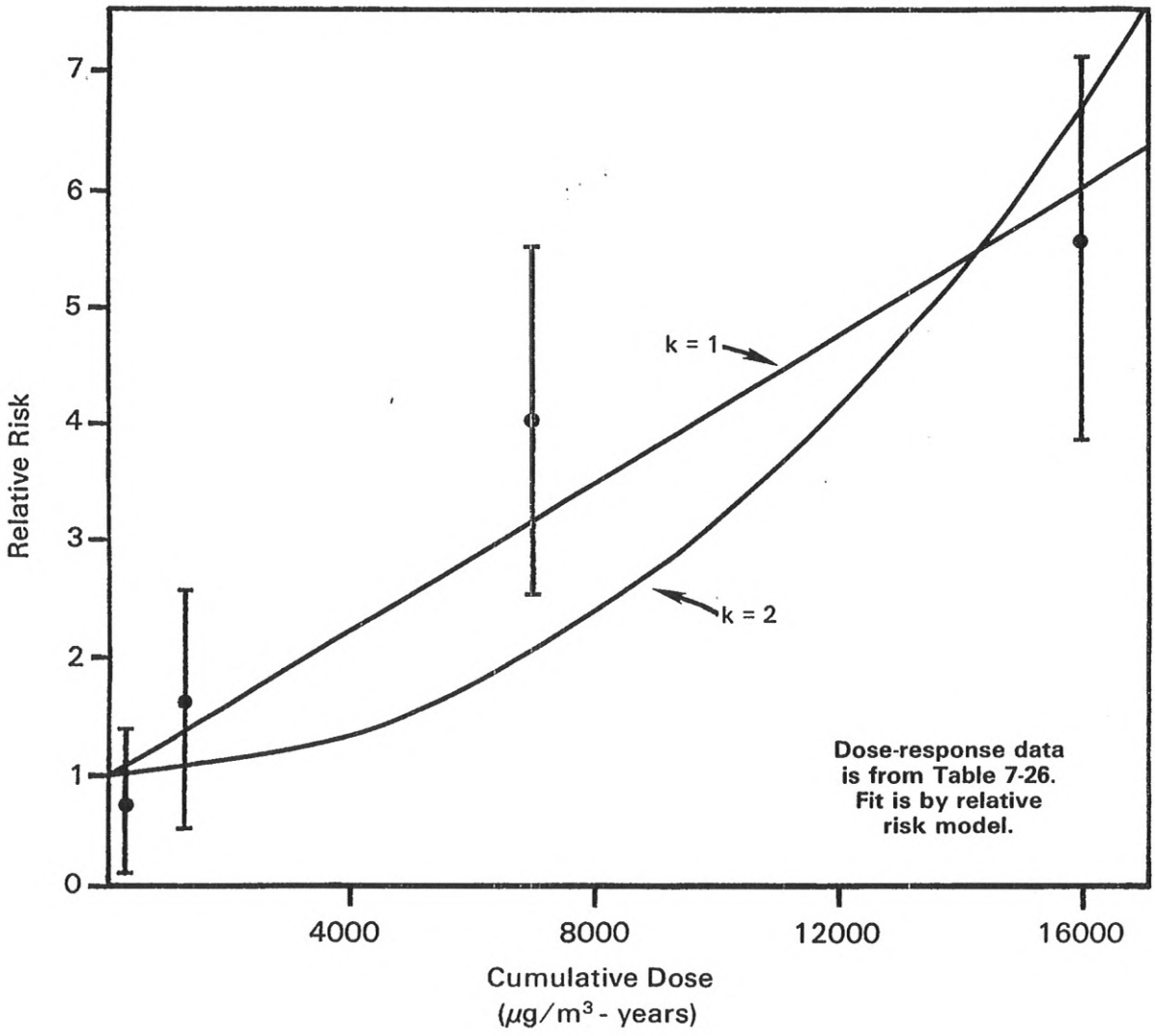

Figure 7-4. Relative risks and 90% confidence limits for data of Higgins (1982).

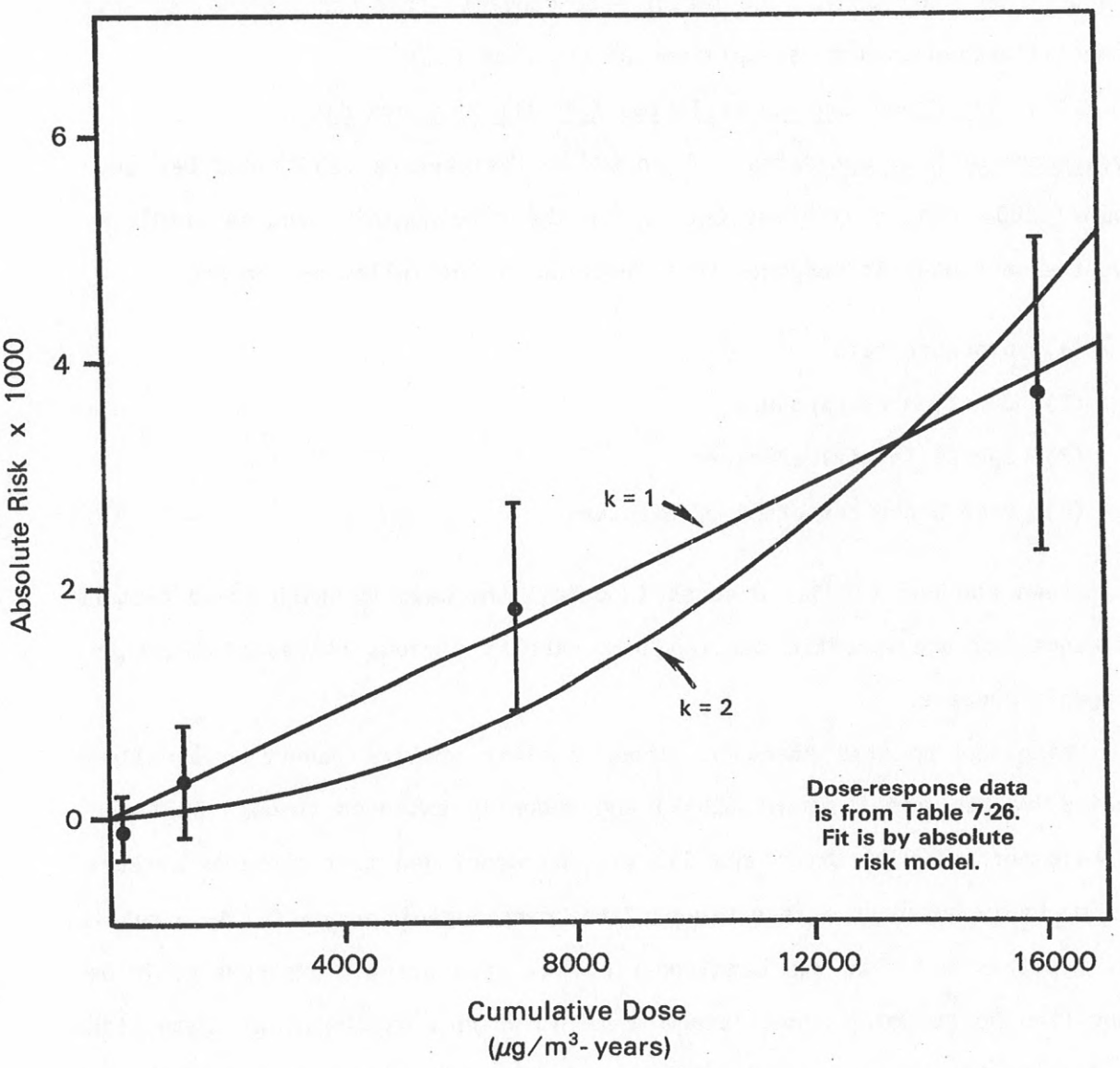

Figure 7-5. Absolute risks and 90% confidence limits for data of Higgins (1982).

would have been more appropriate for purposes of quantitative risk assessment had exposures been related to each 5-year age interval (as was done in the analysis of Enterline and Marsh, 1982) rather than to the total observation period of an individual. The factor 4.56 converts from occupational to environmental exposures and is explained at equation (11).

7.3.2.2.3 The Brown and Chu estimates from the Anaconda data. Development of Risk Estimates. As noted by Whittemore (1977) and Day and Brown (1980), the multistage theory for the carcinogenic process predicts that the carcinogenic response is a function of the following factors:

(1) exposure rate

(2) duration of exposure

(3) age at initial exposure

(4) time since cessation of exposure.

Brown and Chu (1983a) discuss in detail the ways in which these factors influence the age-specific carcinogenic rate at various stages of the carcinogenic process.

Using the updated Anaconda copper smelter workers cohort originally studied by Lee and Fraumeni (1969) and recently extended through 1977 by Lee-Feldstein (1983), Brown and Chu (1983b) concluded that airborne arsenic most probably acted on a late stage of the carcinogenic process. As a result, they hypothesized that the carcinogenic risk from arsenic exposure could be quantified by assuming a multistage model in which only the penultimate stage is affected by exposure. Under this assumption, the risk may be expressed in the form

$$r(d, t_o) = C[(d + t_o)^{k-1} - t_o^{k-1}] \qquad (13)$$

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where d is the duration of exposure, t_o is the age at initial exposure, and C and k are unknown parameters. The parameter C depends upon the exposure rate, and the parameter k upon the time effect of exposure.

Brown and Chu (1983b) noted a deviation from this model on the part of workers who left employment at the copper smelter before the age of 55. As a result, the mortality experience of that group after leaving employment was not included in the analysis.

In order to estimate the unknown parameters C and k, the basic mortality data were arranged in the three-way table reproduced as Table 7-27. The three classifications used in this table are as follows:

(1) Level of exposure, corresponding to Lee and Fraumeni (1969)--classified into heavy, medium, and light exposure groups;

(2) Duration of employment, classified into the following five subgroups; 0-9, 10-19, 20-29, 30-39, and 40+ years;

(3) Age at initial employment, classified into the following five subgroups; 20, 20-29, 30-39, 40-49, and 50+ years.

For each of the 3 x 5 x 5 = 75 cells in the table, the following three variables were given:

Obs = observed number of respiratory cancer deaths;

Exp = expected number of respiratory cancer deaths (based upon the U.S. white male age-specific calendar-time-specific respiratory cancer mortality rates); and

Pyr = person-years of observation

A single individual could supply information for more than one cell as his duration of employment increased over the follow-up period. The person-year weighted average duration of employment, and age at initial employment, were calculated for each cell.

Assuming that age at initial exposure is equivalent to age at initial employment, and that duration of employment and exposure are equivalent, Brown and Chu (1983c) fitted equation 13 to the data in Table 7-27. They used the maximum likelihood method, assuming a binomial distribution where Obs is the number of positive responses, Pyr is the sample size, and the rate of response is $p = Exp/Pyr + r(\bar{d},\bar{t}_o)$, where $\bar{d},\bar{t}_o$ are the averages for each cell. Using this approach, the value for k is estimated to be 6.8, and c = .603, 1.42, 1.74×10^{-13} for the light, medium, and heavy exposure categories, respectively.

Brown and Chu (1983c) did not attempt to give an exposure rate estimate to the heavy, medium, and light exposure groups of Lee and Fraumeni, (1969). One reason for this was that "heavy" and "medium" were defined as "having worked at least one year in a heavy or medium exposure area." The "total time worked" was not necessarily an indication of the total time worked in a heavy or medium exposure area. As a result, the use of the exposure rate in the areas defined as medium or heavy would tend to overestimate the true average exposure over an individual's working history. This bias did not exist for those in the light exposure group, since almost all of their working time was spent in light exposure areas. In addition, these low environmental exposures are of greater utility in estimating risks.

As a result of these factors, only the light exposure group was used to obtain a dose-response model. In this group, Brown and Chu (1983c) estimated that the respiratory cancer rate for an individual first exposed at age t_o for a duration of d years would be

$$r(d,t_o) = .603 \times 10^{-13} [(d + t_o)^{5.8} - t_o^{5.8}]. \qquad (14)$$

Only limited information exists concerning the time-weighted exposure of workers in the light exposure areas. Arsenic concentrations in several light

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TABLE 7-27. OBSERVED AND EXPECTED LUNG CANCER DEATHS AND PERSON-YEARS BY LEVEL OF EXPOSURE, DURATION OF EMPLOYMENT, AND AGE AT INITIAL EMPLOYMENT

Age at Initial Employment		Duration of Employment (years) 0-9	10-19	20-29	30-39	40+
High Exposure Level Group						
<20	Obs	0	0	0	3	0
	Exp	0.001	0.009	0.065	0.249	0.193
	Pyr	206	408	588	499	172
20-29	Obs	0	0	2	0	2
	Exp	0.008	0.051	0.164	0.277	0.082
	Pyr	624	637	495	308	64.4
30-39	Obs	0	0	3	0	0
	Exp	0.030	0.077	0.106	0.053	0.001
	Pyr	398	207	155	59.1	0.86
40-49	Obs	0	0	0	0	0
	Exp	0.083	0.054	0.034	0.007	0.0
	Pyr	210	80.0	49.1	6.88	0.0
50+	Obs	0	0	0	0	0
	Exp	0.066	0.027	0.0	0.0	0.0
	Pyr	78.0	23.2	0.0	0.0	0.0
Medium Exposure Level Group						
<20	Obs	0	0	1	4	1
	Exp	0.010	0.039	0.171	0.591	0.597
	Pyr	1801	1763	1500	1206	579
20-29	Obs	0	0	2	4	7
	Exp	0.035	0.118	0.331	0.717	0.514
	Pyr	2636	1622	1099	951	654
30-39	Obs	0	0	1	3	0
	Exp	0.167	0.473	0.329	0.161	0.045
	Pyr	1939	1137	438	194	68.2
40-49	Obs	0	0	1	3	0
	Exp	0.167	0.414	0.098	0.010	0.0
	Pyr	1190	448	98.9	12.1	0.0
50+	Obs	1	0	0	0	0
	Exp	0.262	0.076	0.011	0.0	0.0
	Pyr	295	71.2	14.5	0.0	0.0

TABLE 7-27. (continued)

Age at Initial Employment		Duration of Employment (years) 0-9	10-19	20-29	30-39	40+
Low Exposure Level Group						
<20	Obs	0	0	1	1	3
	Exp	0.056	0.117	0.478	1.59	1.57
	Pyr	8524	5249	4038	3175	1376
20-29	Obs	0	0	2	5	6
	Exp	0.115	0.334	0.892	1.74	0.796
	Pyr	9951	4724	2965	2117	834
30-39	Obs	0	3	1	0	1
	Exp	0.390	0.802	0.937	0.662	0.062
	Pyr	5218	2218	1364	715	74.6
40-49	Obs	2	1	1	1	0
	Exp	1.29	1.18	0.344	0.035	0.001
	Pyr	3703	1319	386	52.7	2.00
50+	Obs	3	2	0	0	0
	Exp	1.62	0.385	0.041	0.0	0.0
	Pyr	1945	371	65.4	0.0	0.0

Source: Brown and Chu (1983a).

exposure areas, as given in a NIOSH criteria document (1975), are shown in Table 7-28.

In the absence of information to the contrary, it is assumed that the person-hours spent in each area are equal. Thus an estimate of the time-weighted average for workers in the light exposure category is

$$1/3 \times .7 + 1/3 \times .17 + 1/3 \times .004 = .291 \text{ mg As/m}^3.$$

Under the linear assumption, equation 14 may be expressed in terms of mg As/m^3 working exposure by dividing by .291, which gives the result

$$r(d,t_o) = 2.07 \times 10^{-13} [(d + t_o)^{5.8} - t_o^{5.8}]. \qquad (15)$$

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TABLE 7-28. ARSENIC EXPOSURES: 1965 SMELTER SURVEY ATMOSPHERIC ARSENIC CONCENTRATIONS (mg/As/m^3)

"Heavy exposure area" as classified by Lee and Fraumeni

Arsenic Roaster Area		Mean: 1.47
0.10	0.20	Median: 0.185
0.10	0.22	
0.10	0.25	
0.10	0.35	
0.10	1.18	
0.10	5.00	
0.17	12.66	

"Medium exposure areas" as classified by Lee and Fraumeni

Reverberatory Area		Mean: 1.56
0.03	0.93	Median: 0.88
0.22	1.00	
0.23	1.27	
0.36	1.60	
0.56	1.66	
0.63	1.84	
0.66	1.94	
0.76	2.06	
0.78	2.76	
0.78	3.40	
0.80	4.14	
0.83	8.20	
Treater Building and Arsenic Loading		Mean: 1.50
0.10	0.48	Median: 0.295
0.10	0.62	
0.10	3.26	
0.11	7.20	

"Light exposure areas" as classified by Lee and Fraumeni

Copper Concentrate Transfer System		Mean: 0.70
0.25		Median: 0.65
0.65		
1.20		
Samples from Flue Station		Mean: 0.17
0.10		Median: 0.17
0.24		
Reactor Building		Mean: 0.004
0.001	0.003	Median: 0.002
0.002	0.009	
0.002	0.010	
0.002		

Source: Table X-3, NIOSH Criteria Document (1975).

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In this case, exposure is expressed in mg As/m^3 per 8-hr working day. To change the relationship so that it expresses the risk due to a lifetime of continuous exposure to 1 ug As/m^3, we assume 240 days worked per year, one mg As/m^3 on the job gives the same cumulative exposure as 10^3 x $1/3 \times \frac{240}{365} = 219$ µg As/m^3 continuous exposure.

The age-specific rate due to a continuous 1 µg As/m^3 exposure is obtained by substituting $t_o = 0$ and $d = t$ = age into equation (15) and dividing by 219 to arrive at the correct number of exposure units. This gives the result

$$r(t) = 9.45 \times 10^{-16} \, t^{5.8}. \qquad (16)$$

The unit risk is approximately equivalent to the risk of induced respiratory cancer in the median life span. Based upon 1976 U.S. vital statistics, the median life span is 76.2 years, so that the unit risk is expressed approximately as

$$p \simeq \int_o^{76.2} 9.45 \times 10^{-16} \, t^{5.8} = \frac{9.45}{6.8} (76.2)^{6.8} \times 10^{-16} = 8.71 \times 10^{-4}. \qquad (17)$$

An additional approximation consistent with the previous unit calculations is obtained by assuming that

$$r(t) = 9.45 \times 10^{-16} \left[\frac{t_j + t_{j-1}}{2}\right]^{5.8} \quad t_{j-1} < t < t_j \qquad (18)$$

where t_j are the ages at the interval boundaries given in U.S. vital statistics records. This assumes that the age-specific death rate due to the exposure is constant throughout the interval and equal to the true value at the midpoint of the interval. Under this approximation, using 1976 vital statistics, the unit risk is estimated to be $P \simeq 1.25 \times 10^{-3}$.

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Evaluation of Goodness-of-Fit. It is desirable to assess whether the data for the low-exposure group is consistent with the model utilized to estimate the unit risk. However, two factors tend to create a situation that would decrease this goodness-of-fit and bias the results. First, the exact values for each cell of $\bar{d}$, $\bar{t}_o$ are presently not available. Second, the value of k was determined on the basis of all three exposure groups, and does not give as good a fit as would be obtained using the low-exposure group alone.

Brown states (personal communication, 1983) that the exact values of $\bar{d}, \bar{t}_o$ are very close to the midpoint of the interval, and that the values of k appear to be statistically consistent between exposure groups. Thus, distortions of the data because of the use of midpoint values and average k, although inevitable, are not appreciable.

The expected number of cases in each cell are calculated using the relationship

$$E = Exp + Pyr \times .603 \times 10^{-13} [(d + t_o)^{5.8} - t_o^{5.8}], \qquad (19)$$

in which Exp and Pyr are taken from Table 7-27 and d, t_o are the midpoints of the intervals. These results are shown in Table 7-29. A standard chi-square goodness-of-fit test is then run, resulting in a chi-square value of $X^2_{21} = 13.85$ with $23.2 = 21$ degrees of freedom and an associated p-value of .88. Unfortunately, due to the low expected number of cases in many of the cells, the X^2 approximation is of questionable validity for this situation.

To obtain a more stable approximation, cells with low frequency that are as close as possible to each other are usually combined. It is important to have some criteria for combining the data that do not depend upon inspection of the data itself. Two methods of combining the data are used here. The first is across columns (duration exposed), so that the maximum number of

TABLE 7-29. OBSERVED AND EXPECTED NUMBER OF RESPIRATORY CANCER DEATHS FOR EACH CELL IN THE LOW-EXPOSURE GROUP OF TABLE 7-27

	d				
t_o	5	15	25	35	45
18	0 .088	0 .314	1 1.20	1 3.504	3 3.836
25	0 .258	0 .858	2 2.145	5 4.358	6 3.321
35	0 .723	3 1.641	1 2.556	0 2.791	1 .497
45	2 2.023	1 2.508	1 1.428	1 .371	0 .026
55	3 2.582	2 1.234	0 .418		

$X^2_{21} = 13.85$, $p = .88$

cells are obtained, with the constraints that combined cells must have at least three expected cases, and that all cells combined are consecutive within a row. The second approach uses the same technique within a column (age first exposed). The results are shown in Tables 7-30 and 7-31 respectively, giving chi-square values of 7.01 and 7.61, with p-values of .41 and .38. Thus the assumed model is shown to be consistent with the observed low-exposure data.

7.3.2.2.4 The Enterline and Marsh (1982) study. This study included all men (2802 in all) employed at the Tacoma, Washington copper smelter for a year or more during 1940-1964. Their mortality experience was observed through 1976. The study involved over 70,000 person-years of observation, and 104 deaths from cancer of the respiratory system were recorded (Table 7-32). Respiratory cancer deaths had an SMR of 189.4, which was significantly increased at the 1 percent level. Expected deaths for Table 7-32 were based upon U.S. white

TABLE 7-30. CELLS FROM TABLE 7-29 COMBINED WITHIN ROWS TO OBTAIN CELLS WITH THREE OR MORE EXPECTED RESPIRATORY CANCER DEATHS

	d				
t_o	5	15	25	35	45
18				2 5.106	3 3.836
25			2 3.261	5 4.358	6 3.321
35			4 4.920		1 3.288
45					5 6.356
55			5 4.234		

$X^2 = 7.01$, $p = .41$

TABLE 7-31. CELLS FROM TABLE 7-29 COMBINED WITHIN COLUMNS TO OBTAIN CELLS WITH 3 OR MORE EXPECTED RESPIRATORY CANCER DEATHS

	d				
t_o	5	15	25	35	45
18				1 3.504	3 3.836
25			3 3.345	5 4.358	
35					
45				1 3.162	7 3.844
55	5 5.674	6 6.555	2 4.402		

$X^2 = 7.61$, $p = .38$

TABLE 7-32. OBSERVED DEATHS AND SMRs FOR 2802 SMELTER WORKERS WHO WORKED A YEAR OR MORE 1940-64, FOLLOWED THROUGH 1976, BY CAUSE OF DEATH

Cause of death (7th revision code)	Observed Deaths	SMR
All causes of death	1061	103.2
Tuberculosis (001-019)	4	27.6**
Malignant neoplasms (140-148)	231	123.6**
Buccal cavity and pharynx (140-148)	7	110.7
Digestive organs & peritoneum (150-159)	65	108.9
Esophagus (150)	3	66.2
Stomach (151)	17	122.1
Large intestine (153)	21	120.4
Rectum (154)	9	122.4
Biliary passages and liver (155-156)	3	64.1
Pancreas (157)	11	106.0
All other digestive organs (residual)	1	71.6
Respiratory system (160-164)	104	189.4**
Larynx (161)	2	67.7
Bronchus, trachea, and lung (162-163)	100	194.9**
All other respiratory system (residual)	2	305.0
Prostate (177)	11	79.0
Testes and other genital (178-179)	1	92.6
Kidney (180)	6	133.3
Bladder and other urinary organs (181)	4	63.0
Malignant melanoma of skin (19)	0	--
Eye (192)	1	492.7
Central nervous system (193)	3	59.8
Thyroid gland (194)	0	--
Bone (196)	2	175.0
Lymphatic & haematopoietic (200-205)	17	93.8
Lymphosarcoma and reticulosarcoma (200)	4	93.2
Hodgkins' disease (201)	2	83.9
Leukemia and aleukemia (204)	6	78.7
Other lymphopoietic tissue (202, 203, 205)	5	130.4
Other malignant neoplasms (residual)	10	82.3
Benign neoplasms (210-239)	2	78.6
Diabetes mellitus (260)	12	84.8
Stroke (333-334)	91	111.4
Heart disease (400-443)	412	92.5
Hypertension without heart disease (444-447)	1	18.8
Nonmalignant respiratory disease (470-527)	60	108.6
Influenza and pneumonia (480-493)	24	92.9
All other respiratory diseases (residual)	36	122.4
Ulcer of stomach and duodenum (540-541)	7	75.5
Cirrhosis of liver (581)	22	101.9
Chronic nephritis (592)	6	87.5
External causes of death (800-998)	81	94.2
Accidents (899-962)	61	100.6
Suicides (963, 970-979)	17	84.8
Other external causes (residual)	3	56.2
Other causes of death (residual)	85	86.1
Unknown causes	47	--

* $p < .05$, ** $p < .01$
Source: Enterline and Marsh (1982).

male mortality rates. The respiratory cancer SMR increases to 198.1 when Washington State mortality rates are applied.

Enterline and Marsh estimated individual exposures to airborne arsenic using individual work histories, urine arsenic measurements, and an estimated correlation between exposure to airborne arsenic and resulting levels of arsenic in urine. Average urine arsenic levels were available by department for the years 1948-52, 1973, 1974, and 1975. Linear interpolations were used to estimate levels between 1952 and 1973. Levels during 1949-1952 were assumed to hold prior to that time. By coupling these data with employee work histories, Enterline and Marsh estimated individual cumulative exposures for various times in units of μg-years/ℓ urinary arsenic.

Pinto et al. (1977) compared airborne concentrations of arsenic with urinary arsenic levels for 24 workers wearing personal air samplers for 5 successive days. A regression analysis of these data showed a highly significant linear correlation between airborne and urinary arsenic ($p < 0.01$). Average airborne arsenic in units of μg/m^3 was estimated to be 0.304 times average urinary arsenic levels in units of μg/ℓ.

To investigate dose-response, Enterline and Marsh divided the total person-years of observation into 5 groups by cumulative arsenic exposure (0 lag), and also by cumulative arsenic exposure up to 10 years prior to the year of observation (10-year lag). In this type of analysis, as a worker continues to be exposed to arsenic, he or she will contribute person-years to progressively higher exposure categories. The numbers of respiratory cancer deaths and corresponding expected numbers for each of these groups are given in Table 7-33. In this table, urinary arsenic levels provided by Enterline and Marsh have been converted to airborne exposures in μg/m^3-years, using the factor 0.304 estimated by Pinto et al. (1977). The observed numbers of cancers are all significantly increased at the higher exposure levels.

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TABLE 7-33. DATA FROM TABLE 8 OF ENTERLINE AND MARSH (1982) WITH PERSON-YEARS OF OBSERVATION ADDED

Cumulative Exposure[a] $\mu g/m^3$-years	Person-Years of Observation[b]	Observed Deaths	Expected Deaths
	0 Lag		
91.8	10902	8	4.0
263	21642	18	11.0
661	14623	21	10.3
1381	13898	26	14.1
4091	9398	31	12.7
	10-Year Lag		
91.8	27802	10	6.4
263	16453	22	12.5
661	11213	26	11.5
1381	9571	22	12.4
4091	5423	24	9.7

[a]Exposures are in $\mu g/m^3$-years estimated by the formula (I $\mu g/l$-years) (0.304) where I is mean urinary exposure index from Enterline and Marsh (1982) Table 8 and 0.304 is the relation between urinary and airborne arsenic estimated by Pinto et al. (1977).

[b]Furnished by Dr. Enterline (personal communication).

Although the Enterline and Marsh (1982) study is not as large as that of Lee-Feldstein (1983), it does involve a sizable number of respiratory cancer deaths (104). Workers were followed for an extended period--an average of 25 years per individual. Several features of the analysis render it more amenable to quantitative risk estimation than the analysis used by Lee-Feldstein. Enterline and Marsh made estimates of individual exposure histories, whereas Lee-Feldstein did not. The type of dose-response analysis used by Enterline and Marsh is also more suitable for quantitative risk estimation. The exposure estimates based on a 10-year lag probably yield a more realistic dose response than those that do not utilize a lag. Because the latency period for respiratory cancer is generally greater than 10 years (cf. Doll and Peto,

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1978), exposure during the last 10 years prior to observation would not be expected to affect respiratory cancer mortality.

By applying urinary arsenic measurements made during the years 1948-52 to earlier years, Enterline and Marsh probably underestimated exposures prior to 1948. This would result in an overestimate of the carcinogenic potency of arsenic. A calculation by Enterline and Marsh of SMRs by both year of hire and cumulative exposure indicates that workers in a given cumulative exposure category tend to have at least roughly comparable SMRs irrespective of the year of hire. This suggests that exposure estimates for earlier years are not greatly in error. However, further investigation of this problem would be useful.

Because smoking is also an important risk factor for respiratory cancer, it would have been helpful if data on smoking habits had been available for analysis. Pinto and Enterline (undated) report on smoking histories obtained in 1975 from 550 active employees at the Tacoma smelter. Of these employees, 59.6 percent were active smokers, compared to 45.4 percent in 1970 for U.S. males aged 21-64. If this excess of smokers holds in general for the smelter workers, then a small fraction of the excess in respiratory cancer could have been due to smoking.

Development of risk estimates: The data from Table 7-33 were used for quantitative risk assessment. The relative risks (observed/expected) from this table are graphed in Figures 7-6 and 7-7, and the absolute risks ([observed- expected]/person-years) in Figures 7-8 and 7-9. Although there is no clear trend of increasing SMRs with increasing exposures, such a trend is present for absolute risk. Results of applying chi-square goodness-of-fit tests of the relative- and absolute-risk models with $k = 1$ and $k = 2$ are recorded in Table 7-25. The maximum likelihood estimates of the carcinogenic

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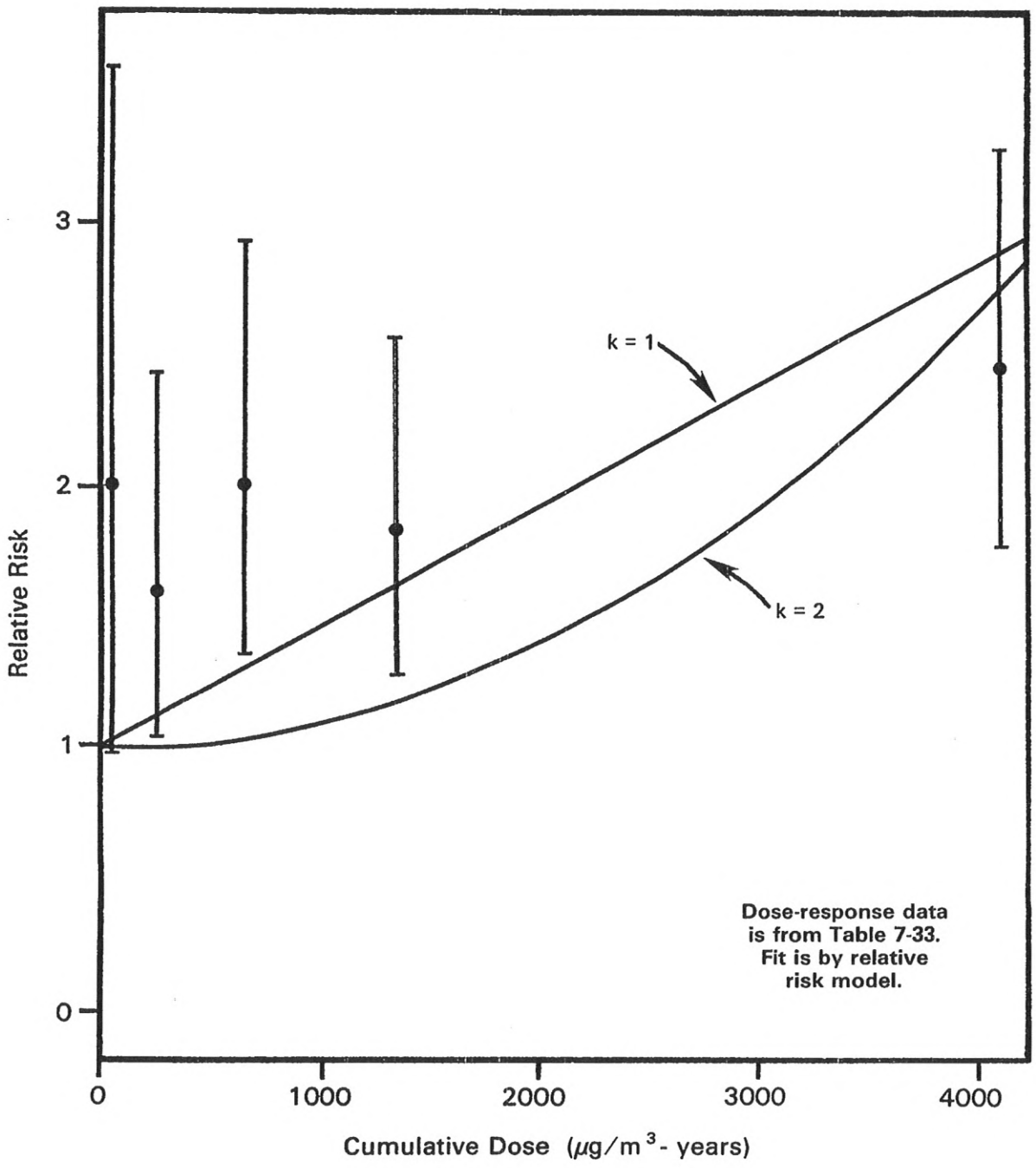

Figure 7-6. Relative risks and 90% confidence limits for zero-lag data of Enterline and Marsh (1982).

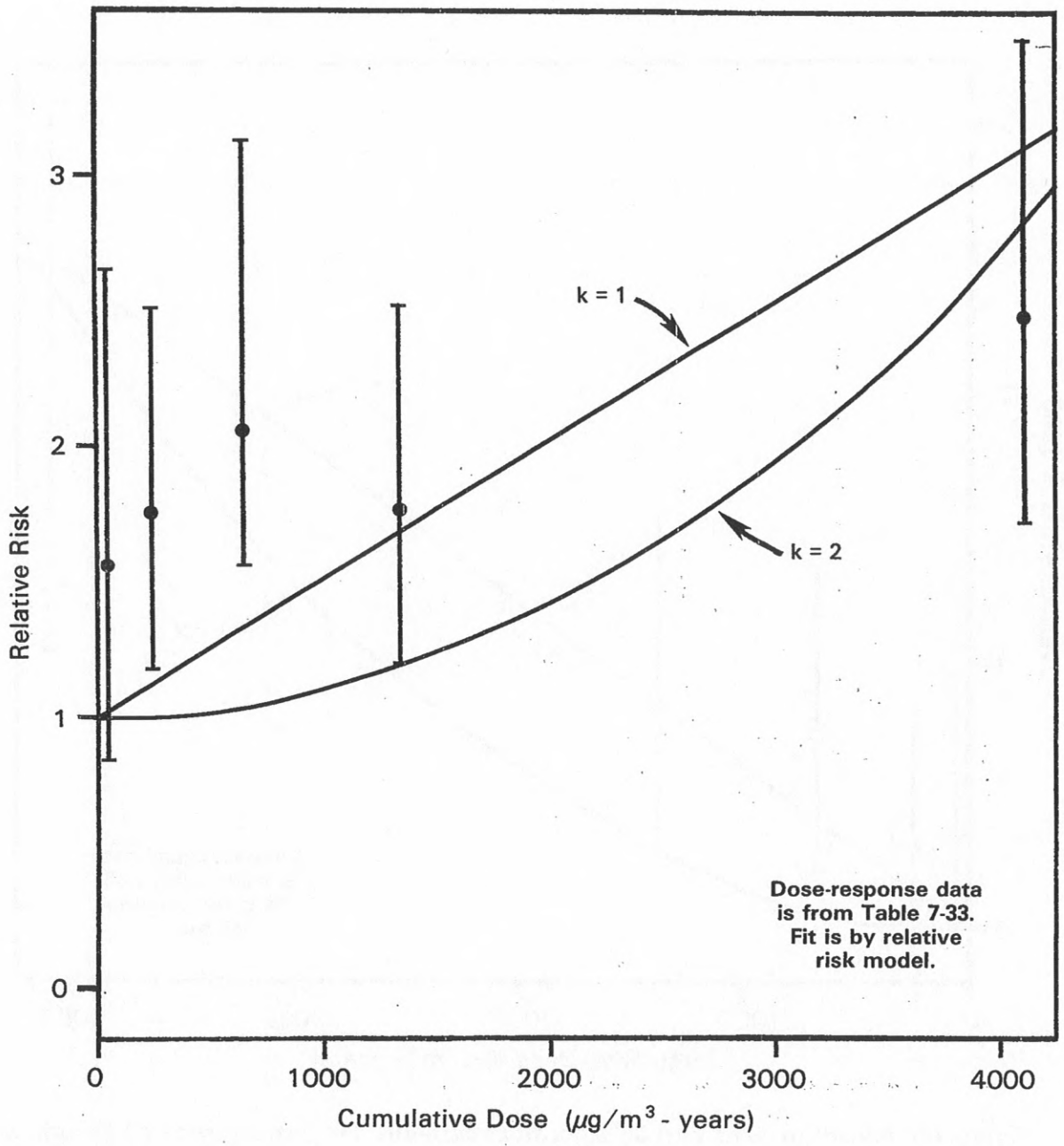

Figure 7-7. Relative risks and 90% confidence limits for 10 year lag data of Enterline and Marsh (1982).

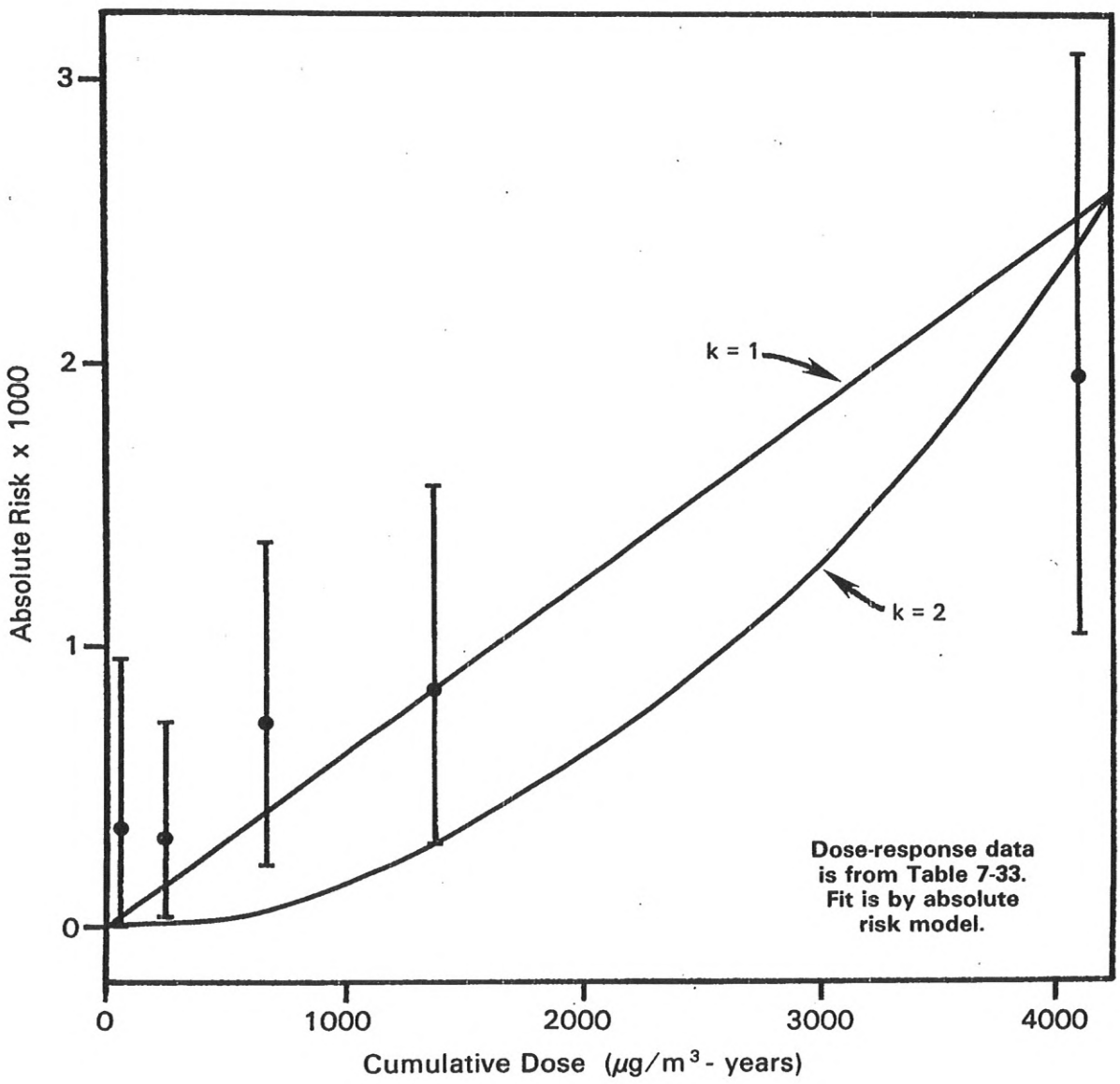

Figure 7-8. Absolute risks and 90% confidence limits for zero-lag data of Enterline and Marsh (1982).

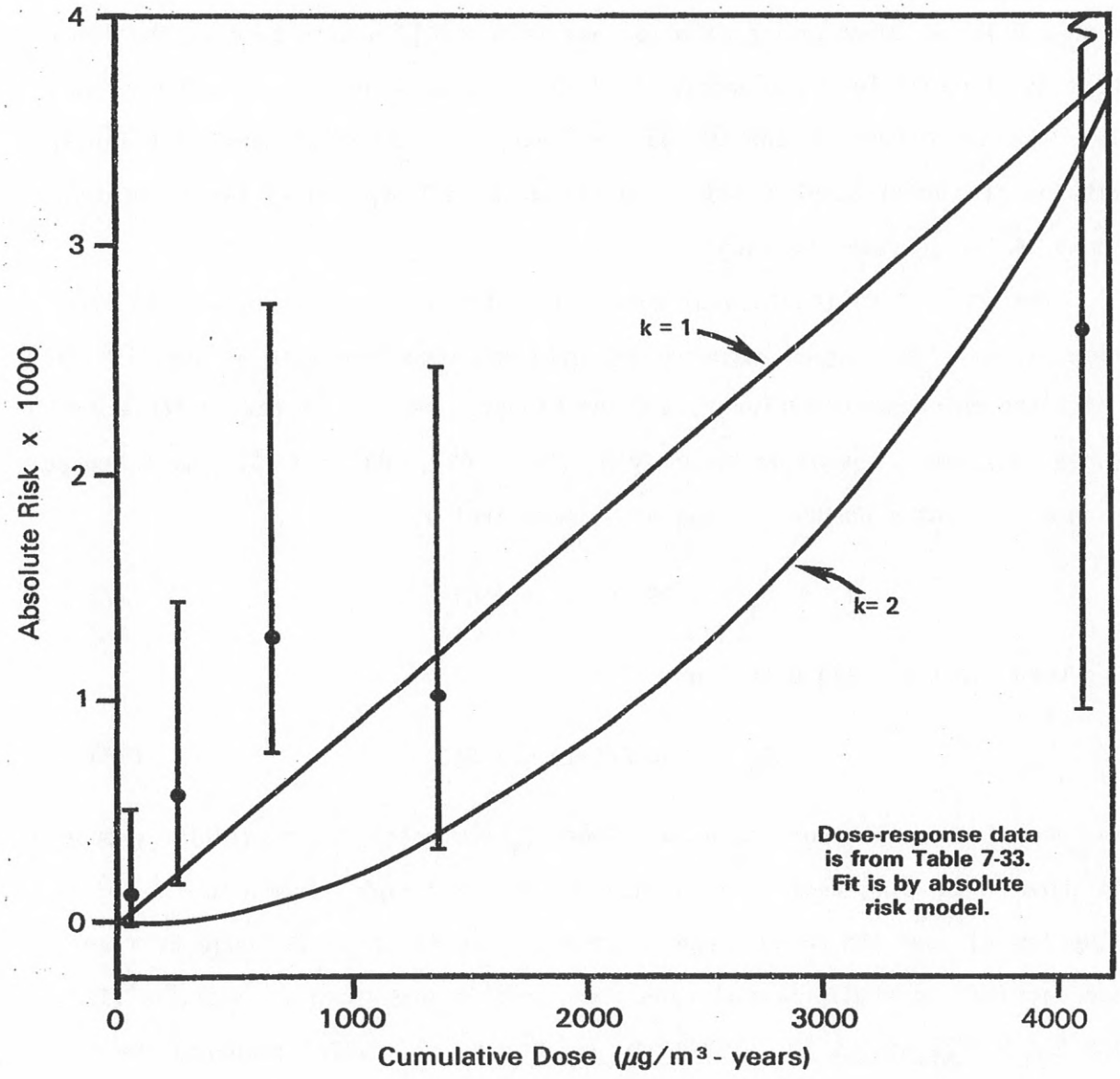

Figure 7-9. Absolute risks and 90% confidence limits for 10 year lag data of Enterline and Marsh (1982).

potency parameter a' are also listed in Table 7-25. The maximum-likelihood fits of these models are graphed in Figures 7-6 through 7-9. The quadratic fit (k = 2) is poor for both the absolute- and relative-risk models with either 0 lag or 10-year lag data (p less than 0.001 in each case). The linear fits to the relative-risk models are also relatively poor (p = 0.02 for the 0 lag data and 0.006 for the 10-year lag data). On the other hand, the linear fits of the absolute-risk model are all acceptable (p = 0.24 for 0 lag data and 0.14 for 10-year lag data).

The unit risks (additional risks of respiratory cancer death from lifetime exposure to 1 $\mu g/m^3$ airborne arsenic) obtained from each of the fits for which the chi-square p-value is 0.01 or higher, are also listed in Table 7-25. These risks were estimated by applying (1) or (2), (8), and (9) with D_i based upon a constant exposure of 1 $\mu g/m^3$. Specifically,

$$D_i = 4.56[5(i-1) + 2.5] \qquad (17)$$

was used for the 0 lag data, and

$$D_i = 4.56[5(i-1) - 7.5] \qquad (18)$$

was used for the 10-year lag data. These D_i represent the cumulative exposure in $\mu g/m^3$ resulting from a constant exposure to 1 $\mu g/m^3$ from birth to the midpoint of the ith 5-year age interval. The factor 4.56 converts from occupational to environmental exposures, and is explained at equation (11).

7.3.2.2.5 The Ott et al. (1974) study. Ott et al. (1974) compared the age-specific death patterns of 174 decedents exposed to arsenic in the production of pesticides to those of 1809 decedents who were not exposed to arsenicals. By fitting the death patterns of the unexposed decedents to a mathematical function, an estimate was obtained of the probability that a death at a parti-

cular age and during a particular epoch was due to respiratory cancer. This function was used to estimate expected respiratory cancer deaths in various exposure categories for the exposed decedents. Cumulative exposures were estimated for exposed decendents, using work histories and estimates of average exposures in various jobs. The exposure estimates were made by industrial hygienists familiar with the processes. Expected cancer deaths were compared with observed to obtain observed-to-expected ratios. Table 7-34 shows the results of Ott et al.'s dose-response analysis. The data in this table are all reproduced directly from Table 4 of Ott et al. (1974), except for the cumulative exposures. Average total exposures in mg provided by Ott et al. were converted to cumulative exposures in $\mu g/m^3$ years by multiplying by the factor

$$\frac{1000\ \mu g/mg}{(4\ m^3/day)(21\ days/mo)(12\ mo/year)} \qquad (19)$$

TABLE 7-34. DATA FROM TABLE 4 OF OTT ET AL. (1974)

Cumulative Exposure[a] $\mu g/m^3$-years	Observed Deaths	Expected Deaths
41.8	1	1.77
125	2	1.01
250	4	1.38
417	3	1.36
790	3	1.70
1544	2	0.97
3505	3	0.77
6451	5	0.79
29497	5	0.72

[a]Exposures are in $\mu g/m^3$-years estimated by:

$$\frac{d\ mg \times 1000\ \mu g/mg}{(4\ m^3/day)(21\ days/month)(12\ months/year)}$$

where d is average total exposure from Table 4 of Ott et al.

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The values included in this factor are not in doubt because use of the factor simply negates the calculation of total exposure made by Ott et al.

Decedent studies such as this are more subject to bias then prospective studies such as those of Lee-Feldstein (1983) and Enterline and Marsh (1982). If, for example, in some age category arsenic exposure increased the mortality from some other disease in addition to respiratory cancer, an analyis of decedents might show an artificially low effect of arsenic upon respiratory cancer for this age group (because there might be an artificially large number of total deaths). It is also of some concern that Ott et al. did not clearly describe how the study cohort was defined.

This study involved primarily short-term exposures, as less than 25 percent of the decedents had worked with arsenicals for more than one year. Thus, this study is less appropriate for estimating risks from lifetime environmental exposure than a comparable study involving longer exposures. The study also was quite small; only 28 respiratory cancer deaths occurred among exposed decedents.

Development of risk estimates: The dose-response data in Table 7-34 were used in an assessment of risk. Because of the nature of the study, only a relative risk model could be applied to these data. The dose-response for relative risk is graphed in Figure 7-10. The response in the most highly exposed group falls far below that predicted by the lower-dose data and is omitted from Figure 7-10. This is possibly due to the fact that some of the more highly exposed workers wore respirators. Because of this shortfall in response, and also because the exposures to this group were the furthest from the low-level environmental exposures of interest, the data from the highest exposure group were omitted from the analysis.

Results of applying chi-square goodness-of-fit tests of the relative-risk model with $k = 1$ and $k = 2$ are listed in Table 7-25. The maximum-likelihood

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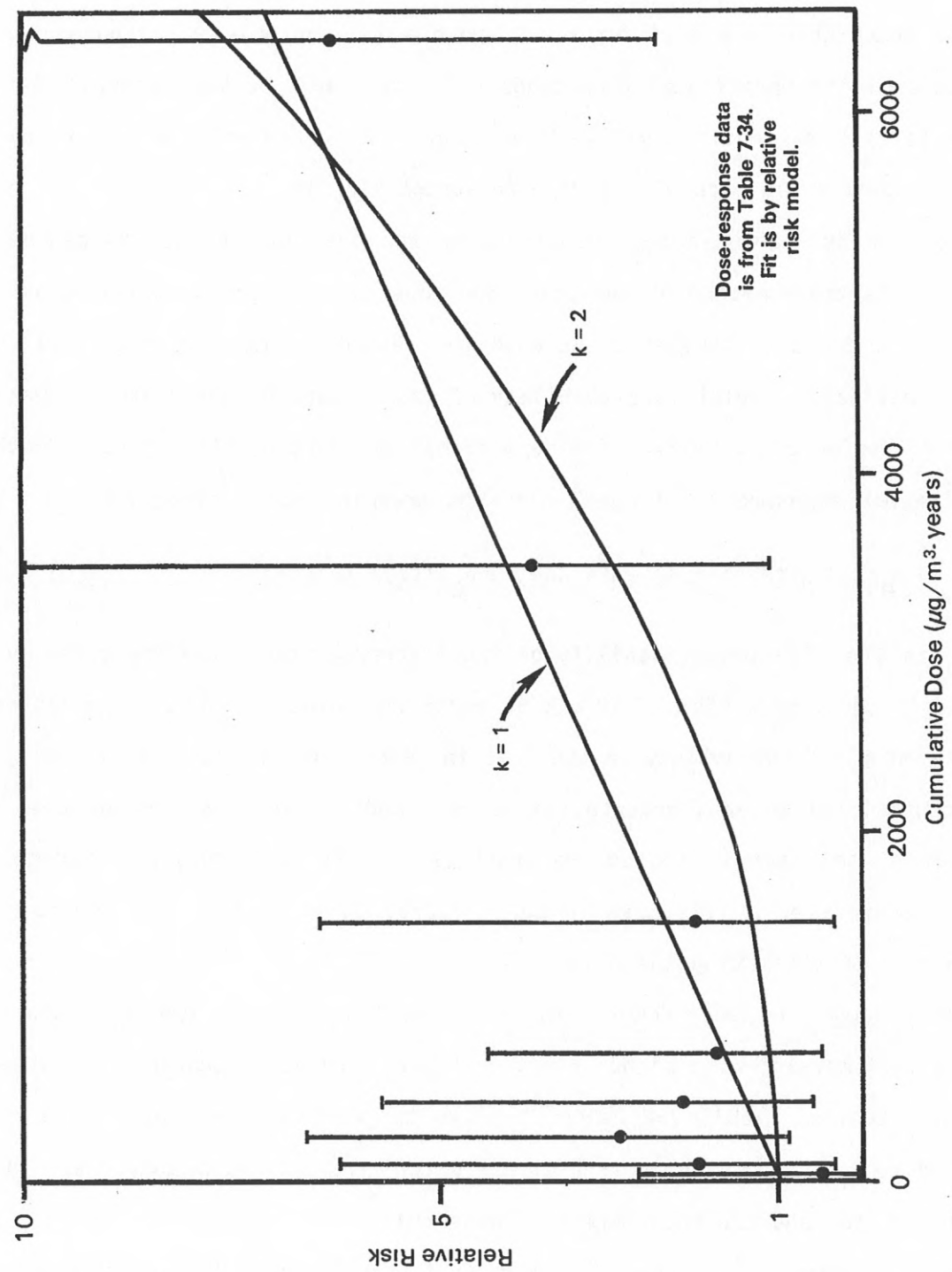

Figure 7-10. Relative risks and 90% confidence limits for data of Ott et al. (1974) with highest exposure group omitted.

estimates of the carcinogenic potency parameter a' are also listed in this table. The maximum-likelihood fits are graphed in Figure 7-10. Both of these fits are acceptable ($p = 0.66$ for $k = 1$ and $p = 0.23$ for $k = 2$), although the data appear to be more linear than quadratic. It should be kept in mind that the sample size was quite small in this study, and consequently a wide range of curve shapes would probably provide an acceptable fit.

The risk estimation method described in the previous section is based upon the life table method of analysis, and does not seem particularly appropriate for a decedent analysis. Because the method employed by Ott et al. seems to estimate a relative probability of respiratory cancer death, it was decided to estimate the extra lifetime probability of respiratory cancer death from lifetime exposure to d $\mu g/m^3$ airborne arsenic, using the expression

$$P_0(1 + a'[(72)(4.56)d]^k) - P_0 = P_0 a'[(72)(4.56)]^k. \qquad (20)$$

Here P_0 is the lifetime probability of respiratory cancer mortality given by (8), and is equal to 0.0451 if 1976 U.S. mortality rates are used. The factor 72 represents life expectancy in the U.S. in years. The factor 4.56 converts from occupational to environmental exposures, and is explained at equation (11). Thus, the term in the square brackets in (20) represents the average total exposure over a life span in $\mu g/m^3$ years, which is the same as the measure used in estimating the potency a'.

7.3.2.3 Discussion--Table 7-25 summarizes the fits of both absolute- and relative-risk models, with either $k = 1$ or $k = 2$, to dose-response data from 4 different studies. Table 7-25 also displays the carcinogenic potencies a'. It should be noted that the potencies estimated from different models are in different units, and are therefore not comparable.

In every case, a linear model ($k = 1$) fitted the data better than the corresponding quadratic model ($k = 2$). In every case but two, the fits of the

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quadratic model could be rejected at the 0.01 level. The two exceptions involved the two smallest data sets (Higgins et al. absolute risk, and Ott et al.) and in the former case the fit was very marginal ($p = 0.017$). On the other hand, for each data set a linear model provided an adequate fit. Also, in every case, an absolute-risk linear model fit the data better than the corresponding relative-risk linear model. The p-values for the fits of the absolute-risk linear model ranged from 0.025 to 0.75.

The estimated unit risk is presented for each fit for which the chi-square goodness-of-fit p-value is greater than 0.01. The unit risks derived from linear models--8 in all--range from 0.0013 to 0.0136. The largest of these is from the Ott et al. study, which probably is the least reliable for developing quantitative estimates, and which also involved exposures to pentavalent arsenic, whereas the other studies involved trivalent arsenic. The unit risks derived from the linear ($k = 1$) absolute-risk models are considered to be the most reliable; although derived from 5 sets of data involving 4 sets of investigators and 2 distinct exposed populations, these estimates are quite consistent, ranging from 0.0013 to 0.0076.

To establish a single point estimate, the geometric mean for data sets is obtained within distinct exposed populations, and the final estimate is taken to be the geometric mean of those values. This process is illustrated in Table 7-35.

The final estimate is 4.29×10^{-3}, where exposure is in $\mu g/m^3$ of continuous exposure. Based upon an assumed 20 m^3 tidal volume of air and a 30 percent absorption rate, this amounts to a unit risk of $4.29 \times 10^{-3} \div (.3 \times 20 \times .001/70) = 50.1$ in units of mg/kg absorbed dose per day.

Although the estimates derived from the various studies are quite consistent, there are a number of uncertainties associated with them. The estimates

TABLE 7-35. COMBINED UNIT RISK ESTIMATES FOR ABSOLUTE-RISK LINEAR MODELS

Exposure Source	Study	Unit Risk	Geometric Mean Unit Risk	Final Estimated Unit Risk
Anaconda smelter	Brown & Chu	1.25×10^{-3}		
	Lee-Feldstein	2.80×10^{-3}	2.56×10^{-3}	
	Higgins	4.90×10^{-3}		4.29×10^{-3}
ASARCO smelter	Enterline & Marsh	6.81×10^{-3}		
		7.60×10^{-3}	7.19×10^{-3}	

were made from occupational studies that involved exposures only after employment age was reached. In estimating risks from environmental exposures throughout life, it was assumed, through either the relative-risk model (1) or the absolute-risk model (2), that the increase in the age-specific mortality rates of lung cancer was a function only of cumulative exposures, irrespective of how the exposure was accumulated. Although this assumption provides an adequate description of all of the data, it may be in error when applied to exposures that begin very early in life. Similarly, the linear models possibly are inaccurate at low exposures, even though they provide excellent descriptions of the experimental data.

The risk assessment methods employed were severely constrained by the fact that they were based only upon the analyses performed and reported by the original authors--analyses that had been performed for purposes other than quantitative risk assessment. For example, although other measures of exposure might be more appropriate, the analyses were necessarily based upon cumulative dose, since that was the only usable measure reported. Given greater access to the data from these studies, other dose measures, as well as models other than the simple relative-risk and absolute-risk models, could be

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studied. It is possible that such wide analyses would indicate that other approaches are more appropriate than the ones applied here.

7.3.3 Unit Risk for Water

The best data available for making quantitative cancer risk estimates for ingestion of arsenic in water are the data collected by Tseng et al. (1968). They surveyed a stable population of 40,421 individuals who lived in a rural area along the southwest coast of Taiwan and who were known to have consumed drinking water containing arsenic. The occurrences of skin cancer among this population, and the arsenic concentrations in their drinking water, were measured. Since the population was stable, the study can be viewed as a lifetime feeding study, and the data may be used to predict the lifetime probability of skin cancer caused by the ingestion of arsenic.

A model estimating the cancer rate as a function of drinking water arsenic concentration was generated using information from the above study in its published form, which is a summary of data collected by the investigators. If the original data had been available, a more exact mathematical analysis would have been possible.

Doll (1971) has suggested that the relationship between the incidence of some site-specific cancers, age, and exposure level of a population may be expressed as:

$$I(x,t) = kBx^m t^{k-1} \qquad (21)$$

where x is the exposure level (which can be measured by the water concentration in ppm), t is the age of the population, and B, m, k are unknown parameters.

However, the data collected by Tseng et al. (1968) was obtained at one point in time, and since skin cancer has only a marginal effect on the death

rate, the obtained rates may be viewed more accurately as the probability of having contracted skin cancer by time t. The relationship between this probability, often referred to as the cumulative probability density or prevalence F(x,t), and the incidence or age-specific or hazard rate, may be expressed as:

$$F(x,t) = 1 - \exp\left[-\int_0^t I(x,s)\, ds\right]. \qquad (22)$$

Utilizing equation (21) as the form of the incidence rate, the prevalence may be expressed as

$$F(x,t) = 1 - \exp\left(-Bx^m t^k\right), \qquad (23)$$

which is a Weibull distribution.

In Table 7-36, adapted from information in Tseng, et al. (1968), estimates are given of F(x,t) for different age and water concentration groupings for males. The prevalence for females is less than for males, and therefore is not used to estimate risk.

To use this data, specific values for x and t had to be obtained for the intervals. Where the intervals were closed, the midpoint was utilized. For the greater than 0.6 ppm group, the midpoint between 0.6 and the greatest recorded value, 1.8, was taken, resulting in 1.2 ppm. For age 60 or greater, a value of 70 was utilized somewhat arbitrarily, being the same increase over the lower level as that in the other two age intervals. The values for (x,t) to relate to the prevalence estimates are shown in parentheses in Table 7-36.

From equation (23) it follows that

$$\ln(-\ln[1-F(x,t)]) = \ln(B) + m\ln(x) + k\ln(t), \qquad (24)$$

which is multiple-linear in form. Estimating the parameters by the usual least-square techniques, the following relationship is obtained:

TABLE 7-36. AGE-EXPOSURE-SPECIFIC PREVALENCE RATES FOR SKIN CANCER

Exposure in ppm[3]	AGE 20-39 (30)	AGE 40-59 (50)	AGE ≥60 (70)
0 - 0.29 (0.15)	0.0013	0.0065	0.0481
0.30 - 0.59 (0.450)	0.0043	0.0477	0.1634
≥0.6 (1.2)	0.0224	0.0983	0.2553

*Source: Tseng et al. (1968).

[a]Range given by authors. Midpoint is in parentheses.

$$\ln(- \ln[1 - F(x,t)]) = 17.548 + 1.192 \ln(x) + 3.881 \ln(t), \quad (25)$$

which is an excellent fit, having a multiple correlation coefficient of 0.986 and a standard error on the exposure regression m of .138.

Equation (25) may be expressed as

$$F(x,t) = 1\text{-}\exp\text{-}[2.429 \times 10^{-8}(X^{1.192})(t^{3.881})]$$
$$= 1\text{-}\exp\text{-}[X^{1.192}\ H(t)] \quad (26)$$

If the parameter m = 1.192 were in fact equal to 1, then for a given value of t, equation (26) would be "one-hit" in form.

To test this hypothesis (i.e., Ho: m = 1) the student "t" test is used, giving the result:

$$t_6 = \frac{1.192 - 1}{0.138} = 1.391,$$

which is not significant at the 0.1 level. Thus, there is insufficient evidence to reject the hypothesis that the dose-response relationship is "one-hit" even at the 0.1 level. However, a quadratic model would be rejected at the $p<.001$ level.

Fixing m = 1, the following relationship is obtained:

$$F(x,t) = 1 - \exp[-g(t)x] \qquad (27)$$

Transforming this equation to its linear form (as in equation 23) and obtaining the least-square linear estimates of B and v, it is found that:

$$g(t) = \exp(-17.5393)\, t^{3.853}, \text{ where } B = 2.41423 \times 10^{-8}, \; k = 3.853.$$

The data used to obtain these estimates are shown in Table 7-37, and the goodness-of-fit is illustrated in Figure 7-11.

TABLE 7-37. DATA UTILIZED TO OBTAIN PREDICTOR EQUATION AND FIGURE 7-11

ppm Arsenic	Age at Medical Examination	Skin Cancer Prevalence Rate		Transformed Skin Cancer Prevalence Rate	
		F(x,t)		$-\ln(-\ln[1-F(x,t)])=$ $-17.5393 + 3.853\ln t + \ln x$	
x	t	Observed Rate	Expected Rate	Observed	Expected
0.15	30	0.0013	0.0031	6.64474	6.33160
	50	0.0063	0.0127	5.03269	4.36341
	70	0.0481	0.0455	3.00993	3.06695
0.45	30	0.0043	0.0053	5.44699	5.23299
	50	0.0477	0.0375	3.01849	3.26480
	70	0.1634	0.1304	1.72368	1.96834
1.20	30	0.0224	0.0141	3.78739	4.25216
	50	0.0983	0.0969	2.26844	2.28397
	70	0.2553	0.3110	1.22155	0.98751

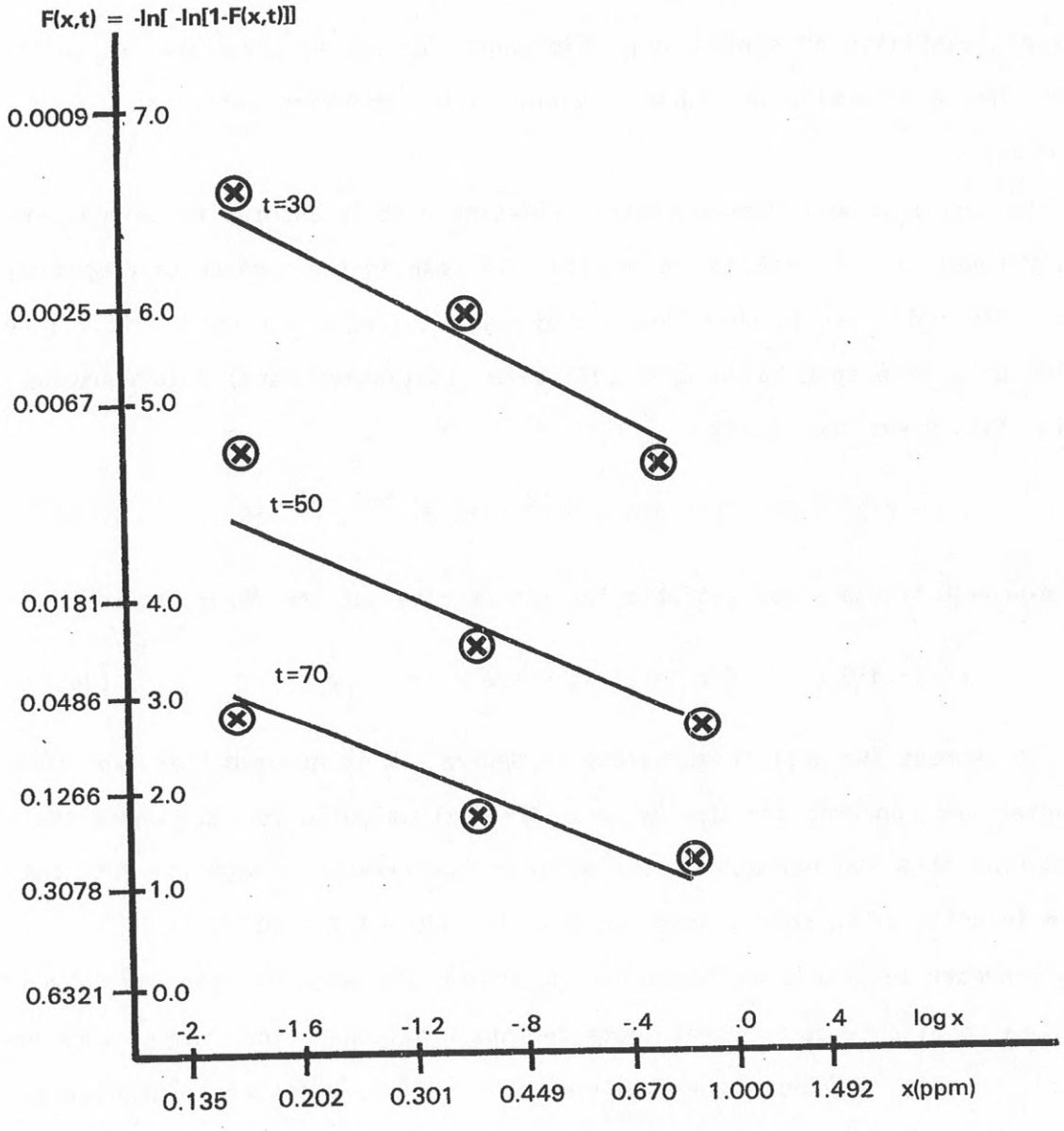

Figure 7-11. Relationship between transformed prevalence and log ppm arsenic in water, log age.

The function

$$F(x,t) = 1-\exp[-2.41423 \times 10^{-8} \times t^{3.853}], \qquad (28)$$

is the probability of contracting skin cancer by age t, given that an individual had a life-time exposure to x ppm in his drinking water (and lived until age t).

To obtain a unit risk estimate, lifetime risk is assumed to be approximately equal to the risk to the median life span in the absence of competing risk. The unit risk is thus obtained by substituting x = 1 and t = 76.2 (the median U.S. life span based upon 1976 vital statistics data) into equation (28). This gives the result

$$P(1) \tilde{=} 1-\exp[-2.414 \times 10^{-8} \times 76.2^{3.853}] = .350 \qquad (29)$$

The exponent is the slope estimate for cancer risks at low doses, so that:

$$P(x) \tilde{=} .430\ x \qquad \text{for small } x, \text{ where } x \text{ is in ppm.} \qquad (30)$$

To express the unit in mg/kg/day exposures, it is assumed that two liters of water are consumed per day by an individual weighing 70 kg. Under the assumption that 100 percent of the arsenic is absorbed through the gut, the slope in units of mg/kg/day absorbed dose is $.430 \div (.2 \div 70) = 15.8$.

A number of potential factors exist that could possibly make the Taiwanese data unsuitable as surrogate data for the U.S. population. Among them are racial, dietary, and nutritional differences. Also, exposure to ergotamine was confounded with arsenic exposure in the well water--a fact which also could have modified the results. However, there is no direct evidence demonstrating the role of these agents in the carcinogenic response to ingested arsenic. Furthermore, a recent extensive review by Andelman and Barnett (1983)

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of the arsenic dose-response model developed here, demonstrates that presently there is no quantitative evidence that is inconsistent with the model. The Andelman and Barnett study also showed that there does not appear to be any population in the U.S. that could be studied that would have a reasonable power to contradict the hypothesis that the Taiwanese dose-response model is consistent with the U.S. dose response.

7.3.4 Relative Potency

One of the uses of the concept of unit risk is to compare the relative potencies of carcinogens. To estimate relative potency on a per-mole basis, the unit risk slope factor is multiplied by the molecular weight, and the resulting number is expressed in terms of $(mMol/kg/day)^{-1}$. This is called the relative potency index.

Figure 7-12 is a histogram representing the frequency distribution of potency indices of 52 chemicals evaluated by the CAG as suspect carcinogens. The actual data summarized by the histogram are presented in Table 7-38. Where human data were available for a compound, they were used to calculate the index. Where no human data were available, animal oral studies and animal inhalation studies were used, in that order. Animal oral studies were selected over animal inhalation studies because they have been made on most of the chemicals, thus allowing potency comparisons by route.

The potency index for arsenic, based on the Tseng et al. study, is 2.25×10^3 $(mMol/kg/day)^{-1}$. This is derived by means of the slope estimate from the Tseng et al. study, which is $15(mg/kg/day)^{-1}$.

Multiplication by the molecular weight of 149.8 gives a potency index of $2.25 \times 10^{+3}$. Rounding off to the nearest order of magnitude gives a value of 10^{+3}, which is the scale presented on the horizontal axis of Figure 7-12. The index of $2.25 \times 10^{+3}$ lies at the bottom of the first quartile of the 52 suspect carcinogens.

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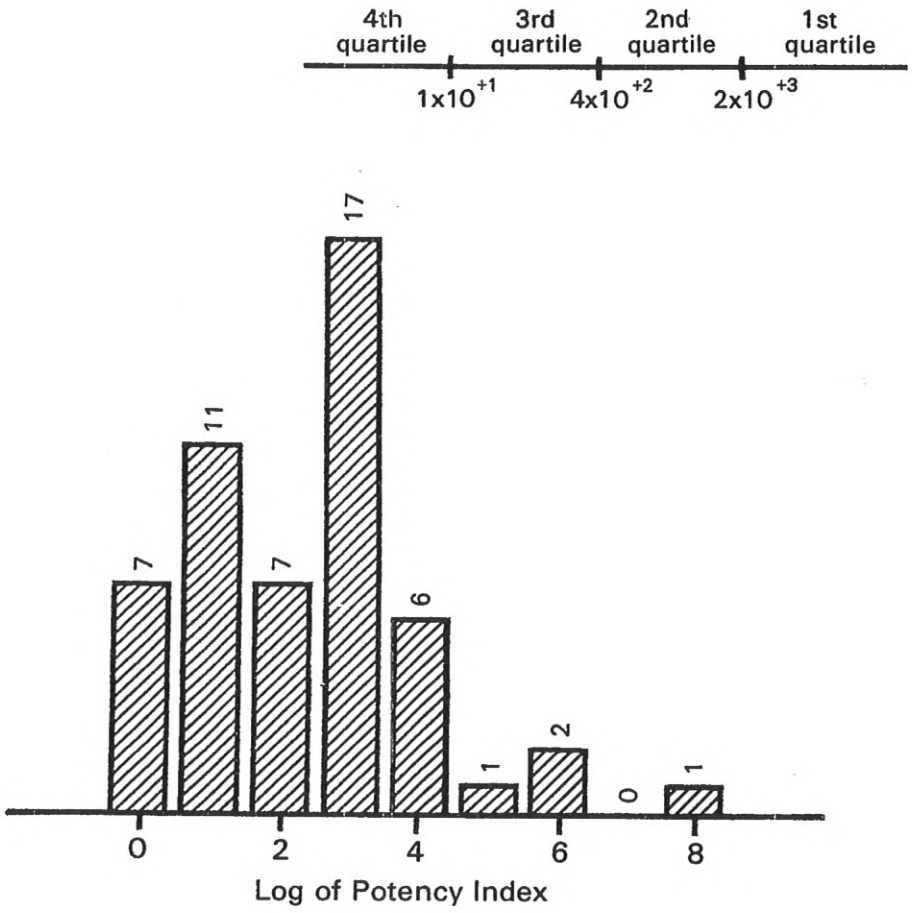

Figure 7-12. Histogram representing the frequency distribution of the potency indices of 52 suspect carcinogens evaluated by the Carcinogen Assessment Group.

TABLE 7-38. RELATIVE CARCINOGENIC POTENCIES AMONG 52 CHEMICALS EVALUATED BY THE CARCINOGEN ASSESSMENT GROUP AS SUSPECT HUMAN CARCINOGENS

Compounds	Slope (mg/kg/day)-1	Molecular Weight	Potency Index	Order of Magnitude (log_{10}) Index
Acrylonitrile	0.24(W)	53.1	$1x10^{+1}$	+1
Aflatoxin B_1	2924	312.3	$9x10^{+5}$	+6
Aldrin	11.4	369.4	$4x10^{+3}$	+4
Allyl Chloride	$1.19x10^{-2}$	76.5	$9x10^{-1}$	0
Arsenic	15(H)	149.8	$2x10^{+3}$	+3
B[a]P	11.5	252.3	$3x10^{+3}$	+3
Benzene	$5.2x10^{-2}$(W)	78	$4x10^{0}$	+1
Benzidine	234(W)	184.2	$4x10^{+4}$	+5
Beryllium	4.86	9	$4x10^{+1}$	+2
Cadmium	6.65(W)	112.4	$7x10^{+2}$	+3
Carbon Tetrachloride	$1.30x10^{-1}$	153.8	$2x10^{+1}$	+1
Chlordane	1.61	409.8	$7x10^{+2}$	+3
Chlorinated Ethanes				
1,2-dichloroethane	$6.90x10^{-2}$	98.9	$7x10^{0}$	+1
1,1,2-trichloroethane	$5.73x10^{-2}$	133.4	$8x10^{0}$	+1
1,1,2,2-tetrachloroethane	0.20	167.9	$3x10^{+1}$	+1
Hexachloroethane	$1.42x10^{-2}$	236.7	$3x10^{0}$	0
Chloroform	$7x10^{-2}$	119.4	$8x10^{0}$	+1
Chromium	41	104	$4x10^{+3}$	+4
DDT	8.42	354.5	$3x10^{+3}$	+3
Dichlorobenzidine	1.69	253.1	$4x10^{+2}$	+3
1,1-dichloroethylene	1.04(I)	97	$1x10^{+2}$	+2
Dieldrin	30.4	380.9	$1x10^{+4}$	+4

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TABLE 7-38. (continued)

Compounds	Slope (mg/kg/day)-1	Molecular Weight	Potency Index	Order of Magnitude (log_{10}) Index
Dinitrotoluene	0.31	182	$6x10^{+1}$	+2
Diphenylhydrazine	0.77	180	$1x10^{+2}$	+2
Epichlorohydrin	$9.9x10^{-3}$	92.5	$9x10^{-1}$	0
Bis(2-chloroethyl)ether	1.14	143	$2x10^{+2}$	+2
Bis(chloromethyl)ether	9300(I)	115	$1x10^{+6}$	+6
Ethylene Dibromide (EDB)	8.51	187.9	$2x10^{+3}$	+3
Ethylene Oxide	0.63(I)	44.0	$3x10^{+1}$	+1
Formaldehyde	$2.14x10^{-2}$(I)	30	$6x10^{-1}$	0
Heptachlor	3.37	373.3	$1x10^{+3}$	+3
Hexachlorobenzene	1.67	284.4	$5x10^{+2}$	+3
Hexachlorobutadiene	$7.75x10^{-2}$	261	$2x10^{+1}$	+1
Hexachlorocyclohexane				
technical grade	4.75	290.9	$1x10^{+3}$	+3
alpha isomer	11.12	290.9	$3x10^{+3}$	+3
beta isomer	1.84	290.9	$5x10^{+2}$	+3
gamma isomer	1.33	290.9	$4x10^{+2}$	+3
Nickel	1.15(W)	58.7	$7x10^{+1}$	+2
Nitrosamines				
Dimethylnitrosamine	25.9(not by q_1^*)	74.1	$2x10^{+3}$	+3
Diethylnitrosamine	43.5(not by q_1^*)	102.1	$4x10^{+3}$	+4
Dibutylnitrosamine	5.43	158.2	$9x10^{+2}$	+3
N-nitrosopyrrolidine	2.13	100.2	$2x10^{+2}$	+2
N-nitroso-N-ethylurea	32.9	117.1	$4x10^{+3}$	+4
N-nitroso-N-methylurea	302.6	103.1	$3x10^{+4}$	+4
N-nitroso-diphenylamine	$4.92x10^{-3}$	198	$1x10^{0}$	0
PCBs	4.34	324	$1x10^{+3}$	+3
Phenols				
2,4,6-trichlorophenol	$1.99x10^{-2}$	197.4	4x10	+1

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TABLE 7-38. (continued)

Compounds	Slope (mg/kg/day)-1	Molecular Weight	Potency Index	Order of Magnitude (log_{10}) Index
Tetrachlorodioxin	$4.25x10^{5}$	322	$1x10^{+8}$	+8
Tetrachloroethylene	$5.31x10^{-2}$	165.8	$9x10^{0}$	+1
Toxaphene	1.13	414	$5x10^{+2}$	+3
Trichloroethylene	$1.26x10^{-2}$	131.4	$2x10^{0}$	0
Vinyl Chloride	$1.75x10^{-2}$(I)	62.5	$1x10^{0}$	0

Remarks:

1. Animal slopes are 95% upperlimit slopes based on the linear multistage model. They are calculated based on animal oral studies, except for those indicated by I (animal inhalation), W (human occupational exposure), and H (human drinking water exposure). Human slopes are point estimate, based on the linear non-threshold model.

2. The potency index is a rounded-off slope in (mMol/kg/day)-1 and is calculated by multiplying the slopes in (mg/kg/day)-1 by the molecular weight of the compound.

3. Not all the carcinogenic potencies presented in this table represent the same degree of certainty. All are subject to change as new evidence becomes available.

Ranking of the relative potency indices is subject to the uncertainty involved in comparing estimates of potency for different chemicals based on different routes of exposure to different species, and using studies of different quality. Furthermore, all the indices are based on estimates of low-dose risk using linear extrapolation from the observational range. Thus, these indices are not valid for the purpose of comparing potencies in the experimental or observational range if linearity does not exist there.

7.3.5 Summary and Conclusions of the Carcinogenicity of Arsenic

7.3.5.1 Qualitative Summary--Human studies of the effects of arsenic from smelters, drinking water, pesticide manufacturing plants, and medicinals have

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been conducted. These are summarized in Table 7-1. Studies of five independent smelter worker populations have all found an association between occupational arsenic exposure and lung cancer mortality. Several of the smelter studies have found a dose response both by intensity and by duration of exposure. The risk of lung cancer mortality in the high dose group of one study of smelter workers in Japan was found to be 10 times that expected. Some of the recent data from these smelter studies suggest that, if the multistage theory of carcinogenesis is correct, arsenic may act as a late-stage carcinogen. It is also possible to hypothesize from some of the data that arsenic may be a promoter. Either of these hypotheses, however, requires further study. In addition, some studies of communities surrounding smelters have found an association between geographic proximity to the smelter and lung cancer mortality.

Both proportionate mortality and cohort studies of pesticide manufacturing workers have demonstrated an excess of lung cancer deaths among workers in that occupation. One study of the population around a pesticide manufacturing plant found that residents of the area surrounding the plant were also at an excess risk of lung cancer. Several case reports of arsenical pesticide applicators have also shown an association between arsenical exposure and lung cancer.

A study of 40,000 persons in Taiwan exposed to arsenic in the drinking water found a significant excess prevalence of skin cancer over that of 7,500 other Taiwanese and residents of Matsu Island who drank water relatively free of arsenic. Water supplies in Chile and Argentina were also reported to be the cause of arsenic-induced skin cancers. In contrast, studies of populations in the United States exposed to relatively high levels of arsenic in the drinking water by U.S. standards did not find any excess of skin cancer.

The difference in response between the Taiwanese and the United States studies may reflect the fact that the drinking water in the study area in Taiwan

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contained much higher levels of arsenic than did the drinking water in the United States. Furthermore, the Taiwanese waters also contained ergotamine-like compounds. Other differences between the two study areas include differences in socioeconomic status, with the Taiwanese who developed skin cancer belonging to a rather low socioeconomic strata which could have had ramifications in terms of diet, personal hygiene and medical care. Racial differences may have also contributed to the differences between the study results. In addition to these physical and cultural differences, the U.S. studies were limited by small sample sizes and would not have detected the risk from skin cancer that would have been predicted, on the basis of arsenic ingestion, from a linear model of the Taiwanese data.

Persons exposed to arsenical medicinals have also been shown to be at a risk of skin cancer.

Using the International Agency for Research on Cancer (IARC) classification scheme for evaluating carcinogens, the evidence for arsenic as a human carcinogen is considered sufficient. This is evidenced by the high relative risks, the consistency in findings in different studies, and the specificity of tumor sites (i.e., skin and lungs).

Consistent demonstration of arsenic carcinogenicity in test animals, using different chemical forms, routes of exposure, and various experimental species, has not been observed. Nevertheless, recent data indicate that tumorigenicity and possibly carcinogenicity can be demonstrated in animals if the retention of arsenic in the lung is increased. The additional observation that calcium arsenate is only slowly cleared from the lung, strongly suggests that this agent may be carcinogenic. In support of the recent animal studies, is the observation that cultured Syrian hamster embryo cells can be transformed by direct exposure to sodium arsenate.

7.3.5.2 Quantitative summary--Unit risks are estimated for both air and water exposures to arsenic. The air estimates were based on data obtained in five separate studies involving three independently exposed worker populations. Linear and quadratic dose-response models in both the absolute and relative form are fitted to the worker data. It was found that for the models that fit the data at the P = .01 or better level that the corresponding unit risk estimates ranged from 1.05×10^{-4} to 1.36×10^{-2}. However, linear models fit better than quadratic models and absolute better than relative models. Also it was felt that exposure to trivalent arsenic was more representive of low environmental exposure than pentavalent arsenic. Restricting unit risk estimates to those obtained from linear absolute models where exposure was to trivalent arsenic gives a range of 1.25×10^{-3} to 7.6×10^{-3}. A weighted average of the five estimates in this range gave a composite estimate of 4.29×10^{-3}.

An extensive drinking water study of the association between arsenic in well water and an examination for skin cancer of a population who lived in a rural area of Taiwan was used to estimate the unit risk for ingestion. Using the male population who appeared to be more susceptible, it was estimated that the unit risk associated with drinking water contaminated with 1 μg/ℓ of arsenic was 4.3×10^{-4}. To compare the air and water unit risks, the exposure units in both cases were converted to mg/kg/day absorbed doses, resulting in unit risk estimates of 50.1 and 15.0, respectively.

The potency of arsenic compared to other carcinogens is evaluated by noting that an arsenic potency of $2.25 \times 10^{+3}$ $(\text{mMol/kg/day})^{-1}$ lies in the first quartile of the 52 suspect carcinogens that have been evaluated by CAG.

7.3.5.3 Conclusions--Skin cancer and lung cancer have been shown by numerous epidemiologic studies to have an association with arsenic exposure. Arsenic

has not definitively been found to be a carcinogen in animal studies, however. In applying the IARC criteria for evaluating a substance as to the weight of evidence for human carcinogenicity, arsenic would be placed in group 1, which IARC characterizes as "carcinogenic to humans."

Using the linear absolute risk model, the composite estimate for cancer risk due to a lifetime exposure to 1 $\mu g/m^3$ trivalent arsenic in the air is estimated to be 4.29×10^{-3}. The unit risk due to lifetime exposure to 1 $\mu g/\ell$ of arsenic in drinking water is estimated to be 4.3×10^{-4}. On the basis of mg/kg/day absorbed dose, the unit-risk slope estimates for air and water are 50.1 and 15, respectively. While it is unlikely that the true risks would be higher than these estimates, they could be substantially lower. Compared to other compounds on a mole unit basis, the carcinogenic potency for arsenic falls towards the lower end of the first quartile.

8. ARSENIC AS AN ESSENTIAL ELEMENT

Mertz (1970) has set forth a set of logical criteria which trace elements should obey in order to be considered physiologically essential for man and/or animals. One of the most obvious of these, and one which should be readily demonstrable, is that the element meet a unique requirement physiologically, and, consequently, that a deficiency in that element be associated with deleterious effects.

In the case of arsenic, early reports attempting to show a nutritional requirement for the element in animals were inconclusive (Arsenic. NAS, 1977; Underwood, 1977). Part of the problem was undoubtedly technical in nature, i.e., the difficulty of carrying out such studies in an experimental environment where rigorous exclusion of a ubiquitous element from the diet is necessary. More recently, however, several carefully controlled studies have been reported to have demonstrated nutritional essentiality for arsenic in at least some mammalian species.

Nielsen et al. (1978) have noted that deprivation of pregnant rats of arsenic-supplemented diets resulted in offspring showing such post-weaning effects as slow growth, enlarged spleens, and increased red cell osmotic fragility. Greater perinatal mortality among pups from arsenic-deprived dams was also noted in a second experimental group.

In a recent review by Uthus et al. (1983), the authors reported on studies with chicks that suggest that arsenic influences arginine metabolism. It was reported that arsenic deprivation influenced the effects of dietary arginine, manganese and zinc, the fluctuations of which variously affected growth, kidney arginase, plasma alkaline phosphatase, plasma urea, plasma uric acid

and hematocrit. The authors suggested that the four components interacted to affect the conversion of arginine into urea and ornithine.

Anke et al. (1978) studied the nutritional requirements for arsenic using goats and mini-pigs and a semi-synthetic diet containing less that 50 ppb arsenic. Effects attributed to arsenic deficiency in both species were seen not only in the adult animals but in their offspring. Arsenic deficiency increased the mortality of adult goats as well as altered the mineral profiles for copper and manganese in the carcass. Significant reproductive effects for both arsenic-deficient goats and mini-pigs included reduction of the normal litter size. Furthermore, the mortality of kids and piglets from the arsenic-deficient groups was significantly higher than controls. Manganese levels were elevated in arsenic-deficient kids and piglets, but no perturbation of hematological indices (hemoglobin, hematocrit or mean corpuscular concentration) was noted. This is in contrast to the experimental observations with rats (Nielsen et al., 1974), where decreased hematocrits, elevated iron content in spleen and increased osmotic fragility of cells are seen. Given the fact that the rat is known to be an anomalous animal model for arsenic metabolism (see Chapter 4), this difference is probably peculiar to this species.

Schwartz (1977) has noted growth effects of arsenite on rats fed an arsenic-supplemented diet, with an optimal effect seen at 0.25 to 0.5 ppm. Interestingly, this worker noted that pentavalent arsenic as sodium arsenate is less effective.

Remaining to be independently demonstrated is a physiological role for arsenic, the existence of any specific carrier agent in the body, or arsenic essentiality in man.

A feature of essential element metabolism is homeostatic control of levels and movement of a particular element *in vivo*. From the information

considered earlier, there is no effective absorption barrier for most soluble inorganic arsenicals, but efficient excretory mechanisms (kidney, hair) and biotransformation appear to provide some control over any absorption-excretion balance.

9. HUMAN HEALTH RISK ASSESSMENT FOR ARSENIC

This portion of the report places the information in the earlier Chapters into a quantitative perspective with regard to non-occupational population exposure and health effects of arsenic germane to such a population.

Data for levels of arsenic encountered by humans in air, water, food and other sources, such as cigarette smoking, were set forth in Chapter 3 and are combined with data on rates of intake and rates of absorption to provide information on the total assimilation of arsenic on a daily basis. Health effects of arsenic most germane to non-occupational population exposures are then summarized. Generally, these are chronic effects associated with long-term intake of relatively low levels of arsenic. In the case of hazardous wastes, however, some health effects of concern may be associated with acute exposures; therefore, acute and sub-acute effects must also be considered.

The section dealing with dose-effect/dose-response data includes consideration of various indices of internal exposure followed by quantitative data for intake and population response.

Populations at risk, identified at least along qualitative lines, are included for discussion.

9.1 AGGREGATE EXPOSURE LEVELS TO ARSENIC IN THE U.S. POPULATION

Among individuals of the general population (not occupationally exposed to arsenic), the main routes of exposure to arsenic are typically via ingestion of food and water, with lesser exposures occurring via inhalation. Representative intake figures are presented in Table 9-1. Intake by inhalation is augmented among smokers in proportion to the level of smoking.

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TABLE 9-1. ROUTES OF DAILY HUMAN ARSENIC INTAKE

Route/level	Rate	Total intake	Absorbed amount
Ambient air/0.006 μg/m^3[(a)]	20 m^3	0.12 μg	0.036 μg[(b)]
Drinking water/≤ 10 μg/liter	2 liters	≤ 20 μg	≤ 20 μg[(c)]
Food/50 μg daily (elemental As)	--	50 μg	40 μg[(d)]
Cigarettes/6 μg in mainstream smoke/pack[(e)]	1/2 pack	3 μg	0.9 μg[(f)]
	1 pack	6 μg	1.8 μg[(f)]
	2 pack	12 μg	2.7 μg[(f)]
Total: ≤ 60 μg nonsmokers			

(a) National average for 1981 (see Section 3.3.1)
(b) Assumes 30 percent respiratory absorption (see Chapter 4).
(c) Assumes total absorption (see Chapter 4).
(d) Assumes 80 percent absorption (see Chapter 4).
(e) Assumes 20 percent of cigarette content in inhaled smoke (see Chapter 4).
(f) Assumes 30 percent absorption of inhaled amount (see Chapter 4).

Assuming a daily ventilation rate of 20 m^3, and a national population inhalation average of 0.006 μg/m^3/As, the total daily inhalation exposure for arsenic can be projected to be approximately 0.12 μg. Assuming 30 percent absorption, approximately 0.03 μg of arsenic would be absorbed on a daily average.

Contribution of tobacco-borne arsenic to the respiratory burden would depend upon the rate of cigarette smoking. If one assumes a mass of 1 gram/cigarette and an average tobacco value of 1.5 ppm, this yields 1.5 μg arsenic/cigarette. With 20 percent of this amount in mainstream smoke, the inhaled amount for each pack of cigarettes would be approximately 6 μg arsenic, and of this amount, 40 percent would be deposited in the respiratory tract (see Chapter 4). Assuming an absorption of 75 percent of the deposited fraction, one arrives at an absorption of approximately 2 μg/pack of cigarettes or a

factor of 10 to 100 times greater than intake for nonsmokers in given ambient air settings. One may assume that the rates of absorption for trivalent and pentavalent arsenic in the respiratory tract are equivalent.

Since drinking water arsenic is mainly in a soluble form (arsenate or arsenite), virtually all of it is absorbed in the GI tract (see Chapter 4). Thus, assuming an average daily consumption of two liters of water containing at most 10 µg As/liter as an outside high figure, one can estimate that the total arsenic absorbed from drinking water would be approximately 20 µg/day. Most individuals would, in reality, take in much less than this amount, while those in the Western U.S. with well water supplies much higher in arsenic content would assimilate proportionately more.

Food arsenic values taken from the 1974 FDA survey indicate a daily total dietary intake of approximately 50 µg elemental arsenic. Based on information presented in Chapter 4, the major portion (80 percent) of food arsenic would be absorbed resulting in a net daily food arsenic absorption of 40 µg total.

Thus, a non-smoker would have a total daily absorption from all exposure media of approximately 60 µg arsenic/day or less. Of this, the diet would be the major contributor, assuming levels in water much below 10 µg/liter. For cigarette smokers, one would add 2 µg arsenic/pack of cigarettes smoked daily.

If one views aggregate intake not in terms of total arsenic intake but in terms of toxicologically significant forms of the element, then much of the dietary fraction, for reasons given earlier, such as complex organoarsenicals being present, becomes relatively less important than the forms in water and air as well as in cigarette smoke. Arsenic forms in such media include: pentavalent arsenic in most water supplies; variable mixtures of tri-and pentavalent arsenic in ambient air; and probably an arsenic oxide in cigarette smoke. From this view point, utilizing the examples already given above, non-

smokers would absorb 20 μg or less daily of toxicologically significant arsenic. Heavy smokers having otherwise very low air and water exposure, conceivably could receive their major exposure via cigarettes.

9.2 SIGNIFICANT HUMAN HEALTH EFFECTS ASSOCIATED WITH AMBIENT EXPOSURES

9.2.1 Acute Exposure Effects

Serious acute effects and late sequelae from exposure to arsenic will appear after single or short-term respiratory or oral exposures to large amounts of arsenic. Available data indicate that inorganic trivalent compounds of arsenic are generally more acutely toxic than inorganic pentavalent compounds, which in turn are more toxic than organic arsenic compounds. Serious effects will also appear after long-term exposure to respiratory or oral doses of arsenic.

The acute symptoms following oral exposure consist of gastrointestinal disturbances, which may be so severe that secondary cardiovascular effects and shock may result and cause death. Also, direct toxic effects on the liver, blood-forming organs, the central and peripheral nervous systems, and the cardiovascular system may appear. Some symptoms, especially those from the nervous system, may appear a long time after exposure has ceased and may not be reversible, whereas the other effects seem to be reversible. Infants and young children especially are susceptible with regard to effects on the central nervous system. The Japanese follow-up after the Morinaga milk poisoning showed that persisting damage, especially mental retardation and epilepsy, is a late sequela in children of short-term oral exposure to large doses of inorganic arsenic. Among adults, the central nervous system is not as susceptible, but peripheral neuropathy has been a common finding.

Both in adults and children, acute oral exposure has resulted in dermal changes, especially hyperpigmentation and keratosis, as a late sequela.

Acute inhalation exposures have also resulted in irritation of the upper respiratory tract, even leading to nasal perforations.

Direct dermal exposure to arsenic may lead to dermal changes; allergic reactions may also be involved.

9.2.2 Chronic Exposure Effects

Both carcinogenic and non-carcinogenic effects are associated with long-term exposures, which do not cause any obvious immediate effects. For the purpose of this document, such chronic effects will be discussed in sequence as follows:

1. Respiratory tract cancer
2. Skin cancer
3. Non-cancerous skin lesions
4. Peripheral neuropathological effects
5. Cardiovascular changes

Cancer of the respiratory system is clearly associated with exposure to arsenic via inhalation. This association has been especially noted among workers engaged in the production and usage of pesticides and among smelter workers. While it is not known to what extent exposure to other compounds in industrial atmospheres has contributed to the excess of lung cancer, the Carcinogen Assessment Group (CAG) has concluded that there is sufficient evidence that inorganic arsenic compounds are lung carcinogens in humans.

Cancer of the skin has been found as a dose-related effect in a population in Taiwan, with lifetime exposure to arsenic in well water. It has also been found among people treated with large doses of arsenite for skin disorders. Skin cancer often has a long latency period on the order of decades, the latency time decreasing with increasing intensity of exposure. The CAG has concluded that there is sufficient evidence that inorganic arsenic compounds are skin carcinogens in humans.

Hyperkeratosis and hyperpigmentation, sometimes with precancerous changes, have been a common finding in persons ingesting arsenic. These skin lesions, as well as the manifest cancer, develop on skin surfaces usually unexposed to sunlight. In studies in the United States, an association between skin lesions or skin cancer has not been demonstrated. These studies have been limited, however, by sample sizes too small to be able to detect the dose response seen in studies outside the U.S.

The effects on the peripheral nervous system range from sensory disturbances to motor weakness and even paralysis. The more severe signs have been noted in subacute poisonings, but more subtle changes after long-term low-level exposure have been found by using electromyography or measuring nerve conduction velocity. These subclinical effects are slow in recovery and may persist for years after cessation of exposure. In a study in Canada, electromyographic (EMG) changes were noted when water concentrations of arsenic exceeded 0.05 mg/l.

Cardiovascular effects have been noted especially in Taiwan, where Blackfoot disease (peripheral vasculopathy) occurred after long-term exposure to arsenic in well water. However, the presence of ergotamine-like compounds raises the possibility of vascular effects from these agents. Peripheral vascular changes were also found among German vintners who were exposed both occupationally, by spraying arsenic-containing pesticides, and orally, by drinking wine with elevated arsenic levels. Studies on occupationally-exposed persons have been inconclusive in showing that arsenic causes an increase in mortality from cardiac disease.

9.3 DOSE-EFFECT/DOSE-RESPONSE RELATIONSHIPS

9.3.1 General Considerations

This section generally attempts to define, as presently feasible, human dose-effect/dose-response relationships for health effects of likely greatest

concern at ambient environment exposure levels for arsenic in the United States. As such, the present section highlights mainly the quantitative carcinogenic risk estimates that were derived in Section 7.3.

The general question of how to define and employ a dose factor in attempts at quantitative assessments of human health risk for any toxicant is highly dependent upon: 1) the available information on the body's ability to metabolize the agent, and 2) the assessment of the relative utility of various internal indices of exposure.

The time period over which a given total intake occurs is highly important. For example, intake of one gram of arsenic over a period of years would be quite different pathophysiologically from assimilating this amount at one time, the latter probably having a lethal outcome. This time-dependent behavior is related in part to the relative ability of the body to detoxify inorganic arsenic by methylation as a function of both dose and time.

In cases of acute and sub-acute exposure, indicators of internal exposure such as blood or urine arsenic levels are probably appropriate for assessing the intensity of exposure.

With chronic, low-level exposure, however, the available data would indicate that the total amount assimilated is probably more important than an indicator concentration without knowledge of the total exposure period. An added problem is the background level of arsenic found in these indicators due to dietary habits. For example, in acute exposures, levels in blood or urine would be greatly elevated over background values while low-level chronic exposures would only result in moderate increases over background.

In regard to hair arsenic levels as an indicator of internal arsenic exposure, no reliable methods exist for distinguishing external contamination levels from those accumulated via absorption and metabolic distribution. Hair arsenic levels cannot, therefore, be employed as reliable indicators of either

current or cumulative long-term exposures for individual subjects, but rather may provide only a rough overall indication of group exposure situations.

Given the above considerations and limitations concerning the use of blood, urinary or hair arsenic concentrations as internal indices of cumulative, long-term low-level arsenic exposures of concern here, the dose-effect/dose-response relationships summarized below are done so mainly in terms of external arsenic exposure levels via either inhalation or ingestion.

9.3.2 Effects and Dose-Response Relationships

It is difficult to define a precise acute lethal dose of arsenic for man, because such exposure situations rarely allow accurate determination of the effective amounts. However, for trivalent arsenic, the figure is believed to range from 70 - 180 milligrams.

For subacute exposure, it appears that for children, about one gram assimilated over a period of 3-4 weeks will induce death with severe effects in survivors, while for adults, that dose will occasion significant clinical effects. In one poisoning episode, intake of approximately 50 milligrams over a period as short as two weeks resulted in clinically demonstrable effects in adults.

9.3.2.1 Respiratory Cancer--A considerable number of studies have shown associations between occupational exposure to arsenic and cancer of the respiratory system. The best information available for making quantitative risk estimates for lung cancer are derived from 5 sets of data involving 4 sets of investigators and 2 distinct exposed populations. The 4 sets of investigators are Brown and Chu (1983a,b,c), Lee-Feldstein (1983) and Higgins (1982)--who conducted studies on workers at the Anaconda smelter in Montana--and Enterline and Marsh (1982)--who conducted a study on the workers at the ASARCO smelter in Tacoma, Washington.

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Using an absolute-risk linear model and the data from the four smelter studies, the lifetime lung cancer risk, due to continuous exposure of 1 μg/As/m^3, was estimated to range from 1.25×10^{-3} to 7.6×10^{-3}. A weighted average of the five estimates* in this range gave a composite estimate of 4.29×10^{-3} (see Section 7.3.2.3). This represents a plausible estimate of the upper limit of risk--that is, the true risk would not likely be more than the estimated risk, but it could be substantially lower.

9.3.2.2 Skin Cancer--Chronic arsenic exposure, both occupational and non-occupational, is associated with a distinctive hyperkeratosis, which is usually followed by a later onset of skin cancer. The best data available for making quantitative risk estimates for skin cancer are the data collected by Tseng et al. (1968). In this study, the authors surveyed a stable population of 40,421 individuals who lived in a rural area along the southwest coast of Taiwan and who were known to have consumed drinking water containing arsenic. The occurrences of skin cancer among this population and the arsenic concentrations in their drinking water were measured. Since the population was stable, the data obtained from the study lends itself to predictions of lifetime probability of skin cancer caused by the ingestion of arsenic.

Using an absolute-risk linear model and the data from Tseng et al., the lifetime skin cancer risk from drinking water containing 1 μg/liter of arsenic was estimated to be 4.3×10^{-4} (see Section 7.3.3). It is not likely that the true risk for skin cancer would be more than this estimated risk, but it could be considerably lower.

9.3.2.3 Non-cancerous Skin Lesions -- As noted above, in man, chronic oral exposure to arsenic induces a sequence of changes in skin epithelium, proceeding from hyperpigmentation to hyperkeratosis, characterized as keratin proliferation

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*Two risk estimates were derived from the Enterline and Marsh study based upon exposure periods lagged 0 and 10 years. See Table 7-25.

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of a verrucose nature and leading, in some cases, to late onset skin cancers. These effects have been noted both in populations which have ingested arsenic via drinking water and among people treated with large doses of arsenite for skin disorders. In a report by Pershagen and Vahter (1979), the authors, using the data from a patient population exposed to arsenic via Fowler's solution (Fierz, 1965), noted an increase in prevalence of hyperkeratosis with increasing dose of arsenic. The U.S. EPA is presently examining this information, along with information from other studies, in order to determine whether quantitative dose-response relationships, similar to those seen for skin cancer, can be established for these precancerous skin lesions.

9.3.2.4 Peripheral Neuropathological Effects and Cardiovascular Changes -- While the qualitative evidence for peripheral neurological effects and cardiovascular changes in arsenic-exposed populations is incontrovertible, the data are insufficient to establish quantitative dose-response relationships at the present time.

9.4 POPULATIONS AT SPECIAL RISK TO ARSENIC EXPOSURE

In reviewing the literature dealing with the acute, subacute and chronic effects of arsenic in children and adults, the evidence suggests that children may be at special risk for the effects of inorganic arsenic under conditions of acute or subacute exposure.

In earlier sections, reference was made to the outbreak of pediatric poisoning by arsenic in Japan due to the presence of arsenic in infant milk formula (Hamamoto et al., 1955). From the clinical reports published at the time of the mass poisoning as well as those from follow-up studies, a number of signs of central nervous system involvement were noted both at the time of the episode and much later, with the follow-up studies showing behavioral problems, abnormal brain wave patterns, marked cognitive deficits, and severe hearing loss in some of those children who survived the acute episode. Some

of these same tardive effects have also been noted in adults but appear to be a much less constant feature of arsenic-induced neurotoxic effects than are the peripheral neuropathies.

Because children consume more water per body weight than do adults, the daily intake of arsenic via drinking water per kilogram body weight would be greater in children. This may have implications regarding chronic exposure effects in children. Zaldivar (1977) developed a regression equation describing this relationship. It should be noted, however, that serious health effects due to chronic exposure of arsenic in drinking water have not been found at a greater frequency in children than adults.

Individuals residing in the vicinity of certain arsenic-emitting sources, e.g., certain types of smelters, may be at risk for increased arsenic intake because of both direct exposure to arsenic in air and indirect exposure via arsenic secondarily deposited from air onto soil or other human exposure media. The relative contribution of such indirect exposures to increased risk of these individuals for arsenic health effects is difficult to define due to the lack of information on this subject. However, it is most likely minimal in relation to the direct effects arising from inhalation of arsenic, including lung cancer.

As a large class of the general population at risk for increased arsenic intake, one would have to include cigarette smokers. However, it is not clear to what extent some increased arsenic intake from tobacco smoke poses a specific heightened health effect risk, although it is clear that internal indicator levels, e.g. blood arsenic, are somewhat elevated in the case of cigarette smokers relative to nonsmokers.

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LIST OF ACRONYMS

µg	Microgram
µm	Micrometer
ADAF	Age Dependent Adjustment Factor
AT	Averaging Time
ATSDR	Agency for Toxic Substances and Disease Registry
BMCL	Benchmark Concentration, Lower confidence limit
BMD	Benchmark Dose
BW	Body Weight
CA	Contaminant Concentration in Air
CERCLA	Comprehensive Environmental Response, Compensation, and Liability Act
CSF	Cancer Slope Factor
DAF	Dosimetric Adjustment Factor
ED	Exposure Duration
EC	Exposure Concentration
EF	Exposure Frequency
EPA	Environmental Protection Agency
ER	Extra-respiratory
ET	Exposure Time
ETh	Extrathoracic
F_r	Fractional Deposition in region r
F_{total}	Total particle deposition in respiratory tract
$H_{b/g\text{-}animal}$	Animal Blood:Gas Partition Coefficient
$H_{b/g\text{-}human}$	Human Blood:Gas Partition Coefficient
HEAST	Health Effects Assessment Summary Table
HEC	Human Equivalent Concentration
HI	Hazard Index
HQ	Hazard Quotient
ICRP	International Commission for Radiological Protection
IR	Inhalation Rate
IRIS	Integrated Risk Information System
IUR	Inhalation Unit Risk
kg	Kilogram
LEC_{10}	Lower limit on Effective Concentration, using a 10 percent response level
LOAEL	Lowest Observable Adverse Effect Level
ME	Microenvironment
MF	Modifying Factor
mg	Milligram
MOA	Mode of Action
MRL	Minimal Risk Level
MW	Molecular Weight
NCEA	National Center for Environmental Assessment
NOAEL	No Observable Adverse Effect Level
ORD	Office of Research and Development
OSRTI	Office of Superfund Remediation and Technology Innovation

LIST OF ACRONYMS (CONT.)

OSWER	Office of Solid Waste and Emergency Response
PBPK	Physiologically Based Pharmacokinetic
POD	Point of Departure
ppm	Parts Per Million
PPRTV	Provisional Peer Reviewed Toxicity Value
PRG	Preliminary Remediation Goal
PU	Pulmonary
Q-alv	Alveolar ventilation rate
QSAR	Quantitative Structure-Activity Relationship
RAGS	Risk Assessment Guidance for Superfund
RBC	Risk-Based Concentration
RfC	Reference Concentration
RfD	Reference Dose
RGDR	Regional Gas Dose Ratio
RDDR	Regional Deposited Dose Ratio
RME	Reasonable Maximum Exposure
SA	Surface Area
SSL	Soil Screening Level
STSC	Superfund Health Risk Technical Support Center
TB	Tracheobronchial
TOT	Total Respiratory System
UF	Uncertainty Factor
V_e	Minute Volume

1. INTRODUCTION

The Environmental Protection Agency's (EPA's) Superfund Program has updated its approach for determining risk from inhaled chemicals to be consistent with the inhalation dosimetry methodology described in *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry* (USEPA, 1994; hereafter, the *Inhalation Dosimetry Methodology*).[1] This document provides Superfund site risk assessors with guidance that should help more consistently address the *Inhalation Dosimetry Methodology*.

This document outlines recommended processes consisting of a series of steps as well as recommended equations for EPA Regions to consider when estimating inhalation exposure and risk at Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) sites. This guidance is intended to provide a recommended methodology for consistently addressing the inhalation pathway in risk assessments for Superfund sites.

Some of the statutory provisions described in this document contain legally binding requirements. However, this document does not substitute for those provisions or regulations, nor is it a regulation itself. Thus, it cannot impose legally binding requirements on EPA, States, or the regulated community, and may not apply to a particular situation based upon the circumstances. Any decisions regarding a particular remedy selection decision will be made based on the statute and regulations, and EPA decisionmakers retain the discretion to adopt approaches on a case-by-case basis that differ from this guidance where appropriate. EPA may change this guidance in the future.

1.1 Background

EPA's *Risk Assessment Guidance for Superfund (RAGS), Part A* (USEPA, 1989; hereafter, *RAGS, Part A*) outlined a previously recommended approach for conducting site-specific baseline risk assessments for inhaled contaminants.[2] According to the original RAGS approach, the inhalation exposure estimate was typically derived in terms of a chronic, daily "air intake" (mg/kg-day) using the following general approach. The intake of the chemical was estimated as a function of the concentration of the chemical in air (CA), inhalation rate (IR), body weight (BW), and the exposure scenario. Age-specific values for BW and IR were used when evaluating childhood exposures. Table 1 presents the *RAGS, Part A* equation for calculating intake for inhalation exposure. Inhalation toxicity values were "converted" into similar units for the risk quantification step. Cancer risk was estimated by multiplying the chronic daily intake of the chemical from the air by the "inhalation cancer slope factor" (CSF_i); the Hazard Quotient (HQ) for non-cancer effects was estimated by dividing the intake of the chemical by an "inhalation reference dose" (RfD_i).[3]

The approach outlined in *RAGS, Part A* was developed before EPA issued the *Inhalation Dosimetry Methodology*, which describes the Agency's refined recommended approach for interpreting

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[1] The *Inhalation Dosimetry Methodology* can be found at the following web address: http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=71993.

[2] See sections 6.6.3, 7.2.3, 7.3.3, and 8.2 of *RAGS, Part A*.

[3] EPA defines an HQ in *RAGS, Part A* as: "The ratio of a single substance exposure level over a specified time period (e.g., subchronic) to a reference dose (RfD) for that substance derived from a similar exposure period" (USEPA, 1989).

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inhalation toxicity studies in laboratory animals or studies of occupational exposures of humans to airborne chemicals. Under the *Inhalation Dosimetry Methodology*, the experimental exposures are typically extrapolated to a Human Equivalent Concentration (HEC), and a reference concentration (RfC) is typically calculated by dividing the HEC by uncertainty factors (UFs). As described in the Agency's *Guidelines for Cancer Risk Assessment* (USEPA, 2005a), the HEC developed in accordance with the *Inhalation Dosimetry Methodology* typically is also used in developing an inhalation unit risk (IUR) for cancer risk assessment (which may also be called an inhalation cancer slope factor).[4] The procedure that was used to calculate the published RfC or IUR is described in the Integrated Risk Information System (IRIS) profile or other toxicological reference document for a chemical.

TABLE 1
RAGS, PART A EQUATION DESCRIBING THE ESTIMATION OF INHALATION EXPOSURE

Equation	Location in RAGS, Part A
Intake (mg/kg-d) = CA x (IR/BW) x (ET x EF x ED)/AT	Exhibit 6-16, Page 6-44
Key: CA (mg/m^3) = contaminant concentration in air; IR (m^3/hr) = inhalation rate; BW (kg) = body weight; ET (hours/day) = exposure time; EF (days/year) = exposure frequency; ED (years) = exposure duration; and AT (days) = averaging time (period over which exposure is averaged).	

The Superfund Program has updated its inhalation risk paradigm to be compatible with the *Inhalation Dosimetry Methodology*, which represents the Agency's current methodology for inhalation dosimetry and derivation of inhalation toxicity values.[5] This document recommends that when estimating risk via inhalation, risk assessors should use the concentration of the chemical in air as the exposure metric (e.g., mg/m^3), rather than inhalation intake of a contaminant in air based on IR and BW (e.g., mg/kg-day).

1.2 Purpose and Scope

The intake equation described above (*RAGS, Part A*, Exhibit 6-16) is not consistent with the principles of EPA's *Inhalation Dosimetry Methodology* because the amount of the chemical that reaches the target site is not a simple function of IR and BW. Instead, the interaction of the inhaled contaminant with the respiratory tract is affected by factors such as species-specific relationships of exposure concentrations (ECs) to deposited/delivered doses and physiochemical characteristics of the inhaled contaminant. The *Inhalation Dosimetry Methodology* also considers the target site where the toxic effect occurs (e.g., the respiratory tract or a location in the body remote from the portal-of-entry) when applying dosimetric adjustments to experimental concentrations (USEPA, 1994). Therefore, this *RAGS, Part A* equation is not recommended for estimating exposures to inhaled contaminants.

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[4] The phrase "inhalation cancer slope factor," as used in this guidance, refers generally to the risk per a measure of inhalation exposure. Inhalation exposure in cancer bioassays or occupational studies from which slope factors may be derived is most commonly expressed as an exposure concentration (e.g., µg agent/m^3 air). Please note that this differs from past use of the phrase "inhalation cancer slope factor" or "CSF_i" by the Superfund program to refer to a cancer slope expressed as an "inhalation intake" (e.g., *RAGS, Part A* (USEPA, 1989)).

[5] For additional information about the Superfund program's adoption of the *Inhalation Dosimetry Methodology*, please refer to the summary of a 2003 Superfund workshop on inhalation risk assessment: http://www.epa.gov/oswer/riskassessment/pdf/finalinhalationriskworkshop.pdf.

The purpose of this document is to provide a recommended approach for developing the information necessary to assist risk assessment and risk management decision-making at waste sites involving potential risks from inhalation exposures.[6, 7] This includes providing equations that may be used in conducting baseline risk assessments and in calculating risk-based concentrations (RBCs). It is intended that *RAGS, Part F* will replace those portions of *RAGS, Part A*, which addressed inhalation risk.

1.3 Effects on Other Office of Superfund Remediation and Technology Innovation Guidance

EPA recommends that the intake equation presented in *RAGS, Part A* (USEPA, 1989, Exhibit 6-16) should no longer be used when evaluating risk from the inhalation pathway. Implementation of a risk assessment approach consistent with the *Inhalation Dosimetry Methodology* will also affect the following guidance documents: *RAGS, Part B*, Section 3.3: Volatilization and Particulate Emission Factors (USEPA, 1991); and the Office of Solid Waste and Emergency Response's (OSWER's) *Draft Guidance for Evaluating the Vapor Intrusion to Indoor Air Pathway from Groundwater and Soils* (USEPA, 2002a; hereafter the *Vapor Intrusion Guidance*). EPA no longer recommends using the equations in Section 3.3 of *RAGS, Part B* nor the inhalation toxicity values generated using simple route-to-route extrapolation, such as those presented in the 2002 draft *Vapor Intrusion Guidance* and related documents.[8]

This guidance does not affect the equations pertaining to risk from inhaled chemicals in the *Soil Screening Guidance* (USEPA, 1996), Section 2.4, or the *Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites* (USEPA, 2002b), Sections 4.2.3, 5.3.2 and Appendix B, other than to clarify that the IURs and RfCs used in the equations are based on continuous exposure (24 hours per day). If the exposure scenario of interest is less than 24 hours per day, the scenario-specific exposure time (ET) in hours per day should be used in the equations and the averaging time should be in units of hours (see Equations 6 and 8 in this document). *RAGS, Part D* (USEPA, 2001) is also not affected by *RAGS, Part F*, as it includes sufficient flexibility to accommodate the revisions described in this guidance. In addition, the screening values presented on the "Regional Screening Levels for Chemical Contaminants at Superfund Sites" screening level/preliminary remediation goal table are consistent with *RAGS, Part F* (USEPA, 2008a).[9] Readers can contact EPA headquarters with questions about the compatibility of specific Superfund documents with *RAGS, Part F*.

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[6] Note that the assessment of risk from inhaled nanoparticles is outside the scope of this document.

[7] If a site contains asbestos contamination, risk assessors should contact EPA's Technical Review Workgroup for Metals and Asbestos for assistance.

[8] Related documents include the *Johnson and Ettinger (1991) Model for Subsurface Vapor Intrusion into Buildings* spreadsheet models (http://www.epa.gov/oswer/riskassessment/airmodel/johnson_ettinger.htm) and the accompanying *User's Guide for Evaluating Subsurface Vapor Intrusion into Buildings* (USEPA, 2004a).

[9] This table can be found on EPA Regions 3, 6, and 9 websites (http://www.epa.gov/reg3hwmd/risk/human/rb-concentration_table/index.htm; http://www.epa.gov/earth1r6/6pd/rcra_c/pd-n/screen.htm; and http://www.epa.gov/region09/waste/sfund/prg/index.html).

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2. BACKGROUND ON DERIVATION OF INHALATION TOXICITY VALUES

For all exposure routes, there are generally two approaches for deriving toxicity values. One involves the derivation of a reference value (e.g., RfC or RfD), while the other involves derivation of a predictive cancer risk estimate (e.g., an oral or inhalation CSF, such as an IUR). For the inhalation route, both approaches rely on EPA's *Inhalation Dosimetry Methodology* for the extrapolation of experimental concentrations to HECs. This extrapolation is described in Section 2.1 and its subsections. The approaches for deriving a toxicity value from the HEC are described in Sections 2.2 and 2.3 and differ depending on the type of toxicity value (e.g., RfC, IUR). This information is provided for background purposes only. **The procedures outlined in Section 2 are typically performed by IRIS chemical managers or by inhalation toxicologists at the National Center for Environmental Assessment's (NCEA's) Superfund Health Risk Technical Support Center (STSC) rather than as part of a baseline risk assessment.**

2.1 Application of Inhalation Dosimetry

The *Inhalation Dosimetry Methodology* recognizes a hierarchy of approaches that can be used for determining the HEC that is used to derive the RfC or IUR. Generally, the preferred approach is to use physiologically-based pharmacokinetic (PBPK) models.[10] With sufficient data, a PBPK model is capable of calculating the amount of the chemical that reaches the target organ in an animal from any exposure scenario and then estimating what human exposure would result in this same amount of chemical reaching the target organ (i.e., the HEC). PBPK models can also be used to derive continuous ECs from human and animal studies with less-than-continuous exposures. Because constructing a valid PBPK model is an information-intensive process that typically requires substantial chemical-specific data, this approach has rarely been used (USEPA, 2004b); an example can be found in the IRIS file for vinyl chloride (USEPA, 2000a). In cases where a complete PBPK model is not available, an intermediate model relying on certain chemical-specific data may be used (USEPA, 1994).[11]

If the database to support the preferred approach is inadequate, an alternative approach, called the Default Chemical Category-Specific Method can be used. This method incorporates the use of limited or categorical chemical-specific and physiological information. The default method is discussed below, followed by the procedures outlined in the *Inhalation Dosimetry Methodology* for deriving the RfC and IUR as they apply to the interpretation of animal and human data.

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[10] EPA defines PBPK models in the IRIS glossary as a model that estimates the dose to a target tissue or organ by taking into account the rate of absorption into the body, distribution among target organs and tissues, metabolism, and excretion (USEPA, 2008b). For further information about PBPK modeling, please refer to *Approaches for the Application of Physiologically Based Pharmacokinetic Models and Supporting Data in Risk Assessment* (USEPA, 2006a).

[11] The *Inhalation Dosimetry Methodology* recognizes the existence of alternate approaches in addition to the two presented in this guidance. The PBPK approach is generally preferred. In the absence of such a model, alternate models may be more optimal than the default approach when default assumptions or parameters can be replaced by more detailed, biologically-motivated descriptions or actual data, respectively. For instance, a model may be considered more optimal if it incorporates chemical or species-specific information or if it accounts for mechanistic determinants. See Table 3-6 in the *Inhalation Dosimetry Methodology* for more details on the hierarchy of approaches (EPA, 1994, page 3-40).

2.1.1 Default Approach - Extrapolation from Experimental Animal Data

The default method involves a two-step procedure that uses limited or categorical chemical-specific and physiological information to calculate the HEC. First, the chosen point of departure (POD) from the experimental data for a chemical is adjusted to derive a concentration intended to represent an equivalent dose under conditions of continuous exposure (7 days a week, 24 hours a day).[12] In the second step, this concentration is then multiplied by a Dosimetric Adjustment Factor (DAF) to generate the HEC. Further details on each step are outlined below.

2.1.1.1 Duration Adjustment to Continuous Exposure

Most of the inhalation studies of laboratory animals used to derive RfCs and IURs involve an exposure regimen of four to six hours per day, five to seven days per week, for 13 weeks or more (equivalent to 10 percent or more of the lifetime of the animal). The POD concentration from an animal study is mathematically adjusted to reflect an equivalent dose under conditions of continuous exposure.[13] Adjustment of duration to a continuous exposure scenario is regularly applied as a default procedure to studies with repeated exposures but not to single-exposure inhalation toxicity studies in animals (USEPA, 1994). Operationally, this is accomplished by applying a c x t product (where "c" is concentration, and "t" is duration of exposure) for both the number of hours in a daily exposure period and the number of days per week that the exposure is experienced. For example, if exposure in a particular study was 6 hours per day, 5 days per week, the experimental exposure is multiplied by 6/24 x 5/7 to calculate an equivalent continuous exposure. The general equation provided in the *Inhalation Dosimetry Methodology* (USEPA, 1994, Equation 4-2) for calculating duration-adjusted exposure levels in mg/m^3 for experimental animals is presented below.

$NOAEL_{[ADJ]}$ = E x D x W **(Equation 1)**

Where:

$NOAEL_{[ADJ]}$ (mg/m^3) = the NOAEL or analogous exposure level obtained with an alternate approach (e.g., LOAEL, LEC_{10}), adjusted for duration of experimental regimen;
E (mg/m^3) = the NOAEL or analogous exposure level observed in the experimental study;
D (h/h) = number of hours exposed/24 hours; and
W (days/days) = number of days of exposure/7days.

Using the example above, the assumption is that the product of c x t, not concentration alone, is associated with the toxicity observed. This is roughly equivalent to implying that if an effect occurs from a chemical at an exposure of 6 hours per day at 40 parts per million (ppm), that same effect will

[12] Examples of PODs include the no-observed-adverse-effect level (NOAEL); the lowest-observed-adverse-effect level (LOAEL); Benchmark Concentration, Lower confidence limit (BMCL); and the Lower limit on an Effective Concentration using a 10 percent response level (LEC_{10}). For definitions of the various PODs, please refer to the IRIS glossary (http://www.epa.gov/ncea/iris/help_gloss.htm).

[13] Continuous exposure refers to 24 hours per day, 7 days per week.

occur at an exposure of 24 hours per day at 10 ppm.[14] Note that this adjustment always produces a lower concentration value than that administered to experimental animals. Thus, as stated in *A Review of the Reference Dose and Reference Concentration Processes* (hereafter, the *RfD/RfC Review*), application of this procedure results in an automatic margin of protectiveness for chemicals for which concentration alone may be the more appropriate dose metric, and it reflects the maximum dose for chemicals for which total or cumulative dose is the appropriate measure (USEPA, 2002c). If a different procedure is used to calculate the continuous exposure, it should be fully discussed in the relevant technical support document for the chemical (e.g., IRIS profile, Provisional Peer Reviewed Toxicity Values (PPRTVs) Assessment). For additional discussion, including the uncertainties associated with this approach, see Section 4.3.2 of the *Inhalation Dosimetry Methodology* and Section 4.4.2.1 of the *RfD/RfC Review* (USEPA, 2002c).

2.1.1.2 Dosimetric Adjustment to Human Equivalent Concentration

Typically, the adjusted POD concentration from the animal study is next converted to an HEC using the following equation (USEPA, 1994, Equation 4-3):

$NOAEL_{[HEC]} = NOAEL_{[ADJ]} \times DAF$ **(Equation 2)**

Where:

$NOAEL_{[HEC]}$ (mg/m^3) = the NOAEL or analogous exposure level obtained with an alternate approach, dosimetrically adjusted to an HEC;

$NOAEL_{[ADJ]}$ (mg/m^3) = the NOAEL or analogous exposure level obtained with an alternate approach, adjusted for duration of experimental regimen; and

DAF = Dosimetric Adjustment Factor for the specific site of effects (e.g., respiratory tract region or extra-respiratory).

The DAF is typically based on ratios of animal and human physiologic parameters. The specific DAF used depends on the nature of the contaminant (e.g., particle or gas) and the target site where the toxic effect occurs (e.g., respiratory tract or a location in the body remote from the portal-of-entry). For example, the DAF can be based on either the Regional Gas Dose Ratio (RGDR), for gases with respiratory effects, or the Regional Deposited Dose Ratio (RDDR) for particles.

Table 2 provides information on the site of effects for the different chemical types. It also lists the physiologic parameters considered when calculating the DAF for specific regions of the body.[15] In addition, the table provides references to the equations from the *Inhalation Dosimetry Methodology* used in deriving the DAFs. Figure 1 provides a schematic of the human respiratory tract, illustrating each of the different regions.

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[14] This assumption is based on Haber's Law, which states that "the incidence and/or severity of an adverse health effect depends on the total exposure to a potentially toxic substance. Total exposure (K) is the concentration of the substance (c) times the duration time of exposure (t), (i.e., $c \times t = K$)" (Gaylor, 2000).

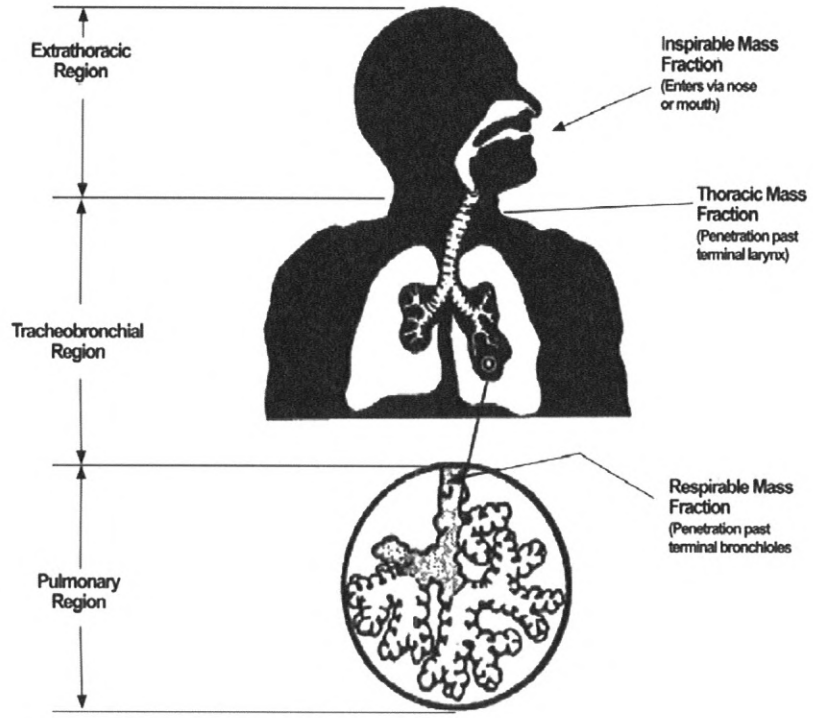
[15] The three main regions of the respiratory tract include the following: 1) Extrathoracic (includes nose, mouth, nasopharynx, oropharynx, laryngopharynx, and larynx); 2) Tracheobronchial (includes trachea, bronchi, and bronchioles); and 3) Pulmonary (includes respiratory bronchioles, alveolar ducts, alveolar sacs and the alveoli).

TABLE 2
CONTAMINANT PROPERTIES AND DOSIMETRIC ADJUSTMENT FACTORS[a]

Chemical Type	Site of Effects	Parameters Considered in Derivation of DAF for Regions of the Body[b]	DAF Equation Numbers in Inhalation Dosimetry Methodology[c]
Category 1 Gases (e.g., acrolein, hydrogen fluoride, chlorine)	Respiratory	-Minute volume (ETh, TB) -Surface area (ETh, TB, PU) -Mass transport coefficient (TB, PU) -Fraction of inhaled chemical penetrating the respiratory region (PU) -Alveolar ventilation rate (PU)	4-18 (ETh), 4-21 & 4-22 (TB), 4-28 (PU)
Category 2 Gases (e.g., acetonitrile, xylene, propanol, isoamyl alcohol)	Respiratory and Remote	-Mass transport coefficients (ETh, TB) -Blood:gas partition coefficient (ET, TB, ER) -Cardiac output (ETh, TB, ER) -Alveolar ventilation rate (PU) -Surface Area (PU) -Minute volume (ER)	4-18 (ETh), 4-21 & 4-22 (TB), 4-28 (PU), 4-48 (ER)[d,e]
Category 3 Gases (e.g., benzene, styrene)	Remote	Blood:gas partition coefficient (ER)	4-48[d]
Particles	Respiratory and Remote	-Minute volume (TOT, ER) -Surface area (TOT) -Fractional deposition of particle (TOT, ER) -Body weight (ER) -Inhaled concentration (ER)	4-14 (TOT), 4-15 (ER)

[a] Due to the complexities inherent in evaluating the health effects associated with exposure to gases, no definitive or comprehensive list of Category 1, 2, or 3 gases is available. Risk assessors should consult with an inhalation toxicologist in order to classify a specific gas as Category 1, 2, or 3, since there is overlap between the sites of effects and the parameters considered in deriving the DAF for different regions of the respiratory tract.
[b] Additional discussion of the terms used in this table can be found in the *Inhalation Dosimetry Methodology*.
[c] The *Inhalation Dosimetry Methodology* provides equations for deriving DAFs for the different contaminant categories. The equations listed in this table are the default equations for each specific region in the body.
[d] This refers to Equation 4-48 that is found on page 4-60 of the *Inhalation Dosimetry Methodology*.
[e] The equations presented for Category 2 gases in the *Inhalation Dosimetry Methodology* contain errors. Therefore, this table refers to the equations for Category 1 and 3 gases, which are expected to cover respiratory and remote effects from Category 2 gases.
Acronyms: ETh = Extrathoracic; TB = Tracheobronchial; PU = Pulmonary; ER = Extra-respiratory; TOT = Total respiratory system.

FIGURE 1
HUMAN RESPIRATORY TRACT



Source: EPA (1994), Figure 3-1, Page 3-5.

Category 1 gases are highly water-soluble and/or are rapidly irreversibly reactive in the respiratory tract (e.g., acrolein, hydrogen fluoride, chlorine). They do not significantly accumulate in the blood, and therefore their effects are usually exclusively respiratory (USEPA, 1994). The DAF for Category 1 gases consists of an RGDR and is based on the animal to human ratio of the minute volume (V_e) divided by the surface area (SA) of the region of the respiratory tract where the effect occurs.[16] See Appendix A, Sections 1, 2, and 3 of this guidance for examples of specific Category 1 DAF equations.

[16] For the purposes of this document, the V_e is defined as the total ventilation per minute and equals the product of the tidal volume (the air volume entering or leaving the lungs with a single breath) and the respiratory frequency.

Category 3 gases are relatively water-insoluble and are unreactive in the respiratory tract (e.g., benzene, styrene). Their toxicity is generally at sites remote to the respiratory tract (USEPA, 1994). The DAF for Category 3 gases is based on the ratio of the animal blood:gas partition coefficient ($H_{b/g\text{-}animal}$) and the human blood:gas partition coefficient ($H_{b/g\text{-}human}$). See Appendix A, Section 4 of this guidance for an example of a Category 3 DAF equation.

Category 2 gases are moderately water-soluble and may be rapidly reversibly reactive or moderately to slowly irreversibly reactive in respiratory tract tissue (e.g., acetonitrile, xylene, propanol, isoamyl alcohol). These gases have potential for significant accumulation in the blood, so they can exhibit both respiratory and remote toxicity (USEPA, 1994). The DAF for respiratory effects of Category 2 gases consists of an RGDR and is based on the animal to human ratio of the V_e and the SA of the region of the respiratory tract where the effect occurs, as for Category 1 gases. The DAF for extra-respiratory (ER) effects of a Category 2 gas is based on the ratio of the $H_{b/g\text{-}animal}$ and the $H_{b/g\text{-}human}$, as for Category 3 gases.

Particles also vary by solubility and reactivity. However, the default equations used to estimate the predicted regional deposition fractions for particles are based on non-soluble, non-hygroscopic particles (USEPA, 1994, Section 4.3.5.3). The DAF for a particle causing an effect in the respiratory tract is the $RDDR_r$. The $RDDR_r$ is based on the animal to human ratio of the V_e and the fractional deposition of the particle in that region (F_r), divided by the SA_r of the region where the effect occurs. This derivation, from the *Inhalation Dosimetry Methodology,* conservatively assumes that 100 percent of the deposited dose remains in the respiratory tract; clearance mechanisms are not considered. The DAF for a particle causing an ER effect, the $RDDR_{ER}$, is based on the animal to human ratio of the V_e and the total deposition of the particle in the entire respiratory tract (F_{total}), divided by BW (USEPA, 1994). The $RDDR_{ER}$ assumes that 100 percent of the deposited dose in the entire respiratory tract is available for uptake into the systemic circulation. See Appendix A, Section 5 for examples of specific particle DAF equations.

2.1.2 Default Approach - Extrapolation from Human Occupational Data

When human data are available to derive an RfC, duration adjustments are often required to account for differences in exposure scenarios (e.g., extrapolation from an 8 hour/day occupational exposure to a continuous chronic exposure). The default approach recommended by the *Inhalation Dosimetry Methodology* for adjusting the POD concentration (e.g., the no observable adverse effect level (NOAEL)) obtained from human study data is provided below in Equation 3 (USEPA, 1994, Equation 4-49).[17,18]

[17] If sufficient data are available, a PBPK model or intermediate approach using chemical-specific information may be employed in preference to the default method for extrapolating human occupational data to an HEC.

[18] EPA's IRIS glossary defines an adverse effect as the following: "A biochemical change, functional impairment, or pathologic lesion that affects the performance of the whole organism, or reduces an organism's ability to respond to an additional environmental challenge" (USEPA, 2008b).

$NOAEL_{[HEC]}$ = NOAEL x (VEho/VEh) x 5 days/7 days **(Equation 3)**

Where: $NOAEL_{[HEC]}$ (mg/m^3) = the NOAEL or analogous exposure level obtained with an alternate approach, dosimetrically adjusted to an ambient HEC;
NOAEL (mg/m^3) = occupational exposure level (time-weighted average over an 8-hour exposure period);
VEho = human occupational default minute volume over 8 hours (10 m^3); and
VEh = human ambient default minute volume over 24 hours (20 m^3).

2.2 Derivation of the Inhalation Unit Risk

The default approach for determining predictive cancer risk recommended by EPA's *Guidelines for Carcinogen Risk Assessment* (USEPA, 2005a; hereafter, *Cancer Guidelines*) is a linear extrapolation from exposures observed in the animal or human occupational study.[19] This approach involves drawing a straight line from the POD to the origin. The default linear extrapolation approach is generally considered to be conservatively protective of public health, including sensitive sub-populations (USEPA, 2005a). The slope of this line is commonly called the slope factor, and when the units are risk per $\mu g/m^3$, it is also called the IUR. EPA defines an IUR in the IRIS glossary as "the upper-bound excess lifetime cancer risk estimated to result from continuous exposure to an agent at a concentration of 1 $\mu g/m^3$ in air" (USEPA, 2008b). Equation 4 below presents a linear extrapolation from a POD of 10 percent response (LEC_{10}).[20]

$IUR = 0.1/LEC_{10[HEC]}$ **(Equation 4)**

Where: IUR $(\mu g/m^3)^{-1}$ = Inhalation Unit Risk; and
$LEC_{10[HEC]}$ ($\mu g/m^3$) = the lowest effective concentration using a 10 percent response level, dosimetrically adjusted to an HEC.

2.3 Derivation of the Reference Concentration

EPA defines an RfC in the IRIS glossary as "an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious effects during a lifetime" (USEPA, 2008b). The RfC is derived after a review of the health effects database for a chemical and identification of the most sensitive and relevant endpoint along with the principal study or studies demonstrating that endpoint. EPA Chemical Managers use UFs to account for recognized

[19] According to the *Cancer Guidelines*, "[a] nonlinear approach should be selected when there are sufficient data to ascertain the mode of action [MOA] and conclude that it is not linear at low doses and the agent does not demonstrate mutagenic or other activity consistent with linearity at low doses" (USEPA, 2005a, page 3-22). In addition, [l]inear extrapolation should be used when there are MOA data to indicate that the dose-response curve is expected to have a linear component below the POD" (USEPA, 2005a, page 3-21). This information will appear on the IRIS profile or other toxicological information source for a chemical. Chemicals with a mutagenic MOA are thought to pose a higher risk during early life. Procedures for assessing cancer risk from these chemicals are outlined in Section 5.1.

[20] The POD used in Equation 4 is an LEC_{10}, which is the lower 95 percent confidence limit on the concentration corresponding to a 10 percent response rate (i.e., the EC_{10}). Other PODs may be substituted for this value, which could be associated with alternative response levels (e.g., 1 percent, 5 percent).

uncertainties in the extrapolations from the experimental data conditions to an estimate appropriate to the assumed human scenario (USEPA, 1994). See Table 3 for a description of the standard UFs. The formula used for deriving the RfC from the HEC is provided below.

$RfC = NOAEL_{[HEC]}/(UF)$[1] **(Equation 5)**

Where: RfC (mg/m^3) = Reference Concentration
$NOAEL_{[HEC]}$ (mg/m^3) = The NOAEL or analogous exposure level obtained with an alternate approach, dosimetrically adjusted to an HEC; and
UF = Uncertainty factor(s) applied to account for the extrapolations required from the characteristics of the experimental regimen.

[1] Some toxicological information sources for RfCs will incorporate an additional factor to account for deficiencies in the available data set, called a modifying factor (MF). In 2002, however, EPA published the *RfD/RfC Review,* which recommended that the use of MFs be discontinued because their purpose is "sufficiently subsumed in the general database UF" (USEPA, 2002c, page xviii). Therefore, RfCs published subsequent to this document will not include MFs.

TABLE 3
THE USE OF UNCERTAINTY FACTORS IN DERIVING AN INHALATION REFERENCE CONCENTRATION

Standard UFs	Processes Considered in the UF Purview
H = Human to sensitive human: Extrapolation of valid experimental results from studies using prolonged exposure to average healthy humans. Intended to account for the variation in sensitivity among the members of the human population.	-Pharmacokinetics/Pharmacodynamics -Sensitivity[2] -Differences in body weight (age, obesity) -Concomitant exposures -Activity pattern -Does not account for idiosyncrasies
A = Animal to human: Extrapolation from valid results of long-term studies on laboratory animals when results of studies of human exposure are not available or are inadequate. Intended to account for the uncertainty in extrapolating laboratory animal data to the case of average healthy humans.	-Pharmacokinetics/Pharmacodynamics -Relevance of laboratory animal model -Species sensitivity
S = Subchronic to chronic: Extrapolation from less-than-chronic exposure results on laboratory animals or humans when there are no useful long-term human data. Intended to account for the uncertainty in extrapolating from less than chronic NOAELs to chronic NOAELs.	-Accumulation/Cumulative damage -Pharmacokinetics/ Pharmacodynamics -Severity of effect -Recovery -Duration of study -Consistency of effect with duration
L = LOAEL to NOAEL: Derivation from a LOAEL instead of a NOAEL. Intended to account for the uncertainty in extrapolating from LOAELs to NOAELs.	-Severity -Pharmacokinetics/Pharmacodynamics -Slope of dose-response curve -Trend, consistency of effect -Relationship of endpoints -Functional vs. histopathological evidence -Exposure uncertainties
D = Incomplete to complete data: Extrapolation from valid results in laboratory animals when the data are "incomplete." Intended to account for the inability of any single laboratory animal study to adequately address all possible adverse outcomes in humans.[1]	-Quality of critical study -Data gaps -Power of critical study/supporting studies -Exposure uncertainties

[1] The *RfD/RfC Review* indicates that this UF accounts for the potential for deriving an underprotective RfD/RfC as a result of an incomplete characterization of the chemical's toxicity or if the existing data suggest that a lower reference value might result if additional data were available (considering both the lacking and available data for particular organ systems as well as life stage) (USEPA, 2002c).

[2] The *RfD/RfC Review* also stresses that susceptible populations and life stages are accounted for with this UF (USEPA, 2002c).

Source: USEPA, 1994, Table 4-9, page 4-77.

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3. CHARACTERIZING EXPOSURE

3.1 Introduction

This section describes an approach for characterizing exposure in a baseline risk assessment that is consistent with the *Inhalation Dosimetry Methodology*. The approach involves the estimation of exposure concentrations (ECs) for each receptor exposed to contaminants via inhalation in the risk assessment. ECs are time-weighted average concentrations derived from measured or modeled contaminant concentrations in air at a site, adjusted based on the characteristics of the exposure scenario being evaluated.[21,22]

Equations for estimating ECs are provided below. This document does not provide default input values for the exposure parameters referenced in these equations. EPA recommends the use of site-specific exposure values consistent with the exposure pathways and receptors at a site wherever practicable and appropriate. If a risk assessor opts to rely on default exposure input values, current Superfund-supported values may be found at the exposure assessment portion of the Superfund website: (http://www.epa.gov/oswer/riskassessment/superfund_hh_exposure.htm).

3.2 Estimating Exposure Concentrations for Assessing Cancer Risks

The estimation of an EC when assessing cancer risks characterized by an IUR involves the CA measured at an exposure point at a site as well as scenario-specific parameters, such as the exposure duration and frequency.[23] The EC typically takes the form of a CA that is time-weighted over the duration of exposure and incorporates information on activity patterns for the specific site or the use of professional judgment. The equation for estimating an EC for use with an IUR is presented below.

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[21] The default method for deriving inhalation toxicity values also involves calculating time-weighted ECs, as discussed in Sections 2.1.1.1 and 2.1.2.

[22] The ECs in this document are in units of $\mu g/m^3$. Inhalation toxicity values presented on IRIS are typically expressed in units of $\mu g/m^3$ or mg/m^3, which are mass units. Some regulatory contexts require the use of volumetric units such as ppm. The conversion from mass units to volumetric units depends on the molecular weight (MW) of the material as well as the ambient temperature and atmospheric pressure. To convert from ppm to mg/m^3, the following equation can be used: $\frac{ppm \times MW}{V} = mg/m^3$; where MW is the molecular weight of the gas and V is the volume of 1 gram molecular weight of the airborne contaminant. This is derived by the formula V = RT/P; where R is the ideal gas constant, T is the temperature in Kelvin (K = 273.16 + T°C) and P is the pressure in mm Hg. The value of R is 62.4 when T is in Kelvin, (K = 273.16 + T°C), the pressure is expressed in units of mm Hg and the volume is in liters. The value of R differs if the temperature is expressed degrees Fahrenheit (°F) or if other units of pressure are used (e.g., atmospheres, kilopascals).

[23] ECs are typically based on either estimated (i.e., modeled) or measured contaminant concentrations in air.

EC = (CA x ET x EF x ED)/AT **(Equation 6)**

Where:
EC ($\mu g/m^3$) = exposure concentration;
CA ($\mu g/m^3$) = contaminant concentration in air;
ET (hours/day) = exposure time;
EF (days/year) = exposure frequency;
ED (years) = exposure duration; and
AT (lifetime in years x 365 days/year x 24 hours/day) = averaging time

3.3 Estimating Exposure Concentrations for Calculating Hazard Quotients

When estimating ECs for non-cancer or cancer hazards characterized by an HQ, risk assessors should match each exposure scenario at a site to the appropriate EC equation, based on the scenario duration and frequency of exposure.[24] Figure 2 presents a flowchart to assist risk assessors with this process and provides recommended equations that can be used to estimate the EC for each type of scenario.[25] As shown in Figure 2, the recommended process for estimating ECs to be used in calculating an HQ involves the following three steps: 1) assess the duration of the exposure scenario; 2) assess the exposure pattern of the exposure scenario; and 3) estimate the scenario-specific EC.

3.3.1 Step 1: Assess Duration

The first step in the recommended process of estimating an EC for use in calculating an HQ involves assessing the duration of the exposure scenario at a site. Step 1 in Figure 2 indicates that the risk assessor first should decide whether the duration of the exposure scenario is generally acute, subchronic, or chronic. Toxicologists have long been aware that effects from a single or short-term exposure can differ markedly from effects resulting from repeated exposures. The response by the exposed person depends upon factors such as whether the chemical accumulates in the body, whether it overwhelms the body's mechanisms of detoxification or elimination, or whether it produces irreversible effects (Eaton & Klaassen, 2001). Therefore, ideally, the chemical-specific elements of metabolism and kinetics, reversibility of effects, and recovery time should be considered as part of this recommended process when defining the duration of a site-specific exposure scenario.

[24] Traditionally, the HQ approach was limited to non-cancer hazard assessment. However, the HQ approach may also be appropriate for carcinogens with a non-linear mode of action. The 2005 *Cancer Guidelines* state the following on this subject: "For cases where the tumors arise through a nonlinear mode of action, an oral reference dose or an inhalation reference concentration, or both, should be developed in accordance with EPA's established practice for developing such values ... this approach expands the past focus of such reference values (previously reserved for effects other than cancer) to include carcinogenic effects determined to have a nonlinear mode of action" (USEPA, 2005a; page 3-24).

[25] Figure 2 was developed for the evaluation of inhalation exposures. While the concepts presented in this flowchart may be useful for assessing other exposure routes (e.g., oral or dermal), these other routes are beyond the scope of this document, and therefore, are not explicitly considered. Caution should be used when using Figure 2 to evaluate other exposure routes, as considerations beyond those outlined in the flowchart may apply (e.g., time to reach steady state for dermal exposures).

To the extent possible, exposure durations (EDs) evaluated in a site-specific risk assessment should be consistent with the ED represented by the toxicity value. However, frequencies or durations of human exposures often are not as clearly defined as those in animal studies with controlled exposures, particularly for intermittent exposures. For example, the emission of some volatile chemicals into the ambient air may vary with temperature and season, providing fluctuating exposures for humans living near the source. Therefore, risk assessors should use best professional judgment to determine if the ED in a given scenario is reasonably similar to the duration associated with the toxicity value. Risk assessors should describe the uncertainties associated with their choice of toxicity value in the risk characterization section of the risk assessment (see Section 9.2.2 of this document). For situations where duration-appropriate toxicity values are not available, please follow the procedures outlined in Section 4.2 and Appendix C of this document.

The specific definition for each exposure duration category may vary depending on the source of the toxicity value being used. For Tier 1 toxicity values obtained from EPA's IRIS database, acute exposures are defined as lasting 24 hours or less; subchronic exposures are defined as repeated exposures by the oral, dermal, or inhalation route for more than 30 days, up to approximately 10 percent of the human lifespan; and chronic exposures are defined as repeated exposures for more than approximately 10 percent of the human lifespan (USEPA, 2008b).[26, 27]

After deciding which duration the exposure scenario most closely matches, risk assessors should then proceed to Step 2, following the path of the selected duration. Note that if an acute duration is selected, risk assessors should proceed directly to Step 3 to estimate an acute EC for each acute exposure period.

3.3.2 Step 2: Assess Exposure Pattern

Step 2 of the recommended process for estimating an EC for use in a hazard quotient involves assessing the exposure pattern for each exposure scenario at a site. This entails comparing the exposure time and frequency at a site to that of a typical subchronic or chronic toxicity test.[28]

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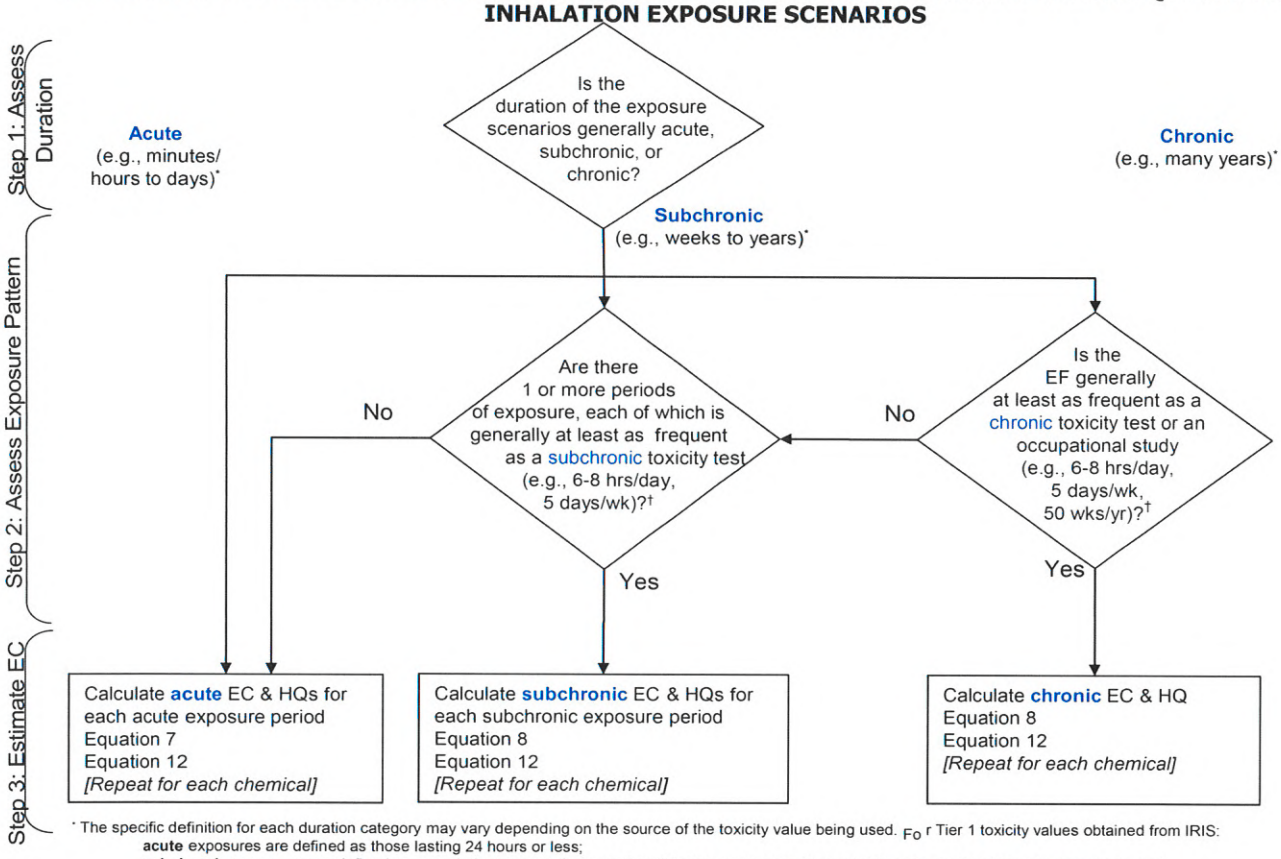
[26] Note that other sources of toxicity values may define exposures differently. For example, the Agency for Toxic Substances and Disease Registry (ATSDR) (which publishes Minimal Risk Levels (MRLs)) defines acute exposures as occurring from one to 14 days, intermediate exposures as greater than 14 to 364 days, and chronic exposures as 365 days or longer. However, the toxicity values are based on the same underlying toxicological concepts described in this section.

[27] Exposures with a duration lasting between 24 hours and 30 days should be treated as subchronic for the purposes of this document.

[28] Exposure regimens vary from study to study. Risk assessors should use best professional judgment to determine if the exposure pattern in a given scenario is reasonably similar to a typical regimen for a subchronic or chronic study.

FIGURE 2
RECOMMENDED PROCEDURE FOR DERIVING EXPOSURE CONCENTRATIONS AND HAZARD QUOTIENTS FOR INHALATION EXPOSURE SCENARIOS



* The specific definition for each duration category may vary depending on the source of the toxicity value being used. For Tier 1 toxicity values obtained from IRIS:
acute exposures are defined as those lasting 24 hours or less;
subchronic exposures are defined as repeated exposures for more than 30 days, up to approximately 10 percent of the life span in humans; and
chronic exposures are defined as repeated exposures for more than approximately 10 percent of the life span in humans (EPA, 2008b).
For the purposes of this document, short-term exposures, defined by the IRIS glossary as repeated exposures for more than 24 hours, up to 30 days, should be treated as subchronic.

† Exposure regimens vary from study to study. Risk assessors should use best professional judgment to determine if the exposure pattern in a given scenario is reasonably similar to a typical regimen for a chronic or subchronic study.

For exposure scenarios with a subchronic duration, risk assessors should follow the center path on the flowchart. Step 2 in this path asks whether there are one or more periods of exposure, each of which is generally as frequent as a subchronic toxicity test (e.g., 6-8 hours per day, 5 days per week). If the exposure scenario matches this description, risk assessors should proceed to Step 3 and estimate a subchronic EC for each subchronic exposure period. However, if the exposure pattern contains periods that are significantly shorter and/or involve significantly less frequent exposures than indicated in the flow chart, risk assessors should derive acute ECs for each of these exposure periods. If it is difficult to determine whether a specific exposure scenario is best modeled as a subchronic exposure or as a series of independent acute exposures, due to uncertainty in the time required to return to baseline following exposure, risk assessors may want to derive ECs using both approaches.

If the exposure scenario has a chronic duration, risk assessors should follow the right hand path on the flowchart. Step 2 in this path asks whether the exposure frequency (EF) is generally as frequent as a chronic animal toxicity test or a human occupational study (e.g., 6-8 hours per day, 5 days per week, for 50 weeks per year). If the exposure scenario matches this description, risk assessors should proceed to Step 3 and estimate a single chronic EC. However, if the scenario differs significantly from this pattern, risk assessors should proceed to the second question under the subchronic duration path and proceed as outlined above.

3.3.3 Step 3: Estimate Exposure Concentration

Step 3 of the recommended process involves estimating the EC for the specific exposure scenario based on the decisions made in Steps 1 and 2. For acute exposures, the EC is equal to the CA. Risk assessors can estimate an acute EC for each acute exposure period at a site using Equation 7. For longer-term exposures, risk assessors should take into consideration the exposure time, frequency, and duration for each receptor being evaluated as well as the period over which the exposure is averaged (i.e., the averaging time (AT)) to arrive at a time-weighted EC. If there are one or more exposure periods that are generally as frequent as a subchronic toxicity test, risk assessors should use Equation 8 to estimate a subchronic EC for each of these exposure periods. (Exposure periods with significantly less frequency should be treated as acute exposures.) If the exposure pattern is generally as frequent as a chronic toxicity test of an occupational study, risk assessors should use Equation 8 to estimate a single chronic EC for the duration of the exposure.

Acute Exposures

EC = CA **(Equation 7)**

Where: EC ($\mu g/m^3$) = exposure concentration;
CA ($\mu g/m^3$) = contaminant concentration in air;

Chronic or Subchronic Exposures

EC = (CA x ET x EF x ED)/AT **(Equation 8)**

Where:
EC ($\mu g/m^3$) = exposure concentration;
CA ($\mu g/m^3$) = contaminant concentration in air;
ET (hours/day) = exposure time;
EF (days/year) = exposure frequency;
ED (years) = exposure duration; and
AT (ED in years x 365 days/year x 24 hours/day) = averaging time

Note: If the duration of the exposure period is less than one year, the units in the above equation can be changed to the following: EF (days/week); ED (weeks/exposure period); and AT (hours/exposure period).

It is important to use the EC equation that most closely matches the exposure pattern and duration at a site. For instance, if the exposure pattern at a site consists of a series of short (e.g., 4-hour) periods of high exposure separated by several days of no exposure, the approach outlined above recommends estimating an acute EC for each acute exposure period. If the chronic EC equation (Equation 8) were to be used instead, the result would be an average EC value that may lead to an underestimate of risk since the inhaled concentrations could be higher than acute toxicity values during periods of exposure.

3.4 Estimating Exposure Concentrations in Multiple Microenvironments

When detailed information on the activity patterns of a receptor at a site is available, risk assessors can use these data to estimate the EC for either non-carcinogenic or carcinogenic effects. The activity pattern data describe how much time a receptor spends, on average, in different microenvironments (MEs), each of which may have a different contaminant concentration level.[29] By combining data on the contaminant concentration level in each ME and the activity pattern data, the risk assessor can calculate a time-weighted average EC for a receptor. Because activity patterns (and hence, MEs) can vary over a receptor's lifetime, EPA recommends that risk assessors pursuing the ME approach first calculate a time-weighted average EC for each exposure period characterized by a specific activity pattern (e.g., separate ECs for a school-aged child resident and a working adult resident). These exposure period-specific ECs can then be combined into a longer term or lifetime average EC by weighting the EC by the duration of each exposure period. The following sections further explain these two steps.

3.4.1 Using Microenvironments to Estimate an Average Exposure Concentration for a Specific Exposure Period

The ME approach can be used to estimate an average EC for a particular exposure period during which a receptor has a specified activity pattern. As a simplified example, a residential receptor may

[29] EPA defines a microenvironment in *Air Quality Criteria for Particulate Matter: Volume II* as a defined space that can be treated as a well-characterized, relatively homogeneous location with respect to pollutant concentration for a specified time period (e.g., rooms in homes, restaurants, schools, offices, inside vehicles, or outdoors) (USEPA, 2004b).

be exposed to a higher concentration of a contaminant in air in the bathroom for 30 minutes per day while showering, and exposed to a lower concentration in the rest of the house for the remaining 23.5 hours per day. In this case, risk assessors can use the CA value experienced in each ME weighted by the amount of time spent in each ME to estimate an average EC for the period of residency in that house using Equation 9.[30] This approach may also be used to address exposures to contaminants in outdoor and indoor environments at sites where both indoor and outdoor samples have been collected or where the vapor intrusion pathway has been characterized.

$$EC_j = \sum_{i=1}^{n} (CA_i \times ET_i \times EF_i) \times ED_j / AT_j \qquad \textbf{(Equation 9)}$$

Where:
EC_j ($\mu g/m^3$) = average exposure concentration for exposure period j;
CA_i ($\mu g/m^3$) = contaminant concentration in air in ME i;
ET_i (hours/day) = exposure time spent in ME i;
EF_i (days/year) = exposure frequency for ME i;
ED_j (years) = exposure duration for exposure period j; and
AT_j (hours) = averaging time = ED_j x 24 hours/day x 365 days/year.

3.4.2 Estimating an Average Exposure Concentration Across Multiple Exposure Periods

To derive an average EC for a receptor over multiple exposure periods, the average EC from each period (as calculated above in Equation 9) can be weighted by the fraction of the total exposure time that each period represents, using Equation 10. For example, when estimating cancer risks, the risk assessor may calculate a lifetime average EC where the weights of the individual exposure periods are the duration of the period, ED_j, divided by the total lifetime of the receptor. Alternatively, when estimating an HQ, risk assessors can use Equation 10 to calculate less-than-lifetime average ECs across multiple exposure periods. In that case, the AT will equal the sum of the individual EDs for all of the exposure periods.

$$EC_{LT} = \sum_{i=1}^{n} (EC_j \times ED_j) / AT \qquad \textbf{(Equation 10)}$$

Where:
EC_{LT} ($\mu g/m^3$) = long-term average exposure concentration;
EC_j ($\mu g/m^3$) = average exposure concentration of a contaminant in air for exposure period j;
ED_j (years) = duration of exposure period j; and
AT (years)[1] = averaging time.

[1] When evaluating cancer risk, the AT is equal to lifetime in years. When evaluating non-cancer hazard, the AT is equal to the sum of the EDs for each exposure period.

[30] If one or more MEs involve acute exposures, risk assessors should conduct a supplemental analysis comparing the CA for each of those MEs to a corresponding acute toxicity value to ensure that receptors are protected from potential acute health effects.

4. SELECTING APPROPRIATE TOXICITY VALUES

After characterizing the exposure scenarios and estimating ECs for each receptor at a site, the risk assessor should select appropriate inhalation toxicity values for each inhaled contaminant. For estimating cancer risks, this typically involves identifying and evaluating available published cancer potency estimates. For estimating HQs, this typically involves identifying and evaluating reference values that match the characterization of the exposure scenario from Figure 2 (i.e., acute, subchronic, or chronic reference values).

This section provides guidance for the selection of toxicity values appropriate for assessing risk under inhalation exposure scenarios. It describes sources for the most current inhalation data and provides guidance for proceeding when published inhalation toxicity data are not available.

4.1 Sources for Inhalation Toxicity Data

The OSWER Directive, *Human Health Toxicity Values in Superfund Risk Assessment* (USEPA, 2003), provides a recommended hierarchy of toxicological data sources to guide risk assessors when selecting appropriate toxicity values. This document sets out a recommended three-tiered framework for selecting human toxicity values. Tier 1 consists of EPA's IRIS, Tier 2 consists of EPA's PPRTVs, and Tier 3 includes other toxicity values as recommended by NCEA, such as the California EPA toxicity values, the Agency for Toxic Substances and Disease Registry's (ATSDR's) Minimal Risk Levels (MRLs), and Health Effects Assessment Summary Table (HEAST) toxicity values. Priority in Tier 3 should be given to sources that are the most current and those that are peer reviewed. Consultation with the Superfund Headquarters office is recommended regarding the use of Tier 3 values for Superfund response decisions when the contaminant appears to be a risk driver for the site.

The most up-to-date information on Superfund-supported cancer potency estimates and chronic and subchronic cancer and non-cancer reference values for inhaled contaminants are available on the Superfund risk assessment website (www.epa.gov/oswer/riskassessment/superfund_toxicity.htm). Superfund-recommended sources for acute non-cancer toxicity values can be found at www.epa.gov/oswer/riskassessment/superfund_acute.htm.[31]

In situations where the desired reference value (e.g., acute, subchronic, chronic) is not available, risk assessors may use a reference value based on the next longer duration of exposure as a conservative estimate that would be protective for a shorter-term ED (USEPA, 2002c). For example, if a risk assessor determines that an ED at a site is subchronic, but no subchronic toxicity value is available, a chronic RfC can be used to assess hazard.

EPA recommends that toxicity values published in Superfund-supported sources should generally be used in the risk equations presented in this guidance, without modification. This includes IURs on IRIS that were calculated from oral values using a default ventilation rate and BW (see Appendix B for a list of these chemicals). It is not generally appropriate to make adjustments to these values

[31] In selecting an acute toxicity value, risk assessors should consider the duration associated with their estimate of exposure (e.g., a 1-hour versus a 24-hour air sample). Use of a toxicity value specified for a longer duration than that of the exposure estimate may overestimate hazard, while the use of a shorter duration acute reference value may underestimate hazard.

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based on IR and BW using the intake equation, because the amount of the chemical that reaches the target site through the inhalation pathway is not a simple function of these parameters (see Section 1.2). Use of the toxicity values listed in Appendix B should be noted in the uncertainty section of the risk assessment (see Section 9).

4.2 Recommended Procedures for Assessing Risk in the Absence of Inhalation Toxicity Values

The following section provides guidance on recommended procedures for situations where inhalation toxicity values are not available in any of the toxicity data sources described in Section 4.1.

If RfC and IUR values are not available for an inhaled contaminant, risk assessors should first contact NCEA's STSC for guidance.[32] Risk assessors working on Superfund sites can contact STSC to determine whether a provisional peer-reviewed toxicity value (PPRTV) exists for a contaminant; if not, the risk assessor, in cooperation with the appropriate EPA Regional office may request that STSC develop a PPRTV document or that STSC develop an inhalation toxicity value as a "consult". The latter would be specific to the site in question only. Additional information on STSC's current process for developing alternative toxicity values is described in Appendix C.

If STSC indicates that no quantitative toxicity information for the inhalation route is available, the risk assessor should conduct a qualitative evaluation of this exposure route. The risk assessor should discuss in the uncertainty section of the risk assessment report the implications of not quantitatively assessing risks due to inhalation exposures to chemicals lacking inhalation toxicity data. See the section on Risk Characterization (Section 9) in this guidance for more information.

Performing simple route-to-route extrapolation without the assistance of STSC is generally not appropriate because hazard may be misrepresented when data from one route are substituted for another without any consideration of the pharmacokinetic differences between the routes (USEPA, 1998). The following circumstances, outlined in the *Inhalation Dosimetry Methodology* (page 4-6), are specific examples of situations when route-to-route extrapolation from oral toxicity values might not be appropriate, even for use during screening:

- When groups of chemicals are expected to have different toxicity by the two routes – for example, metals, irritants, and sensitizers;
- When a first-pass effect by the respiratory tract is expected;
- When a first-pass effect by the liver is expected;
- When a respiratory tract effect is established, but dosimetry comparison cannot be clearly established between the two routes;
- When the respiratory tract was not adequately studied in the oral studies; and
- When short-term inhalation studies, dermal irritation, in vitro studies, or characteristics of the chemical indicate the potential for portal-of-entry effects at the respiratory tract, but studies themselves are not adequate for inhalation toxicity value development.

[32] All contact with STSC should be performed by an EPA regional risk assessor. States and other entities should first contact their EPA regional risk assessor with questions on inhalation toxicity values. Regional risk assessors can then contact STSC on their behalf.

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The *Cancer Guidelines* (USEPA, 2005a) includes the following statement regarding route-to-route extrapolation:

> "When a qualitative extrapolation can be supported, quantitative extrapolation may still be problematic due to the absence of adequate data. The differences in biological processes among routes of exposure (oral, inhalation, dermal) can be great because of, for example, first-pass effects and different results from different exposure patterns. There is no generally applicable method for accounting for these differences in uptake processes in a quantitative route-to-route extrapolation of dose-response data in the absence of good data on the agent of interest. Therefore, route-to-route extrapolation of dose data relies on a case-by-case analysis of available data" (page 3-10).

5. ESTIMATING RISKS

This section provides updated equations recommended for estimating excess cancer risks and HQs from inhaled contaminants of concern at Superfund sites. Please see Section 8.2.1 of *RAGS, Part A* for further information about how to interpret calculated excess cancer risks and HQs.

5.1 Cancer Risks Characterized by an Inhalation Unit Risk

The excess cancer risk for a receptor exposed via the inhalation pathway can be estimated with the following equation:

Risk = IUR x EC **(Equation 11)**

Where: IUR $(\mu g/m^3)^{-1}$ = Inhalation Unit Risk; and
EC $(\mu g/m^3)$ = exposure concentration (See Equation 6).

When estimated ECs are above the POD used for the low dose extrapolation described in Section 2.3, a linear concentration-response relationship may not hold.[33] In such situations, the risk assessor should not use toxicity values developed through low dose extrapolation techniques. Instead, the risk assessor may report semi-quantitative risk estimates (e.g., risks are greater than 10^{-2}) or estimate risk using the original model underlying the toxicity value, which can be found in the technical support document for the value (e.g., IRIS profile, PPRTV Assessment).

When estimating cancer risks for children, risk assessors should be aware of chemicals that pose a higher risk of cancer when exposure occurs during early life. If evidence exists suggesting differences in risk across age groups for a chemical, this typically will be considered in the derivation of the toxicity value and described in the chemical's technical support document.

[33] Reviews of chemical-specific IRIS files indicate that the risk level corresponding to the concentration level above which the IUR should not be used often falls at or near 10^{-2}. However, this risk level varies by chemical and, therefore, risk assessors should refer to the toxicity value's technical support document for information on the concentration range for which the IUR was intended to be used.

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Chemicals that have been determined to cause cancer by a mutagenic mode of action (MOA) are thought to pose a higher risk during early life. An EPA-recommended procedure exists for assessing risks from these chemicals. Figure 3 summarizes the recommendations of the *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* (USEPA, 2005b; hereafter *Supplemental Cancer Guidelines*) on how to adjust childhood risk calculations to account for chemicals with a mutagenic MOA for carcinogenicity. Please refer to the *Supplemental Cancer Guidelines* (USEPA, 2005b) for a list of chemicals with a mutagenic MOA that were used in the development of that document.

In addition, EPA's website for the "Handbook for Implementing the Supplemental Cancer Guidance at Waste and Cleanup Sites" contains an up-to-date list of chemicals that EPA has determined to have a mutagenic MOA (http://www.epa.gov/oswer/riskassessment/sghandbook/index.htm). As chemicals receive new assessments for mutagenicity, this information will appear in the IRIS profile or PPRTV assessment.

FIGURE 3
GUIDANCE ON ASSESSING RISK FROM EARLY-LIFE EXPOSURES FOR CHEMICALS ACTING BY A MUTAGENIC MODE OF ACTION FOR CARCINOGENICITY

If a chemical has been determined to cause cancer by a mutagenic MOA, it is possible that exposures to that chemical in early-life may result in higher lifetime cancer risks than a comparable duration adult exposure.

In risk assessments of exposure to chemicals for which a mutagenic MOA for carcinogenicity has been determined by EPA and a linear low-dose extrapolation performed, one of the following generally pertains:

1) If chemical-specific data on susceptibility from early-life exposures were available for derivation of CSFs, those slope factors are used for risk characterization, and Age Dependent Adjustment Factors (ADAFs) are not applied.
2) If chemical-specific data on susceptibility from early-life exposures were not available, the ADAFs are applied in calculating or estimating risks associated with early-life exposures (USEPA, 2005c).

If the latter case applies, the *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* (USEPA, 2005b) recommends the following default ADAFs be applied in risk assessments:

- 10-fold adjustment for exposures during the first 2 years of life;
- 3-fold adjustment for exposures from ages 2 to <16 years of age; and
- No adjustment for exposures after turning 16 years of age.

In such cases, Equation 11 can be altered to include the ADAFs in the following way:

$$\text{Risk} = (\text{IUR} \times \text{EC}_{<2} \times \text{ADAF}_{<2}) + (\text{IUR} \times \text{EC}_{2\text{-}16} \times \text{ADAF}_{2\text{-}16}) + (\text{IUR} \times \text{EC}_{>16})$$

Sources: USEPA, 2005b and USEPA, 2005c.
Note: All communications and factsheets pertaining to the implementation of the 2005 *Cancer Guidelines* can be found at www.epa.gov/osa/spc/cancer_guidelines.htm.

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5.2 Hazard Quotients

The HQ for the inhalation pathway can be calculated with the following general equation:

HQ = EC/(Toxicity Value[1] x 1000 µg/mg) **(Equation 12)**

Where: HQ (unitless) = Hazard Quotient;
EC ($\mu g/m^3$) = exposure concentration (See Equations 7 or 8);
Toxicity Value (mg/m^3) = Inhalation toxicity value (e.g., RfC) that is appropriate for the exposure scenario (acute, subchronic, or chronic).

[1] Risk assessors should refer to the flowchart (Figure 2) to select an appropriate inhalation toxicity value for the exposure scenario at a site in order to calculate the HQ.

6. EXAMPLE EXPOSURE SCENARIOS

This section of the guidance includes examples of the types of exposure scenarios risk assessors may encounter when evaluating inhalation exposures at waste sites. Each scenario includes sample values for exposure parameters and reviews the process of estimating the EC and risks for cancer and other health effects. These examples are provided for illustrative purposes only and are not representative of every exposure scenario that could be encountered at a site. Furthermore, risk assessors should use site-specific values for exposure parameters if practicable when estimating ECs and risk levels or HQs. This would typically require some information on activity patterns for the specific site or the use of professional judgment. If default values are to be used for certain exposure parameters, please consult the Superfund website for up-to-date information on Superfund-recommended default exposure parameters.[34]

6.1 Residential Receptor

An example of a residential scenario could consist of inhalation exposure for up to 24 hours per day, up to 350 days per year for 6 to 30 years. When estimating cancer risk for this type of scenario, Equation 6 is recommended to calculate an EC and Equation 11 is recommended to estimate risk. For estimating hazard quotients for cancer or non-cancer effects, this scenario can be evaluated using the steps outlined in Figure 2. The duration of this scenario ranges from 6 to 30 years, which can be considered chronic (because it consists of repeated exposures for approximately 10 percent of a receptor's lifespan). The frequency of this scenario is generally as frequent as a chronic toxicity test and therefore Equation 8 is recommended to derive a chronic EC and Equation 12 with a chronic toxicity value is recommended to calculate an HQ. If information about multiple MEs is available, risk assessors should proceed according to Section 3.4 to estimate ECs to use in estimating cancer risks or HQs.

When assessing the risk under the residential scenario for children, the risk assessor should keep in mind that exposure parameters, specifically those related to activity patterns (e.g., exposure time, frequency, and duration) may be different for children and adults at the same site. For example, due

[34] http://www.epa.gov/oswer/riskassessment/superfund_hh_exposure.htm.

to outdoor play patterns, children may spend more time near the source of contamination than adults, and thus would have higher exposure time and/or exposure frequency values than adults living in the same location.[35] For indoor vapor intrusion from the subsurface, very young children might be more highly exposed due to substantial time spent indoors.

Beyond the consideration of activity patterns, MEs, and chemicals with a mutagenic MOA for carcinogenicity (as described in Section 5.1), no additional adjustments to account for specific child receptors should be made to the default values. Appendix A of this document is intended to illustrate that the use of default values sufficiently covers age-related variation in DAF or HEC values derived using the EPA *Inhalation Dosimetry Methodology's* default approach.

6.2 Commercial-Industrial/Occupational Receptor

An example of a commercial-industrial or occupational inhalation exposure scenario could be characterized by full-time workers (e.g., 8 hours per day, 5 days per week) in an indoor setting, such as an office building, exposed via vapor intrusion of subsurface contamination on a daily basis for 5 to 25 years. When estimating cancer risk for this type of scenario, Equation 6 is recommended to calculate an EC and Equation 11 is recommended to estimate risk. Following the flowchart in Figure 2, the duration and exposure pattern of this scenario would typically be considered chronic. Therefore, Equation 8 is recommended to derive a chronic EC and Equation 12 is recommended (with a chronic RfC) when calculating an HQ for cancer or non-cancer effects. If information about multiple MEs is available, risk assessors should proceed according to Section 3.4 when deriving ECs to use in estimating cancer risks or HQs. Exposure parameters should be adjusted to consider the exposure time, frequency and duration for this scenario, which may differ from a residential scenario. Risk assessors should also use appropriate exposure parameters for outdoor workers who, similar to children, may spend more time near a source of contamination than indoor workers.

6.3 Construction Worker

One example of a construction worker scenario could involve a long-term project (1-2 years) with workers exposed regularly to contaminant vapors and fugitive dust (8 hours per day, 5 days per week). When estimating cancer risk for this type of scenario, Equations 6 and 11 are recommended to calculate an EC and the risk estimate, respectively. Following the flowchart in Figure 2, the duration of this exposure scenario would typically be considered subchronic. In addition, this exposure is generally as frequent as a subchronic toxicity test. Therefore, Equation 8 is recommended to derive a subchronic EC, and Equation 12 is recommended for use with a subchronic toxicity value to calculate the HQ. If information about multiple MEs is available, risk assessors should proceed according to Section 3.4 when deriving ECs to use in estimating cancer risks or HQs.

6.4 Trespasser/Recreational Receptor

An example trespasser/recreational scenario could consist of an exposure of 1 to 2 hours per day, for 100 days per year or less. When estimating cancer risk for this type of scenario, Equations 6 and 11

[35] For additional information about early-lifestage age groups to consider when assessing children's exposure to environmental contaminants, please consult EPA's *Guidance on Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants* (EPA, 2005d).

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are recommended to calculate an EC and the risk estimate, respectively. Following the steps in Figure 2 for cancer or non-cancer effects characterized by an RfC, each exposure period should be assessed separately because this exposure lasts only one to two hours each day for an average of two days per week. Therefore, Equation 7 is recommended to derive acute ECs for each exposure period. In addition, Equation 12 is recommended for use with an acute toxicity value to calculate HQs for each exposure period.

7. TARGET CONCENTRATIONS FOR SCREENING ANALYSIS OF INHALATION PATHWAYS

For purposes of this guidance, risk-based screening levels are values that may be compared to the contaminant concentration in air to help risk assessors identify potential contaminants of concern. Screening levels can also be calculated for comparison with samples from source media at a site, such as soil. Screening levels are generally not appropriate for use as clean-up levels; they are intended to aid in initial evaluation of contaminants and exposure pathways of concern prior to proceeding with a baseline risk assessment.[36] If contaminant concentrations in air exceed the risk-based screening levels appropriate for the receptor population of interest, risk assessors should gather site-specific information to determine the need for any remedial action. The following sections outline a recommended approach for calculating screening levels in air as well as source media.

7.1 Target Contaminant Concentrations in Air

The equations recommended for estimating ECs and risk (Equations 6 through 12) can be used to calculate target contaminant concentrations in air by following the four steps outlined below in Table 4.[37]

If air samples from a site are found to be below the target concentration, the risk assessor can generally conclude that this pathway does not pose an unacceptable level of risk from the contaminant. If the concentrations are found to exceed the screening levels, the risk assessor should evaluate the inhalation pathway further by gathering additional site-specific data on contaminant levels, site conditions, and receptor characteristics.

7.2 Screening Levels for Other Media

Inhalation risk-based screening levels may also be calculated for media other than air, including soils, tap water, soil gas, and ground water. The soil gas and ground water values may be derived specifically to address concerns about vapor intrusion from subsurface contamination into indoor spaces.

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[36] EPA regions, states, or other agencies may support unique screening levels for specific purposes that may differ from the method presented in this document. Generally, when using screening levels it is important that risk assessors understand the target risks, toxicity, and exposure assumptions as well as migration-attenuation assumptions on which they are based, and to apply them for their intended use.

[37] Target contaminant concentrations in air calculated according to the procedure outlined in this document are generally protective for direct inhalation exposures. This process should not be used to calculate concentrations in air to be protective of indirect exposures (e.g., ingestion of crops contaminated through air delivery or vapor phase transfer, ingestion of livestock or fish contaminated indirectly through air deposition or vapor phase transfer).

TABLE 4
RECOMMENDED PROCEDURE FOR CALCULATING RISK-BASED SCREENING CONCENTRATIONS FOR CONTAMINANTS IN AIR

	Cancer Risk-Based	Hazard-Based[1]
Step 1: Select Target Levels	Select target cancer risk (e.g., 1 x 10^{-6}).	Select target HQ (e.g., 1).
Step 2: Identify Toxicity Value[2]	Identify inhalation cancer potency value (e.g., IUR). If none exists, proceed with hazard-based screening level calculation.	Identify inhalation reference value (e.g., RfC) to match exposure scenario (acute, subchronic, or chronic). If none exist, proceed with cancer screening level calculation.
Step 3: Calculate CA	Using target cancer risk from Step 1 along with the receptor- and scenario-specific exposure parameter values, calculate CA; the following equation is recommended: CA = (AT x Target Risk)/(IUR x ET x EF x ED)	Using target HQ from Step 1 along with the receptor- and scenario-specific exposure parameter values, calculate CA; the following equation is recommended: CA = (AT x Target HQ x RfC x 1000 µg/mg)/(ET x EF x ED)
Step 4: Select Screening Concentration	Select minimum of predicted cancer risk- and hazard-based values as screening concentrations.[3] Repeat for each receptor/scenario combination of interest.	

[1] Hazard-based screening concentrations are typically derived from reference values such as RfCs. These values may be available for non-cancer effects but may include cancer, if a nonlinear MOA is thought to operate for a chemical.
[2] If no inhalation toxicity value is available for a chemical, contact STSC for further direction on how to proceed.
[3] Screening levels estimated from the equations presented in Step 3 could yield concentrations that exceed the maximum possible vapor concentration for a chemical. In such cases, it may be useful to calculate the maximum possible vapor concentration of the pure contaminant at the temperature of interest, using the following formula: C_{max} = S x H x 10^3 L/m^3, where S = solubility at 25° C (or temperature of interest) and H (unitless) = Henry's Law Constant at 25° C (or temperature of interest). This equation is based on an established relationship (see, for example, Schwartzenbach et al. 1993), that allows the Henry's Law Constant to be estimated as the ratio of a compound's vapor pressure and aqueous solubility for compounds that are slightly to moderately soluble in water. When the dimensionless Henry's Law constant, H, is used, the relationship described above can be used to calculate the vapor concentration of a saturated solution of a given compound, assuming equilibrium between the vapor and aqueous phases.

7.2.1 Soil Screening Levels

When evaluating risk in a source medium, such as soil, it is typically possible to calculate screening levels for that medium that are expected to be protective of inhalation exposures based on the expected transfer of a contaminant from the source medium to the air. Soil Screening Levels (SSLs) can be described as "risk-based soil concentrations derived for individual chemicals of concern from standardized sets of equations. These equations combine EPA chemical toxicity data with parameters defined by assumed future land uses and exposure scenarios, including receptor characteristics and potential exposure pathways" (USEPA, 2002b). These SSLs may be used for screening analyses and may serve as the basis for the development of Preliminary Remediation Goals (PRGs). Refer to the *Soil Screening Guidance* (USEPA, 1996) and the *Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites* (USEPA, 2002b) for recommended equations that can be used to calculate SSLs for volatilization of chemicals from soil to air and for particulate emissions.

7.2.2 Tap Water Screening Values

Contaminated tap water may pose risk by the inhalation route if the contaminants present are volatile. Screening levels can be calculated for tap water that account for inhalation exposures resulting from the household use of water (e.g., showering, laundering, dishwashing). Risk assessors should consult their local EPA regional risk assessor for direction on how to calculate appropriate screening levels for tap water.

7.2.3 Soil Gas or Ground Water Screening Values for Vapor Intrusion

If there is concern at a site about the possibility of migration of vapor-forming chemicals from contaminated soil gas or ground water into the indoor air of overlying buildings ("vapor intrusion"), screening values can be calculated for these media. Risk assessors should first follow the procedure outlined in Section 7.1 and Table 4 to calculate a risk-based target concentration for the contaminant in air.

For the calculation of a soil gas screening-level concentration, the target air concentration is then divided by an assumed screening-level attenuation factor. The attenuation factor (the ratio of indoor air divided by subsurface source concentration) represents the factor by which subsurface vapor concentrations migrating into indoor air spaces are reduced due to a variety of attenuating mechanisms.

For the calculation of a ground water screening-level concentration, the target air concentration is divided by an assumed screening-level attenuation factor, and the resulting soil gas concentration is converted to a corresponding ground water concentration, assuming equilibrium between the aqueous and vapor phases at the water table.

Risk assessors should consult their local EPA regional risk assessor for direction on how to calculate appropriate screening levels for soil gas and ground water when vapor intrusion is an issue at a site.

8. DEVELOPING AGGREGATE AND CUMULATIVE RISK ESTIMATES

EPA's current approach to estimating cumulative risk or hazard at a site from multiple chemicals, set forth in *RAGS, Part A* (USEPA, 1989), is not affected by the *Inhalation Dosimetry Methodology* and therefore is not being updated at this time. In addition, the aggregation of risks and hazards across multiple exposure routes should remain unchanged. The recommended approaches for aggregating risk and hazard estimates are outlined below.

8.1 Estimating Cumulative Risks and Hazards Across Multiple Chemicals

The recommended method for estimating cumulative risk and hazard at a site from exposure to multiple chemicals is described in *RAGS, Part A*, Section 8.2.2. This method is based on the default approaches described in *Guidelines for the Health Risk Assessment of Chemical Mixtures* (USEPA, 1986). Additional information on this method was subsequently published in the *Supplementary Guidance for Conducting Health Risk Assessment of Chemical Mixtures* (USEPA, 2000b). The recommended methods to use with quantitative cancer risk estimates as well as with HQs are outlined below.

8.1.1 Cancer Risks

When evaluating predicted cancer risks from multiple contaminants, risk assessors should estimate the cancer risk for each substance and then sum these risks. This yields an estimate of total cancer risk, which represents the cumulative predicted cancer risk for the chemicals at a site.

Risk assessors should note, however, that this recommended method assumes "independence of action by the compounds involved (i.e., that there are no synergistic or antagonistic chemical interactions and that all chemicals produce the same effect, i.e., cancer)" (USEPA, 1989). In addition, this simple additive approach is generally most appropriate for total cancer risks less than 0.1. If these assumptions are incorrect, over- or under-estimation of actual multiple-substance risk could result (USEPA, 1989).

8.1.2 Hazard Quotients

When the evaluation involves multiple chemicals assessed via HQs, risk assessors typically first calculate the HQ for each substance, and then sum the individual HQ values. This generally yields an estimated hazard index (HI) for the multiple chemicals assessed via a hazard-based approach. Separate HIs should be calculated for each type of exposure period (i.e., chronic, subchronic, acute). If an HI is greater than 1, it is generally appropriate to derive separate HIs for each target organ of concern (for more information, see *RAGS, Part A*, page 8-14).[38] When multiple acute exposures are present at a site, risk assessors should evaluate each acute exposure event separately. Hazards from multiple chemicals generally should be summed only when the exposures to these chemicals occur simultaneously.[39]

8.2 Aggregating Risk and Hazard Quotients Across Exposure Routes

Guidance for combining the multi-chemical risk estimates and hazard quotients across exposure pathways is described in *RAGS, Part A*, Section 8.3 (USEPA, 1989). In order to determine whether risks or HIs should be combined across exposure pathways, risk assessors should first identify reasonable exposure pathway combinations. Then, risk assessors should examine whether it is likely that the same individuals would consistently face the reasonable maximum exposure (RME) by more than one pathway.

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[38] This recommended method assumes that "the dose for each individual component is at a level at which effects are not expected to occur, be observable, or be of concern; however, when the doses are combined, effects of concern may be expected or observed in response to the higher dose level of the mixture" (EPA, 2000b, page 12). Another assumption of the HI approach is that the compounds induce the same effect by the same mechanism of action. Therefore, "application of the HI equation to a number of compounds that are not expected to induce the same type of effects or that do not act by the same mechanism, although appropriate as a screening-level approach, could overestimate the potential for effects" (EPA, 1989, page 8-14). This is generally less of a concern if one to two substances are responsible for driving the HI above 1.

[39] In cases where a single chemical is present at a site and receptors are exposed through a series of acute exposure events, the highest single EC should be compared to an acute reference value of the appropriate duration to assess hazard.

The recommended approach for estimating excess cancer risk from exposure via multiple routes is to first estimate cancer risk from each exposure pathway and then sum across the multiple routes.[40]

For the effects assessed via a reference value, risk assessors should calculate the HI for each exposure pathway and sum across the multiple routes. Separate total HIs should be calculated for each type of exposure period (i.e., chronic, subchronic or acute). If the HI exceeds one, there may be concern for potential adverse effects and risk assessors should consider deriving separate HIs for each target organ of concern.

9. RISK CHARACTERIZATION

Risk characterization is the final, summarizing step in conducting a risk assessment. Generally, the purpose of the risk characterization section of a report is to:[41]

- Describe the key findings of the risk assessment in a transparent manner, including identifying hazard, characterizing the dose-response relationship, and describing receptor exposures;
- Identify and describe the scientific and policy assumptions used in the assessment;
- Characterize uncertainties in results; and
- Provide an overall conclusion about the risks present at a site (USEPA, 2000c).

A well-crafted risk characterization section puts risk calculations into context for risk managers so that they may effectively weigh and interpret risk assessment results (i.e., it is the interface between risk assessment and risk management). A few of the key issues and uncertainties involved in calculating risks from inhalation exposures are outlined below.

9.1 Highly Exposed or Susceptible Populations and Life Stages

EPA recommends that the risk characterization portion of the risk assessment explain any particular susceptibilities to inhaled toxicants or potential for increased inhalation exposures among the various receptor groups at a site.[42] We discuss below two possible examples, children and worker receptors, though this discussion could apply to other receptor characteristics as well (e.g., age, disease, gender, genetic characteristics).

9.1.1 Children

One population group that could potentially be more highly exposed to inhalation exposures at a site is children. As discussed in Section 6.2, exposure parameters related to activity patterns (e.g., exposure time, frequency, and duration) and MEs, may vary across age groups. For example, due to outdoor play patterns, children may spend more time near the source of contamination than adults,

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[40] Note that this approach is generally most appropriate for total cancer risks of less than 0.1 (EPA, 1989).

[41] For specific information on the format of risk characterizations, refer to *Elements to Consider when Drafting EPA Risk Characterizations* (EPA, 1995c).

[42] EPA's IRIS glossary defines susceptibility as the following: "Increased likelihood of an adverse effect, often discussed in terms of relationship to a factor that can be used to describe a human subpopulation (e.g., life stage, demographic feature, or genetic characteristic)" (EPA, 2008b).

and thus would have higher exposure time and/or exposure frequency values than adults living in the same location. Therefore, it is important to carefully describe site-specific exposures to children, and assumptions made in risk calculations.[43]

If chemical-specific data on susceptibility to the toxic effects from early life exposures are available, these data are considered when developing toxicity values that specifically address differential toxicity to the young (e.g., vinyl chloride) (USEPA, 2005c). Toxicity values derived using the default approach from the *Inhalation Dosimetry Methodology* are developed for the human population as a whole, including sensitive subgroups. Therefore, as described in Section 6 of Appendix A, no quantitative adjustment of toxicity values derived using the default approach in the *Inhalation Dosimetry Methodology* is recommended for specific age groups to account for different ventilation rates or body weights of specific age groups.

When evaluating risk to carcinogenic chemicals with a demonstrated mutagenic MOA but which lack chemical-specific information on susceptibility from early life exposures, EPA recommends a quantitative adjustment of the toxicity value to account for early life susceptibility, as described in the *Supplemental Cancer Guidelines* (see USEPA, 2005b & 2005c; and Section 5.1 of this guidance for further information).

9.1.2 Workers

Workers could have increased exposure under certain occupational scenarios. Some outdoor workers might spend more time near a source of contamination in the course of their job and this should be reflected in adjustments to the exposure parameters (e.g., ET, Exposure Frequency (EF), and ED) describing the worker exposure scenario. Toxicity values derived using the *Inhalation Dosimetry Methodology* are developed for the human population as a whole, including sensitive populations and life stages. In the default *Inhalation Dosimetry Methodology* approach, typical variation in IRs between periods of high activity and rest is considered. However, if workers have especially high levels of exertion with correspondingly high ventilation rates, these workers could be at the upper end of the risk range, particularly if they are exposed to Category 1 gases, which have direct effects in the respiratory tract. This implication should be recognized in the risk characterization section.

9.2 Uncertainties in Inhalation Risk Assessment

This guidance recommends including an assessment of the key uncertainties that may significantly impact risk estimates for inhaled chemicals. This should ensure transparency, clarity, reasonableness and consistency in risk assessments, as recommended by EPA's *Policy for Risk Characterization* (USEPA, 1995a). Other sources of uncertainty may be present and other EPA documents provide guidance on characterizing uncertainty in risk the assessment process (USEPA, 1992, 1995a, 1995b, 1995c, 1997a, 1997b). Key uncertainties related to inhalation risk assessment, which is the focus of this section, include the development of ECs, choice of toxicity value, lack of quantitative toxicity information via inhalation, and the approach to estimating and aggregating risks. According to EPA's *Guidance for Risk Characterization*, the discussion of uncertainty "should reflect the type and complexity of the risk assessment, with the level of effort for analysis and discussion of uncertainty

[43] For additional information on children's health risk assessment, please consult *A Framework for Assessing Health Risks of Environmental Exposures to Children* (EPA, 2006b).

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corresponding to the level of effort for the assessment" (USEPA, 1995b). Therefore, risk assessors should provide a qualitative and/or quantitative evaluation of key uncertainties pertaining to inhalation risk, and their impact on the outcome of the assessment, consistent with the level of effort of the specific risk assessment.

9.2.1 Development of Exposure Concentrations

As described in Section 3 of this guidance, with the exception of acute exposures, time-weighted averages are typically used to represent intermittent or variable inhalation exposures to receptors at a site. This recommended approach is consistent with the duration adjustment approach (based on Haber's Law) that is generally used in deriving the toxicity values (see Section 2.1.1.1 for further information). As mentioned in Section 3, when evaluating situations in which the exposure is long-term, yet there are short periods of significantly higher exposure, those periods should also be assessed using appropriate short-term toxicity values. This ensures that periods of much higher exposure can be appropriately assessed and not "diluted out" in the assessment of longer-term exposure.

When information on multiple MEs exists at a site, risk assessors may choose to estimate ECs as outlined in Section 3.4. However, this typically requires sufficient time-activity information of receptors at a site to accurately determine the time spent in each ME. Incomplete or low quality data on time-activity pattern may introduce uncertainty into the estimation of the ECs for MEs. Risk assessors should describe the quality and completeness of these data.

The recommended method for determining the CA at a site can potentially introduce uncertainty into the EC calculations. For instance, if contaminant concentrations in air are measured, risk assessors should consider uncertainties related to how well the set of air samples available at a site represents the duration and time period being assessed as well as measurement uncertainty related to the methods and equipment used. In addition, risk assessors should describe any potential confounding of indoor air samples by other sources of contaminants (e.g., household products). If contaminant concentrations in air are modeled, (e.g., by EPA's spreadsheet models for vapor intrusion) risk assessors should address model-related uncertainties and their potential impact on the estimate of contaminant concentrations in air. Considerations of particle size at the site versus particle size used to derive the toxicity value are also important.

9.2.2 Toxicity Assessment

Section 4.1 of this document indicates that some IURs on IRIS were developed through extrapolation from oral CSFs (see Appendix B of this document). The use of toxicity values derived through simple route-to-route extrapolation introduces additional uncertainty into risk calculations. Therefore, risk assessors should indicate when extrapolated IURs are used and should characterize the potential impact of the uncertainty associated with using these values, if known.

Section 4.2 and Appendix C of this guidance recommends contacting STSC to help identify appropriate toxicity values for conducting a risk assessment at Superfund sites in the absence of published inhalation toxicity values. If STSC is unable to recommend a toxicity value, risk assessors should acknowledge the resulting uncertainty in risk associated with the chemical(s) lacking inhalation toxicity data. If STSC provides risk assessors with a toxicity value based on a PBPK

model, model uncertainty should be discussed. In addition, if STSC provides risk assessors with one or more structurally analogous chemicals, risk assessors can use toxicity data for these chemicals to help characterize the potential magnitude of the inhalation risk associated with the chemical(s) lacking data. In this case, risk assessors should acknowledge the uncertainty associated with relying on toxicity data for analogous chemicals to characterize risk at the site.

Risk assessors should also acknowledge chemicals that lack duration-appropriate toxicity values and discuss the potential impacts of substituting alternative toxicity values for HQ calculations. For instance, if the ED is determined to be subchronic but no subchronic inhalation RfC or analogous toxicity value is available for that chemical, the risk assessor should address the uncertainty associated with calculating an HQ using a toxicity value for a different duration, such as chronic, or the impact of not quantifying those risks. In addition, if risk assessors use an acute toxicity value that does not match the duration of the acute exposure being assessed, the possibility of under or overestimating hazard should be discussed.

When conducting a screening-level risk assessment using screening values such as those described in Section 7, it is important to further evaluate and clearly describe the quality and uncertainties associated with the inhalation toxicity values used in the risk assessment if measured sample contaminant concentrations at a site exceed these screening values.

9.2.3 Estimating Cancer Risks

For high exposures, for example those within the range of epidemiological studies (usually those predicted to have risks greater than 10^{-2}), the IUR derived from the linear extrapolation below the range of observation is generally not appropriate for use (see Section 5.1 of this document for further information).[44] Risk assessors should provide specific information in the risk characterization describing how these high exposures were addressed in the risk assessment. For instance, if a risk assessor chose to provide a semi-quantitative approach (e.g., indicating that risks are above 10^{-2}), this should be indicated, along with a description of the uncertainties involved in not fully quantifying risk associated with exposure to this chemical. If a risk assessor chose to use the original model in the IRIS file or other technical background document, the risk characterization section should include a description of any uncertainties in the model used and could contain examples of the risks estimated.

9.2.4 Estimating Risk and Hazard from Multiple Chemicals and Exposure Pathways

Risk assessors should also describe uncertainties involved in aggregating risk and hazard across multiple chemicals and exposure pathways. For instance, the approaches described in Section 8 of this document are associated with several assumptions (e.g., independence of action and doses for individual compounds at levels not expected to be of concern). If these assumptions are not met, aggregation may not be appropriate. This should be fully described in the risk characterization section and any uncertainties involved in the lack of quantitative information should be indicated.

[44] Also refer to Section 8.2.1 of *RAGS, Part A* for further discussion of this topic (EPA, 1989, page 8-6).

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APPENDIX A

APPENDIX A

ANALYSIS OF DEFAULT APPROACH FOR HEC DERIVATION AS COMPARED TO POPULATION- AND LIFESTAGE-SPECIFIC CALCULATIONS

NOTE: The Agency's inhalation dosimetry methodology (USEPA, 1994; hereafter, "the *Inhalation Dosimetry Methodology*") is a technical report that describes the derivation of human equivalent concentrations (HECs) from animal (or human) studies, as well as the other steps involved in developing a chronic Reference Concentration (RfC). This appendix is included to illustrate the HEC derivation using the *Inhalation Dosimetry Methodology*'s default approach (with the recommended default values for humans), and to also illustrate the impact of substituting alternate age- and activity-specific human values into the default calculations. The default approach is employed for chemicals for which more chemical-specific dosimetric and pharmacokinetic data are not available, thus precluding the use of more advanced models for deriving the HEC. The calculations in this appendix do not represent a refined or optimal model for assessing intra-human variability (e.g., age- and activity-specific risks), and are not intended to imply that risk assessors should deviate from the *Inhalation Dosimetry Methodology* by substituting alternate values into the default calculations. Age-specific data are limited. Because of these limitations, the calculations made for different ages and exposure groups in this appendix are not recommended for use in quantitative risk assessment (i.e., they are only for the purpose of illustration), but may be useful in discussions of uncertainty and variability associated with the default approach.

It is also noted that, as of this writing, the Agency is involved in a routine reevaluation of scientific advancements in the field, with consideration of the need for improvement to the *Inhalation Dosimetry Methodology*. Any revisions will consider current understanding of inhalation dosimetry and differences across and within species, as well as the Agency's risk assessment needs. In order to transparently and quantitatively address children's inhalation dosimetry and risk assessment, this guidance document will be updated (on-line) when Agency methodology updates are available that are specific to early life. Until that time, the 1994 *Inhalation Dosimetry Methodology* is the appropriate Agency methodology.

INTRODUCTION

This appendix consists of examples and discussions illustrating the current default chemical category-specific approach to inhalation dosimetry for the various categories of gases and particles as described in *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry* (USEPA, 1994; hereafter, the *Inhalation Dosimetry Methodology*). This default inhalation dosimetry approach is used to convert toxicological and epidemiological study data to an HEC that can then be used to derive chronic RfCs for the human population (inclusive of susceptible populations and life stages, such as children) and also in the development of Inhalation Unit Risks (IURs) (USEPA, 2005). The default approach does not rely on age- or activity-specific values for physiological parameters when calculating HECs; however the default approach has been designed by EPA to derive reference values that are protective across the entire population.

The appendix includes six sections. Sections 1 through 3 address Category 1 gases. These sections provide example calculations for Category 1 highly reactive, high water solubility gases that are typically absorbed in the upper airways, exhibiting adverse effects in the extrathoracic (ETh), tracheobronchial (TB), and pulmonary (PU) regions of the respiratory tract, respectively. These examples include comparisons of HEC calculations based on default parameters with those derived using age- and activity-specific parameters for the respiratory region affected. Section 4 addresses Category 3 low reactivity, limited water solubility gases that exhibit systemic effects outside the respiratory tract. Section 5 addresses changes in particle deposition in the respiratory tract across age groups. The conclusions are summarized in Section 6.

When reviewing the examples, please note the following:

- An RfC derived using the *Inhalation Dosimetry Methodology* is defined as "an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime" (USEPA, 2008).

- All examples in this appendix are based on the *Inhalation Dosimetry Methodology*. EPA is committed to periodically reviewing and updating the *Inhalation Dosimetry Methodology* to ensure that it reflects the current state of the science and that it yields toxicity values that sufficiently cover potential age- and activity-related variation in inhalation exposure. A review and update is currently underway.

- The examples in this appendix are all based on calculating HECs from a point of departure (POD) for non-cancer effects (e.g., a No Observed Adverse Effect Level (NOAEL), Lowest Observed Adverse Effect Level (LOAEL), or Benchmark Concentration, Lower confidence limit (BMCL)). These calculations could also be performed in an identical manner for carcinogens using a POD for cancer risk estimate derivation (e.g., a Lower limit on the Effective Concentration (LEC) value).

- The default animal and human values for minute volume (V_e) and surface area (SA) used in these examples were obtained from *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry* (USEPA, 1994).[45] The age- and activity-specific V_e values were obtained from the International Commission on Radiological Protection (ICRP) Publication 66, *Human Respiratory Tract Model for Radiological Protection* (ICRP, 1994).[46] Age-specific SA values used in Examples 1 and 2 were calculated using scaled estimates for the mass and thickness of respiratory region-specific target tissue from ICRP (1994); Values for Example 3 were calculated from an allometric scaling equation presented in a publication by Zeltner et al. (1987). EPA's Office of Research and Development (ORD) selected these data following review of the available physiological data for the age groups indicated in the examples.

- Chemical-specific data from the Integrated Risk Information System (IRIS) file for acrolein were used in the ETh example (Example 1). However, the other two examples, which focus on effects in the TB and PU regions, respectively, use hypothetical data for the POD because there are currently no chemicals on IRIS exhibiting Critical Effects (for RfC derivation) in those regions.[47] The conclusions of these two examples are unaffected by the use of hypothetical data because the results are driven by the values of parameters that are not chemical-specific (i.e., SA and V_e).

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[45] The minute volume is the total ventilation per minute and equals the product of the tidal volume (the air volume entering or leaving the lungs with a single breath) and the respiratory frequency.

[46] For further information on inhalation rates in humans under different scenarios, refer to Chapter 5 of EPA's *Exposure Factors Handbook* (EPA, 1997).

[47] Hypothetical examples for the TB and PU regions were included in this appendix because currently no RfCs for gases on IRIS are calculated based on animal studies showing health effects occurring in these regions of the respiratory system

1. EXAMPLE 1: CATEGORY 1 GAS, EXTRATHORACIC EFFECTS, ACROLEIN

The Dosimetric Adjustment Factor (DAF) for a Category 1 gases, the Regional Gas Dose Ratio (RGDR), is based on the animal to human ratio of the V_e divided by the SA of the region of the respiratory tract where the effect occurs. For acrolein, the effect occurs in the ETh region. The DAF is typically calculated using the following equation (USEPA, 1994, Equation 4-18):

$$RGDR_{ETh} = \frac{\left(\frac{V_e}{SA_{ETh}}\right)_{animal}}{\left(\frac{V_e}{SA_{ETh}}\right)_{human}} = \frac{\frac{0.14\,L/min}{15\,cm^2}}{\frac{13.8\,L/min}{200\,cm^2}} = 0.14 \qquad \textbf{(Equation A-1)}$$

The default *Inhalation Dosimetry Methodology*-recommended values for the V_e and SA_{ETh} of the Wistar rat (the animal in the principal study for acrolein) are 0.14 L/min (0.20 m^3/day) and 15 cm^2, respectively (USEPA, 1994). EPA's default human values are 13.8 L/min (20 m^3/day) for V_e and 200 cm^2 for SA_{ETh} (USEPA, 1994). The RGDR for the ETh region ($RGDR_{ETh}$) was calculated using these values for the rat and the human as shown in Equation A-1. In the laboratory animal study on acrolein, the LOAEL adjusted for continuous exposure ($LOAEL_{[ADJ]}$) of 0.16 mg/m^3 (USEPA, 2003) is used as the point of departure. The $LOAEL_{[HEC]}$ is the $LOAEL_{[ADJ]}$ multiplied by the $RGDR_{ETh}$.

To illustrate any potential age- or activity-related variation in the $LOAEL_{[HEC]}$ that might result from using human parameter values other than the defaults, scaled estimates for the mass and thickness of ETh target tissue from ICRP (1994) at different ages are used to calculate the SA_{ETh} values in Table A-1. Age- and activity-related V_e reported in ICRP (1994) are based on daily time-budgeted reference values. Table A-1 shows little variation in the resultant $LOAEL_{[HEC]}$ across the groups in this example. The default procedure produces the lowest $LOAEL_{[HEC]}$ value in Table A-1 and is, therefore, sufficient to cover all of these groups.

TABLE A-1
COMPARISON OF THE HEC-DEFAULT (EPA, 1994) WITH EXAMPLE $LOAEL_{[HEC]}$ VALUES FOR HUMANS OF DIFFERENT AGES AND ACTIVITY PATTERNS FOR THE EXTRATHORACIC REGION

	Total $V_{e\ (human)}$ (L/min)[a]	$SA_{ETh\ (human)}$ (cm^2)[b]	$(V_e/SA_{ETh})_{human}$ (L/min-cm^2)	$RGDR_{ETh}$	$LOAEL_{[HEC]}$ (mg/m^3)
Outdoor Worker, Male	17.5	470	0.037	0.25	0.04
Sedentary Worker, Male	15.4	470	0.033	0.28	0.04
Sedentary Worker, Female	12.6	407	0.031	0.30	0.05
15 Year-Old Male	14.0	439	0.032	0.29	0.05
15 Year-Old Female	10.9	397	0.027	0.35	0.06
10 Year-Old	10.6	293	0.036	0.26	0.04
5 Year-Old	6.1	198	0.031	0.30	0.05
1 Year-Old	3.6	97.1	0.037	0.25	0.04
3 Month-Old	2.0	65.8	0.030	0.31	0.05
HEC - Default	13.8	200	0.069	0.14	0.02

[a] These values are from the ICRP publication, Tables 8, 27, B.16a, B.16b and B.17 (ICRP, 1994).
[b] These values are from the ICRP publication, Tables 1 and 5 (ICRP, 1994).

2. EXAMPLE 2: CATEGORY 1 GAS, TRACHEOBRONCHIAL EFFECTS, HYPOTHETICAL CHEMICAL

The DAF for a Category 1 gas or vapor exhibiting effects in the TB region is based on the animal to human ratio of the V_e divided by the SA of the TB region for each species. The DAF is typically calculated using the following equation:

$$RGDR_{TB} = \frac{\left(\frac{V_e}{SA_{TB}}\right)_{animal}}{\left(\frac{V_e}{SA_{TB}}\right)_{human}} = \frac{\frac{0.14\ L/min}{22.5\ cm^2}}{\frac{13.8\ L/min}{3200\ cm^2}} = 1.4 \qquad \textbf{(Equation A-2)}^{48}$$

This example assumes that the hypothetical chemical has been tested on Wistar rats and therefore utilizes the EPA animal default values for that strain. The V_e value used is 0.14 L/min (0.20 m^3/day) and the default SA_{TB} is 22.5 cm^2 (USEPA, 1994). EPA's default human values are 13.8 L/min (20 m^3/day) for V_e and 3200 cm^2 for SA_{TB} (USEPA, 1994). The RGDR for the TB region ($RGDR_{TB}$) is calculated using these values for the rat and the human, as shown in Equation A-2. The example also assumes a NOAEL adjusted for continuous exposure ($NOAEL_{[ADJ]}$) of 0.16 mg/m^3 as the point of departure. The $NOAEL_{[HEC]}$ is the $NOAEL_{[ADJ]}$ multiplied by the $RGDR_{TB}$.

Table A-2 shows little variation across age and activity groups in the $NOAEL_{[HEC]}$. The variation from the default (less than a factor of 2) is less than the default value of 10 used for the uncertainty factor for intraspecies variability when deriving the RfC. Application of the normal procedure for

[48] This equation is the reduced, default version of Equation 4-19 of the *Inhalation Dosimetry Methodology*. Equation 4-19 is reduced to this form consistent with the derivation of the reduced form of the RGDR equation of extrathoracic effects described in section 4.3.6.1 and Appendix I of the *Inhalation Dosimetry Methodology*.

determining the RfC will accommodate the observed variation. In addition, RfCs and IURs are developed for chronic exposure and will generally involve an exposure for multiple years.

TABLE A-2
COMPARISON OF THE HEC-DEFAULT (EPA, 1994) WITH EXAMPLE $LOAEL_{[HEC]}$ VALUES FOR HUMANS OF DIFFERENT AGES AND ACTIVITY PATTERNS FOR THE TRACHEOBRONCHIAL REGION

	Total $V_{e\,(human)}$ (L/min)[a]	$SA_{TB\,(human)}$ (cm^2)[b]	$(V_e/SA_{TB})_{human}$ (L/min-cm^2)	$RGDR_{TB}$	$NOAEL_{[HEC]}$ (mg/m^3)
Outdoor Worker M	17.5	2660	0.0066	0.94	0.15
Sedentary Worker M	15.4	2660	0.0058	1.1	0.18
Sedentary Worker F	12.6	2640	0.0048	1.3	0.21
15 year M	14.0	2520	0.0056	1.1	0.18
15 year F	10.9	2250	0.0048	1.3	0.21
10 Year	10.6	1830	0.0058	1.1	0.18
5 Year	6.1	1340	0.0046	1.4	0.22
1 Year	3.6	857	0.0042	1.5	0.24
3 Months	2.0	712	0.0028	2.2	0.35
HEC-default	13.8	3200	0.0043	1.4	0.22

[a] These values are from the ICRP publication, Tables 8, 27, B.16a, B.16b and B.17 (ICRP, 1994).
[b] These values are from the ICRP publication, Tables 1 and 5 (ICRP, 1994).

3. EXAMPLE 3: CATEGORY 1 GAS, PULMONARY EFFECTS, HYPOTHETICAL CHEMICAL

The DAF for a Category 1 gas or vapor with an effect in the PU region is based on the animal to human ratio of the alveolar ventilation rate (Q-alv) divided by the SA of the PU region (SA_{PU}) for each species. The Q-alv is approximately equal to the V_e multiplied by 0.7. This adjustment accounts for the anatomic/physiologic deadspace in the PU region, making the Q-alv equivalent to the amount of inspired air available for gas exchange (West, 2000). The DAF for this region of the respiratory tract is typically calculated using the following equation:

$$RGDR_{PU} = \frac{\left(\frac{Q-alv}{SA_{PU}}\right)_{animal}}{\left(\frac{Q-alv}{SA_{PU}}\right)_{human}} = \frac{\frac{0.1\,L/min}{0.34\,m^2}}{\frac{9.7\,L/min}{54\,m^2}} = 1.6 \qquad \textbf{(Equation A-3)}^{49}$$

This example assumes that the hypothetical chemical has been tested on Wistar rats and therefore utilizes the EPA animal default values for that strain. The V_e valued used is 0.14 L/min (0.20 m^3/day), which when multiplied by 0.7, yields a Q-alv of 0.1 L/min. The example uses the EPA default rat SA_{PU} of 0.34 m^2 (USEPA, 1994). EPA's default human values are 13.8 L/min (20

[49] This equation is the reduced, default version of Equation 4-23 of the *Inhalation Dosimetry Methodology*. Equation 4-23 is reduced to this form consistent with the derivation of the reduced form of the RGDR equation of extrathoracic effects described in section 4.3.6.1 and Appendix I of the *Inhalation Dosimetry Methodology*.

m^3/day) for V_e (which yields a Q-alv of 9.7 L/min) and 54 m^2 for SA_{PU} (USEPA, 1994). The RGDR for the PU region ($RGDR_{PU}$) is calculated using these values for the rat and the human, as shown in Equation A-3. The example also assumes a $NOAEL_{[ADJ]}$ of 0.16 mg/m^3 as the point of departure. The $NOAEL_{[HEC]}$ is the $NOAEL_{[ADJ]}$ multiplied by the $RGDR_{PU}$.

Table A-3 below provides the Q-alv values for humans based on the daily time-budgeted V_e for different ages and activity levels from the ICRP publication (1994). SA data for the PU region in the ICRP publication are estimated using an allometric scaling model fitted to data from a morphometric analysis of SA_{PU} in a sample of seven children (ranging in age from 26 days to 5 years) and eight adults (Zeltner et al., 1987). ORD selected the Zeltner analysis for this example because these SA_{PU} data are based on empirical morphometric measurements of human lungs as opposed to scaled estimates determined from lung models (such as those done by Yu and Xu, 1987 or Yu and Yoon, 1991). In addition, the children and adult SA_{PU} values calculated in the Zeltner analysis are supported by several independent studies that measured SA_{PU} in children (Langston et al., 1984) or in adults using similar morphometric techniques (Crapo et al., 1982 & 1983; Stone et al., 1992; Mercer et al., 1994).

Table A-3 shows little variation in the resultant $NOAEL_{[HEC]}$ across the groups in this example. The default procedure produces the lowest $NOAEL_{[HEC]}$ value in Table A-3 and is, therefore, sufficient to cover all of these groups.

TABLE A-3

COMPARISON OF THE HEC-DEFAULT (EPA, 1994) WITH EXAMPLE $LOAEL_{[HEC]}$ VALUES FOR HUMANS OF DIFFERENT AGES AND ACTIVITY PATTERNS FOR THE PULMONARY REGION

	Total V_e (L/min)[a]	Q-$alv_{(human)}$ (L/min)[b]	$SA_{PU\ (human)}$ (m^2)	$(Q\text{-}alv/SA_{PU})_{human}$ (L/min-m^2)	$RGDR_{PU}$	$NOAEL_{HEC}$ (mg/m^3)
Outdoor Worker, Male	17.5	12	139	0.088	3.3	0.53
Sedentary Worker, Male	15.4	11	139	0.078	3.7	0.59
Sedentary Worker, Female	12.6	8.8	114	0.077	3.8	0.61
15 Year-Old Male	14.0	9.8	108	0.091	3.2	0.51
15 Year-Old Female	10.9	7.6	100	0.076	3.8	0.61
10 Year-Old	10.6	7.4	62.0	0.12	2.4	0.38
5 Year-Old	6.1	4.3	37.3	0.11	2.6	0.42
1 Year-Old	3.6	2.5	18.5	0.14	2.1	0.34
3 Month-Old	2.0	1.4	11.0	0.13	2.2	0.35
HEC-Default	13.8	9.7	54.0	0.18	1.6	0.26

[a] These values are from the ICRP publication, Tables 8, 27, B.16a, B.16b and B.17 (ICRP, 1994).
[b] These values are from Zeltner et al. (1987).

4. CATEGORY 3 GASES

The DAF for a Category 3 gas or vapor is based on the ratio of the animal blood:gas partition coefficient to the human blood:gas partition coefficient and is typically calculated using the following equation:

$$DAF = \frac{(H_{b/g})_{animal}}{(H_{b/g})_{human}} \qquad \textbf{(Equation A-4)}$$

The blood:gas partition coefficient is primarily determined by the solubility of the gas in an aqueous medium as well as the protein and lipid content of the blood. There is little reason to suspect that the blood:gas partition coefficient for a non-metabolized chemical will vary greatly across the human population. The limited data available indicate no difference in the blood:gas partition coefficient with age for methylene chloride in mice (Thomas et al., 1996), and for sevoflurane, isoflurane, and halothane in humans (Malviya and Lerman, 1990). Two studies examining the solubility of volatile anesthetics (isoflurane, enflurane, halothane, and methoxyflurane) in the blood and body tissues found higher blood:gas partition coefficients in adults compared with children (Lerman, et al., 1984 & 1986). Any variability in the blood:gas partition coefficient with age is expected to be less than the default value of 10 used for the uncertainty factor for intraspecies variability when deriving the RfC. Any variability in the blood:gas partition coefficient with age is also not expected to cause a large overestimate or underestimate in the calculated cancer risk.

Because of the limited data available, the *Inhalation Dosimetry Methodology* makes the science policy decision to use a value of one for the ratio of the partition coefficients when the animal to human ratio exceeds one or when the animal or human value is unknown. At this time, all chemicals on IRIS for which both human and animal data are available have an animal to human ratio of partition coefficient greater than 1.[50] Therefore, the default assumption of one is a conservative approach that is not likely to underestimate the chemical-specific DAF.

5. PARTICLE DEPOSITION ACROSS AGE GROUPS

The DAF for a particle causing an effect in the respiratory tract, the Regional Dose Deposition Ratio ($RDDR_r$), is based on the animal to human ratio of the V_e and the fractional deposition of the particle in that region (F_r), divided by the surface area of the region where the effect occurs (SA_r) (USEPA, 1994). Inherent in this derivation is the assumption that 100 percent of the deposited dose remains in the respiratory tract and any clearance mechanisms are not considered. The $RDDR_r$ is typically calculated using the following equation:

$$RDDR_r = \frac{\left(\frac{V_e}{SA_r} \times F_r\right)_{animal}}{\left(\frac{V_e}{SA_r} \times F_r\right)_{human}} \qquad \textbf{(Equation A-5)}$$

[50] While 1,4-dioxane has not yet been evaluated on IRIS, it provides an exception to this statement, in that the blood:gas partition coefficient is 2750 for mice, 1850 for rats, and 3650 for humans, yielding an animal to human ratio of 0.75 for mice and 0.51 for rats (Reitz et al., 1990).

The DAF for a particle causing an extra-respiratory (ER) effect, the $RDDR_{ER}$, is based on the animal to human ratio of the V_e and the total deposition of the particle in the entire respiratory tract (F_{total}), divided by body weight (BW) (USEPA, 1994). The $RDDR_{ER}$ assumes that 100 percent of the deposited dose in the entire respiratory tract is available for uptake into the systemic circulation. The following general equation can be used to estimate the $RDDR_{ER}$:

$$RDDR_{ER} = \frac{\left(\frac{V_e}{BW} \times F_{total}\right)_{animal}}{\left(\frac{V_e}{BW} \times F_{total}\right)_{human}} \qquad \textbf{(Equation A-6)}$$

The information on particle deposition in various age groups is quite limited. A discussion of the current state of the science can be found in the *Air Quality Criteria for Particulate Matter Volume II*, Section 6.2.3.2 (USEPA, 2004; hereafter, *PM Criteria Document*).

Experimental and modeling results are summarized in Table A-4. The results for experimental studies are mixed, some suggesting higher deposition in children and others finding no difference across age groups. Bennett and Zeman (1998) and Schiller-Scotland et al. (1994) found no difference between total deposition of particles in the respiratory tract of children (aged 7 to14 and 6 to12, respectively) and adults for 1 to 2 micrometer particles. Schiller-Scotland et al. did find two- to three-fold higher total particulate deposition in 6 to 12 year olds for particles of 2 to 3 micrometers in size. In addition, Bennett et al. (1997) found that deposition in the ETh region was 50 percent greater in children than adults. The *PM Criteria Document* concludes that "these...studies ...do not provide unequivocal evidence for significant differences in deposition between adults and children" (USEPA, 2004, page 6-29). The document notes, however, that children may have higher activity levels and higher associated minute ventilation per lung size, potentially causing a greater size-specific dose of particles to the lung.

Modeled results suggest a higher deposition of particles in the TB region of children when compared to adults, depending on the particle size (Xu and Yu (1986); Hofmann et al. (1989); Musante and Martonen (1999); Phalen and Oldham (2001); Asgharian et al. (2004); Jarabek et al. (2005); Ginsberg et al. (2005)). Mixed results again are found in modeling studies for total deposition and deposition in other respiratory regions. In general, where differences are observed in either experimental or modeled studies, variability in deposition between age groups has been reported to be most often in the range of 1- to 3-fold greater for children than for adults, but ranging from equivalency or less up to 7-fold greater.[51]

[51] A modeling analysis examining deposition fraction per unit area at various airway generations of the lung as a function of age for various particle sizes (ranging from 0.01 to 10 μm) reported comparisons between a 3-month old and 21-year old that ranged from equivalency up to a 14-fold difference in this metric for some specific airway generations (Asgharian et al., 2004).

TABLE A-4
PARTICLE DEPOSITION ACROSS AGE GROUPS

Study	Particle Size	Results
Experimental Studies		
Becquemin et al. (1991)	Various	Nasal deposition higher in adults (up to 1.8-fold higher at rest and up to 3.4-fold higher during exercise) than children – meaning that thoracic airways of children are less protected than those of adults.
Bennett et al. (1997)	4.5 µm	-ETh deposition of particles 50 percent greater in children (higher for younger ages). -No significant difference in total respiratory tract deposition.
Bennett and Zeman (1998)	1-2 µm	No difference between 7-14 year olds and adults in total deposition of particles in the respiratory tract.
Schiller-Scotland et al. (1994)	1-2 µm	No difference between 6-12 year olds and adults in total deposition of particles in the respiratory tract.
	2-3 µm	Two- to three-fold higher total deposition of particles in 6-12 year olds versus adults.
Modeled Studies		
Asgharian et al. (2004)	0.01-10 µm	-Up to 1.2-fold higher total deposition in 3 month olds compared to adults in the TB region. -Up to 1.5-fold higher total deposition in 8 year olds compared to adults in the alveolar region. Total deposition higher in adults than 3 and 23 month olds (up to 2-fold). -Estimates of deposition fraction per unit area at various airway generations of the lung and various particle sizes highest for 3 month olds compared to adults (up to 14-fold). Higher deposition also seen for 23 month olds (up to 5-fold) and 8 year olds (up to 3-fold) compared with adults. No difference in deposition in 14 year olds compared to adults.
Cheng et al. (1995)	0.0046-0.2 µm	Nasal casts of children's airways found increased deposition efficiency for ultrafine particles with decreasing age, suggesting that young children may receive a higher dose of ultrafine particles to the upper airways.
ınsberg et al. (2005)	0.001-10 µm	-Higher deposition in 3 month olds compared with adults for coarse and fine particles in the upper TB (up to 2-fold) and PU (up to 4-fold) regions. -Higher deposition in adults in the lower TB region.
Hoffmann et al. (1989)	1-2 µm	-1.5- to 2-fold higher total deposition in the TB region for particles in resting 8 year olds versus adults. -40-50 percent lower total deposition of particles in 8 year olds under conditions of exercise.
Jarabek et al. (2005)	0.3-6 µm	-Retained mass in the TB region normalized to regional SA was compared across age groups. -Up to 2-fold lower deposition in 3 month olds compared to adults. -Up to 2-fold higher deposition in 3 year olds and 14 year olds compared to adults.
Musante and Martonen (1999)	0.25-5 µm	-Total deposition was generally higher in children (ages 7, 22, 48, and 98 months) than adults (e.g., total lung deposition in 48-month olds was 38 percent higher than adults for 1µm particles). -TB deposition monotonically decreased as a function of age (i.e., younger children had increased TB deposition). -PU deposition greatest in the 48 and 98-month children.
Musante and Martonen (2000)	2 µm	3-fold higher deposition of particles in the PU region for 7 month olds versus adults.
Oldham et al. (1997)	Various	Airway models of trachea and bronchial airways showed total deposition in children (ages 4 and 7) greater than adult (up to approximately 7-fold higher for 4 year olds compared to adults for 4.5 µm particles).
Phalen and Oldham (2001)	0.1-10 µm	-No difference in total deposition of particles in 2 year olds versus adults. -Somewhat higher (13-81 percent; depending on particle size) deposition of particles in the TB region. -Lower deposition of particles in the PU region.
Xu and Yu (1986)	Various	Increased total deposition (up to 1.5-fold higher) in children aged 6 months, 2 years, and 8 years compared with adults for particles of varying sizes.

6. CONCLUSIONS

The examples and discussions included in this appendix suggest that the *Inhalation Dosimetry Methodology's* default approaches for derivation of the HEC for Category 1 gases with effects in the ETh, TB, and PU regions and for Category 3 gases typically are sufficient to cover variation across human age- and activity-level groups. The process for deriving an RfC from the HEC includes applying an uncertainty factor (UF) to account for within-species variability, adding further protection. When deriving an IUR for a carcinogen, UFs are not used. However the procedures for estimating an IUR incorporate conservative assumptions that would likely accommodate the degree of variation observed in these examples.

Experimental and modeling results for particles suggest the potential for small differences in deposition of particles in the respiratory tract as a function of age. The assumption that 100 percent of the deposited dose is available for uptake into the systemic circulation (for remote acting toxicants), or for activity in the respiratory tract (for local toxicity) is likely to result in an overestimation of dose to the target tissue. Any small variation in deposition among age groups should be considered against the potential magnitude of such overestimation. These differences in calculated deposition are small relative to the default 10-fold UF that accounts for intra-species variability in the derivation of the RfC. In addition, RfCs and IURs are developed for chronic exposure and will generally involve an exposure for multiple years. No additional correction of the toxicity values for these age groups is needed when the RfC or IUR is used in a risk assessment. Calculations in these examples are based on empirical data from sources listed and referenced in ICRP Publication 66 (ICRP, 1994). While ORD selected the ICRP values as the best estimates for these examples, other published values for V_e and SA exist. The use of alternate values may change the $LOAEL_{[HEC]}$ calculated for the various populations and life stages and may show more or less variability in results across the age and activity groups. In addition, the examples for the TB and PU regions are based on a hypothetical chemical, since currently no RfCs for gases on IRIS are calculated based on animal studies showing health effects occurring in these regions of the respiratory system. Given the parameter values used in the default method for calculating the HEC, it is likely that the process would yield results sufficient to cover populations and life stages with varying activities and physiologic characteristics.

Note that the available data, albeit limited, generally support these conclusions. As recommended by the Reference Dose (RfD)/RfC Technical Panel (USEPA, 2002), EPA has been exploring issues involving dose to the young from inhalation exposures, both theoretically and experimentally as well as further considering the existing animal-to-human extrapolation procedures described in current methodologies (e.g., USEPA, 1994). This is especially important because of the significant developmental changes that occur in the lung from birth well into adolescence (Pinkerton and Joad, 2000). The review and updating of these methodologies will be based on the best available science.

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APPENDIX B

APPENDIX B

CHEMICALS ON IRIS WITH EXTRAPOLATED INHALATION UNIT RISKS

Table B-1 contains chemicals on the Environmental Protection Agency's (EPA's) Integrated Risk Information System (IRIS) with Inhalation Unit Risk (IUR) values calculated by extrapolation using the default ventilation rate and body weight from the oral Cancer Slope Factor (CSF). These chemicals cause tumors remote from the respiratory tract. Also listed is the year EPA verified the cancer assessment. The list was compiled in September 2008.

EPA recommends that extrapolated IURs should be used with risk Equations 6 and 11 in the main document without additional modification for calculation of cancer risk by the inhalation route of exposure. It is generally not appropriate to make adjustments based on ventilation rate and body weight using the intake equation, because the amount of the chemical that reaches the target site of the chemical through the inhalation pathway is not a simple function of the inhalation rate and body weight. Risk assessors should outline the uncertainties involved in using extrapolated IURs in the risk characterization section of the risk assessment.

TABLE B-1 CHEMICALS WITH EXTRAPOLATED INHALATION UNIT RISKS ON IRIS	
Chemical	**Year of Verification**
Acrylamide[1]	1988
Aldrin	1987
Aramite	1991
Azobenzene	1988
Bromoform	1989
Chlordane	1997
Chloroform[1]	1987
DDT	1987
1,2-Dichloroethane	1986
Dieldrin	1987
1,2-Diphenylhydrazine	1986
Heptachlor	1987
Heptachlor epoxide	1987
Hexachlorobenzene	1989
Hexachlorobutadiene[1]	1986
Alpha-hexachlorocyclohexane	1986
Beta-hexachlorocyclohexane	1986
Technical-hexachlorocyclohexane	1986
Hexachlorodibenzo-p-dioxin mixture	1987
Hexachloroethane	1986
N-nitroso-di-n-butylamine	1986
N-nitrosodiethylamine	1986
N-nitrosodimethylamine	1986
N-nitrosopyrrolidine	1986
Polychlorinated biphenyls	1996
1,1,2,2-Tetrachloroethane	1986
1,1,1,2-Tetrachloroethane	1988
Toxaphene	1987
1,1,2-Trichloroethane	1986
2,4,6-Trichlorophenol	1989
[1] Note that this chemical's IUR is currently under review.	

APPENDIX C

APPENDIX C

STSC's PROCESS FOR DERIVING ALTERNATIVE INHALATION TOXICITY VALUES

If Reference Concentration (RfC) and/or Inhalation Unit Risk (IUR) values for an inhaled contaminant are not available from the sources in the Environmental Protection Agency's (EPA's) Office of Solid Waste and Emergency Response (OSWER) hierarchy, risk assessors should first contact the National Center for Environmental Assessment's (NCEA's) Superfund Health Risk Technical Support Center (STSC) for guidance.[52] Risk assessors working on Superfund sites can contact STSC to determine whether a provisional peer-reviewed toxicity value (PPRTV) exists for a contaminant; if not, the risk assessor, in cooperation with the appropriate EPA Regional office may request that STSC develop a PPRTV document or that STSC develop an inhalation toxicity value as a "consult." The latter would be specific to the site in question only.

As a first choice, if human or whole animal studies exist providing a suitable No Observable Adverse Effect Level (NOAEL)/Lowest Observable Adverse Effect Level (LOAEL) or Point of Departure (POD) from a Benchmark Dose (BMD) analysis, this data normally will be used by STSC to develop an inhalation toxicity value. If, in addition, a suitable human inhalation physiologically based pharmacokinetic (PBPK) model exists that can be utilized to refine the dose metric to the target organ, then this information generally will be included in developing an inhalation toxicity value.

If no appropriate whole animal or human studies exist, but an appropriate peer reviewed human inhalation PBPK model exists that has been validated by experimental results, then STSC usually will attempt to derive an inhalation toxicity value from this model. If none exists, but a suitable PBPK animal inhalation models exists, STSC may attempt developing a human model and deriving an inhalation value.

PBPK modeling quantitatively describes the absorption/metabolism/distribution and elimination of the chemical from a point of entry (oral, inhalation, dermal) to the target organ(s). In some cases, an oral PBPK model can be extrapolated to the inhalation pathway, but care must be taken to consider direct pulmonary effects that may not be evident by oral dosing.

As a next approach, STSC typically will evaluate development of an inhalation toxicity value using a suitable surrogate chemical based on a quantitative structure-activity relationship (QSAR) model with structural selection criteria and solubility/toxicity considerations. STSC may evaluate possible surrogate chemicals based on several available structural models and provide a comparison. Selection of the appropriate surrogate may depend on the weight of evidence of these models.

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[52] All contact with STSC should be performed by an EPA regional risk assessor. States and other entities should first contact their EPA regional risk assessor with questions on inhalation toxicity values. Regional risk assessors can then contact STSC on their behalf.

If STSC uses any of the methods for developing toxicity values other than from human or whole animal data, the value normally will be presented as a "screening" value with the caveat that it should not be used as a risk driver for a site without consultation with the STSC. The uncertainties associated with using toxicity values derived through PBPK modeling or QSAR, or with using a surrogate value should be described in the risk characterization portion of the risk assessment (see Section 9). Risk assessors are discouraged from performing simplistic route-to-route extrapolations from oral data using default assumptions about Inhalation Rate (IR) and body weight (BW).[53]

[53] If STSC indicates that no quantitative toxicity information for the inhalation route is available, the risk assessor should conduct a qualitative evaluation of this exposure route. The risk assessor should discuss in the uncertainty section of the risk assessment report the implications of not quantitatively assessing risks due to inhalation exposures to chemicals lacking inhalation toxicity data. See the section on Risk Characterization (Section 9) in the main text of this guidance for more information.

An official website of the United States government

Conducting a Human Health Risk Assessment

On this page:

Planning | Hazard Identification | Dose-Response | Exposure Assessment | Risk Characterization

Planning and Scoping

Even a human health risk assessment starts with a good plan. Before anything though there is a need to make judgments early when planning major risk assessments regarding the purpose, scope, and technical approaches that will be used. To start, risk assessors will typically ask the following questions:

1. Who/What/Where is at risk?
    - Individual
    - General population
    - Lifestages such as children, teenagers, pregnant/nursing women
    - Population subgroups - highly susceptible (for example, due to asthma, genetics, etc.) and/or highly exposed (for example, based on geographic area, gender, racial or ethnic group, or economic status)

2. What is the environmental hazard of concern?

- Chemicals (single or multiple/cumulative risk)
- Radiation
- Physical (dust, heat)
- Microbiological or biological
- Nutritional (for example, diet, fitness, or metabolic state)
- Socio-Economic (for example, access to health care)

3. Where do these environmental hazards come from?

- Point sources (for example, smoke or water discharge from a factory; contamination from a Superfund site)
- Non-point sources (for example, automobile exhaust; agricultural runoff)
- Natural sources

4. How does exposure occur?

- Pathways (recognizing that one or more may be involved)
  - Air
  - Surface Water
  - Groundwater
  - Soil
  - Solid Waste
  - Food
  - Non-food consumer products, pharmaceuticals
- Routes (and related human activities that lead to exposure)
  - Ingestion (both food and water)
  - Contact with skin
  - Inhalation
  - Non-dietary ingestion (for example, "hand-to-mouth" behavior)

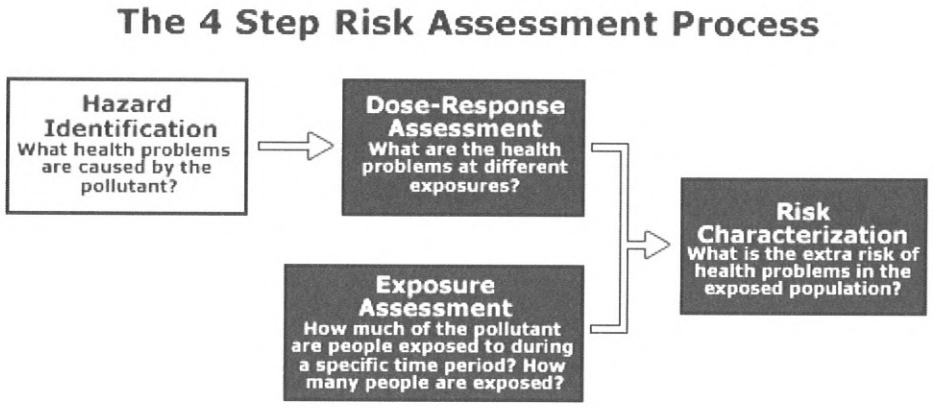
5. What does the body do with the environmental hazard and how is this impacted by factors such as age, race, sex, genetics, etc.?)
    - Absorption - does the body take up the environmental hazard
    - Distribution - does the environmental hazard travel throughout the body or does it stay in one place?
    - Metabolism - does the body break down the environmental hazard?
    - Excretion - how does the body get rid of it?

6. What are the health effects?
    - Example of some health effects include cancer, heart disease, liver disease and nerve disease.

7. How long does it take for an environmental hazard to cause a toxic effect? Does it matter when in a lifetime exposure occurs?
    - How long?
        - Acute - right away or within a few hours to a day
        - Subchronic - weeks or months (for humans generally less than 10% of their lifespan)
        - Chronic - a significant part of a lifetime or a lifetime (for humans at least seven years)
        - Intermittent
    - Timing
      Is there a critical time during a lifetime when a chemical is most toxic (e.g., fetal development, childhood, during aging)?

Step 1: Hazard Identification

The objective of Step 1 is to identify the types of adverse health effects that can be caused by exposure to some agent in question, and to characterize the quality and weight of evidence supporting this identification.



Step 1: Hazard identification is the first step of a human health risk assessment.

Hazard Identification is the process of determining whether exposure to a stressor can cause an increase in the incidence of specific adverse health effects (e.g., cancer, birth defects). It is also whether the adverse health effect is likely to occur in humans.

In the case of chemical stressors, the process examines the available scientific data for a given chemical (or group of chemicals) and develops a weight of evidence to characterize the link between the negative effects and the chemical agent.

Exposure to a stressor may generate many different adverse effects in a human: diseases, formation of tumors, reproductive defects, death, or other effects.

Sources of Data

Statistically controlled clinical studies on humans provide the best evidence linking a stressor, often a chemical, to a resulting effect. However, such studies are frequently not available since there are significant ethical concerns associated with human testing of environmental hazards.

Epidemiological studies involve a statistical evaluation of human populations to examine whether there is an association between exposure to a stressor and a human health effect. The advantage of these studies is that they involve humans while their weakness results from generally not having accurate exposure information and the difficulty of teasing out the effects of multiple stressors.

When data from human studies are unavailable, data from animal studies (rats, mice, rabbits, monkeys, dogs, etc) are relied on to draw inference about the potential hazard to humans. Animal studies can be designed, controlled, and conducted to address specific gaps in knowledge, but there are uncertainties associated with extrapolating results from animal subjects to humans.

Key Components of Hazard Identification

A wide variety of studies and analysis are used to support a hazard identification analysis.

- Toxicokinetics considers how the body absorbs, distributes, metabolizes, and eliminates specific chemicals.

- Toxicodynamics focus on the effects that chemicals have on the human body. Models based on these studies can describe mechanisms by which a chemical may impact human health, thus providing insights into the possible effects of a chemical.

When assessing a chemical for potential carcinogenic behavior, current EPA practice is to focus on analysis of a mode of action. Mode of action is a sequence of key events and processes, starting with interaction of an agent and a cell, proceeding through operational and anatomical changes, and resulting in cancer formation. A given agent may work by more than one mode of action, both at different tumor sites as well as at the same site.

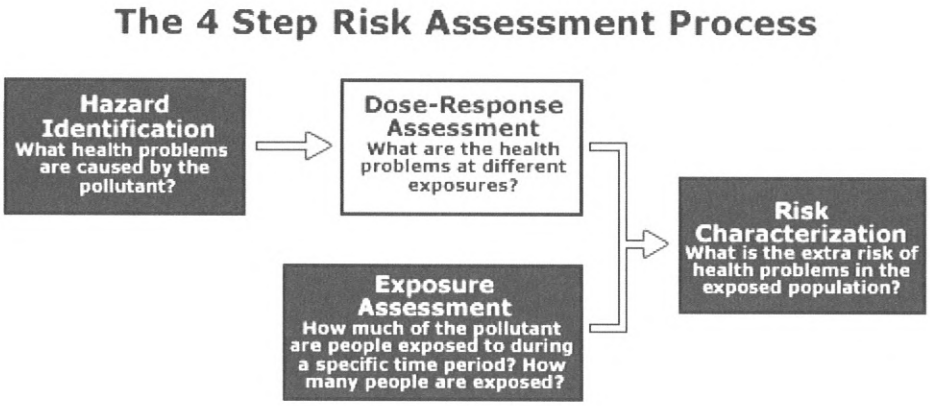
Analysis of mode of action is based on physical, chemical, and biological information that helps to explain key events in an agent's influence on tumor development.

A key component of hazard characterization involves evaluating the weight of evidence regarding a chemical's potential to cause adverse human health effects. The weight of evidence narrative may include some standard 'descriptors' that signify certain qualitative threshold levels of evidence or confidence have been met, such as 'Carcinogenic to humans' or 'Suggestive evidence of carcinogenic potential'.

Note: More specific information on hazard assessment approaches can be found in the specific risk assessment guidelines relevant for the kind of effect being considered.

Step 2: Dose Response

The objective of Step 2 is to document the relationship between dose and toxic effect.



Step 2: Dose-response assessment is the second step of a human health risk assessment.

A dose-response relationship describes how the likelihood and severity of adverse health effects (the responses) are related to the amount and condition of exposure to an agent (the dose provided). Although this webpage refers to the "dose-response" relationship, the same principles generally apply for studies where the exposure is to a concentration of the agent (e.g., airborne concentrations applied in inhalation exposure studies), and the resulting information is referred to as the "concentration-response" relationship.

The term "exposure-response" relationship may be used to describe either a dose-response or a concentration-response, or other specific exposure conditions.

Typically, as the dose increases, the measured response also increases. At low doses there may be no response. At some level of dose the responses begin to occur in a small fraction of the study population or at a low probability rate. Both the dose at which response begin to appear and the rate at which it increases given increasing dose can be variable between different pollutants, individuals, exposure routes, etc.

The shape of the dose-response relationship depends on the agent, the kind of response (tumor, incidence of disease, death, etc), and the experimental subject (human, animal) in question. For example, there may be one relationship for a response such as 'weight loss' and a different relationship for another response such as 'death'. Since it is impractical to study all possible relationships for all possible responses, toxicity research typically focuses on testing for a limited number of adverse effects.

> Typically, as the dose increases, the measured response also increases.

Upon considering all available studies, the response (adverse effect), or a measure of response that leads to an adverse effect (known as a 'precursor' to the effect), that occurs at the lowest dose is selected as the critical effect for risk assessment. The underlying assumption is that if the critical effect is prevented from occurring, then no other effects of concern will occur.

As with hazard identification, there is frequently a lack of dose-response data available for human subjects. When data are available, they often cover only a portion of the possible range of the dose-response relationship, in which case some extrapolation must be done in order to extrapolate to dose levels that are lower than the range of data obtained from scientific studies. Also, as with hazard identification, animal studies are frequently done to augment the available data.

Studies using animal subjects permit the use of study design to control the number and composition (age, gender, species) of test subjects, the levels of dose tested, and the measurement of specific responses. Use of a designed study typically leads to more meaningful statistical conclusions than does an uncontrolled observational study were additional confounding factors must also be considered for their impact on the conclusions.

However, dose-response relationships observed from animal studies are often at much higher doses that would be anticipated for humans, so must be extrapolated to lower doses, and animal studies must also be extrapolated from that animal species to

humans in order to predict the relationship for humans. These extrapolations, among others, introduce uncertainty into the dose-response analysis.

Basic Dose-Response Calculations & Concepts

As a component of the first step of the process discussed below, the scientific information is evaluated for a better biological understanding of how each type of toxicity or response (adverse effect) occurs; the understanding of how the toxicity is caused is called the "mode of action" (which is defined as a sequence of key events and processes, starting with interaction of an agent with a cell, proceeding through operational and anatomical changes, and resulting in the effect, for example, cancer formation).

Based on this mode of action, the Agency determines the nature of the extrapolation used in the second step of the process discussed above, either through non-linear or linear dose-response assessment.

A two-step process...

Step 1: Take an assessment of all data that are available or can be gathered through experiments. This is in order to document the dose-response relationship(s) over the range of observed doses (i.e, the doses that are reported in the data collected).

However, frequently this range of observation may not include sufficient data to identify a dose where the adverse effect is not observed (i.e., the dose that is low enough to prevent the effect) in the human population.

Step 2: This consists of extrapolation to estimate the risk (probably of adverse effect) beyond the lower range of available observed data. This is in order to make inferences about the critical region where the dose level begins to cause the adverse effect in the human population.

Non-linear dose-response assessment

Non-linear dose response assessment has its origins in the threshold hypothesis, which holds that a range of exposures from zero to some finite value can be tolerated by the organism with essentially no chance of expression of the toxic effect, and the threshold of toxicity is where the effects (or their precursors) begin to occur. It is often prudent to focus on the most sensitive members of the population; therefore, regulatory efforts are generally made to keep exposures below the population threshold, which is defined as the lowest of the thresholds of the individuals within a population.

If the "mode of action" information (discussed above) suggests that the toxicity has a threshold, which is defined as the dose below which no deleterious effect is expected to occur, then type of assessment is referred to by the Agency as a "non-linear" dose-response assessment. The term "nonlinear" is used here in a narrower sense than its usual meaning in the field of mathematics; a nonlinear assessment uses a dose-response relationship whose slope is zero (i.e., no response) at (and perhaps above) a dose of zero.

A No-Observed-Adverse-Effect Level (NOAEL) is the highest exposure level at which no statistically or biologically significant increases are seen in the frequency or severity of adverse effect between the exposed population and its appropriate control population. In an experiment with several NOAELs, the regulatory focus is normally on the highest one, leading to the common usage of the term NOAEL as the highest experimentally determined dose without a statistically or biologically significant adverse effect. In cases in which a NOAEL has not been demonstrated experimentally, the term "lowest-observed-adverse-effect level (LOAEL)" is used, which this is the lowest dose tested.

Mathematical modeling, which can incorporate more than one effect level (i.e., evaluates more data than a single NOAEL or LOAEL), is sometimes used to develop an alternative to a NOAEL known as a Benchmark Dose (BMD) or Benchmark Dose Lower-confidence Limit (BMDL). In developing the BMDL, a predetermined change in the response rate of an adverse effect (called the benchmark response or BMR; generally in the range of 1 to 10% depending on the power of a toxicity study) is selected, and the BMDL is a statistical lower confidence limit on the dose that produces the selected response. When the non-linear approach is applied, the LOAEL, NOAEL, or BMDL is used as the point of departure for extrapolation to lower doses.

The reference dose (RfD) is an oral or dermal dose derived from the NOAEL, LOAEL or BMDL by application of generally order-of-magnitude uncertainty factors (UFs). These uncertainty factors take into account the variability and uncertainty that are reflected in possible differences between test animals and humans (generally 10-fold or 10x) and variability within the human population (generally another 10x); the UFs are multiplied together: **10 x 10 = 100x.**

If a LOAEL is used, another uncertainty factor, generally 10x, is also used. In the absence of key toxicity data (duration or key effects), an extra uncertainty factor(s) may also be employed. Sometimes a partial UF is applied instead of the default value of 10x, and this value can be less than or greater than the default. Often the partial value is ½ log unit (the square root of 10) or 3.16 (rounded to 3-fold in risk assessment). Note, that when two UFs derived from ½ log units are multiplied together (3 x 3) the result is a 10 (equal to the full UF from which the two partial factors were derived).

Thus, the RfD is determined by use of the following equation: **RfD = NOAEL (or LOAEL or BMDL) / UFs**

In general, the RfD is defined as an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive groups, such as asthmatics, or life stages, such as children or the elderly) that is likely to be without an appreciable risk of deleterious effects during a lifetime.

The **RfD is generally expressed** in **units of milligrams per kilogram of bodyweight per day: mg/kg/day**.

A similar term, know as reference concentration (RfC), is used to assess inhalation risks, where concentration refers to levels in the air (generally expressed in the units of milligrams agent per cubic meter of air: mg/m^3).

- For more information, please see A Review of the Reference Dose and Reference Concentration Processes <https://epa.gov/scientific-leadership/review-reference-dose-and-reference-concentration-processes>.

Linear dose-response assessment

If the "mode of action" information (discussed above) suggests that the toxicity does not have a threshold, then this type of assessment is referred to by the Agency as a "linear" dose-response assessment. In the case of carcinogens, if "mode of action" information is insufficient, then linear extrapolation is typically used as the default approach for dose-response assessment.

- For more detailed information, please see EPA's Guidelines for Carcinogen Risk Assessment <https://epa.gov/risk/guidelines-carcinogen-risk-assessment>.

In this type of assessment, there is theoretically no level of exposure for such a chemical that does not pose a small, but finite, probability of generating a carcinogenic response. The extrapolation phase of this type of assessment does not use UFs; rather, a straight line is drawn from the point of departure for the observed data (typically the BMDL) to the origin (where there is zero dose and zero response).

The slope of this straight line, called the slope factor or cancer slope factor, is use to estimate risk at exposure levels that fall along the line. When linear dose-response is used to assess cancer risk, EPA calculates excess lifetime cancer risk (i.e., probability that an individual will contract cancer over a lifetime) resulting from exposure to a contaminant by considering the degree to which individuals were exposed, as compared to the slope factor.

Thus, the cancer risk is determined by use of the following equation: **Cancer Risk = Exposure x Slope Factor**

Total cancer risk is calculated by adding the individual cancer risks for each pollutant in each pathway of concern (i.e., inhalation, ingestion, and dermal absorption), then summing the risk for all pathways.

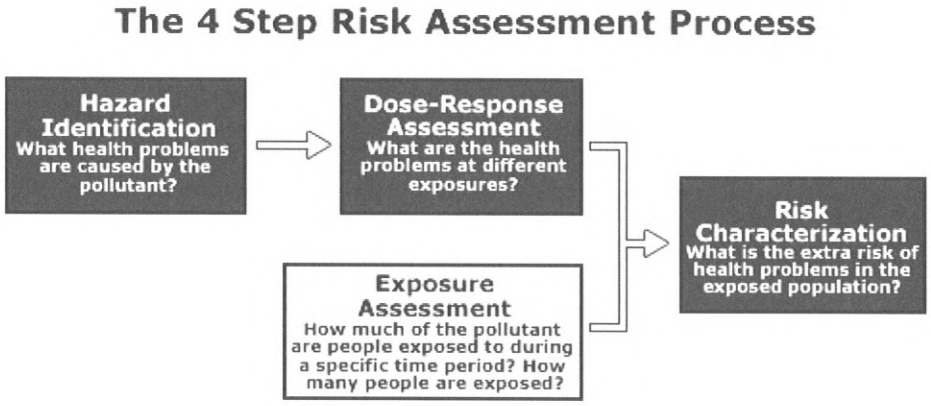
A similar term, know as inhalation unit risk (IUR), is used to assess inhalation risks, where the exposure-response relationship refers to concentrations in the air.

Note: When there are alternative procedures having significant biological support, the Agency encourages assessments to be performed using these alternative procedures, if feasible, in order to shed light on the uncertainties in the assessment, recognizing that

the Agency may decide to give greater weight to one set of procedures than another in a specific assessment or management decision.

Step 3: Exposure Assessment

The objective of Step 3 is to calculate a numerical estimate of exposure or dose.



Step 3: Exposure Assessment is the third step of a human health risk assessment.

Exposure assessment is the process of measuring or estimating the magnitude, frequency, and duration of human exposure to an agent in the environment, or estimating future exposures for an agent that has not yet been released. An exposure assessment includes some discussion of the size, nature, and types of human populations exposed to the agent, as well as discussion of the uncertainties in the above information.

Exposure can be measured directly, but more commonly is estimated indirectly through consideration of measured concentrations in the environment, consideration of models of chemical transport and fate in the environment, and estimates of human intake over time.

Different Kinds of Doses. Exposure assessment considers both the exposure pathway (the course an agent takes from its source to the person(s) being contacted) as well as the exposure route (means of entry of the agent into the body). The exposure route is

generally further described as intake (taken in through a body opening, e.g. as eating, drinking, or inhaling) or uptake (absorption through tissues, e.g. through the skin or eye).

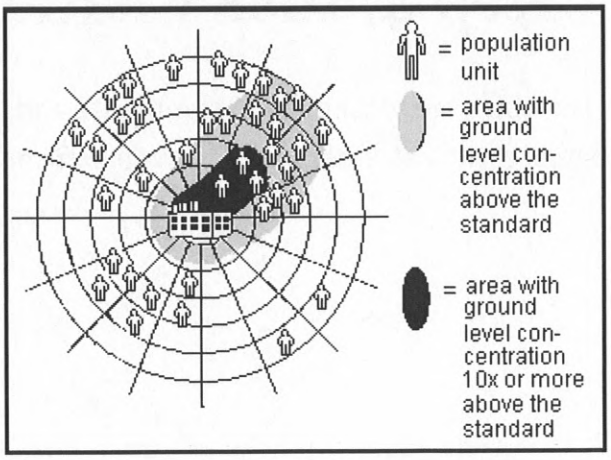
> EPA defines exposure as 'contact between an agent and the visible exterior of a person (e.g. skin and openings into the body)'.

The applied dose is the amount of agent at the absorption barrier that is available for absorption. The potential dose is the amount of agent that is ingested, inhaled, or applied to the skin. The applied dose may be less than the potential dose if the agent is only partly bioavailable.

The internal dose or absorbed dose is the amount of an agent that has been absorbed and is available for interaction with biologically significant receptors within the human body. Finally, the delivered dose is the amount of agent available for interaction with any specific organ or cell.

Range of Exposure. For any specific agent or site, there is a range of exposures actually experienced by individuals. Some individuals may have a high degree of contact for an extended period (e.g. factory workers exposed to an agent on the job). Other individuals may have a lower degree of contact for a shorter period (e.g. individuals using a recreational site downwind of the factory). EPA policy for exposure assessment requires consideration of a range of possible exposure levels.

Two common scenarios for possible exposure are "Central Tendency" and "High End". "Central Tendency" exposure is an estimate of the average experienced by the affected population, based on the amount of agent present in the environment and the frequency and duration of exposure.



"High End" exposure is the highest dose estimated to be experienced by some individuals, commonly stated as approximately equal to the 90th percentile exposure category for individuals.

Figure: Showing the "range of exposure"

Quantifying Exposure. There are three basic approaches for quantifying exposure. Each approach is based on different data, and has different strengths and weaknesses; using the approaches in combination can greatly strengthen the credibility of an exposure risk assessment.

- **Point of Contact Measurement** - The exposure can be measured at the point of contact (the outer boundary of the body) while it is taking place, measuring both exposure concentration and time of contact, then integrating them;

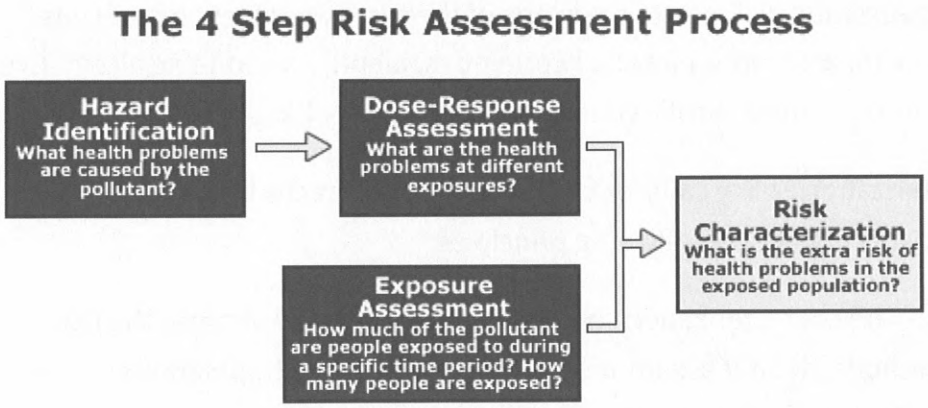
- **Scenario Evaluation** - The exposure can be estimated by separately evaluating the exposure concentration and the time of contact, then combining this information;

- **Reconstruction** - the exposure can be estimated from dose, which in turn can be reconstructed through internal indicators (biomarkers, body burden, excretion levels, etc) after the exposure has taken place (reconstruction).

- For more information on exposure assessment methods, see the Guidelines for Exposure Assessment <https://epa.gov/risk/guidelines-exposure-assessment>.

Step 4: Risk Characterization

The objective of Step 4 is to summarize and integrate information from the proceeding steps of the risk assessment to synthesize an overall conclusion about risk.



Step 4: Risk characterization is the last step of a human health risk assessment.

A risk characterization conveys the risk assessor's judgment as to the nature and presence or absence of risks, along with information about how the risk was assessed, where assumptions and uncertainties still exist, and where policy choices will need to be made. Risk characterization takes place in both human health risk assessments and ecological risk assessments.

In practice, each component of the risk assessment (e.g. hazard assessment, dose-response assessment, exposure assessment) has an individual risk characterization written to carry forward the key findings, assumptions, limitations, and uncertainties. The set of these individual risk characterizations provide the information basis to write an integrative risk characterization analysis.

The final, overall risk characterization thus consists of the individual risk characterizations plus an integrative analysis.

The overall risk characterization informs the risk manager and others about the rationale behind EPA's approach to conducting the risk assessment.

Such as: Why EPA did what it did to assess the risk?

Principles of Conducting Risk Characterizations

A good risk characterization will restate the scope of the assessment, express results clearly, articulate major assumptions and uncertainties, identify reasonable alternative interpretations, and separate scientific conclusions from policy judgments.

EPA's Risk Characterization Policy calls for conducting risk characterizations in a manner that is consistent with the following principles:

- **Transparency** - The characterization should fully and explicitly disclose the risk assessment methods, default assumptions, logic, rationale, extrapolations, uncertainties, and overall strength of each step in the assessment.

- **Clarity** - The products from the risk assessment should be readily understood by readers inside and outside of the risk assessment process. Documents should be concise, free of jargon, and should use understandable tables, graphs, and equations as needed.

- **Consistency** - The risk assessment should be conducted and presented in a manner which is consistent with EPA policy, and consistent with other risk characterizations of similar scope prepared across programs within the EPA.

- **Reasonableness** - The risk assessment should be based on sound judgment, with methods and assumptions consistent with the current state-of-the-science and conveyed in a manner that is complete and balanced, informative.

These four principles are referred to collectively as TCCR. In order to achieve TCCR in a risk characterization, the same principles need to have been applied in all of the prior steps in the risk assessment which lead up to the risk characterization.

- For more information read the Risk Characterization Handbook <https://epa.gov/risk/risk-characterization-handbook>.

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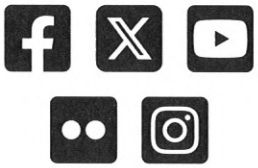

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Risk Assessment for Carcinogenic Effects

EPA's first carcinogen risk assessment guidelines [1], published in 1986, were the product of nearly two decades of experience and scientific consensus building. EPA has since gained considerable experience in applying cancer risk assessment approaches. Concurrently, the science of risk assessment and toxicological testing has continued to evolve, and EPA has had to address situations not explicitly discussed in the 1986 guidelines, e.g., children's risk assessment. The update of EPA's carcinogen risk assessment guidelines in 2005 consolidated the Agency's experience, providing more comprehensive and transparent guidance on topics not fully developed in the original guidelines, and providing flexibility to accommodate anticipated advances in the science.

During the time between 1996 and 2005, EPA applied the principles and procedures of the draft revised guidelines on a case-by-case basis for new hazard identifications and dose-response assessments using interim draft guidelines that represented the

Dose–Response Assessment for Assessing Health Risks Associated With Exposure to Hazardous Air Pollutants

- Summary and Tables <https://epa.gov/fera/dose-response-assessment-assessing-health-risks-associated-exposure-hazardous-air-pollutants>

evolution of risk assessment methods rather than a dramatic shift in methodology. Since 2005, EPA has applied the new 2005 guidelines which reflect EPA's accumulated experience and advances in our knowledge on cancer assessment. On the other hand, assessments for many substances that were prepared under the 1986 guidelines continue to be valid. Therefore, the dose-response assessments of carcinogens reflect a mixture of the application of 1986 guidelines and the more recent guidelines.

Hazard Identification for Carcinogenic Effects. EPA's guidelines recognize three broad categories of data: (1) human data (primarily epidemiological); (2) results of long-term experimental animal bioassays; and (3) supporting data, including a variety of short-term tests for genotoxicity and other relevant properties, pharmacokinetic and metabolic studies, and structure-activity relationships. In hazard identification of carcinogens under the guidelines, human data, animal data, and supporting evidence are combined to characterize the weight-of-evidence (WOE) regarding the agent's potential as a human carcinogen. The current guidelines <https://epa.gov/risk/guidelines-carcinogen-risk-assessment>, finalized in 2005, recommend expressing WOE by narrative statements rather than only hierarchical categories, and expressing them separately for the oral and inhalation routes. The general categories recognized by the 2005 guidelines are [2]:

- Carcinogenic to Humans
- Likely to be Carcinogenic to Humans
- Suggestive Evidence of Carcinogenic Potential

- Sources of Chronic Dose-Response Information <https://epa.gov/fera/sources-chronic-dose-response-information>
- Prioritization of Data Sources for Chronic Exposure <https://epa.gov/fera/prioritization-data-sources-chronic-exposure>
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- Sources of Acute Dose-Response Information <https://epa.gov/fera/sources-acute-dose-response-information>

- Inadequate Information to Assess Carcinogenic Potential
- Not Likely to be Carcinogenic to Humans

Under the 1986 guidelines, this WOE was summarized as fitting one of several hierarchic categories [1]:

Group A - Carcinogenic to Humans: Agents with adequate human data to demonstrate the causal association of the agent with human cancer (typically epidemiologic data).

Group B - Probably Carcinogenic to Humans: Agents with sufficient evidence (i.e., indicative of a causal relationship) from animal bioassay data, but either limited human evidence (i.e., indicative of a possible causal relationship, but not exclusive of alternative explanations; Group B1), or with little or no human data (Group B2).

Group C - Possibly Carcinogenic to Humans: Agents with limited animal evidence and little or no human data.

Group D - Not Classifiable as to Human Carcinogenicity: Agents without adequate data either to support or refute human carcinogenicity.

Group E - Evidence of Non-carcinogenicity for Humans: Agents that show no evidence for carcinogenicity in at least two adequate animal tests in different species or in both adequate epidemiologic and animal studies.

For each HAP that has been assessed for carcinogenicity under either set of guidelines, Table 1 of dose-response assessments compiled by the Office of Air Quality Planning and Standards <https://epa.gov/fera/dose-response-assessment-assessing-health-risks-associated-exposure-hazardous-air-pollutants> presents the category label specified by the most recent assessment (which may be via the current or past guidelines). At some point in the future, the table may also include excerpts of narrative WOEs. These WOE categories express the relative level of certainty that these agents may cause cancer in humans.

- The NRC Risk Assessment Paradigm <https://epa.gov/fera/nrc-risk-assessment-paradigm>
- **Risk Assessment for Carcinogens**
- Risk Assessment for Noncancer Effects <https://epa.gov/fera/risk-assessment-other-effects>

The categories specifically do not connote relative levels of hazard or degree of conservatism applied in developing a dose-response assessment. For example, a substance in group C (possible human carcinogen), under the 1986 guidelines, may impart a greater cancer risk to more people than another substance in group A (known human carcinogen), yet there is a greater certainty with regard to the risk associated with the latter. EPA's WOE classifications are focused on the amount and quality of evidence regarding whether or not a substance is carcinogenic to humans, not on the level of risk a substance might present. Dose-Response Assessment for Carcinogens. Since the publication of EPA's original cancer guidelines in 1986, considerable new knowledge has been developed regarding the processes of chemical carcinogenesis and the evaluation of human cancer risk. The 2005 guidelines [2] recognize both linear and nonlinear modes of action for carcinogens. When assessing the dose-response relationship under the guidelines, cancer data in the observable range are analyzed using a common dose-response model regardless of mode of action. The method of extrapolation to lower doses from the point of departure may vary depending on whether the available data indicate a linear or nonlinear mode of action.

Under the guidelines, linear extrapolation is appropriate when the evidence supports the mode of action of gene mutation due to direct DNA reactivity or another mode of action that is thought to be linear in the low dose region. A linear mode of action will also be the approach when available evidence is not sufficient to support a nonlinear extrapolation procedure, even in the absence of evidence of DNA reactivity. Nonlinear methods (including derivation of an oral reference dose or inhalation reference concentration) are to be used if there is sufficient evidence to support a nonlinear mode of action.

For linear carcinogens, EPA's current process of estimating cancer risk is based on the unit risk estimate (URE) for inhalation, and the carcinogenic potency slope (CPS) for ingestion. The URE represents the upper-bound excess lifetime cancer risk estimated to result from continuous exposure to an agent over a lifetime at a concentration of 1 $\mu g/m^3$ in air. The interpretation of the URE would be as follows: if the URE = 1.5 x 10-6 $\mu g/m^3$, no more than 1.5 excess tumors are expected to develop per 1,000,000 people if exposed all day, every day for a lifetime to a concentration of 1 µg of the chemical per cubic meter of air. The CPS is an upper bound, usually approximating a 95% confidence limit, on the increased cancer risk from a lifetime oral exposure to an agent. This estimate, usually expressed in units of proportion (of a population) affected per

mg/kg/day, is generally reserved for use in the low-dose region of the dose-response relationship, that is, for exposures corresponding to risks less than 1 in 100. The URE and CPS are plausible upper-bound estimates of the risk (i.e., the actual risk is likely to be lower, but may be greater). However, because the URE and CPS reflect unquantifiable assumptions about effects at low doses, their upper bounds are not true statistical confidence limits. The tabulated UREs and CPSs were developed by EPA and the California EPA, and were selected for use by a priority system <https://epa.gov/fera/prioritization-data-sources-chronic-exposure>.

References

1. U.S. EPA. 1986. Guidelines for Carcinogen Risk Assessment. 51 FR 33992-34003.
2. U.S. EPA. 2005. Guidelines for Carcinogen Risk Assessment. 70 FR 17765-17817

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Exposure Assessment Tools by Routes - Inhalation

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Overview



An exposure route is the way that a contaminant enters an individual or population after contact (IPCS, 2004). Typically, exposure occurs by one of three exposure routes—inhalation, ingestion, or dermal.

Inhalation exposure can result from breathing air that is contaminated with particulate matter (e.g., dust), vapors (e.g., volatile or semivolatile contaminants), or aerosols. Individuals can be exposed via the inhalation route during a variety of activities outdoors and indoors. Indoor receptors could also be exposed to outdoor air contaminants that infiltrate the indoor environment.

Estimating exposure from inhalation requires information on the concentrations of contaminants in the air and the timeframe over which inhalation exposure occurs. To calculate an inhaled dose, inhalation rates and receptor body weights might also be needed.

Calculations to estimate dose from inhalation are provided in this module as are various tools available for evaluating potential exposure concentrations. Exposure scenarios, exposure factors, and guidance for assessing exposure via inhalation are also provided.

Methods

When a contaminant is taken into the body via inhalation, the amount that gets into the body in a biologically available form is called the dose. There are a few different ways to measure dose (U.S. EPA, 1992):

- **Potential dose** is the amount of contaminant inhaled (i.e., amount that gets in the mouth or nose), not all of which is actually absorbed.

- **Applied dose** is the amount of contaminant at the absorption barrier (e.g., respiratory tract) that can be absorbed by the body.
- **Internal dose** is the amount of contaminant that gets past the exchange boundary (lung) and into the blood, or the amount of the contaminant that can interact with organs and tissues to cause biological effects.
- **Biologically effective dose** is the amount of contaminant that interacts with the internal target tissue or organ.

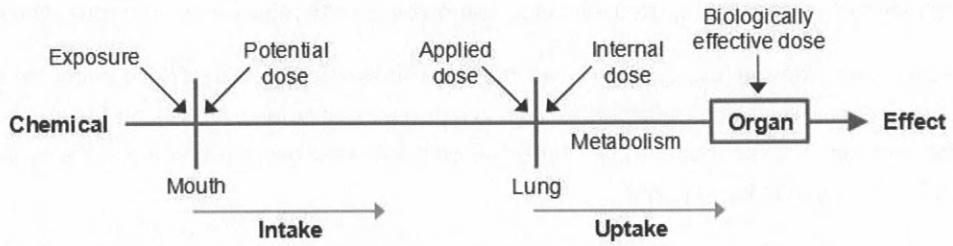

Illustration of Inhalation Route: Exposure and Dose (U.S. EPA, 1992)

The amount of chemical that is absorbed through the lung may vary from the amount of the substance that is inhaled. Thus, internal dose might differ from potential dose.

When using inhalation reference concentrations [RfCs] or inhalation unit risk [IURs] from the Integrated Risk Information System (IRIS) <https://epa.gov/iris> to characterize risk, it is not necessary to calculate the inhaled dose. This is because the IRIS methodology accounts for inhalation rates in the development of "dose-response" relationships. Instead, only an air concentration is needed to evaluate health concerns.

The methods used in developing noncancer inhalation dose-response values for IRIS are discussed in more detail in the U.S. EPA report entitled *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry* <https://epa.gov/risk/methods-derivation-inhalation-reference-concentrations-and-application-inhalation-dosimetry> (U.S. EPA, 1994).

The Superfund Program has also recently updated its approach for determining inhalation risk. It has eliminated the use of inhalation rates when evaluating exposure to air contaminants. This is described in *Risk Assessment Guidance for Superfund (Part F, Supplemental Guidance for Inhalation Risk Assessment)* <https://epa.gov/risk/risk-assessment-guidance-superfund-rags-part-f> (U.S. EPA, 2009).

Inhalation - A Complicating Factor

The Agency defines exposure as the chemical concentration at the boundary of the body (U.S. EPA, 1992). In the case of inhalation, the situation is complicated by the fact that oxygen exchange with carbon dioxide takes place in the distal portion of the lung. The anatomy and physiology of the respiratory system as well as the characteristics of the inhaled agent diminishes the pollutant concentration in inspired air (potential dose) such that the amount of a pollutant that actually enters the body through the upper respiratory tract (especially

This updated methodology recommends that risk assessors use the concentration of the contaminant in air (C_{air}) as the exposure metric (e.g., mg/m^3) instead of the intake of a contaminant in air based on inhalation rate and body weight (dose; e.g., mg/kg-day).

the nasal-pharyngeal and tracheo-bronchial regions) and lung (internal dose) is less than that measured at the boundary of the body.

Calculations

Using EPA's current methodology, it is unnecessary to calculate an inhaled dose when using dose-response factors from IRIS in a risk assessment. However, inhalation risk assessments may require that an adjusted air concentration be used to represent continuous exposure.

The adjusted air concentration ($\mathbf{C_{air\text{-}adj}}$) may be estimated as shown below. As described under the Methods tab, for noncarcinogens, the air concentration is adjusted based on the time over which exposure occurs (i.e., the exposure duration). For carcinogens, the concentration is averaged over the lifetime of the exposed individual (often assumed to be 70 years).

$$\text{Cair-adj} = \text{Cair} \times \text{ET} \times \frac{1\text{day}}{24\text{ hours}} \times \text{EF} \times \frac{\text{ED}}{\text{AT}}$$

Where:
$\mathbf{C_{air}}$ = Concentration of contaminant in air (mg/m^3)
ET = Exposure time (hours/day)
EF = Exposure frequency (days/year)
ED = Exposure duration (years)
AT = Averaging time (days)

- The concentration in air ($\mathbf{C_{air}}$) is either a measured or modeled value. Air concentrations may be measured in the breathing zone of individuals using personal monitoring equipment or in indoor or outdoor air using stationary or portable monitoring devices. Air measurements may represent gas phase or particulate-phase contaminants, or both.
- **Temporal parameters** in the equation include the following:
  - Exposure time (**ET**) and exposure frequency (**EF**) refer to the frequency with which the exposure occurs and might be provided in hours per day and days per year, respectively.
  - Exposure duration (**ED**) is the amount of time that an individual or population is exposed to the contaminant being evaluated and is typically given in years.
  - Averaging time (**AT**) is the amount of time over which exposure is averaged and is equal to ED for assessing non-cancer risks. For chronic assessments (e.g., cancer), potential lifetime average daily dose (LADD) is calculated in which lifetime (LT, in days) is substituted for AT.

In some cases, it may be necessary to calculate an inhalation dose using the equation below. This algorithm can be used to calculate the average daily potential dose from inhalation of a contaminant in air.

The **potential dose** of a contaminant is the product of the contaminant concentration, inhalation rate, exposure time, exposure frequency, and exposure duration divided by the product of averaging time and body weight. The equation parameters below must be defined for each inhalation exposure scenario, and all parameters must be expressed in consistent units.

In some cases, unit conversion factors may be necessary. Average Daily Dose (ADD) is generally expressed as mass of contaminant per unit body weight over time (e.g., mg/kg-day).

$$\mathbf{ADD = Cair \times InhR \times ET \times EF \times ED/BW \times AT}$$

Where:
ADD = Average daily dose (mg/kg-day)
$\mathbf{C_{air}}$ = Concentration of contaminant in air (mg/m^3)
InhR = Inhalation rate (m^3/hour)
ET = Exposure time (hours/day)
EF = Exposure frequency (days/year)
ED = Exposure duration (years)
BW = Body weight (kg)
AT = Averaging time (days)

See above for descriptions for many of the relevant equation parameters. The additional parameters are described below.

- Inhalation rate (**InhR**) represents the volume of air inhaled over a specified timeframe. Long-term inhalation rates are typically expressed in units of m^3/day. Short-term inhalation rates are typically indexed to activity levels and are expressed in units of m^3/hour or m^3/minute. Assessors should choose inhalation rate data that best represent the population for which exposures are being assessed. Chapter 6 of the Handbook provides inhalation rate data for various age groups (see the Factors tab in this module).
- Body weight (**BW**) of an individual, typically expressed in kilograms (kg), is also included so that the dose is normalized to that value. Sometimes the inhalation rate is already normalized to body weight (e.g., in units of m^3/kg-day). In this case, a separate term for body weight would not be necessary.

Additional information on exposure scenarios involving the inhalation route can be found in the Indirect Estimation Module in the Approaches Tool Set.

- **Key:** Information sources
- Data sources
- Models

Tool Type	Tools	Description

d	Agency for Toxic Substances and Disease Registry (ATSDR). ATSDR Comparison Value Viewer <https://www.atsdr.cdc.gov/sites/brownfields/cvviewer.html>	ATSDR's Comparison Value Viewer is a computer program that provides users with ATSDR health comparison values for chemicals in air, soil, and water.
m	Dutch National Institute for Health and Environment (RIVM). ConsExpo <https://www.rivm.nl/en/consexpo>	ConsExpo is a set of models that can be used to estimate and assess human exposure to substances from consumer products used indoors. This model is primarily used in the European Union's assessment of industrial chemicals (REACH).
m	The Lifeline Group. LifeLine™ User Manual v1.0 (Archived) <https://archive.epa.gov/scipoly/sap/meetings/web/pdf/lifeline.pdf>	LifeLine™ software for modeling aggregate and cumulative exposure to pesticides was designed to characterize population-based risks from pesticide residues in food and tap water as well as in the home following residential uses.
m	U.S. EPA. Air Pollutants Exposure Model (APEX) <https://www.epa.gov/fera/human-exposure-modeling-air-pollutants-exposure-model>	The APEX model can be used to estimate inhalation exposures that may occur at the local level or in specific microenvironments.
m	U.S. EPA. Chemical Screening Tool For Exposures and Environmental Releases (ChemSTEER) <https://www.epa.gov/tsca-screening-tools/chemsteer-chemical-screening-tool-exposures-and-environmental-releases>	ChemSTEER is used to estimate inhalation and dermal exposures to chemicals during chemical use and manufacture. Estimates also cover the releases of a chemical into the air, water, and land associated with occupational use.

	U.S. EPA. (2016). ExpoFIRST (Exposure Factors Interactive Resource for Scenarios Tool) <https://assessments.epa.gov/risk/document/&deid=322489>	ExpoFIRST is a standalone tool that draws from data in the EPA's Exposure Factors Handbook for quick, easy, and flexible development of human exposure scenarios. The tool develops these scenarios based on the selections made by the user in terms of the route of exposure of interest, the media of interest, exposure descriptor, receptor (age groups) and other demographics.
	U.S. EPA. Exposure and Fate Assessment Screening Tool (E-FAST) <https://www.epa.gov/tsca-screening-tools/e-fast-exposure-and-fate-assessment-screening-tool-version-2014>	Exposure and Fate Assessment Screening Tool (E-FAST) provides screening-level estimates of the concentrations of chemicals released to surface water and other media from consumer products.
	U.S. EPA. Industrial Source Complex Model (ISC3) <https://www.epa.gov/scram/air-quality-dispersion-modeling-alternative-models#isc3 >	ISC3 is a steady-state Gaussian plume model which can be used to assess pollutant concentrations from a wide variety of sources associated with an industrial complex.
	U.S. EPA. Industrial Waste Air Model (IWAIR) <https://www.epa.gov/smm/industrial-waste-air-model-iwair>	IWAIR is used to evaluate inhalation risks for workers and residents in the vicinity of waste management units. It includes models to estimate emissions, dispersion, and risk.

	U.S. EPA. (1997). Johnson and Ettinger Model for Subsurface Vapor Intrusion into Buildings <https://rais.ornl.gov/epa/je/guide.pdf>	This resource includes a series of models used to evaluate vapor intrusion into buildings. Several modifications have been made to the original models including the ability to edit data for existing chemicals, add new chemicals, and default values recommended in Appendix G of the EPA OSWER Draft Guidance for Evaluating the Vapor Intrusion to Indoor Air Pathway have been incorporated into the models. EPA has revised the models and added a series of new models.
	U.S. EPA. Multi-Chamber Concentration And Exposure Model (MCCEM) <https://www.epa.gov/tsca-screening-tools/forms/mccem-multi-chamber-concentration-and-exposure-model-download-and-install>	The MCCEM estimates average and peak indoor air concentrations of chemicals released from products or materials in residential buildings.
	U.S. EPA. Multimedia, Multipathway, and Multireceptor Exposure and Risk Assessment (3MRA) <https://www.epa.gov/ceam/3mra >	The Multimedia, Multipathway, Multireceptor Exposure and Risk Assessment (3MRA) is a screening-level tool that allows the assessment of potential human and ecological health risks resulting from long-term exposure to chemicals related to waste management.
	U.S. EPA. Swimmer Exposure Assessment Model (SWIMODEL) <https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/swimmer-exposure-assessment-model-swimodel>	SWIMODEL is a screening tool to conduct exposure assessments of pesticides found in indoor swimming pools and spas.
	U.S. EPA. Wall Paint Exposure Assessment Model (WPEM) <https://www.epa.gov/tsca-screening-tools/wall-paint-exposure-assessment-model-wpem>	WPEM is used to estimate the potential exposure of consumers and workers to the chemicals emitted from wall paint applied using a roller or a brush.

Concentrations

- Measuring Concentrations
- Modeling Concentrations
- Available Data

Sources of contamination to air, water, and soil and dust are discussed in the Media Tool Set. Media-specific concentrations are needed for estimating exposure via the inhalation route. Data and tools that can be used to estimate media-specific concentrations can also be found in the Media Tool Set.

Contamination of ambient (outdoor) air can occur from anthropogenic or natural sources. Examples of anthropogenic sources include: driving cars, trucks, or buses; burning coal, oil, and other fossil fuels; manufacturing chemicals or other products; degreasing, painting, or other industrial operations; and dry cleaning. Examples of natural sources include: gases emitted by the earth's crust [e.g., radon], and smoke and carbon dioxide [CO_2] released during forest fires.

Activities such as these may add gases and/or particles to the air. Some air pollutants can remain in the environment for long periods of time and can be transported in the atmosphere (e.g., by wind) hundreds of miles from their original source.

There are many sources of indoor air contaminants. These contaminants can enter buildings from the outside or may be generated from inside sources. Examples of indoor sources include: combustion of oil, gas, kerosene, coal, wood, and tobacco products; building materials and furnishings; and consumer products).

Reductions in building ventilation may increase indoor pollutant levels because indoor emissions are not being diluted by outdoor air or carried out of the indoor environment. Temperature and humidity can also contribute to increases in contaminant concentrations indoors.

Contaminant concentrations in air can be characterized based on measurements, modeling, and/or available monitoring data.

Measuring Concentrations

Information on sampling techniques and analytical methods is available to support the measurement of contaminants in potentially inhaled media.

- **Key:** Information sources
- Data sources
- Models

Tool Type	Tools	Description
	American Society for Testing and Materials (ASTM). (2008). D6178: Standard Practice for Estimation of Short-term Inhalation Exposure to Volatile Organic Chemicals Emitted from Bedding Sets <https://www.astm.org/standards/d6178.htm>	This document describes procedures for estimating human inhalation exposure to volatile compounds emitted from bedding sets for the purpose of characterizing health risks due to short-term VOC exposures. Exposure estimates for specific raw materials and other components of different bedding sets could be evaluated and compared.

d	American Society for Testing and Materials (ASTM). Standards by Category <https://www.astm.org/products-services/standards-and-publications.html>	ASTM International (formerly known as the American Society for Testing and Materials, or ASTM) develops and provides support related to international voluntary consensus standards. Standards developed by ASTM include those relevant to occupational settings, including industrial hygiene and safety standards that specify methods for measuring the presence and amounts of chemical hazards used in the workplace. ASTM has also developed consumer product and related standards that cover methods for measuring chemicals related to a wide range of products.
d	National Institute for Occupational Safety and Health (NIOSH). (2016). NIOSH Pocket Guide to Chemical Hazards <https://www.cdc.gov/niosh/npg/>	The NIOSH Pocket Guide to Chemical Hazards informs workers, employers, and occupational health professionals about workplace chemicals and their hazards. The NPG gives general industrial hygiene information for hundreds of chemicals/classes. The NPG clearly presents key data for chemicals or substance groupings (such as cyanides, fluorides, manganese compounds) that are found in workplaces.
i	U.S. EPA. Air Modeling - Guidance for Air Toxics Modeling <https://www.epa.gov/scram/air-modeling-guidance-air-toxics-modeling>	This section provides miscellaneous guidance documents other than permit modeling or State Implementation Plan (SIP) attainment demonstrations.
i	U.S. EPA. Air Monitoring Methods <https://www.epa.gov/amtic/air-monitoring-methods>	This EPA site provides an approved method for conducting open-path remote sensing for ambient air concentrations with a Fourier transform infrared spectrometer.
i	U.S. EPA. Air Monitoring Methods – Criteria Pollutants <https://www.epa.gov/amtic/air-monitoring-methods-criteria-pollutants>	This EPA site lists designated reference or equivalent methods for monitoring and measuring ambient concentrations of criteria air pollutants—total suspended particulates (TSP), PM10, PM2.5, PM10–2.5, SO2, O3, CO, NO2, and Pb.

	U.S. EPA. Air Toxics – Monitoring Methods <https://www3.epa.gov/ttnamti1/airtox.html>	This EPA site provides descriptions and methodologies for monitoring and measuring hazardous air pollutants in ambient air.
	U.S. EPA. Compendium of Methods for the Determination of Inorganic Compounds in Ambient Air <https://www.epa.gov/amtic/compendium-methods-determination-inorganic-compounds-ambient-air>	This EPA site lists designated reference or equivalent methods for monitoring and measuring ambient concentrations of criteria air pollutants—total suspended particulates (TSP), PM10, PM2.5, PM10–2.5, SO2, O3, CO, NO2, and Pb.
	U.S. EPA. (2002). Guidance on Choosing a Sampling Design for Environmental Data Collection for Use in Developing a Quality Assurance Project Plan <https://www.epa.gov/quality/guidance-choosing-sampling-design-environmental-data-collection-use-developing-quality>	This guidance document provides information on how to develop sampling designs to collect environmental measurement data.
	U.S. EPA. (1992). Guidelines for Exposure Assessment: Table 2. Examples of Types of Measurements to Characterize Exposure-Related Media and Parameters <https://assessments.epa.gov/risk/document/&deid=15263>	This table illustrates some of the types of measurements used by exposure assessors, along with notes describing additional information often needed to use these measurements in estimating exposure or dose.
	U.S. EPA. (2004). Identification of Time-integrated Sampling and Measurement Techniques to Support Human Exposure Studies	This resource presents a literature review on the identification and evaluation of methods used to classify exposure.
	U.S. EPA. Superfund Analytical Services and Contract Laboratory Program (CLP) <https://www.epa.gov/clp>	This document is designed to offer the data reviewer guidance in determining the usability of analytical data generated through the U.S. EPA Contract Laboratory Program (CLP).

Modeling Concentrations

In the absence of measurement data, a variety of models can be used to estimate contaminant concentrations in air or dust that may be inhaled. Ambient air quality models may be used to estimate contaminant concentrations in air considering spatial-temporal characteristics (e.g., urban versus rural, geographic scale;

climate, season). Some models also account for population demographics and the time that the exposed populations spend in various microenvironments.

Indoor air models and models that evaluate air concentrations for specific exposure scenarios are also available. Examples include: inhalation of contaminants that volatilize from water while showering, and inhalation of contaminants that volatilize from pool water while swimming.

- **Key:** Information sources
- Data sources
- Models

Tool Type	Tools	Description
	American Industrial Hygiene Association (AIHA). Industrial Hygiene Model (IH Mod) <https://www.aiha.org/get-involved/volunteergroups/pages/exposure-assessment-strategies-committee.aspx >	This website for the Exposure Assessment Strategies Committee provides links to tools for the practicing Industrial Hygienist including IH-Mod which is an Excel spreadsheet containing several algorithms used for calculating airborne concentrations of chemicals. Algorithms are provided for 12 models including well-mixed room, eddy diffusion, two-zone, field plume, and estimating contamination from small spills.
	California Air Resource Board (CARB). (2002). California Population Indoor Exposure Model (CPIEM) Version 2.0 User's Guide <https://www.arb.ca.gov/research/apr/past/98-327_usera.pdf>	This user's guide is comprehensive reference document for CPIEM, a Monte Carlo simulation model for estimating inhalation exposure for several indoor microenvironments (plus outdoors). CPIEM employs a mass-balance algorithm to estimate indoor pollutant concentration distributions using airborne concentrations and location/activity profiles.

	California Department of Toxic Substances Control (DTSC). CalTOX 1.5 Multimedia Risk Assessment Model <http://www.dtsc.ca.gov/assessingrisk/ctox_model.cfm>	The CalTOX Multimedia Risk Assessment model is a spreadsheet-based model for use in health-risk assessments that address contaminated soils and the contamination of adjacent air, surface water, sediments, and ground water. It includes a multimedia and transport transformation model, exposure scenario models, and addresses uncertainty in multimedia multi-pathway models.
	Dutch National Institute for Health and Environment (RIVM). ConsExpo <https://www.rivm.nl/en/consexpo>	ConsExpo is a set of models that can be used to estimate and assess human exposure to substances from consumer products used indoors. This model is primarily used in the European Union's assessment of industrial chemicals (REACH).
	ENVIRON. Comprehensive Air Quality Model with Extensions (CAMx) <http://www.camx.com/ >	The CAMx model allows for the assessment of gaseous and particulate air pollution (i.e., ozone, PM2.5, PM10, air toxics) over many scales ranging from sub-urban to continental. It also enables examination of source attribution.
	ICF International/Systems Applications International. (2006). Regional Modeling System for Aerosols and Deposition (REMSAD) <http://remsad.icfconsulting.com/>	REMSAD is used to provide a better understanding of the distributions, sources, and removal processes related to regional haze, particulate matter and other airborne pollutants, including soluble acidic components and toxics. Air concentrations and (wet and dry) deposition values are also available.

	The Lifeline Group. LifeLine™ User Manual v1.0 (Archived) <https://archive.epa.gov/scipoly/sap/meetings/web/pdf/lifeline.pdf>	LifeLine™ software for modeling aggregate and cumulative exposure to pesticides was designed to characterize population-based risks from pesticide residues in food and tap water as well as in the home following residential uses.
	U.S. EPA. AERMOD Modeling System <https://www.epa.gov/scram/air-quality-dispersion-modeling-preferred-and-recommended-models#aermod>	AERMOD can be used to model the movement of chemicals released from one or multiple sources through air; it incorporates air dispersion based on boundary layer turbulence structure and scaling concepts, including treatment of both surface and elevated sources, and both simple and complex terrain.
	U.S. EPA. Air: Fate, Exposure, and Risk Analysis (FERA) <https://www.epa.gov/fera>	This site describes multimedia fate and transport models (Total Risk Integrated Methodology [TRIM] - TRIM.FaTE); human exposure models (Air Pollutants Exposure Model [APEX/TRIM.Expo Inhalation], Hazardous Air Pollutant Exposure Model [HAPEM]); risk models (TRIM.Risk, Human Exposure Model [HEM]); as well as available documentation of methods for Fate, Exposure, and Risk Analysis as compiled by the Office of Air.
	U.S. EPA. Chemical Screening Tool For Exposures and Environmental Releases (ChemSTEER) <https://www.epa.gov/tsca-screening-tools/chemsteer-chemical-screening-tool-exposures-and-environmental-releases>	ChemSTEER is used to estimate inhalation and dermal exposures to chemicals during chemical use and manufacture. Estimates also cover the releases of a chemical into the air, water, and land associated with occupational use.

	U.S. EPA. Community Multiscale Air Quality Modeling System (CMAQ) <https://www.epa.gov/cmaq>	CMAQ is an air quality model and software suite designed to model multiple pollutants at multiple scales (from urban to regional). CMAQ can model tropospheric ozone, fine particles, toxics, acid deposition, and visibility degradation. It allows regulatory agencies to evaluate the impact of air quality management decisions and gives scientists the ability to probe, simulate, and understand chemical and physical interactions in the atmosphere.
	U.S. EPA. Estimation Program Interface (EPI) Suite <https://www.epa.gov/tsca-screening-tools/epi-suitetm-estimation-program-interface >	EPI Suite is a Microsoft Windows-based collection of physical/chemical property and environmental fate estimation programs developed by EPA's Office of Pollution Prevention Toxics (OPPT) and Syracuse Research Corporation (SRC).
	U.S. EPA. Exposure and Fate Assessment Screening Tool (E-FAST) <https://www.epa.gov/tsca-screening-tools/e-fast-exposure-and-fate-assessment-screening-tool-version-2014>	Exposure and Fate Assessment Screening Tool (E-FAST) provides screening-level estimates of the concentrations of chemicals released to surface water and other media from consumer products.
	U.S. EPA. Exposure Model for Soil-Organic Fate and Transport (EMSOFT) <https://assessments.epa.gov/risk/document/&deid=241704>	EMSOFT is used to explore how chemicals in the soil can vaporize and become an inhalation exposure risk in humans. The model can predict concentrations of soil contaminants, rates of transfer into the atmosphere, and potential ingestion and dermal contact risks. EMSOFT can also estimate average contaminant concentrations at a given soil depth over time.

	U.S. EPA. (2008). Guidance for the Sampling and Analysis of Lead in Indoor Residential Dust for Use in the Integrated Exposure Uptake Biokinetic (IEUBK) Model	This document recommends "methods for collecting and analyzing indoor residential dust data to estimate the mean concentration of lead in dust for use in the IEUBK model".
	U.S. EPA. Hazardous Air Pollutant Exposure Model (HAPEM) <https://www.epa.gov/fera/human-exposure-modeling-hazardous-air-pollutant-exposure-model-hapem>	HAPEM is a screening-level exposure model designed to assess average long-term inhalation exposures of the general population or a specific sub-population to various air toxics over spatial scales ranging from urban (large city) to national; activity patterns and multiple microenvironments can be considered.
	U.S. EPA. (2005). Human Health Risk Assessment Protocol (HHRAP) for Hazardous Waste Combustion Facilities	HHRAP describes the evaluation of multi-pathway, site-specific human health risk assessments and was developed specifically for assessment of hazardous waste combustors; it is applicable to other exposure scenarios as well.
	U.S. EPA. (2001). Indoor Air Quality Building Education and Assessment Model (I-BEAM), [CD-ROM]	I-BEAM is a guidance tool designed for use by building professionals and others interested in indoor air quality in commercial buildings. I-BEAM supplements EPA's Building Air Quality guidance and was designed to provide information about managing IAQ in commercial buildings. I-BEAM contains text, animation/visual, and interactive/calculation components that can be used to perform a number of diverse tasks.

	U.S. EPA. Integrated Exposure Uptake Biokinetic (IEUBK) Model for Lead in Children <https://www.epa.gov/superfund/lead-superfund-sites-software-and-users-manuals >	The IEUBK Model is designed to model exposure from lead in air, water, soil, dust, diet, and paint and other sources with pharmacokinetic modeling to predict blood lead levels in children 6 months to 7 years old. Links to the model and supporting documentation are provided at this website. (EPA's Adult Lead Model is used to predict blood lead levels in adults.)
	U.S. EPA. Internet Geographical Exposure Modeling System (IGEMS) <https://www.epa.gov/tsca-screening-tools/igemscsm-internet-geographical-exposure-modeling-systemchemical-safety-mapper>	IGEMS incorporates models and data for ambient air, surface water, soil, and ground water in one system. Each model produces results files that can be saved and used with statistical software applications or other database programs. IGEMS can create graphics and Geographical Information System (GIS) files for displaying environmental modeling results.
	U.S. EPA. Landfill Gas Emissions Model (LandGEM) <https://www.epa.gov/catc/clean-air-technology-center-products#software >	LandGem is an automated estimation tool with a Microsoft Excel interface to estimate emission rates for total landfill gas, methane, carbon dioxide, non-methane organic compounds, and individual air pollutants from municipal solid waste landfills.

	U.S. EPA. Lead at Superfund Sites: Software and Users' Manuals <https://www.epa.gov/superfund/lead-superfund-sites-software-and-users-manuals>	EPA's Integrated Exposure Uptake Biokinetic Model for Lead in Children is used to predict blood lead levels for children aged 6 months to 7 years. The ALM Model is designed to model exposure from lead in air, water, soil, dust, diet, and paint and other sources with pharmacokinetic modeling to predict blood lead levels adults. This page provides links for downloading these lead models and supporting documentation, including technical reports, guidance documents, FAQs, short sheets related to use of the IEUBK model and the ALM, and other links with additional information related to lead and lead cleanup.
	U.S. EPA. Models for Pesticide Risk Assessment: Atmospheric Models <https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/models-pesticide-risk-assessment#atmospheric >	EPA's Models for Pesticide Risk Assessment webpage provides links to aquatic, terrestrial, and atmospheric exposure models as well as health effects models used to assess the risk of a pesticide to human health or the environment. This website provides links to atmospheric models used to predict the deposition patterns of pesticides released into the atmosphere. Models include AGDISP (AGricultural DISPersal), AgDRIFT (modified version of AGDISP), PERFUM (Probabilistic Exposure and Risk Model for FUMigants), SOFEA (SOil Fumigant Exposure Assessment), and FEMS (Fumigant Exposure Modeling System).

	U.S. EPA. MOtor Vehicle Emission Simulator (MOVES) Model and Other Mobile Source Emissions Models <https://www.epa.gov/moves>	This website provides links to the MOtor Vehicle Emission Simulator (MOVES) and older models including the NONROAD model, National Mobile Inventory Model (NMIM), and MOBILE Model. MOVES is an emission modeling system that estimates emissions for mobile sources covering a broad range of pollutants. This tool allows users to perform multiple-scale analysis.
	U.S. EPA. Multimedia Models to Assess Exposures <https://www.epa.gov/ceam/multimedia-models-assess-exposures>	This site provides links to five multimedia models maintained by CEAM designed to quantify the movement and concentration of contaminants traveling through groundwater, surface water, and food chain media: Multimedia, Multi-pathway, Multi-receptor Exposure and Risk Assessment (3MRA) system; MINTEQA2 equilibrium speciation model; Multimedia Contaminant Fate, Transport, and Exposure Model (MMSOILS); Multimedia Exposure Assessment Model (MULTIMED); and Watershed Health Assessment Tools Investigating Fisheries (WHATIF) software.
	U.S. EPA. Risk Assessment and Modeling – Human Exposure Model (HEM) <https://www.epa.gov/fera/risk-assessment-and-modeling-human-exposure-model-hem>	HEM is used in performing risk assessments for major point sources of air toxics specifically for the inhalation exposure pathway. HEM provides ambient air concentrations for use with unit risk estimates and inhalation reference concentrations to estimate cancer risk and noncancer hazard, respectively, for the air toxics modeled.

	U.S. EPA. RISK, Indoor Air Quality Model	The RISK model allows calculation of individual exposure to indoor air pollutants from sources. RISK runs in the MS-Windows operating environment and allows users to calculate risk based on the calculated exposure.
	U.S. EPA. Simulation Tool Kit for Indoor Air Quality and Inhalation Exposure (IAQX), Version 1.0 User's Guide	This resource is a comprehensive guide to using IAQX version 1.
	U.S. EPA. Support Center for Regulatory Atmospheric Modeling (SCRAM) <https://www.epa.gov/scram>	This Web site is maintained by EPA's Air Quality Modeling Group (AQMG) and provides links to various air quality models, such as dispersion models, photochemical models, and receptor models. It also provides additional resources such as modeling applications and tools, and documentation and guidance for air quality models.

	U.S. EPA. Support Center for Regulatory Atmospheric Modeling – Air Quality Models <https://www.epa.gov/scram/air-quality-models>	EPA's Air Quality Modeling group maintains this site with documentation, guidance, and model code for dispersion, photochemical, and receptor models commonly used to support policy and regulatory decisions, including the assessment of control strategies and source impacts. Preferred/recommended dispersion models include the AERMOD Modeling System and the CALPUFF Modeling System. Links are provided to several photochemical models: Community Multi-scale Air Quality (CMAQ); Comprehensive Air quality Model with extensions (CAMx); Regional Modeling System for Aerosols and Deposition (REMSAD); and Urban Airshed Model Variable Grid (UAM-V®) as well as receptor models: Chemical Mass Balance (CMB); UNMIX; and Positive Matrix Factorization (PMF).
	U.S. EPA. TANKS Model <https://www3.epa.gov/ttn/chief/software/tanks/index.html>	TANKS is a Windows-based computer software program that estimates volatile organic compound (VOC) and hazardous air pollutant (HAP) emissions from fixed- and floating-roof storage tanks.
	U.S. EPA. Total Risk Integrated Methodology (TRIM) – TRIM.FaTE <https://www.epa.gov/fera/total-risk-integrated-methodology-trim-trimfate>	The TRIM.FaTE model estimates movement and transformation of pollutants over time. Outputs provide exposure estimates for environmental and human receptors that can be used in other models.

	U.S. EPA. (2007). User's Guide for the Integrated Exposure Uptake Model for Lead in Children (IEUBK)	This user's guide is a comprehensive reference for the IEUBK model, including installation, model inputs, analysis, and interpretation.
	U.S. EPA. (2000). Volatilization Rates from Water to Indoor Air Phase II <https://assessments.epa.gov/risk/document/&deid=20677>	EPA developed mass balance models for estimating chemical emissions for 5 tracer chemicals (acetone, ethyl acetate, toluene, ethylbenzene, and cyclohexane) from 4 sources (showers, dishwashers, washing machines, and bathtubs) to better characterize chemical volatilization from drinking water to indoor air. These experiments led to the development of source- and chemical-specific mass transfer coefficients, air exchange (ventilation) rates, and chemical stripping efficiencies. EPA also describes a set of protocols for estimating emission rates for chemicals other than the 5 tracer chemicals examined for this study.
	U.S. EPA. WATER9 Model <https://www3.epa.gov/ttn/chief/software/water/water9_3/index.html>	WATER9, a wastewater treatment model, estimates air emissions of individual waste constituents in wastewater collection, storage, treatment, and disposal facilities.
	U.S. EPA Region 3. Air Quality Analysis <https://www.epa.gov/air-quality-analysis >	This webpage includes information for air quality data analysts inside and outside EPA. The information provided supports EPA's NAAQS Review Process.

Available Data

Personal or stationary monitors can be used to measure air concentrations in the breathing zone of individuals who are closest to a source. Area monitors may be used to measure air concentrations that are representative of particular areas. In some cases, measurement data are used directly to estimate exposure concentrations. In other cases, measured data are used along with modeling to predict potential levels of exposure.

There are a number of information sources that provide monitoring data on contaminant concentrations in potentially inhaled media. Many of these data sources provide ambient air concentrations of contaminants at the national level and for other broad geographic areas such as cities, counties, and states. As such, they help EPA identify specific air toxics, and specific source sectors such as stationary sources or mobile sources, that generally produce the highest exposures and risks.

- **Key:** Information sources
- Data sources
- Models

Tool Type	Tools	Description

di	Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological Profiles for Hazardous Substances <https://www.atsdr.cdc.gov/toxprofiles/index.asp>	ATSDR has prepared approximately 300 toxicological profiles for hazardous substances found at National Priorities List (NPL) sites and other federal sites. Chemical names may be searched using the A to Z list on the ATSDR Toxic Substances Portal. Each Toxicological Profile contains a review of key studies and other data characterizing the exposure-related health effects and pertinent characteristics and processes that affect human exposures. Sections include other relevant information on releases to the environment, environmental fate, levels monitored in the environment, potential exposures, and analytical methods.
d	AIRNow. AIRNow website <https://airnow.gov/ >	AirNow provides air quality information in terms of the Air Quality Index (AQI) for five criteria air pollutants; data on trends as well as real-time indices are available from this collaboration between EPA and other federal, state and local agencies.

d	DeLima Associates. Consumer Product Information Database (CPID) <https://www.whatsinproducts.com/pages/index/1>	The CPID contains health effects information for nine categories of products used in the home and in some commercial/institutional settings that contain chemicals. The databases links brand names to health effects and provides label information, including brand name, ingredients and warnings, manufacturer information, health effect information, and properties and health studies for the chemical ingredients of brands.
d i	Health Canada. The Canadian House Dust Study <https://www.canada.ca/en/health-canada/services/environmental-workplace-health/environmental-contaminants/canadian-house-dust-study.html>	The Canadian House Dust Study sampled households between 2007 and 2010 to provide background levels of lead in Canadian homes. This web page provides links to several publications based on the results of the House Dust Study.
d	Jantunen, MJ; Hanninen, O; Katsouyanni, K; Knoppel, H; Kuenzli, N; Lebret, E; Maroni, M; Saarela, K; Sram, R; Zmirou, D. (1998). Air Pollution Exposure in European Cities: The EXPOLIS STUDY <https://www.thl.fi/expolis/files/final_report.pdf>	The EXPOLIS study measured personal exposure to PM2.5, 30 VOCs, CO, and NO2 in six European cities.

d	POET FP5 European project. (2006). POET Emission Inventory Documentation <http://accent.aero.jussieu.fr/documents/poet_documentation.pdf>	NASA estimated global emissions of gases (ozone precursors) from anthropogenic, natural, and biomass burning sources for the period 1990-2000. The emissions estimates are based on national activity data and emission factors.
d	U.S. Department of Health and Human Services (HHS). (2010). NLM® Household Products Database <https://www.nlm.nih.gov/pubs/techbull/ja10/ja10_sis_reprint_household_prods.html>	The Household Products Database (HPD) is based on the Consumer Product Information Database (CPID). The HPD contains information on products, manufacturers, chemical ingredients, safety and handling, and potential health effects for various product categories, including auto, inside the home, landscape/yard, home maintenance, pet care, arts/crafts, personal care products, home office, and pesticides. The National Library of Medicine® (NLM) HPD has been updated and now includes 10,000 brand name products, 3,214 ingredients, and 395 manufacturers. In addition, 4,111 products are now linked to the complete Material Safety Data Sheet (MSDS).

d	U.S. EPA. Air Data: Air Quality Data Collected at Outdoor Monitors Across the US <https://www.epa.gov/outdoor-air-quality-data>	The Air Data site provides access to yearly summaries of U.S. air pollution data collected at outdoor monitors across the US. This site has information about where air pollution comes from (emissions) and how much pollution is in the air outside our homes and work places (monitoring). Reports, visualization tools, and interactive maps are available on the site.
d i	U.S. EPA. (2018). Air Emissions Sources <https://www.epa.gov/air-emissions-inventories/national-emissions-inventory-nei>	This interactive National Emissions Inventory (NEI) Report explains how air emissions data are generated and used, and provides tools that explore emission trends and source contributions to air pollution. It highlights the most recent comprehensive and complete NEI, 2014 version 2, released in February 2018.
d	U.S. EPA. Air Quality System (AQS) <https://www.epa.gov/aqs >	AQS is EPA's database of ambient air monitoring data for criteria and hazardous air pollutants collected by states and tribes at more than 10,000 monitors across the country.

d	U.S. EPA. Air Toxics – National Air Toxics Trends Stations <https://www3.epa.gov/ttn/amtic/natts.html>	The NATTS Network was developed to monitor concentrations and trends in hazardous air pollutants (air toxics) at multiple sites across the U.S. The data can also be used to assess the effectiveness of emission reduction programs, assess and verify air quality models, and can serve as a direct input to source-receptor models.
d	U.S. EPA. Analysis and Products from NHEXAS; National Human Exposure Assessment Survey	This website provides links to NHEXAS work products.
d	U.S. EPA. Building Assessment Survey and Evaluation (BASE) Study <https://www.epa.gov/indoor-air-quality-iaq/building-assessment-survey-and-evaluation-study >	During the five year Building Assessment Survey and Evaluation (BASE) study, EPA collected measurements of indoor air quality in a nationally representative sample of public and commercial office buildings. Survey information about occupant perceptions of air quality is also available along with building specifications such as age and HV/AC characteristics. This site links to the raw data from this study as well as summary statistics and reports published using the data.

d	U.S. EPA. Chemical Data Reporting (CDR) <https://www.epa.gov/chemical-data-reporting>	CDR data are a collection of screening-level, exposure-related information on chemical substances. The CDR rule requires manufacturers and importers to submit information on the production and use of chemicals in commerce in large quantities. The CDR data constitute the most comprehensive source of basic screening-level, exposure-related information on chemicals available to EPA and include the following information when available: production volume, maximum concentration and physical form(s), total number of manufacturing, processing and use sites, total number of reasonably likely to be exposed manufacturing and industrial workers, and industrial processing and use and commercial and consumer use data.

d	U.S. EPA. Clean Air Status and Trends Network (CASTNET) Data <https://www.epa.gov/castnet>	CASTNET provides access to measured concentrations of criteria air pollutants from various rural monitoring sites around the United States; data can be used to assess trends in air quality, ecological effects, and atmospheric deposition.
d	U.S. EPA. Clearinghouse for Inventories and Emissions Factors (CHIEF) <https://www.epa.gov/chief>	This web site provides links to emissions inventories, air quality emission factors from the Emissions Factors and Policy Applications Center (EFPAC), Emissions Modeling Clearinghouse (EMCH), and monitoring techniques for air pollution control.

	U.S. EPA. CompTox Chemicals Dashboard <https://www.epa.gov/chemical-research/comptox-chemicals-dashboard>	The CompTox Chemicals Dashboard can be searched by chemical identifiers (e.g. DTXSID and CASRN), consumer product categories (i.e. view chemicals found in certain product types), and assays/genes associated with high-throughput screening data. Using high-throughput screening, living cells or proteins are exposed to chemicals and examined for subsequent changes that suggest potential biological responses. The Dashboard contains chemistry, toxicity and exposure information for over 900,000 chemicals, with over 300 chemical lists based on structure or category. Data and models within the Dashboard also help with efforts to identify chemicals of most need of further testing and reducing the use of animals in chemical testing.

d	U.S. EPA. Database of Sources of Environmental Releases of Dioxin-Like Compounds in the United States <https://assessments.epa.gov/risk/document/&deid=20797>	This resource is a repository of specific CDD/CDF emissions data from all known sources in the United States. The database information can be analyzed to track emissions of CDD/CDF over time, compare specific profiles between and among source categories, and develop source specific emission factors that can then be used to develop emission estimates.
d	U.S. EPA. Emission & Generation Resource Integrated Database (eGRID) < https://www.epa.gov/energy/emissions-generation-resource-integrated-database-egrid>	eGRID contains data on the environmental characteristics of almost all U.S.-based generated power. Characteristics recorded include air emissions for nitrogen oxides, sulfur dioxide, and other emissions as well as net generation, emission rates, and other attributes.

d	U.S. EPA. The Facility Registry Service (FRS) Query Page <https://www.epa.gov/enviro/frs-query-page>	The FRS Query Page allows users to retrieve selected facility data from the national systems listed. Search strategies include combinations of the facility name, geographic location, facility industrial classification, affiliated organization and contact, program category, and national systems.
i	U.S. EPA. (2011). Global Anthropogenic Non-CO2 Greenhouse Gas Emissions: 1990-2030 <https://www.epa.gov/sites/production/files/2016-08/documents/epa_global_nonco2_projections_dec2012.pdf>	This 2012 report provides estimated projections to 2030 for emissions from more than twenty emissions sources. The gases included in this report are methane, nitrous oxide, and fluorinated greenhouse gases (hydrofluorocarbons, perfluorocarbons, and sulfur hexafluoride).

d	U.S. EPA. (2008). Mobile Source Observation Database (MSOD) User Guide and Reference	The MSOD database contained emission test data from in-use mobile air pollution sources such as cars, trucks, and engines from trucks and nonroad vehicles. Data are available from 1982 to present and are intended to be representative of in-use vehicle emissions in the United States. A user and reference guide is available for this database.
d	U.S. EPA. National Air Quality: Status and Trends of Key Air Pollutants <https://www.epa.gov/air-trends>	This EPA website describes the trends in ambient air pollutants as well as emissions of those pollutants from different sources across the country.
d i	U.S. EPA. National Air Toxics Assessments (NATA) <https://www.epa.gov/national-air-toxics-assessment>	NATA is EPA's ongoing comprehensive evaluation of air toxics in the U.S. It is a screening tool for state/local/tribal agencies to prioritize pollutants, emission sources, and areas of interest for further study to gain a better understanding of risks.

d	U.S. EPA. National Emission Inventory (NEI) <https://www.epa.gov/air-emissions-inventories/national-emissions-inventory-nei>	EPA's NEI database contains information about sources that emit criteria air pollutants and their precursors, and hazardous air pollutants. The database includes estimates of annual air pollutant emissions from point, nonpoint, and mobile sources in the 50 States, the District of Columbia, Puerto Rico, and the Virgin Islands. EPA collects information about sources and releases an updated version of the NEI database every three years.
d	U.S. EPA. Ozone-Depleting Substances (ODS) <https://www.epa.gov/ozone-layer-protection/ozone-depleting-substances >	This site lists ozone-depleting substances (ODS) categorized by class, number scheme, and global warming potentials for ODS substitutes.
i	U.S. EPA. The Plain English Guide to the Clean Air Act <https://www.epa.gov/clean-air-act-overview/plain-english-guide-clean-air-act>	This site provides information on pollution prevention as it relates to consumer products use. Information on the contribution of consumer products to indoor and outdoor air pollution is provided.

d	U.S. EPA. RadNet <https://www.epa.gov/radnet>	RadNet, formerly Environmental Radiation Ambient Monitoring System (ERAMS), tracks radiation in the nation's air, precipitation, drinking water, and milk samples through a nationwide monitoring system.
d	U.S. EPA. Source Ranking Database <https://www.epa.gov/tsca-screening-tools/srd-source-ranking-database-users-guide-and-documentation-vol-1-and-vol-2>	The Source Ranking Database includes preliminary screening-level reviews of over 12,000 potential indoor pollution sources and allows for the identification of high-priority product and material categories for further evaluation.

d	U.S. EPA. SPECIATE Database <https://www.epa.gov/air-emissions-modeling/speciate-version-45-through-40>	SPECIATE is EPA's repository of total organic compound (TOC) and particulate matter (PM) speciation profiles of air pollution sources. The database can be used to create speciated emissions inventories for air quality modeling, estimate hazardous and toxic air pollutant emissions from total PM and TOC primary emissions, provide input to chemical mass balance receptor models, and verify profiles derived from ambient measurements using multivariate receptor models (e.g., factor analysis and positive matrix factorization).
d	U.S. EPA. (1987). Total Exposure Assessment Methodology (TEAM) Study <https://nepis.epa.gov/adobe/pdf/2000tty7.pdf>	EPA designed this study to develop methods to measure individual total exposure (through air, food, and water) to toxic and carcinogenic chemicals, including VOCs, pesticides, and carbon monoxide. Breath, personal air, outdoor air, and water samples were collected for 30 VOCs.

Scenarios

Inhalation exposure can be relevant for ambient air, indoor air, or both depending on the source and nature of the pollutant. Inhalation exposure can be estimated by first defining the exposure scenario of interest.

Exposure scenarios typically include information on the sources and pathways of exposure, contaminants of concern, and receptor populations. They might also describe a receptor population's activities that may affect exposure and the timeframe over which exposure occurs.

Inhalation exposure could occur over short durations (e.g., more than 24 hours, up to 30 days) or longer timeframes (e.g., more than 30 days), and can be associated with various types of activities (e.g., occupational, recreational, residential) in different indoor or outdoor environments.

The table below provides some examples of inhalation scenarios. The list of examples is not meant to be exhaustive; there are numerous other inhalation scenarios that may be constructed based on the specific needs of the assessment. There are also numerous variations of the examples provided in the table.

Examples of Inhalation Exposure Scenarios and Related Exposure Factors Handbook: 2011 Edition <https://epa.gov/expobox/about-exposure-factors-handbook> **Tables**

Medium	Receptor Population	Activity/Timeframe	Inhalation Rate	Exposure Period
Ambient air	General population; adults	Routine activity; long-term; adjusted air concentration	Not applicable	Chronic
Ambient air; contaminated site	School children	Playing during time spent in elementary school; dose calculation [Table 16-17]	Short-tem, activity-specific [Table 6-2]	Sub-chronic
Ambient air; source-related contaminant	Highly-exposed local population; adults and children	Routine; long-term-dose calculation	Daily [Table 6-1]	Chronic or sub-chronic, depending on lifestage
Outdoor air; particulates from contaminated site	Occupational; adults	Site-specific construction; short-term; adjusted air concentration	Not applicable	Acute
Indoor air	Infants or home-bound elderly adults	Routine; less than lifetime; adjusted air concentration	Not applicable	Sub-chronic

Medium	Receptor Population	Activity/Timeframe	Inhalation Rate	Exposure Period
Indoor air	Occupational	Working in contaminated office building; long-term occupational; adjusted air concentration [Table 16-8]	Not applicable	Chronic
Indoor air; consumer product use	Consumers	Cleaning with same consumer product over long timeframe [Chapter 17]	Short-term, activity-specific [Table 6-2]	Chronic
Indoor air; vapor intrusion from under-foundation source	Residential adults and children	Routine over lifetime; adjusted air concentration	Not applicable	Chronic
Indoor air; volatilization from water while showering	Residential adults and children	Showering daily [Table 16-1]	Short-term, activity-specific [Table 6-2]	Chronic or sub-chronic, depending on lifestage
Outdoor or indoor air; volatilization from swimming pool water	Recreators	Swimming over less than lifetime [Table 16-1]	Short-term, activity-specific [Table 6-2]	Sub-chronic
Indoor air; contamination in vehicle	Commuters; adults	Traveling in vehicle to and from work; less than lifetime [Table 16-24]	Short-term, activity-specific [Table 6-2]	Sub-chronic

Several resources are available that illustrate inhalation exposure scenarios.

- **Key:** Information sources
- Data sources
- Models

Tool Type	Tools	Description

	U.S. EPA. (2014). Child-Specific Exposure Scenarios Examples	The Child-Specific Exposure Scenarios Examples provides common exposure pathways and tools for estimating exposure, dose, and adverse health effects in children. The scenarios provided in the document use data found in EPA's Child-Specific Exposure Factors Handbook and the Exposures Factors Handbook: 2011 Edition.
	U.S. EPA. (2004). Example Exposure Scenarios Assessment Tool <https://assessments.epa.gov/risk/document/&deid=85843>	This document presents a series of example exposure scenarios for various exposure pathways organized by route (i.e., ingestion, inhalation, or dermal) and demonstrates how data from the Exposure Factors Handbook can be applied for estimating exposures.
	U.S. EPA. (2016). ExpoFIRST (Exposure Factors Interactive Resource for Scenarios Tool) <https://assessments.epa.gov/risk/document/&deid=322489>	ExpoFIRST is a standalone tool that draws from data in the EPA's Exposure Factors Handbook for quick, easy, and flexible development of human exposure scenarios. The tool develops these scenarios based on the selections made by the user in terms of the route of exposure of interest, the media of interest, exposure descriptor, receptor (age groups) and other demographics.
	U.S. EPA. (2010). An Exposure Assessment of Polybrominated Diphenyl Ether <https://assessments.epa.gov/risk/document/&deid=210404>	EPA's exposure assessment of polybrominated diphenyl ether (PBDE) provides a comprehensive assessment of the exposure of Americans to PBDEs. The report includes information on the production, use, lifecycle, and environmental fate of these persistent organic chemicals, as well as measured environmental levels and human exposure.

	U.S. EPA. (2005). Human Health Risk Assessment Protocol (HHRAP) for Hazardous Waste Combustion Facilities	HHRAP describes the evaluation of multi-pathway, site-specific human health risk assessments and was developed specifically for assessment of hazardous waste combustors; it is applicable to other exposure scenarios as well.
	U.S. EPA. (1994). Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry <https://assessments.epa.gov/risk/document/&deid=71993>	This document describes EPA's methodology for estimation of inhalation reference concentrations (RfCs) as benchmark estimates of the quantitative dose-response assessment of chronic noncancer toxicity for individual inhaled chemicals. It also includes discussions of general principles of dose-response assessment for noncancer assessment process, criteria to select key studies for RfC derivation, and uncertainty and data gaps using this methodology.
	U.S. EPA. (1989). Risk Assessment Guidance for Superfund (RAGS): Volume I: Human Health Evaluation Manual (Part A) <https://www.epa.gov/risk/risk-assessment-guidance-superfund-rags-part>	The Risk Assessment Guidance for Superfund (RAGS): Volume I: Human Health Evaluation Manual (Part A) provides guidance for evaluating human health effects as part of a baseline risk assessment. This guidance document includes 10 chapters and two appendices describing topics including: planning, data collection and evaluation, exposure and toxicity assessment, and risk characterization.
	U.S. EPA. (2009). Risk Assessment Guidance for Superfund (RAGS): Volume I: Human Health Evaluation Manual (Part F, Supplemental Guidance for Inhalation Risk Assessment) <https://www.epa.gov/risk/risk-assessment-guidance-superfund-rags-part-f>	This document provides guidance for conducting inhalation risk assessments for Superfund sites.

	U.S. EPA. (2012). Standard Operating Procedures (SOPs) for Residential Pesticide Exposure Assessment <https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide >	The 2012 Residential SOPs are based on the Guidelines for Exposure Assessment and present scenario-based assessments of exposure to pesticides in residential settings. New scenarios have been added to this edition for new products and uses; exposure algorithms for some existing exposure scenarios have been modified. Links to spreadsheets that can be used to perform the calculations are also available from this resource.
	U.S. EPA. (1996). Superfund Soil Screening Guidance <https://www.epa.gov/superfund/superfund-soil-screening-guidance>	The Soil Screening Guidance (SSG) is a framework proposed by U.S. EPA for developing risk-based, soil screening levels for protection of human health. The framework presents a tiered approach for site evaluation and screening-level development. The SSG is presented in three documents (fact sheet, user's guide, and technical background document) with an additional supplemental guidance. The supplemental guidance describes additional scenarios for soil screening evaluations for residential land use. It also updated the residential scenario presented in the original guidance, adding exposure pathways and incorporating new modeling data. The 2002 version includes updated dispersion modeling data for the residential air exposure model and new methods to develop SSLs for the migration of volatiles from subsurface sources into indoor air that supersede the 1996 guidance.

Factors

To estimate human exposure to contaminants in ambient or indoor air, information is needed about the exposed population(s), exposure pathways, and the concentrations of contaminants in air. When determining inhalation risk, inhalation rate and body weight

Microenvironments are the various changing spaces in which people spend their time that will influence how they will be exposed to contaminants. A

might not be needed. The Superfund Program's updated approach for determining inhalation risk eliminates use of inhalation rates when evaluating exposure to air contaminants (U.S. EPA, 2009).

However, if inhalation rates are needed, data are available in Chapter 6 of the Handbook. Inhalation rate is a volume of air inhaled per unit time. Long-term inhalation rates are reported as daily rates in units of m^3/day or m^3/kg-day. Short-term rates are described for various activities (e.g., walking, running, playing, housework, yard work) or activity levels (e.g., light, moderate, heavy) in units of m^3/minute.

Characteristics of the exposed individual and population are important to define because they determine inhalation rate. For example, inhalation rates will vary between children and adults due to differences in size, physiology, behavior, and activity levels. Individuals in an occupational setting are often assumed to be working harder than residents and so might be assumed to have a higher inhalation rate.

Personal characteristics also dictate activity patterns, which determine where a person is located (i.e., his/her microenvironments; see text box). They also pertain to the intensity of the activities in which the individual is engaged.

microenvironment can be defined as a space with a contaminant concentration that is assumed to be relatively well-mixed, homogeneous, and temporally constant while an individual is located within the microenvironment. Examples of microenvironments included in EPA assessments are automobiles, schools, work places, and other buildings. The *Exposure Factors Handbook: 2011 Edition* presents data on the amount of time that an individual is expected to spend in various microenvironments. For buildings, important factors might include size, volume, number of windows, and air exchange rates, and the Handbook provides information about these factors for both residential and nonresidential buildings (U.S. EPA, 2011).

The Exposure Factors Tab <https://epa.gov/expobox/exposure-assessment-tools-approaches-indirect-estimation-scenario-evaluation#factors> of the Indirect Estimation Module provides links to data on inhalation rates.

Activity-specific factors that may be relevant for assessing inhalation exposures associated with specific activity levels are available in Chapter 16 of the Handbook. Other exposure factors that might be needed for assessing inhalation exposures include:

Other exposure factors that might be needed for assessing inhalation exposures include:

- Body weight (**Chapter 8**)
- Consumer product use (**Chapter 17**)

- Life expectancy values, specifically when evaluating cancer risk (**Chapter 18**)
- Building characteristics when assessing indoor air exposures (**Chapter 19**)

Inhalation exposure factors should be selected to represent the age, gender (if appropriate), timeframe/activity level, and population group (e.g., resident, occupational worker) for the exposure scenario of interest.

> The Exposure Factors Tab <https://epa.gov/expobox/exposure-assessment-tools-approaches-indirect-estimation-scenario-evaluation#factors> of the Indirect Estimation Module provides links to data on other factors.

Guidance

The following sources provide helpful information for conducting exposure assessments involving the inhalation route of exposure.

- **Key:** Information sources
- Data sources
- Models

Tool Type	Tools	Description
	Australian Government Department of Health. (2012). Environmental Health Risk Assessment: Guidelines for Assessing Human Health Risks from Environmental Hazards <https://www.health.gov.au/sites/default/files/documents/2022/07/enhealth-guidance-guidelines-for-assessing-human-health-risks-from-environmental-hazards.pdf>	This guidance document provides information on basic concepts in environmental health risk assessment, including problem formulation, tiered approaches to exposure assessment. Specific guidance is provided for several topics related to exposure assessment including: assessing exposure from multiple routes and sources of exposure, probabilistic exposure modelling, and biomonitoring.

	California Air Resource Board (CARB). California Air Toxics Program <https://www.arb.ca.gov/toxics/toxics.htm>	The CARB Air Toxics Program institutes the process for identifying and controlling toxic air contaminants related to diesel activities, composite wood products, automobile coatings, residential waste burning, automotive maintenance and repair, dry cleaning, asbestos, ocean-going ship onboard incineration, and chrome plating and anodizing. The program also helps to increase public awareness regarding significant toxic exposures and methods for reducing risk.
	European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC). (2010). Guidance on Assessment Factors to Derive a Derived No-Effect Levels (DNEL) <http://www.ecetoc.org/wp-content/uploads/2014/08/ecetoc-tr-110-guidance-on-assessment-factors-to-derive-a-dnel.pdf>	This European guidance document provides a review of assessment factors (AF) used in Derived No-Effect Levels (DNEL), which are used by chemical manufacturers and importers to justify chemical safety assessments (CSA), as required by REACH. The review examined the validity of AF used in R.8 Guidance and predicts the increased difficulty of balancing DNEL with exposure predictions if the use of default AF continues.
	National Institute for Occupational Safety and Health (NIOSH). Respirator Selection Logic Guidance <https://www.cdc.gov/niosh/docs/2005-100/>	This document provides guidance to respirator program administrators on respirator selection in accordance with current respirator use and certification regulations and NIOSH policy.

	Occupational Safety and Health Administration (OSHA). Respiratory Protection eTool <https://www.osha.gov/sltc/etools/respiratory/respirator_selection.html>	This OSHA eTool provides guidance on selecting the appropriate respirator, developing a respirator change schedule, and complying with the OSHA respirator standard.
	Occupational Safety and Health Administration (OSHA). Technical Manual on Ventilation <https://www.osha.gov/otm/section-3-health-hazards/chapter-3>	This OSHA manual provides technical information and guidance on occupational safety and health issues and can be used by OSHA Compliance Safety and Health Officers to assist in hazard recognition and provide guidance in accident prevention.
	U.S. Consumer Product Safety Commission (CPSC). Carbon Monoxide <https://www.cpsc.gov/safety-education/safety-education-centers/carbon-monoxide-information-center>	This website provides links to various publications related to indoor air quality and consumer products.

m	U.S. Department of Energy (DOE). (1997). Office of Scientific and Technical Information (OSTI) Case Study Comparisons of Vapor Inhalation Risk Estimates <https://www.osti.gov/scitech/biblio/641268>	This paper describes two case studies that compare exposure concentrations and estimated human health risks from the RBCA vapor transport models and actual soil vapor concentration and soil vapor flux data. The first case study examines a residential property with petroleum hydrocarbon contamination; the second case study examines chlorinated hydrocarbon contamination in soil and groundwater at a Superfund site. The two approaches compared were the American Society for Testing and Materials (ASTM) Risk-Based Corrective Action (RBCA) model predictions versus site specific soil vapor data.
d	U.S. EPA. Acute Exposure Guideline Levels (AEGLs) Chemical Listing <https://www.epa.gov/aegl/access-acute-exposure-guideline-levels-aegls-values#chemicals >	AEGLs are airborne concentrations (expressed as ppm or mg/m3) that represent threshold exposure limits for the general public and are applicable to exposure periods up to 8 hours. There are three AEGL severity levels—AEGL-1, AEGL-2, and AEGL-3—with AEGL-3 being the most severe. From this website, AEGL information can be obtained using chemical name or cas. no. A compilation of AEGLs is also available for download.

i	U.S. EPA. Air Modeling Guidance and Support <https://www.epa.gov/scram/modeling-guidance-and-support>	The EPA's Air Quality Modeling Group (AQMG) provides leadership to the EPA Regions and State/local/tribal agencies on the selection and use of models in regulatory settings through national modeling guidance. This website provides links to models and guidance.
i	U.S. EPA. (2009). Asbestos: Protect Your Family <https://www.epa.gov/asbestos/protect-your-family>	This EPA website provides information on vermiculite consumer products that may contain asbestos.
i	U.S. EPA. Consumer Products: National Volatile Organic Compound Emission Standards <https://www.epa.gov/stationary-sources-air-pollution/consumer-products-national-volatile-organic-compound-emission>	EPA promulgated national volatile organic compound (VOC) emission standards for certain categories of consumer products pursuant to section 183(e) of the Clean Air Act (Act). Information on these standards can be found at this website.
d	U.S. EPA. Formaldehyde website <https://www.epa.gov/formaldehyde>	Building materials, smoking, household products, and the use of un-vented, fuel-burning appliances can be sources of formaldehyde in buildings. An important source of formaldehyde in homes may be pressed wood products made using adhesives that contain urea-formaldehyde (UF) resins. Information on formaldehyde sources may be found at this website.

i	U.S. EPA. (2007). Framework for Metals Risk Assessment <https://www.epa.gov/risk/framework-metals-risk-assessment>	The Framework for Metals Risk Assessment identifies the unique properties, issues, and processes that risk assessors need to consider when evaluating metal compounds in EPA risk assessments.
i	U.S. EPA. (1992). Guidelines for Exposure Assessment <https://assessments.epa.gov/risk/document/&deid=15263>	The Guidelines for Exposure Assessment is the "go to" resource for planning and conducting human exposure assessments. Guidance is also provided on general concepts of exposure, including definitions, uncertainty, suggestions for presenting results, and tools used for conducing exposure assessments. Information relevant to wildlife exposure to chemicals and human exposure to biological, radiological, and noise agents is also discussed in this resource.
d	U.S. EPA. Health Effects Assessment Summary Tables (HEAST) <https://assessments.epa.gov/risk/document/&deid=2877>	HEAST was developed by EPA for the Superfund and Resource Conservation and Recovery Act (RCRA) hazardous waste programs and includes human health risk and toxicity reference values for key contaminants at hazardous waste sites.

	U.S. EPA. (2005). Human Health Risk Assessment Protocol (HHRAP) for Hazardous Waste Combustion Facilities	HHRAP describes the evaluation of multi-pathway, site-specific human health risk assessments and was developed specifically for assessment of hazardous waste combustors; it is applicable to other exposure scenarios as well.
	U.S. EPA. Indoor Air Quality (IAQ) <https://www.epa.gov/indoor-air-quality-iaq>	This resource provides links to fact sheets, reports, and other sources of information related to indoor air quality.
	U.S. EPA. Indoor Air Quality (IAQ): Volatile Organic Compounds' (VOCs) Impact on Indoor Air Quality <https://www.epa.gov/indoor-air-quality-iaq/volatile-organic-compounds-impact-indoor-air-quality >	This website provides introductory-level information VOCs, including sources, health effects, levels in homes, steps to reduce exposure, and standards/guidelines.
	U.S. EPA. (2009). Metabolically-Derived Human Ventilation Rates: A Revised Approach Based upon Oxygen Consumption Rates <https://assessments.epa.gov/risk/document/&deid=202543>	This EPA report is a companion book to the EPA Exposure Factors Handbook. It provides a revised approach for calculating individual ventilation rates directly from oxygen consumption rate. This revised approach replaces previous approaches that relied on a ventilatory equivalent based on a person's fitness level.
	U.S. EPA. (1998). Methodology for Assessing Health Risks Associated with Multiple Pathways of Exposure to Combustor Emissions <https://assessments.epa.gov/risk/document/&deid=55525>	This guidance provides methodology on conducting indirect risk assessments for multiple pathways of exposure to combustor emissions.

	U.S. EPA. Mobile Source Pollution and Related Health Effects <https://www.epa.gov/mobile-source-pollution>	This website presents information on mobile source pollution, health effects, and strategies for reducing risk to the public from these pollutants.
	U.S. EPA. (1996). Occupational and Residential Exposure Test Guidelines for Indoor Inhalation Exposure <https://permanent.fdlp.gov/fbb/library/epa_875/875-1400.pdf>	This document is one of a series of test guidelines that have been developed by the Office of Prevention, Pesticides and Toxic Substances (OPPTS) for use in the testing of pesticides and toxic substances, and the development of test data that must be submitted to the Agency for review.
	U.S. EPA. (1996). Occupational and Residential Exposure Test Guidelines for Outdoor Inhalation Exposure <https://permanent.fdlp.gov/fbb/library/epa_875/875-1300.pdf>	This document is one of a series of test guidelines that have been developed by the Office of Prevention, Pesticides and Toxic Substances (OPPTS) for use in the testing of pesticides and toxic substances, and the development of test data that must be submitted to the Agency for review.

	U.S. EPA. (2015). OSWER Technical Guide for Assessing and Mitigating the Vapor Intrusion Pathway from Subsurface Vapor Sources to Indoor Air <https://www.epa.gov/sites/production/files/2015-09/documents/oswer-vapor-intrusion-technical-guide-final.pdf>	This OSWER guidance provides technical and policy recommendations for evaluation of subsurface vapor intrusion that may occur from subsurface soil and/or groundwater to building indoor air. It describes a recommended framework for assessing vapor intrusion to support risk management decisions. It also provides technical recommendations about monitoring and terminating building mitigation systems.
	U.S. EPA. (1989). Risk Assessment Guidance for Superfund (RAGS): Volume I: Human Health Evaluation Manual (Part A) <https://www.epa.gov/risk/risk-assessment-guidance-superfund-rags-part>	The Risk Assessment Guidance for Superfund (RAGS): Volume I: Human Health Evaluation Manual (Part A) provides guidance for evaluating human health effects as part of a baseline risk assessment. This guidance document includes 10 chapters and two appendices describing topics including: planning, data collection and evaluation, exposure and toxicity assessment, and risk characterization.
	U.S. EPA. (2009). Risk Assessment Guidance for Superfund (RAGS): Volume I: Human Health Evaluation Manual (Part F, Supplemental Guidance for Inhalation Risk Assessment) <https://www.epa.gov/risk/risk-assessment-guidance-superfund-rags-part-f>	This document provides guidance for conducting inhalation risk assessments for Superfund sites.

	U.S. EPA. (2012). Standard Operating Procedures (SOPs) for Residential Pesticide Exposure Assessment <https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide >	The 2012 Residential SOPs are based on the Guidelines for Exposure Assessment and present scenario-based assessments of exposure to pesticides in residential settings. New scenarios have been added to this edition for new products and uses; exposure algorithms for some existing exposure scenarios have been modified. Links to spreadsheets that can be used to perform the calculations are also available from this resource.

	U.S. EPA. (1996). Superfund Soil Screening Guidance <https://www.epa.gov/superfund/superfund-soil-screening-guidance>	The Soil Screening Guidance (SSG) is a framework proposed by U.S. EPA for developing risk-based, soil screening levels for protection of human health. The framework presents a tiered approach for site evaluation and screening-level development. The SSG is presented in three documents (fact sheet, user's guide, and technical background document) with an additional supplemental guidance. The supplemental guidance describes additional scenarios for soil screening evaluations for residential land use. It also updated the residential scenario presented in the original guidance, adding exposure pathways and incorporating new modeling data. The 2002 version includes updated dispersion modeling data for the residential air exposure model and new methods to develop SSLs for the migration of volatiles from subsurface sources into indoor air that supersede the 1996 guidance.
	U.S. EPA. Technical Air Pollution Resources <https://www.epa.gov/technical-air-pollution-resources>	This resource provides links to various web sites related to air pollution, including resources for air quality monitoring, modeling, fate exposure and risk analysis (FERA), policy and guidance.

	U.S. EPA. Transportation, Air Pollution, and Climate Change <https://www.epa.gov/transportation-air-pollution-and-climate-change>	This website provides information on transportation-related carbon pollution and other air pollution that cause harmful health effects and climate change.
	U.S. EPA. (2004). User's Guide for the Johnson and Ettinger (1991) Model for Subsurface Vapor Intrusion into Buildings <https://www.epa.gov/sites/default/files/2015-11/documents/2004_0222_3phase_users_guide.pdf>	This resource provides guidance for the use of the Johnson and Ettinger Subsurface Vapor Intrusion Model. This revised version (Feb 2004) of the User's Guide corresponds with the release of Version 3.1 of the Johnson and Ettinger (1991) model (J&E) spreadsheets for estimating subsurface vapor intrusion into buildings. The spreadsheet tool was updated in September 2017, and is version 6.0.
	U.S. EPA. Vapor Intrusion website <https://www.epa.gov/vaporintrusion>	This web site provides basic information on vapor intrusion for the general public, homeowners, community leaders, environmental professionals, and other interested parties. Also, included at this site are links to current guidance documents, including Assessing and Mitigating the Vapor Intrusion Pathway from Subsurface Vapor Sources to Indoor Air and Addressing Petroleum Vapor Intrusion At Leaking Underground Storage Tank Sites.

	U.S. EPA Region 3. Air Quality Analysis <https://www.epa.gov/air-quality-analysis >	This webpage includes information for air quality data analysts inside and outside EPA. The information provided supports EPA's NAAQS Review Process.
	U.S.EPA. Air Sensor Toolbox <https://www.epa.gov/air-sensor-toolbox>	This website provides information for citizen scientists, researchers, and developers on how to select and use low-cost, portable air sensor technology and understand results from monitoring activities. The information can help the public learn more about air quality in their communities.

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- U.S. EPA. (2011). Exposure Factors Handbook 2011 Edition (Final) <https://epa.gov/expobox/about-exposure-factors-handbook>. (EPA/600/R-09/052F). Washington, DC.

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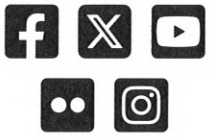

Arsenic, inorganic; CASRN 7440-38-2

Human health assessment information on a chemical substance is included in the IRIS database only after a comprehensive review of toxicity data, as outlined in the IRIS assessment development process. Sections I (Health Hazard Assessments for Noncarcinogenic Effects) and II (Carcinogenicity Assessment for Lifetime Exposure) present the conclusions that were reached during the assessment development process. Supporting information and explanations of the methods used to derive the values given in IRIS are provided in the guidance documents located on the IRIS website.

STATUS OF DATA FOR Arsenic, inorganic

File First On-Line 02/10/1988

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	09/01/1991
Inhalation RfC (I.B.)	not evaluated	
Carcinogenicity Assessment (II.)	yes	06/01/1995

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

I.A. Reference Dose for Chronic Oral Exposure (RfD)

Substance Name — Arsenic, inorganic
CASRN — 7440-38-2
Last Revised — 09/01/1991

The oral Reference Dose (RfD) is based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. It is expressed in units of mg/kg-day. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Please refer to the Background Document for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of substances that are also carcinogens. Therefore, it is essential to refer to other sources of information concerning the carcinogenicity of this

substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

NOTE: There was not a clear consensus among Agency scientists on the oral RfD. Applying the Agency's RfD methodology, strong scientific arguments can be made for various values within a factor of 2 or 3 of the currently recommended RfD value, i.e., 0.1 to 0.8 ug/kg/day. It should be noted, however, that the RfD methodology, by definition, yields a number with inherent uncertainty spanning perhaps an order of magnitude. New data that possibly impact on the recommended RfD for arsenic will be evaluated by the Work Group as it becomes available. Risk managers should recognize the considerable flexibility afforded them in formulating regulatory decisions when uncertainty and lack of clear consensus are taken into account.

I.A.1. Oral RfD Summary

Critical Effect	Experimental Doses*	UF	MF	RfD
Hyperpigmentation, keratosis and possible vascular complications **Human Chronic oral exposure** **Tseng, 1977; Tseng et al., 1968**	NOAEL: 0.009 mg/L converted to 0.0008 mg/kg-day LOAEL: 0.17 mg/L converted to 0.014 mg/kg-day	3	1	3E-4 mg/kg-day

*Conversion Factors -- NOAEL was based on an arithmetic mean of 0.009 mg/L in a range of arsenic concentration of 0.001 to 0.017 mg/L. This NOAEL also included estimation of arsenic from food. Since experimental data were missing, arsenic concentrations in sweet potatoes and rice were estimated as 0.002 mg/day. Other assumptions included consumption of 4.5 L water/day and 55 kg bw (Abernathy et al., 1989). NOAEL = [(0.009 mg/L x 4.5 L/day) + 0.002 mg/day] / 55 kg = 0.0008 mg/kg-day. The LOAEL dose was estimated using the same assumptions as the NOAEL starting with an arithmetic mean water concentration from Tseng (1977) of 0.17 mg/L. LOAEL = [(0.17 mg/L x 4.5 L/day) + 0.002 mg/day] / 55 kg = 0.014 mg/kg-day.

I.A.2. Principal and Supporting Studies (Oral RfD)

Tseng, W.P. 1977. Effects and dose-response relationships of skin cancer and blackfoot disease with arsenic. Environ. Health Perspect. 19: 109-119.

Tseng, W.P., H.M. Chu, S.W. How, J.M. Fong, C.S. Lin and S. Yeh. 1968. Prevalence of skin cancer in an endemic area of chronic arsenicism in Taiwan. J. Natl. Cancer Inst. 40: 453-463.

The data reported in Tseng (1977) show an increased incidence of blackfoot disease that increases with age and dose. Blackfoot disease is a significant adverse effect. The prevalences (males and females combined) at the low dose are 4.6 per 1000 for the 20-39 year group, 10.5 per 1000 for the 40-59 year group, and 20.3 per 1000 for the >60 year group. Moreover, the prevalence of blackfoot disease in each age group increases with increasing dose. However, a recent report indicates that it may not be strictly due to arsenic exposure (Lu, 1990). The data in Tseng et al. (1968) also show increased incidences of hyperpigmentation and keratosis with age. The overall prevalences of hyperpigmentation and keratosis in the exposed groups are 184 and 71 per 1000, respectively. The text states that the incidence increases with dose, but data for the individual doses are not shown. These data show that the skin lesions are the more sensitive endpoint. The low dose in the Tseng (1977) study is considered a LOAEL.

The control group described in Tseng et al. (1968; Table 3) shows no evidence of skin lesions and presumably blackfoot disease, although this latter point is not explicitly stated. This group is considered a NOAEL.

The arithmetic mean of the arsenic concentration in the wells used by the individuals in the NOAEL group is 9 ug/L (range: 1-17 ug/L) (Abernathy et al., 1989). The arithmetic mean of the arsenic concentration in the wells used by the individuals in the LOAEL group is 170 ug/L (Tseng, 1977; Figure 4). Using estimates provided by Abernathy et al. (1989), the NOAEL and LOAEL doses for both food and water are as follows: LOAEL - [170 ug/L x 4.5 L/day + 2 ug/day (contribution of food)] x (1/55 kg) = 14 ug/kg/day; NOAEL - [9 ug/L x 4.5 L/day + 2 ug/day (contribution of food)] x (1/55 kg) = 0.8 ug/kg/day.

Although the control group contained 2552 individuals, only 957 (approximately 38%) were older than 20, and only 431 (approximately 17%) were older than 40. The incidence of skin lesions increases sharply in individuals above 20; the incidence of blackfoot disease increases sharply in individuals above 40 (Tseng, 1968; Figures 5, 6 and 7). This study is less powerful than it appears at first glance. However, it is certainly the most powerful study available on arsenic exposure to people.

This study shows an increase in skin lesions, 22% (64/296) at the high dose vs. 2.2% (7/318) at the low dose. The average arsenic concentration in the wells at the high dose is 410 ug/L and at the low dose is 5 ug/L (Cebrian et al., 1983; Figure 2 and Table 1) or 7 ug/L (cited in the abstract). The average water consumption is 3.5 L/day for males and 2.5 L/day for females. There were about an equal number of males and females in the study. For the dose estimates given below we therefore assume an average of 3 L/day. No data are given on the arsenic exposure from food or the body weight of the participants (we therefore assume 55 kg). The paper states that exposure times are directly related to chronological age in 75% of the cases. Approximately 35% of the participants in the study are more than 20 years old (Figure 1).

Exposure estimates (water only) are: high dose - 410 ug/L x 3 L/day x (1/55 kg) = 22 ug/kg/day; low dose - 5-7 ug/L x 3 L/day x (1/55 kg) = 0.3-0.4 ug/kg/day.

The high-dose group shows a clear increase in skin lesions and is therefore designated a LOAEL. There is some question whether the low dose is a NOAEL or a LOAEL since there is no way of knowing what the incidence of skin lesions would be in a group where the exposure to arsenic is zero. The 2.2% incidence of skin lesions in the low-dose group is higher than that reported in the Tseng et al. (1968) control group, but the dose is lower (0.4 vs. 0.8 ug/kg/day).

The Southwick et al. (1983) study shows a marginally increased incidence of a variety of skin lesions (palmar and plantar keratosis, diffuse palmar or plantar hyperkeratosis, diffuse pigmentation, and arterial insufficiency) in the individuals exposed to arsenic. The incidences are 2.9% (3/105) in the control group and 6.3% (9/144) in the exposed group. There is a slight, but not statistically significant increase in the percent of exposed individuals that have abnormal nerve conduction (8/67 vs. 13/83, or 12% vs. 16% (Southwick et al., 1983; Table 8). The investigators excluded all individuals older than 47 from the nerve conduction portion of the study. These are the individuals most likely to have the longest exposure to arsenic.

Although neither the increased incidence of skin lesions nor the increase in abnormal nerve conduction is statistically significant, these effects may be biologically significant because the same abnormalities occur at higher doses in other studies. The number of subjects in this study was insufficient to establish statistical significance.

Table 3 (Southwick et al., 1983) shows the annual arsenic exposure from drinking water. No data are given on arsenic exposure from food or the body weight (assume 70 kg). Exposure times are not clearly defined, but are > 5 years, and dose groups are ranges of exposure.

Exposure estimates (water only) are: dosed group - 152.4 mg/year x 1 year/365 days x (1/70) kg = 6 ug/kg/day; control group - 24.2 mg/year x year/365 days x (1/70) kg = 0.9 ug/kg/day.

Again because there are no data for a group not exposed to arsenic, there is some question if the control group is a NOAEL or a LOAEL. The incidence of skin lesions in this group is about the same as in the low-dose group from the Cebrian et al. (1983) study; the incidence of abnormal nerve conduction in the control group is higher than that from the low-dose group in the Hindmarsh et al. (1977) study described below. The control dose is comparable to the dose to the control group in the Tseng et al. (1968) and Hindmarsh et al. (1977) studies. The dosed group may or may not be a LOAEL, since it is does not report statistically significant effects when compared to the control.

This study shows an increased incidence of abnormal clinical findings and abnormal electromyographic findings with increasing dose of arsenic (Hindmarsh et al., 1977; Tables III and VI). However, the sample size is extremely small. Percentages of abnormal clinical signs possibly attributed to As were 10, 16, and 40% at the low, mid and high doses, respectively. Abnormal EMG were 0, 17 and 53% in the same three groups.

The exact doses are not given in the Hindmarsh et al. (1977) paper; however, some well data are reported in Table V. The arithmetic mean of the arsenic concentration in the high-dose and mid-dose wells is 680 and 70 ug/L, respectively. Figure 1 (Hindmarsh et al., 1977) shows that the average arsenic concentration of the low-dose wells is about 25 ug/L. No data are given on arsenic exposure from food. We assume daily water consumption of 2 liters and body weight of 70 kg. Exposure times are not clearly stated.

Exposure estimates (water only) are: low - 25 ug/L x 2 L/day x (1/70) kg = 0.7 ug/kg/day; mid - 70 ug/L x 2 L/day x (1/70) kg = 2 ug/kg/day; high - 680 ug/L x 2 L/day x (1/70) kg = 19 ug/kg/day.

The low dose is a no-effect level for abnormal EMG findings. However, because there is no information on the background incidence of abnormal clinical findings in a population with zero exposure to arsenic, there is no way of knowing if the low dose is a no-effect level or another marginal effect level for abnormal clinical findings. The low dose is comparable to the dose received by the control group in the Tseng (1977) and Southwick et al. (1983) studies.

The responses at the mid dose do not show a statistically significant increase but are part of a statistically significant trend and are biologically significant. This dose is an equivocal NOAEL/LOAEL. The high dose is a clear LOAEL for both responses.

As discussed previously there is no way of knowing whether the low doses in the Cebrian et al. (1983), Southwick et al. (1983) and Hindmarsh et al. (1977) studies are NOAELs for skin lesions and/or abnormal nerve conduction. However, because the next higher dose in the

Southwick and Hindmarsh studies only shows marginal effects at doses 3-7 times higher, the Agency feels comfortable in assigning the low doses in these studies as NOAELs.

The Tseng (1977) and Tseng et al. (1968) studies are therefore considered superior for the purposes of developing an RfD and show a NOAEL for a sensitive endpoint. Even discounting the people < 20 years of age, the control group consisted of 957 people that had a lengthy exposure to arsenic with no evidence of skin lesions.

The following is a summary of the defined doses in mg/kg-day from the principal and supporting studies:

1) Tseng (1977): NOAEL = 8E-4; LOAEL = 1.4E-2

2) Cebrian et al. (1983): NOAEL = 4E-4; LOAEL = 2.2E-2

3) Southwick et al. (1983): NOAEL = 9E-4; LOAEL = none (equivocal effects at 6E-3)

4) Hindmarsh et al., 1977: NOAEL = 7E-4; LOAEL = 1.9E-2 (equivocal effects at 2E-3)

I.A.3. Uncertainty and Modifying Factors (Oral RfD)

UF — The UF of 3 is to account for both the lack of data to preclude reproductive toxicity as a critical effect and to account for some uncertainty in whether the NOAEL of the critical study accounts for all sensitive individuals.

MF — None

I.A.4. Additional Studies/Comments (Oral RfD)

Ferm and Carpenter (1968) produced malformations in 15-day hamster fetuses via intravenous injections of sodium arsenate into pregnant dams on day 8 of gestation at dose levels of 15, 17.5, or 20 mg/kg bw. Exencephaly, encephaloceles, skeletal defects and genitourinary systems defects were produced. These and other terata were produced in mice and rats all at levels around 20 mg/kg bw. Minimal effects or no effects on fetal development have been observed in studies on chronic oral exposure of pregnant rats or mice to relatively low levels of arsenic via drinking water (Schroeder and Mitchner, 1971). Nadeenko et al. (1978) reported that intubation of rats with arsenic solution at a dose level of 25 ug/kg/day for a period of 7 months, including pregnancy, produced no significant embryotoxic effects and only infrequent slight expansion of ventricles of the cerebrum, renal pelvis and urinary bladder. Hood et al. (1977) reported that very high single oral doses of arsenate solutions (120 mg/kg) to pregnant

mice were necessary to cause prenatal fetal toxicity, while multiple doses of 60 mg/kg on 3 days had little effect.

Extensive human pharmacokinetic, metabolic, enzymic and long-term information is known about arsenic and its metabolism. Valentine et al. (1987) established that human blood arsenic levels did not increase until daily water ingestion of arsenic exceeded approximately 250 ug/day (approximately 120 ug of arsenic/L. Methylated species of arsenic are successively 1 order of magnitude less toxic and less teratogenic (Marcus and Rispin, 1988). Some evidence suggests that inorganic arsenic is an essential nutrient in goats, chicks, minipigs and rats (NRC, 1989). No comparable data are available for humans.

I.A.5. Confidence in the Oral RfD

Study — Medium
Database — Medium
RfD — Medium

Confidence in the chosen study is considered medium. An extremely large number of people were included in the assessment (> 40,000) but the doses were not well-characterized and other contaminants were present. The supporting human toxicity database is extensive but somewhat flawed. Problems exist with all of the epidemiological studies. For example, the Tseng studies do not look at potential exposure from food or other source. A similar criticism can be made of the Cebrian et al. (1983) study. The U.S. studies are too small in number to resolve several issues. However, the database does support the choice of NOAEL. It garners medium confidence. Medium confidence in the RfD follows.

I.A.6. EPA Documentation and Review of the Oral RfD

Source Document — This assessment is not presented in any existing U.S. EPA document.

This analysis has been reviewed by EPA's Risk Assessment Council on 11/15/1990. This assessment was discussed by the Risk Assessment Council of EPA on 11/15/1990 and verified through a series of meetings during the 1st, 2nd and 3rd quarters of FY91.

Other EPA Documentation — U.S. EPA, 1984, 1988

Agency Work Group Review — 03/24/1988, 05/25/1988, 03/21/1989, 09/19/1989, 08/22/1990, 09/20/1990

Verification Date — 11/15/1990

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the RfD for Arsenic (inorganic) conducted in September 2002 identified one or more significant new studies. IRIS users may request the references for those studies from the IRIS Hotline at hotline.iris@epa.gov or (202)566-1676.

I.A.7. EPA Contacts (Oral RfD)

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202)566-1676 (phone), (202)566-1749 (FAX) or hotline.iris@epa.gov (internet address).

I.B. Reference Concentration for Chronic Inhalation Exposure (RfC)

Substance Name — Arsenic, inorganic
CASRN — 7440-38-2

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Arsenic, inorganic
CASRN — 7440-38-2
Last Revised — 06/01/1995

Section II provides information on three aspects of the carcinogenic assessment for the substance in question; the weight-of-evidence judgment of the likelihood that the substance is a human carcinogen, and quantitative estimates of risk from oral exposure and from inhalation exposure. The quantitative risk estimates are presented in three ways. The slope factor is the result of application of a low-dose extrapolation procedure and is presented as the risk per (mg/kg)/day. The unit risk is the quantitative estimate in terms of either risk per ug/L drinking water or risk per ug/cu.m air breathed. The third form in which risk is presented is a drinking water or air concentration providing cancer risks of 1 in 10,000, 1 in 100,000 or 1 in 1,000,000. The rationale and methods used to develop the carcinogenicity information in IRIS are described in The Risk Assessment Guidelines of 1986 (EPA/600/8-87/045) and in the IRIS Background Document. IRIS summaries developed since the publication of EPA's more recent Proposed Guidelines for Carcinogen Risk Assessment also utilize those Guidelines where

indicated (Federal Register 61(79):17960-18011, April 23, 1996). Users are referred to Section I of this IRIS file for information on long-term toxic effects other than carcinogenicity.

II.A. Evidence for Human Carcinogenicity

II.A.1. Weight-of-Evidence Characterization

Classification — A; human carcinogen

Basis — based on sufficient evidence from human data. An increased lung cancer mortality was observed in multiple human populations exposed primarily through inhalation. Also, increased mortality from multiple internal organ cancers (liver, kidney, lung, and bladder) and an increased incidence of skin cancer were observed in populations consuming drinking water high in inorganic arsenic.

II.A.2. Human Carcinogenicity Data

Sufficient. Studies of smelter worker populations (Tacoma, WA; Magma, UT; Anaconda, MT; Ronnskar, Sweden; Saganoseki-Machii, Japan) have all found an association between occupational arsenic exposure and lung cancer mortality (Enterline and Marsh, 1982; Lee-Feldstein, 1983; Axelson et al., 1978; Tokudome and Kuratsune, 1976; Rencher et al., 1977). Both proportionate mortality and cohort studies of pesticide manufacturing workers have shown an excess of lung cancer deaths among exposed persons (Ott et al., 1974; Mabuchi et al., 1979). One study of a population residing near a pesticide manufacturing plant revealed that these residents were also at an excess risk of lung cancer (Matanoski et al., 1981). Case reports of arsenical pesticide applicators have also corroborated an association between arsenic exposure and lung cancer (Roth, 1958).

A cross-sectional study of 40,000 Taiwanese exposed to arsenic in drinking water found significant excess skin cancer prevalence by comparison to 7500 residents of Taiwan and Matsu who consumed relatively arsenic-free water (Tseng et al., 1968; Tseng, 1977). Although this study demonstrated an association between arsenic exposure and development of skin cancer, it has several weaknesses and uncertainties, including poor nutritional status of the exposed populations, their genetic susceptibility, and their exposure to inorganic arsenic from non-water sources, that limit the study's usefulness in risk estimation. Dietary inorganic arsenic was not considered nor was the potential confounding by contaminants other than arsenic in drinking water. There may have been bias of examiners in the original study since no skin cancer or preneoplastic lesions were seen in 7500 controls; prevalence rates rather than mortality rates are the endpoint; and furthermore there is concern of the applicability of extrapolating data from Taiwanese to the U.S. population because of different background

rates of cancer, possibly genetically determined, and differences in diet other than arsenic (e.g., low protein and fat and high carbohydrate) (U.S. EPA, 1988).

A prevalence study of skin lesions was conducted in two towns in Mexico, one with 296 persons exposed to drinking water with 0.4 mg/L arsenic and a similar group with exposure at 0.005 mg/L. The more exposed group had an increased incidence of palmar keratosis, skin hyperpigmentation and hypopigmentation, and four skin cancers (histologically unconfirmed) (Cebrian et al. (1983). The association between skin cancer and arsenic is weak because of the small number of cases, small cohort size, and short duration follow-up; also there was no unexposed group in either town. No excess skin cancer incidence has been observed in U.S. residents consuming relatively high levels of arsenic in drinking water but the numbers of exposed persons were low (Morton et al., 1976; Southwick et al., 1981). Therapeutic use of Fowler's solution (potassium arsenite) has also been associated with development of skin cancer and hyperkeratosis (Sommers and McManus, 1953; Fierz, 1965); several case reports implicate exposure to Fowler's solution in skin cancer development (U.S. EPA, 1988).

Several follow-up studies of the Taiwanese population exposed to inorganic arsenic in drinking water showed an increase in fatal internal organ cancers as well as an increase in skin cancer. Chen et al. (1985) found that the standard mortality ratios (SMR) and cumulative mortality rates for cancers of the bladder, kidney, skin, lung and liver were significantly greater in the Blackfoot disease endemic area of Taiwan when compared with the age adjusted rates for the general population of Taiwan. Blackfoot disease (BFD, an endemic peripheral artery disease) and these cancers were all associated with high levels of arsenic in drinking water. In the endemic area, SMRs were greater in villages that used only artesian well water (high in arsenic) compared with villages that partially or completely used surface well water (low in arsenic). However, dose-response data were not developed (Chen et al. 1985).

A retrospective case-control study showed a significant association between duration of consuming high-arsenic well water and cancers of the liver, lung and bladder (Chen et al., 1986). In this study, cancer deaths in the Blackfoot disease endemic area between January 1980 and December 1982 were chosen for the case group. About 90% of the 86 lung cancers and 95 bladder cancers in the registry were histologically or cytologically confirmed and over 70% of the liver cancers were confirmed by biopsy or à-fetoprotein presence with a positive liver x-ray image. Only confirmed cancer cases were included in the study. A control group of 400 persons living in the same area was frequency-matched with cases by age and sex. Standardized questionnaires of the cases (by proxy) and controls determined the history of artesian well water use, socioeconomic variables, disease history, dietary habits, and lifestyle. For the cancer cases, the age-sex adjusted odds ratios were increased for bladder (3.90), lung (3.39), and liver (2.67) cancer for persons who had used artesian well water for 40 or more years when compared with controls who had never used artesian well water. Similarly, in a

15-year study of a cohort of 789 patients of Blackfoot disease, an increased mortality from cancers of the liver, lung, bladder and kidney was seen among BFD patients when compared with the general population in the endemic area or when compared with the general population of Taiwan. Multiple logistic regression analysis to adjust for other risk factors including cigarette smoking did not markedly affect the exposure-response relationships or odds ratios (Chen et al., 1988).

A significant dose-response relationship was found between arsenic levels in artesian well water in 42 villages in the southwestern Taiwan and age- adjusted mortality rates from cancers at all sites, cancers of the bladder, kidney, skin, lung, liver and prostate (Wu et al., 1989). An ecological study of cancer mortality rates and arsenic levels in drinking water in 314 townships in Taiwan also corroborated the association between arsenic levels and mortality from the internal cancers (Chen and Wang, 1990).

Chen et al. (1992) conducted a recent analysis of cancer mortality data from the arsenic-exposed population to compare risk of various internal cancers and compare risk between males and females. The study area and population have been described by Wu et al. (1989). It is limited to 42 southwestern coastal villages where residents have used water high in arsenic from deep artesian wells for more than 70 years. Arsenic levels in drinking water ranged from 0.010 to 1.752 ppm. The study population had 898,806 person-years of observation and 202 liver cancer, 304 lung cancer, 202 bladder cancer and 64 kidney cancer deaths. The study population was stratified into four groups according to median arsenic level in well water (< 0.10 ppm, 0.10- 0.29 ppm, 0.30-0.59 ppm and 60+ ppm), and also stratified into four age groups (< 30 years, 30-49 years, 50-69 years and 70+ years). Mortality rates were found to increase significantly with age for all cancers and significant dose- response relationships were observed between arsenic level and mortality from cancer of the liver, lung, bladder and kidney in most age groups of both males and females. The data generated by Chen et al. (1992) provide evidence for an association of the levels of arsenic in drinking water and duration of exposure with the rate of mortality from cancers of the liver, lung, bladder, and kidney. Dose-response relationships are clearly shown by the tabulated data (Tables II-V of Chen et al., 1992). Previous studies summarized in U.S. EPA (1988) showed a similar association in the same Taiwanese population with the prevalence of skin cancers (which are often non-fatal). Bates et al. (1992) and Smith et al. (1992) have recently reviewed and evaluated the evidence for arsenic ingestion and internal cancers.

II.A.3. Animal Carcinogenicity Data

Inadequate. There has not been consistent demonstration of carcinogenicity in test animals for various chemical forms of arsenic administered by different routes to several species (IARC, 1980). Furst (1983) has cited or reviewed animal carcinogenicity testing studies of nine

inorganic arsenic compounds in over nine strains of mice, five strains of rats, in dogs, rabbits, swine and chickens. Testing was by the oral, dermal, inhalation, and parenteral routes. All oxidation states of arsenic were tested. No study demonstrated that inorganic arsenic was carcinogenic in animals. Dimethylarsonic acid (DMA), the end metabolite predominant in humans and animals, has been tested for carcinogenicity in two strains of mice and was not found positive (Innes et al., 1969); however, this was a screening study and no data were provided. The meaning of non-positive data for carcinogenicity of inorganic arsenic is uncertain, the mechanism of action in causing human cancer is not known, and rodents may not be a good model for arsenic carcinogenicity testing. There are some data to indicate that arsenic may produce animal lung tumors if retention time in the lung can be increased (Pershagen et al., 1982, 1984).

II.A.4. Supporting Data for Carcinogenicity

A retrospective cohort mortality study was conducted on 478 British patients treated between 1945-1969 with Fowler's solution (potassium arsenite). The mean duration of treatment was 8.9 months and the average total oral consumption of arsenic was about 1890 mg (daily dose x duration). In 1980, 139 deaths had occurred. No excess deaths from internal cancers were seen after this 20-year follow-up. Three bladder cancer deaths were observed (1.19 expected, SMR 2.5) (Cuzick et al., 1982). A recent follow-up (Cuzick et al., 1992) indicated no increased mortality from all cancers but a significant excess from bladder cancer (5 cases observed/1.6 expected; SMR of 3.07). A subset of the original cohort (143 persons) had been examined by a dermatologist in 1970 for signs of arsenicism (palmar keratosis). In 1990, there were 80 deaths in the subcohort and 11 deaths from internal cancers. All 11 subjects had skin signs (keratosis-10, hyperpigmentation-5 and skin cancer-3). A case-control study of the prevalence of palmar keratoses in 69 bladder cancer patients, 66 lung cancer patients and 218 hospital controls (Cuzick et al., 1984), indicated an association between skin keratosis (as an indicator of arsenic exposure) and lung and bladder cancer. Above the age of 50, 87% of bladder cancer patients and 71% of lung cancer patients but only 36% of controls had one or more keratoses. Several case reports implicate internal cancers with arsenic ingestion or specifically with use of Fowler's solution but the associations are tentative (U.S. EPA, 1988).

Sodium arsenate has been shown to transform Syrian hamster embryo cells (Dipaolo and Casto, 1979) and to produce sister chromatid-exchange in DON cells, CHO cells, and human peripheral lymphocytes exposed in vitro (Wan et al., 1982; Ohno et al., 1982; Larramendy et al., 1981; Andersen, 1983; Crossen, 1983). Jacobson-Kram and Montalbano (1985) have reviewed the mutagenicity of inorganic arsenic and concluded that inorganic arsenic is inactive or very weak for induction of gene mutations in vitro but it is clastogenic with trivalent arsenic being an order of magnitude more potent than pentavalent arsenic.

Both the pentavalent and trivalent forms of inorganic arsenic are found in drinking water. In both animals and humans, arsenate (As+5) is reduced to arsenite (As+3) and the trivalent form is methylated to give the metabolites mononomethylarsinic acid (MMA) and dimethylarsonic acid (DMA) (Vahter and Marafante, 1988). The genotoxicity of arsenate (As+5) and arsenite (As+3) and the two methylated metabolites, MMA and DMA were compared in the thymidine kinase forward mutation assay in mouse lymphoma cells (Harrington-Brock et al. 1993; Moore et al., 1995, in press). Sodium arsenite (+3) and sodium arsenate (+5) were mutagenic at concentration of 1-2 ug/mL and 10-14 ug/mL, respectively, whereas MMA and DMA were significantly less potent, requiring 2.5-5 mg/mL and 10 mg/mL, respectively, to induce a genotoxic response. Based on small colony size the mutations induced were judged chromosomal rather than point mutations. The authors have previously shown that for chemicals having clastogenic activity (i.e., cause chromosomal mutations), the mutated cells grow more slowly than cells with single gene mutations and this results in small colony size. In the mouse lymphoma assay, chromosomal abberations were seen at approximately the same arsenic levels as TK forward mutations. Arsenate, arsenite and MMA were considered clastogenic but the abberation response with DMA was insufficient to consider it a clastogen. Since arsenic exerts its genotoxicity by causing chromosomal mutations, it has been suggested by the above authors that it may act in a latter stage of carcinogenesis as a progressor, rather than as a classical initiator or promotor (Moore et al., 1994). A finding which supports this process is that arsenate (8-16 uM) and arsenite (3 uM) have been shown to induce 2-10 fold amplification of the dihydrofolate reductase gene in culture in methotrexate resistant 3T6 mouse cells (Lee et al., 1988). Although the mechanism of induction in rodent cells is not known, gene amplification of oncogenes is observed in many human tumors. Inorganic arsenic has not been shown to mutate bacterial strains, it produces preferential killing of repair deficient strains (Rossman, 1981). Sodium arsenite (As+3) induces DNA-strand breaks which are associated with DNA-protein crosslinks in cultured human fibroblasts at 3 mM but not 10 mM (Dong and Luo, 1993) and it appears that arsenite inhibits the DNA repair process by inhibiting both excision and ligation (Jha et al., 1992; Lee-Chen et al., 1993).

The inhibitory effect of arsenite on strand-break rejoining during DNA repair was found to be reduced by adding glutathione to cell cultures (Huang et al., 1993). The cytotoxic effects of sodium arsenite in Chinese hamster ovary cells also has also found to correlate with the intracellular glutathione levels (Lee et al., 1989).

In vivo studies in rodents have shown that oral exposure of rats to arsenate (As+5) for 2-3 weeks resulted in major chromosomal abnormalities in bone marrow (Datta et al., 1986) and exposure of mice to As (+3) in drinking water for 4 weeks (250 mg As/L as arsenic trioxide) caused chromosomal aberrations in bone marrow cells but not spermatogonia (Poma et al., 1987); micronuclei in bone marrow cells were also induced by intraperitoneal dosing of mice with arsenate (DeKnudt et al., 1986; Tinwell et al., 1991). Chromosomal aberrations and sister

chromatid exchange have been seen in patients exposed to arsenic from treatment with Fowler's solution (Burgdorf et al., 1977) and subjects exposed occupationally (Beckman et al., 1977) but no increase in either endpoint was seen in lymphocytes of subjects exposed to arsenic in drinking water (Vig et al., 1984).

II.B. Quantitative Estimate of Carcinogenic Risk from Oral Exposure

II.B.1. Summary of Risk Estimates

Oral Slope Factor — 1.5E+0 per (mg/kg)/day

Drinking Water Unit Risk — 5E-5 per (ug/L)

Extrapolation Method — Time- and dose-related formulation of the multistage model (U.S. EPA, 1988)

Drinking Water Concentrations at Specified Risk Levels:

Risk Level	Concentration
E-4 (1 in 10,000)	2E+0 ug/L
E-5 (1 in 100,000)	2E-1 ug/L
E-6 (1 in 1,000,000)	2E-2 ug/L

II.B.2. Dose-Response Data (Carcinogenicity, Oral Exposure)

The Risk Assessment Forum has completed a reassessment of the carcinogenicity risk associated with ingestion of inorganic arsenic (U.S. EPA, 1988). The data provided in Tseng et al., 1968 and Tseng, 1977 on about 40,000 persons exposed to arsenic in drinking water and 7500 relatively unexposed controls were used to develop dose-response data. The number of persons at risk over three dose intervals and four exposure durations, for males and females separately, were estimated from the reported prevalence rates as percentages. It was assumed that the Taiwanese persons had a constant exposure from birth, and that males consumed 3.5 L drinking water/day and females consumed 2.0 L/day. Doses were converted to equivalent

doses for U.S. males and females based on differences in body weights and differences in water consumption and it was assumed that skin cancer risk in the U.S. population would be similar to the Taiwanese population. The multistage model with time was used to predict dose-specific and age-specific skin cancer prevalence rates associated with ingestion of inorganic arsenic; both linear and quadratic model fitting of the data were conducted. The maximum likelihood estimate (MLE) of skin cancer risk for a 70 kg person drinking 2 L of water per day ranged from 1E-3 to 2E-3 for an arsenic intake of 1 ug/kg/day. Expressed as a single value, the cancer unit risk for drinking water is 5E-5 per (ug/L). Details of the assessment are in U.S. EPA (1988).

Dose response data have not been developed for internal cancers for the Taiwanese population. The data of Chen et al. (1992) are considered inadequate at present.

II.B.3. Additional Comments (Carcinogenicity, Oral Exposure)

Eastern Research Group, under contract to EPA, convened an Expert Panel on Arsenic Carcinogenicity on May 21 and 22, 1997 (Eastern Research Group, 1997). The Expert Panel believed that, "it is clear from epidemiological studies that arsenic is a human carcinogen via the oral and inhalation routes (p. 20)." They also concluded, "that one important mode of action is unlikely to be operative for arsenic". The panel agreed that arsenic and its metabolites do not appear to directly interact with DNA (pp. 30-31)." In addition, the panel agreed that, "for each of the modes of action regarded as plausible, the dose-response would either show a threshold or would be nonlinear (p. 31)". The panel agreed, however, "that the dose-response for arsenic at low doses would likely be truly nonlinear, i.e., with a decreasing slope as the dose decreased. However, at very low doses such a curve might be linear but with a very shallow slope, probably indistinguishable from a threshold (p. 31)."

II.B.4. Discussion of Confidence (Carcinogenicity, Oral Exposure)

This assessment is based on prevalence of skin cancer rather than mortality because the types of skin cancer studied are not normally fatal. However, competing mortality from Blackfoot disease in the endemic area of Taiwan would cause the risk of skin cancer to be underestimated. Other sources of inorganic arsenic, in particular those in food sources have not been considered because of lack of reliable information. There is also uncertainty on the amount of water consumed/day by Taiwanese males (3.5 L or 4.5 L) and the temporal variability of arsenic concentrations in specific wells was not known. The concentrations of arsenic in the wells was measured in the early 1960s and varied between 0.01 and 1.82 ppm. For many villages 2 to 5 analyses were conducted on well water and for other villages only one analysis was performed; ranges of values were not provided. Since tap water was supplied to many areas after 1966, the arsenic-containing wells were only used in dry periods. Because

of the study design, particular wells used by those developing skin cancer could not be identified and arsenic intake could not be assigned except by village. Several uncertainties in exposure measurement reliability existed and subsequent analysis of drinking water found fluorescent substances in water that are possible confounders or caused synergistic effects. Uncertainties have been discussed in detail in U.S. EPA (1988). Uncertainties in exposure measurement can affect the outcome of dose- response estimation.

II.C. Quantitative Estimate of Carcinogenic Risk from Inhalation Exposure

II.C.1. Summary of Risk Estimates

Inhalation Unit Risk — 4.3E-3 per (ug/cu.m)

Extrapolation Method — absolute-risk linear model

Air Concentrations at Specified Risk Levels:

Risk Level	Concentration
E-4 (1 in 10,000)	2E-2 ug/cu.m
E-5 (1 in 100,000)	2E-3 ug/cu.m
E-6 (1 in 1,000,000)	2E-4 ug/cu.m

II.C.2. Dose-Response Data for Carcinogenicity, Inhalation Exposure

Tumor Type — lung cancer
Test animals — human, male
Route — inhalation, occupational exposure
Reference — Brown and Chu, 1983a,b,c; Lee-Feldstein, 1983; Higgins, 1982; Enterline and Marsh, 1982

Ambient Unit Risk Estimates (per µg/cu.m)

Ambient Unit Risk Estimates (per µg/cu.m)				
Exposure Source	**Study**	**Unit Risk**	**Geometric Mean Unit Risk**	**Final Estimated Geometric Mean Unit Risk**
Anaconda smelter	Brown and Chu Lee-Feldstein Higgins et al.	1.25E-3 2.80E-3 4.90E-3	2.56E-3	4.29E-3
ASARCO smelter	Enterline & Marsh	6.81E-3 7.60E-3	7.19E-3	4.29E-3

II.C.3. Additional Comments (Carcinogenicity, Inhalation Exposure)

A geometric mean was obtained for data sets obtained with distinct exposed populations (U.S. EPA, 1984). The final estimate is the geometric mean of those two values. It was assumed that the increase in age-specific mortality rate of lung cancer was a function only of cumulative exposures.

The unit risk should not be used if the air concentration exceeds 2 ug/cu.m, since above this concentration the unit risk may not be appropriate.

II.C.4. Discussion of Confidence (Carcinogenicity, Inhalation Exposure)

Overall a large study population was observed. Exposure assessments included air measurements for the Anaconda smelter and both air measurements and urinary arsenic for the ASARCO smelter. Observed lung cancer incidence was significantly increased over expected values. The range of the estimates derived from data from two different exposure areas was within a factor of 6.

II.D. EPA Documentation, Review, and Contacts (Carcinogenicity Assessment)

II.D.1. EPA Documentation

U.S. EPA. 1984, 1988, 1993

A draft of the 1984 Health Assessment Document for Inorganic Arsenic was independently reviewed in public session by the Environmental Health Committee of the U.S. EPA Science Advisory Board on September 22-23, 1983. A draft of the 1988 Special Report on Ingested Inorganic Arsenic; Skin Cancer; Nutritional Essentiality was externally peer reviewed at a two-day workshop of scientific experts on December 2-3, 1986. A draft of the Drinking Water Criteria Document for Arsenic was reviewed by the Drinking Water Committee of the U.S. EPA Science Advisory Board on March 10, 1993. The comments from these reviews were evaluated and considered in the revision and finalization of these reports.

II.D.2. EPA Review (Carcinogenicity Assessment)

Agency Work Group Review — 01/13/1988, 12/07/1989, 02/03/1994

Verification Date — 02/03/1994

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the cancer assessment for Arsenic (inorganic) conducted in September 2002 identified one or more significant new studies. IRIS users may request the references for those studies from the IRIS Hotline at hotline.iris@epa.gov or (202)566-1676.

II.D.3. EPA Contacts (Carcinogenicity Assessment)

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202)566-1676 (phone), (202)566-1749 (FAX) or hotline.iris@epa.gov (internet address).

III. [reserved]
IV. [reserved]
V. [reserved]

VI. Bibliography

Substance Name — Arsenic, inorganic
CASRN — 7440-38-2

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None

VI.C. Carcinogenicity Assessment References

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VII. Revision History

Substance Name — Arsenic, inorganic
CASRN — 7440-38-2

Date	Section	Description
06/30/1988	II.C.1.	Inhalation slope factor changed
09/01/1991	I.A.	Oral RfD summary now on-line
06/01/1995	II.	Carcinogenicity assessment replaced

Date	Section	Description
12/03/2002	I.A.6., II.D.2.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — Arsenic, inorganic
CASRN — 7440-38-2
Last Revised — 02/10/1988

- 7440-38-2
- Arsenic
- Arsenic, inorganic
- gray-arsenic

Symbol	Definition (units)	Default	Reference
	Resident SLs		
$SL_{res\text{-}sol\text{-}ingnc}$	Resident Soil Noncarcinogenic Child Ingestion (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{res\text{-}sol\text{-}dernc}$	Resident Soil Noncarcinogenic Child Dermal (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{res\text{-}sol\text{-}inhnc}$	Resident Soil Noncarcinogenic Child Inhalation (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{res\text{-}sol\text{-}totnc}$	Resident Soil Noncarcinogenic Child Total (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{res\text{-}sol\text{-}ingna}$	Resident Soil Noncarcinogenic Adult Ingestion (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{res\text{-}sol\text{-}derna}$	Resident Soil Noncarcinogenic Adult Dermal (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{res\text{-}sol\text{-}inhna}$	Resident Soil Noncarcinogenic Adult Inhalation (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{res\text{-}sol\text{-}totna}$	Resident Soil Noncarcinogenic Adult Total (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{res\text{-}sol\text{-}ingc}$	Resident Soil Carcinogenic Ingestion (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{res\text{-}sol\text{-}derc}$	Resident Soil Carcinogenic Dermal (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{res\text{-}sol\text{-}inhc}$	Resident Soil Carcinogenic Inhalation (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{res\text{-}sol\text{-}totc}$	Resident Soil Carcinogenic Total (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{res\text{-}sol\text{-}ingmu}$	Resident Soil Mutagenic Ingestion (mg/kg)	Mutagen-specific	Determined in this calculator
$SL_{res\text{-}sol\text{-}dermu}$	Resident Soil Mutagenic Dermal (mg/kg)	Mutagen-specific	Determined in this calculator
$SL_{res\text{-}sol\text{-}inhmu}$	Resident Soil Mutagenic Inhalation (mg/kg)	Mutagen-specific	Determined in this calculator
$SL_{res\text{-}sol\text{-}totmu}$	Resident Soil Mutagenic Total (mg/kg)	Mutagen-specific	Determined in this calculator
$SL_{res\text{-}sol\text{-}ingvc}$	Resident Soil Carcinogenic Vinyl Chloride Ingestion (mg/kg)	Vinyl Chloride -specific	Determined in this calcula
$SL_{res\text{-}sol\text{-}dervc}$	Resident Soil Carcinogenic Vinyl Chloride Dermal (mg/kg)	Vinyl Chloride-specific	Determined in this calcula
$SL_{res\text{-}sol\text{-}inhvc}$	Resident Soil Carcinogenic Vinyl Chloride Inhalation (mg/kg)	Vinyl Chloride-specific	Determined in this calculator
$SL_{res\text{-}sol\text{-}totvc}$	Resident Soil Carcinogenic Vinyl Chloride Total (mg/kg)	Vinyl Chloride-specific	Determined in this calculator
$SL_{res\text{-}sol\text{-}ingtce}$	Resident Soil Trichloroethylene Ingestion (mg/kg)	Trichloroethylene-specific	Determined in this calculator
$SL_{res\text{-}sol\text{-}dertce}$	Resident Soil Trichloroethylene Dermal (mg/kg)	Trichloroethylene-specific	Determined in this calculator
$SL_{res\text{-}sol\text{-}inhtce}$	Resident Soil Trichloroethylene Inhalation (mg/kg)	Trichloroethylene-specific	Determined in this calculator
$SL_{res\text{-}sol\text{-}tottce}$	Resident Soil Trichloroethylene Total (mg/kg)	Trichloroethylene-specific	Determined in this calculator
$SL_{res\text{-}wat\text{-}ingnc}$	Resident Tapwater Noncarcinogenic Child Ingestion (µg/L)	Contaminant-specific	Determined in this calculator
$SL_{res\text{-}wat\text{-}dernc}$	Resident Tapwater Noncarcinogenic Child Dermal (µg/L)	Contaminant-specific	Determined in this calculator
$SL_{res\text{-}wat\text{-}inhnc}$	Resident Tapwater Noncarcinogenic Child Inhalation (µg/L)	Contaminant-specific	Determined in this calculator
$SL_{res\text{-}wat\text{-}totnc}$	Resident Tapwater Noncarcinogenic Child Total (µg/L)	Contaminant-specific	Determined in this calculator
$SL_{res\text{-}wat\text{-}ingna}$	Resident Tapwater Noncarcinogenic Adult Ingestion (µg/L)	Contaminant-specific	Determined in this calculator
$SL_{res\text{-}wat\text{-}derna}$	Resident Tapwater Noncarcinogenic Adult Dermal (µg/L)	Contaminant-specific	Determined in this calculator
$SL_{res\text{-}wat\text{-}inhna}$	Resident Tapwater Noncarcinogenic Adult Inhalation (µg/L)	Contaminant-specific	Determined in this calculator
$SL_{res\text{-}wat\text{-}totna}$	Resident Tapwater Noncarcinogenic Adult Total (µg/L)	Contaminant-specific	Determined in this calculator
$SL_{res\text{-}wat\text{-}ingc}$	Resident Tapwater Carcinogenic Ingestion (µg/L)	Contaminant-specific	Determined in this calculator
$SL_{res\text{-}wat\text{-}derc}$	Resident Tapwater Carcinogenic Dermal (µg/L)	Contaminant-specific	Determined in this calculator
$SL_{res\text{-}wat\text{-}inhc}$	Resident Tapwater Carcinogenic Inhalation (µg/L)	Contaminant-specific	Determined in this calculator

Symbol	Definition (units)	Default	Reference
$SL_{res\text{-}wat\text{-}totc}$	Resident Tapwater Carcinogenic Total (µg/L)	Contaminant-specific	Determined in this calculator
$SL_{res\text{-}wat\text{-}ingmu}$	Resident Tapwater Mutagenic Ingestion (µg/L)	Mutagen-specific	Determined in this calculator
$SL_{res\text{-}wat\text{-}dermu}$	Resident Tapwater Mutagenic Dermal (µg/L)	Mutagen-specific	Determined in this calculator
$SL_{res\text{-}wat\text{-}inhmu}$	Resident Tapwater Mutagenic Inhalation (µg/L)	Mutagen-specific	Determined in this calculator
$SL_{res\text{-}wat\text{-}totmu}$	Resident Tapwater Mutagenic Total (µg/L)	Mutagen-specific	Determined in this calculator
$SL_{res\text{-}wat\text{-}ingvc}$	Resident Tapwater Carcinogenic Vinyl Chloride Ingestion (µg/L)	Vinyl Chloride-specific	Determined in this calculator
$SL_{res\text{-}wat\text{-}dervc}$	Resident Tapwater Carcinogenic Vinyl Chloride Dermal (µg/L)	Vinyl Chloride-specific	Determined in this calculator
$SL_{res\text{-}wat\text{-}inhvc}$	Resident Tapwater Carcinogenic Vinyl Chloride Inhalation (µg/L)	Vinyl Chloride-specific	Determined in this calculator
$SL_{res\text{-}wat\text{-}totvc}$	Resident Tapwater Carcinogenic Vinyl Chloride Total (µg/L)	Vinyl Chloride-specific	Determined in this calculator
$SL_{res\text{-}wat\text{-}ingtce}$	Resident Tapwater Trichloroethylene Ingestion (µg/L)	Trichloroethylene-specific	Determined in this calculator
$SL_{res\text{-}wat\text{-}dertce}$	Resident Tapwater Trichloroethylene Dermal (µg/L)	Trichloroethylene-specific	Determined in this calculator
$SL_{res\text{-}wat\text{-}inhtce}$	Resident Tapwater Trichloroethylene Inhalation (µg/L)	Trichloroethylene-specific	Determined in this calculator
$SL_{res\text{-}wat\text{-}tottce}$	Resident Tapwater Trichloroethylene Total (µg/L)	Trichloroethylene-specific	Determined in this calculator
$SL_{res\text{-}air\text{-}inhn}$	Resident Air Noncarcinogenic (µg/m^3)	Contaminant-specific	Determined in this calculator
$SL_{res\text{-}air\text{-}inhc}$	Resident Air Carcinogenic (µg/m^3)	Contaminant-specific	Determined in this calculator
$SL_{res\text{-}air\text{-}inhmu}$	Resident Air Mutagenic (µg/m^3)	Mutagen-specific	Determined in this calculator
$SL_{res\text{-}air\text{-}inhvc}$	Resident Air Carcinogenic Vinyl Chloride (µg/m^3)	Vinyl Chloride-specific	Determined in this calculator
$SL_{\text{-}air\text{-}inhtce}$	Resident Air Trichloroethylene (µg/m^3)	Trichloroethylene-specific	Determined in this calculator
	Worker SLs		
$SL_{com\text{-}sol\text{-}ingn}$	Composite Worker Soil Noncarcinogenic Ingestion (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{com\text{-}sol\text{-}dern}$	Composite Worker Soil Noncarcinogenic Dermal (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{com\text{-}sol\text{-}inhn}$	Composite Worker Soil Noncarcinogenic Inhalation (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{com\text{-}sol\text{-}totn}$	Composite Worker Soil Noncarcinogenic Total (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{com\text{-}sol\text{-}ingc}$	Composite Worker Soil Carcinogenic Ingestion (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{com\text{-}sol\text{-}derc}$	Composite Worker Soil Carcinogenic Dermal (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{com\text{-}sol\text{-}inhc}$	Composite Worker Soil Carcinogenic Inhalation (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{com\text{-}sol\text{-}totc}$	Composite Worker Soil Carcinogenic Total (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{com\text{-}air\text{-}inhn}$	Composite Worker Air Noncarcinogenic (µg/m^3)	Contaminant-specific	Determined in this calculator
$SL_{com\text{-}air\text{-}inhc}$	Composite Worker Air Carcinogenic (µg/m^3)	Contaminant-specific	Determined in this calculator
$SL_{out\text{-}sol\text{-}ingn}$	Outdoor Worker Soil Noncarcinogenic Ingestion (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{out\text{-}sol\text{-}dern}$	Outdoor Worker Soil Noncarcinogenic Dermal (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{out\text{-}sol\text{-}inhn}$	Outdoor Worker Soil Noncarcinogenic Inhalation (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{out\text{-}sol\text{-}totn}$	Outdoor Worker Soil Noncarcinogenic Total (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{out\text{-}sol\text{-}ingc}$	Outdoor Worker Soil Carcinogenic Ingestion (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{out\text{-}sol\text{-}derc}$	Outdoor Worker Soil Carcinogenic Dermal (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{out\text{-}sol\text{-}inhc}$	Outdoor Worker Soil Carcinogenic Inhalation (mg/kg)	Contaminant-specific	Determined in this calculator

Symbol	Definition (units)	Default	Reference
$SL_{out\text{-}sol\text{-}totc}$	Outdoor Worker Soil Carcinogenic Total (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{out\text{-}air\text{-}inhn}$	Outdoor Worker Air Noncarcinogenic (µg/m³)	Contaminant-specific	Determined in this calculator
$SL_{out\text{-}air\text{-}inhc}$	Outdoor Worker Air Carcinogenic (µg/m³)	Contaminant-specific	Determined in this calculator
$SL_{ind\text{-}sol\text{-}ingn}$	Indoor Worker Soil Noncarcinogenic Ingestion (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{ind\text{-}sol\text{-}inhn}$	Indoor Worker Soil Noncarcinogenic Inhalation (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{ind\text{-}sol\text{-}totn}$	Indoor Worker Soil Noncarcinogenic Total (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{ind\text{-}sol\text{-}ingc}$	Indoor Worker Soil Carcinogenic Ingestion (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{ind\text{-}sol\text{-}inhc}$	Indoor Worker Soil Carcinogenic Inhalation (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{ind\text{-}sol\text{-}totc}$	Indoor Worker Soil Carcinogenic Total (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{ind\text{-}air\text{-}inhn}$	Indoor Worker Air Noncarcinogenic (µg/m³)	Contaminant-specific	Determined in this calculator
$SL_{ind\text{-}air\text{-}inhc}$	Indoor Worker Air Carcinogenic (µg/m³)	Contaminant-specific	Determined in this calculator
$SL_{con\text{-}sol\text{-}ingn}$	Construction Worker Soil Noncarcinogenic Ingestion (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{con\text{-}sol\text{-}dern}$	Construction Worker Soil Noncarcinogenic Dermal (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{con\text{-}sol\text{-}inhn}$	Construction Worker Soil Noncarcinogenic Inhalation (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{con\text{-}sol\text{-}totn}$	Construction Worker Soil Noncarcinogenic Total (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{con\text{-}sol\text{-}ingc}$	Construction Worker Soil Carcinogenic Ingestion (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{con\text{-}sol\text{-}derc}$	Construction Worker Soil Carcinogenic Dermal (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{con\text{-}sol\text{-}inhc}$	Construction Worker Soil Carcinogenic Inhalation (mg/kg)	Contaminant-specific	Determined in this calcula
$SL_{con\text{-}sol\text{-}totc}$	Construction Worker Soil Carcinogenic Total (mg/kg)	Contaminant-specific	Determined in this calcula
Recreator SLs			
$SL_{rec\text{-}sol\text{-}ingnc}$	Recreator Soil Noncarcinogenic Child Ingestion (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{rec\text{-}sol\text{-}dernc}$	Recreator Soil Noncarcinogenic Child Dermal (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{rec\text{-}sol\text{-}inhnc}$	Recreator Soil Noncarcinogenic Child Inhalation (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{rec\text{-}sol\text{-}totnc}$	Recreator Soil Noncarcinogenic Child Total (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{rec\text{-}sol\text{-}ingna}$	Recreator Soil Noncarcinogenic Adult Ingestion (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{rec\text{-}sol\text{-}derna}$	Recreator Soil Noncarcinogenic Adult Dermal (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{rec\text{-}sol\text{-}inhna}$	Recreator Soil Noncarcinogenic Adult Inhalation (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{rec\text{-}sol\text{-}totna}$	Recreator Soil Noncarcinogenic Adult Total (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{rec\text{-}sol\text{-}ingc}$	Recreator Soil Carcinogenic Ingestion (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{rec\text{-}sol\text{-}derc}$	Recreator Soil Carcinogenic Dermal (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{rec\text{-}sol\text{-}inhc}$	Recreator Soil Carcinogenic Inhalation (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{rec\text{-}sol\text{-}totc}$	Recreator Soil Carcinogenic Total (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{rec\text{-}sol\text{-}ingmu}$	Recreator Soil Mutagenic Ingestion (mg/kg)	Mutagenic-specific	Determined in this calculator
$SL_{rec\text{-}sol\text{-}dermu}$	Recreator Soil Mutagenic Dermal (mg/kg)	Mutagenic-specific	Determined in this calculator
$SL_{rec\text{-}sol\text{-}inhmu}$	Recreator Soil Mutagenic Inhalation (mg/kg)	Mutagenic-specific	Determined in this calculator
$SL_{rec\text{-}sol\text{-}totmu}$	Recreator Soil Mutagenic Total (mg/kg)	Mutagenic-specific	Determined in this calculator

Symbol	Definition (units)	Default	Reference
$SL_{rec\text{-}sol\text{-}ingvc}$	Recreator Soil Carcinogenic Vinyl Chloride Ingestion (mg/kg)	Vinyl Chloride-specific	Determined in this calculator
$SL_{rec\text{-}sol\text{-}dervc}$	Recreator Soil Carcinogenic Vinyl Chloride Dermal (mg/kg)	Vinyl Chloride-specific	Determined in this calculator
$SL_{rec\text{-}sol\text{-}inhvc}$	Recreator Soil Carcinogenic Vinyl Chloride Inhalation (mg/kg)	Vinyl Chloride-specific	Determined in this calculator
$SL_{rec\text{-}sol\text{-}totvc}$	Recreator Soil Carcinogenic Vinyl Chloride Total (mg/kg)	Vinyl Chloride-specific	Determined in this calculator
$SL_{rec\text{-}sol\text{-}ingtce}$	Recreator Soil Trichloroethylene Ingestion (mg/kg)	Trichloroethylene-specific	Determined in this calculator
$SL_{rec\text{-}sol\text{-}dertce}$	Recreator Soil Trichloroethylene Dermal (mg/kg)	Trichloroethylene-specific	Determined in this calculator
$SL_{rec\text{-}sol\text{-}inhtce}$	Recreator Soil Trichloroethylene Inhalation (mg/kg)	Trichloroethylene-specific	Determined in this calculator
$SL_{rec\text{-}sol\text{-}tottce}$	Recreator Soil Trichloroethylene Total (mg/kg)	Trichloroethylene-specific	Determined in this calculator
$SL_{rec\text{-}wat\text{-}ingnc}$	Recreator Surface Water Noncarcinogenic Child Ingestion (µg/L)	Contaminant-specific	Determined in this calculator
$SL_{rec\text{-}wat\text{-}dernc}$	Recreator Surface Water Noncarcinogenic Child Dermal (µg/L)	Contaminant-specific	Determined in this calculator
$SL_{rec\text{-}wat\text{-}totnc}$	Recreator Surface Water Noncarcinogenic Child Total (µg/L)	Contaminant-specific	Determined in this calculator
$SL_{rec\text{-}wat\text{-}ingna}$	Recreator Surface Water Noncarcinogenic Adult Ingestion (µg/L)	Contaminant-specific	Determined in this calculator
$SL_{rec\text{-}wat\text{-}derna}$	Recreator Surface Water Noncarcinogenic Adult Dermal (µg/L)	Contaminant-specific	Determined in this calculator
$SL_{rec\text{-}wat\text{-}totna}$	Recreator Surface Water Noncarcinogenic Adult Total (µg/L)	Contaminant-specific	Determined in this calculator
$SL_{rec\text{-}wat\text{-}ingc}$	Recreator Surface Water Carcinogenic Ingestion (µg/L)	Contaminant-specific	Determined in this calculator
$SL_{rec\text{-}wat\text{-}derc}$	Recreator Surface Water Carcinogenic Dermal (µg/L)	Contaminant-specific	Determined in this calculator
$SL_{rec\text{-}wat\text{-}totc}$	Recreator Surface Water Carcinogenic Total (µg/L)	Contaminant-specific	Determined in this calculator
$SL_{\text{-}wat\text{-}ingmu}$	Recreator Surface Water Mutagenic Ingestion (µg/L)	Mutagen-specific	Determined in this calculator
$SL_{rec\text{-}wat\text{-}dermu}$	Recreator Surface Water Mutagenic Dermal (µg/L)	Mutagen-specific	Determined in this calculator
$SL_{rec\text{-}wat\text{-}totmu}$	Recreator Surface Water Mutagenic Total (µg/L)	Mutagen-specific	Determined in this calculator
$SL_{rec\text{-}wat\text{-}ingvc}$	Recreator Surface Water Carcinogenic Vinyl Chloride Ingestion (µg/L)	Vinyl Chloride-specific	Determined in this calculator
$SL_{rec\text{-}wat\text{-}dervc}$	Recreator Surface Water Carcinogenic Vinyl Chloride Dermal (µg/L)	Vinyl Chloride-specific	Determined in this calculator
$SL_{rec\text{-}wat\text{-}totvc}$	Recreator Surface Water Carcinogenic Vinyl Chloride Total (µg/L)	Vinyl Chloride-specific	Determined in this calculator
$SL_{rec\text{-}wat\text{-}ingtce}$	Recreator Surface Water Trichloroethylene Ingestion (µg/L)	Trichloroethylene-specific	Determined in this calculator
$SL_{rec\text{-}wat\text{-}dertce}$	Recreator Surface Water Trichloroethylene Dermal (µg/L)	Trichloroethylene-specific	Determined in this calculator
$SL_{rec\text{-}wat\text{-}tottce}$	Recreator Surface Water Trichloroethylene Total (µg/L)	Trichloroethylene-specific	Determined in this calculator
Fish SLs			
$SL_{res\text{-}fsh\text{-}ingn}$	Resident Fish Noncarcinogenic Ingestion (mg/kg)	Contaminant-specific	Determined in this calculator
$SL_{res\text{-}fsh\text{-}ingc}$	Resident Fish Carcinogenic Ingestion (mg/kg)	Contaminant-specific	Determined in this calculator

Symbol	Definition (units)	Default	Reference
	Miscellaneous Variables		
TR	target risk	1×10^{-6}	Selected by user
THQ	target hazard quotient	0.1	Selected by user
RBA	relative bioavailability factor	Arsenic = 0.6 All Others = 1	U.S. EPA 2012
K	Andelman Volatilization Factor (L/m^3)	0.5	U.S. EPA 1991b (pg. 20)
K_p	Dermal Permeability Constant (cm/hour)	Contaminant-specific Inorganic default = 0.001	U.S. EPA 2004 Exhibit 3-1 and Section 3.1.2.1
$K_{p,ve}$	Steady-state Permeability Coefficient (cm/hour)	Contaminant-specific $K_{p,ve} = K_{ew} D_e / L_e$, K_{ew} = 1 assuming the viable epidermis (ve) (cm/hr) behaves essentially as water; $L_e = 10^{-2}$ cm, $De = 7.1 \times 10^{-6}$/MW cm^2/s assuming $D_e = 10^{-6}$ cm^2/s when MW = 50 (Bunge and Cleek, 1995)	U.S. EPA 2004
K_{ew}	Equilibrium Partition Coefficient between epidermis and water for the absorbing chemical (unitless)	Contaminant-specific	U.S. EPA 2004
D_{sc}	Effective diffusion coefficient for chemical transfer through the stratum corneum (cm2/hr)	Contaminant-specific	U.S. EPA 2004
B	Dimensionless ratio of the permeability coefficient of a compound through the stratum corneum relative to its permeability coefficient across the viable epidermis (ve) (unitless)	Contaminant-specific	U.S. EPA 2004
t^*	Time to reach steady-state (hr)	Contaminant-specific	U.S. EPA 2004
τ_{event}	Lag time per event (hr/event)	Contaminant-specific	U.S. EPA 2004
D_e	Effective Diffusivity of absorbing chemical in the epidermis (cm^2/sec)	$(7.1 \times 10^{-6}) / (\sqrt{MW})$	U.S. EPA 2004
I_{sc}	Apparent thickness of stratum corneum (cm)	0.001	U.S. EPA 2004
b,c	Correlation coefficients	Contaminant-specific see User's Guide section 4.9.8	U.S. EPA 2004
L_e	Effective Thickness of the Epidermis (cm)	0.01	U.S. EPA 2004
AT_{res-c}	Averaging time - resident child (days)	365 x ED_{res-c} = 2190	U.S. EPA 1989 (pg. 6-23)
AT_{res-a}	Averaging time - resident adult (days)	365 x ED_{res} = 9490	U.S. EPA 1989 (pg. 6-23)
AT_{res}	Averaging time - resident age adjusted (days)	365 x LT = 25550	U.S. EPA 1989 (pg. 6-23)
AT_{com-a}	Averaging time - composite worker (days)	365 x ED_{com} = 9125 (non-carcinogenic)	U.S. EPA 1989 (pg. 6-23)
AT_{com}	Averaging time - composite worker (days)	365 x LT = 25550 (carcinogenic)	U.S. EPA 1989 (pg. 6-23)
AT_{ind-a}	Averaging time - indoor worker (days)	365 x ED_{ind} = 9125 (non-carcinogenic)	U.S. EPA 1989 (pg. 6-23)
AT_{ind}	Averaging time - indoor worker soil (days)	365 x LT = 25550 (carcinogenic)	U.S. EPA 1989 (pg. 6-23)
AT_{out-a}	Averaging time - outdoor worker (days)	365 x ED_{out} = 9125 (non-carcinogenic)	U.S. EPA 1989 (pg. 6-23)
AT_{out}	Averaging time - outdoor worker (days)	365 x LT = 25550 (carcinogenic)	U.S. EPA 1989 (pg. 6-23)
AT_{con-a}	Averaging time - construction worker (days)	EW_{con} x 7 (d/wk) x ED_{con} = 350 (non-carcinogenic)	U.S. EPA 1989 (pg. 6-23)
AT_{con}	Averaging time - construction worker (days)	365 x LT = 25550 (carcinogenic)	U.S. EPA 1989 (pg. 6-23)
AT_{rec-c}	Averaging time - recreator child (days)	365 x ED_{rec-c}	U.S. EPA 1989 (pg. 6-23)
AT_{rec-a}	Averaging time - recreator adult (days)	365 x ED_{rec-a}	U.S. EPA 1989 (pg. 6-23)
AT_{rec}	Averaging time - recreator (days)	365 x LT	U.S. EPA 1989 (pg. 6-23)
LT	Lifetime (years)	70	U.S. EPA 1989 (pg. 6-22)
$\Delta H_{v,b}$	Enthalpy of vaporization at the normal boiling point (cal/mol)	Contaminant-specific	See Chemical-specific hierarchy
$\Delta H_{v,gw}$	Enthalpy of vaporization at temperature of groundwater (cal/mol)	Contaminant-specific	Determined in this calculator
HLC	Henry's Law Constant at specified groundwater temperature (atm-m^3/mol)	Contaminant-specific	See Chemical-specific hierarchy
T_{gw}	Groundwater Temperatures (Kelvin)	Site-Specific	Site-Specific
T_c	Critical Temperatures (Kelvin)	Contaminant-specific	See Chemical-specific hierarchy
T_b	Normal Boiling Point (Kelvin)	Contaminant-specific	See Chemical-specific hierarchy
n	If (T_{gw}/T_c < 0.57)	n = 0.3	U.S. EPA Fact Sheet
	If (T_{gw}/T_c > 0.71)	n = 0.41	Unitless exponent values used to determine $\Delta H_{v,gw}$

Symbol	Definition (units)	Default	Reference
	Miscellaneous Variables		
	If $(0.57 < T_s/T_c \leq 0.71)$	$n = (0.74 \times T_s/T_c - 0.116)$	
VPT_{gw}	Vapor Pressure at Groundwater Temperature (mmHg)	Contaminant-specific	Determined in this calculator
VP	Vapor Pressure at 25°C (mmHg)	Contaminant-specific	Contaminant-specific

Symbol	Definition (units)	Default	Reference
	Toxicity Values		
RfD_o or RFDOC	Chronic Oral Reference Dose (mg/kg-day)	Contaminant-specific	EPA Superfund hierarchy
RfC or RFCIC	Chronic Inhalation Reference Concentration (mg/m^3)	Contaminant-specific	EPA Superfund hierarchy
$SRfD_o$ or RFDOS	Subhronic Oral Reference Dose (mg/kg-day)	Contaminant-specific	EPA Superfund hierarchy
SRfC or RFCIS	Subchronic Inhalation Reference Concentration (mg/m^3)	Contaminant-specific	EPA Superfund hierarchy
CSF_o or SFO	Oral Slope Factor $(mg/kg\text{-}day)^{-1}$	Contaminant-specific	EPA Superfund hierarchy
IUR	Inhalation Unit Risk $(\mu g/m^3)^{-1}$	Contaminant-specific	EPA Superfund hierarchy

Symbol	Definition (units)	Default	Reference
Ingestion and Dermal Contact Rates			
IRW_{res-c}	Resident Drinking Water Ingestion Rate - Child (L/day)	0.78	U.S. EPA 2011, Tables 3-15 and 3-33; weighted average of 90th percentile consumer-only ingestion of drinking water (birth to <6 years)
IRW_{res-a}	Resident Drinking Water Ingestion Rate - Adult (L/day)	2.5	U.S. EPA 2011, Table 3-33; 90th percentile of consumer-only ingestion of drinking water (>= 21 years)
$IFW_{res-adj}$	Resident Drinking Water Ingestion Rate - Age-adjusted (L/kg)	327.95	Calculated using the age adjusted intake factors equation
$IFWM_{res-adj}$	Resident Mutagenic Drinking Water Ingestion Rate - Age-adjusted (L/kg)	1019.9	Calculated using the age adjusted intake factors equation
IRS_{res-c}	Resident Soil Ingestion Rate - Child (mg/day)	200	U.S. EPA 1991a (pg. 15)
IRS_{res-a}	Resident Soil Ingestion Rate - Adult (mg/day)	100	U.S. EPA 1991a (pg. 15)
$IFS_{res-adj}$	Resident Soil Ingestion Rate - Age-adjusted (mg/kg)	36750	Calculated using the age adjusted intake factors equation
$IFSM_{res-adj}$	Resident Mutagenic Soil Ingestion Rate - Age-adjusted (mg/kg)	166833.33	Calculated using the age adjusted intake factors equation
IR_{ind}	Indoor Worker Soil Ingestion Rate (mg/day)	50	U.S. EPA 1991a (pg. 15)
IR_{out}	Outdoor Worker Soil Ingestion Rate (mg/day)	100	U.S. EPA 1991a (pg. 15)
IR_{con}	Construction Worker Soil Ingestion Rate (mg/day)	330	U.S. EPA 2002 Exhibit 5-1
IR_{com}	Composite Worker Soil Ingestion Rate (mg/day)	100	U.S. EPA 1991a (pg. 15)
IR_{rec-c}	Recreator Surface Water Ingestion Rate - Child (L/hour)	0.12	U.S. EPA 2011, Table 3.5
IRW_{rec-a}	Recreator Surface Water Ingestion Rate - Adult (L/hour)	0.11	Time weighted average was calculated based on the upper percentile from U.S. EPA 2019, Table 3.7
$IFW_{rec-adj}$	Recreator Surface Water Ingestion Rate - Age-adjusted (L/kg)	Site-Specific	Calculated using the age adjusted intake factors equation
IRW_{0-2}	Surface Water Ingestion Rate - Age Segment 0-2 (L/hour)	0.12	U.S. EPA 2011, Table 3.5
IRW_{2-6}	Surface Water Ingestion Rate - Age Segment 2-6 (L/hour)	0.12	U.S. EPA 2011, Table 3.5
IRW_{6-16}	Surface Water Ingestion Rate - Age Segment 6-16 (L/hour)	0.124	Time weighted average was calculated based on the upper percentile from U.S. EPA 2019, Table 3.7
IRW_{16-26}	Surface Water Ingestion Rate - Age Segment 16-26 (L/hour)	0.0985	Time weighted average was calculated based on the upper percentile from U.S. EPA 2019, Table 3.7
$IFWM_{rec-adj}$	Recreator Mutagenic Surface Water Ingestion Rate - Age-adjusted (L/kg)	Site-Specific	Calculated using the age adjusted intake factors equation
IRS_{rec-c}	Recreator Soil Ingestion Rate - Child (mg/day)	Site-Specific	U.S. EPA 1991a (pg. 15)
IRS_{rec-a}	Recreator Soil Ingestion Rate - Adult (mg/day)	Site-Specific	U.S. EPA 1991a (pg. 15)
$IFS_{rec-adj}$	Recreator Soil Ingestion Rate - Age-adjusted (mg/kg)	Site-Specific	Calculated using the age adjusted intake factors equation
IRS_{0-2}	Soil Ingestion Rate - Age-segment 0-2 (mg/day)	200	U.S. EPA 1991a (pg. 15)
IRS_{2-6}	Soil Ingestion Rate - Age-segment 2-6 (mg/day)	200	U.S. EPA 1991a (pg. 15)
IRS_{6-16}	Soil Ingestion Rate - Age-segment 6-16 (mg/day)	100	U.S. EPA 1991a (pg. 15)
IRS_{16-26}	Soil Ingestion Rate - Age-segment 16-26 (mg/day)	100	U.S. EPA 1991a (pg. 15)

Symbol	Definition (units)	Default	Reference
	Ingestion and Dermal Contact Rates		
$IFSM_{rec-adj}$	Recreator Mutagenic Soil Ingestion Rate - Age-adjusted (mg/kg)	Site-Specific	Calculated using the age adjusted intake factors equation
$DFS_{res-adj}$	Resident soil dermal contact factor- age-adjusted (mg/kg)	103390	Calculated using the age adjusted intake factors equation
$DFSM_{res-adj}$	Resident Mutagenic soil dermal contact factor- age-adjusted (mg/kg)	428260	Calculated using the age adjusted intake factors equation
$DFS_{rec-adj}$	Recreator soil dermal contact factor- age-adjusted (mg/kg)	Site-Specific	Calculated using the age adjusted intake factors equation
$DFSM_{rec-adj}$	Recreator Mutagenic soil dermal contact factor- age-adjusted (mg/kg)	Site-Specific	Calculated using the age adjusted intake factors equation
$DFW_{res-adj}$	Resident water dermal contact factor- age-adjusted (cm_2 - event/kg)	2610650	Calculated using the age adjusted intake factors equation
$DFWM_{res-adj}$	Resident Mutagenic water dermal contact factor- age-adjusted (cm_2 - event/kg)	8191633	Calculated using the age adjusted intake factors equation
$DFW_{rec-adj}$	Recreator water dermal contact factor- age-adjusted (cm_2 - event/kg)	Site-Specific	Calculated using the age adjusted intake factors equation
$DFWM_{rec-adj}$	Recreator Mutagenic water dermal contact factor- age-adjusted (cm^2 - event/kg)	Site-Specific	Calculated using the age adjusted intake factors equation
IRF_{res-a}	Fish Ingestion Rate (mg/day)	Site-Specific	Recommend using Site-Specific values
SA_{res-c}	Resident surface area soil - child (cm^2/day)	2373	U.S. EPA 2011a, Tables 7-2 and 7-8; weighted average of mean values for head, hands, forearms, lower legs, and feet (male and female, birth to < 6 years)(forearm and lower leg-specific data used when available, ratios for nearest available age group used elsewhere)
SA_{res-a}	Resident surface area soil - adult (cm^2/day)	6032	U.S. EPA 2011, Tables 7-2 and 7-12; weighted average of mean values for head, hands, forearms, lower legs, and feet (male and female, 21+ years)(forearm and lower leg-specific data used for males and female lower leg; ratio of male forearm to arm applied to female arm data.
SA_{res-c}	Resident surface area water - child (cm^2)	6365	U.S. EPA 2014, weighted average of mean values for children <6 years.
SA_{res-a}	Resident surface area water - adult (cm^2)	19652	U.S. EPA 2014, weighted average of mean values for adults, male and female 21+.
SA_{out}	Outdoor Worker soil surface area - adult (cm^2/day)	3527	US EPA 2011a, Table 7-2; weighted average of mean values for head, hands, and forearms (male and female, 21+years)
SA_{con}	Construction Worker soil surface area - adult (cm^2/day)	3527	US EPA 2011a, Table 7-2; weighted average of mean values for head, hands, and forearms (male and female, 21+years)
SA_{com}	Composite Worker soil surface area - adult (cm^2/day)	3527	US EPA 2011a, Table 7-2; weighted average of mean values for head, hands, and forearms (male and female, 21+years)

Symbol	Definition (units)	Default	Reference
Ingestion and Dermal Contact Rates			
SA_{rec-c}	Recreator surface area soil - child (cm^2/day)	Site-Specific	Site-Specific
SA_{rec-a}	Recreator surface area soil - adult (cm^2/day)	Site-Specific	Site-Specific
SA_{rec-c}	Recreator surface area water - child (cm^2)	6365	U.S. EPA 2014, weighted average of mean values for children <6 years.
SA_{rec-a}	Recreator surface area water - adult (cm^2)	19652	U.S. EPA 2014, weighted average of mean values for adults, male and female 21+.
SA_{0-2}	Resident/Recreator surface area soil - age segment 0-2 (cm2/day)	Resident 2373	U.S. EPA 2011, Tables 7-2 and 7-12; weighted average of mean values for head, hands, forearms, lower legs, and feet (male and female, 21+ years)(forearm and lower leg-specific data used for males and female lower leg; ratio of male forearm to arm applied to female arm data.
		Recreator - Site-Specific	Recreator - Site-Specific
SA_{2-6}	Resident/Recreator surface area soil - age segment 2-6 (cm^2/day)	Resident 2373	U.S. EPA 2011, Tables 7-2 and 7-12; weighted average of mean values for head, hands, forearms, lower legs, and feet (male and female, 21+ years)(forearm and lower leg-specific data used for males and female lower leg; ratio of male forearm to arm applied to female arm data.
		Recreator - Site-Specific	Recreator - Site-Specific
SA_{6-16}	Resident/Recreator surface area soil - age segment 6-16 (cm^2/day)	Resident 6032	U.S. EPA 2011, Tables 7-2 and 7-12; weighted average of mean values for head, hands, forearms, lower legs, and feet (male and female, 21+ years)(forearm and lower leg-specific data used for males and female lower leg; ratio of male forearm to arm applied to female arm data.
		Recreator - Site-Specific	Recreator - Site-Specific
SA_{16-26}	Resident/Recreator surface area soil - age segment 16-26 (cm^2/day)	Resident 6032	U.S. EPA 2011, Tables 7-2 and 7-12; weighted average of mean values for head, hands, forearms, lower legs, and feet (male and female, 21+ years)(forearm and lower leg-specific data used for males and female lower leg; ratio of male forearm to arm applied to female arm data.
		Recreator - Site-Specific	Recreator - Site-Specific
SA_{0-2}	Resident/Recreator surface area water - age segment 0-2 (cm^2)	6365	U.S. EPA 2014, weighted average of mean values for children <6 years.
SA_{2-6}	Resident/Recreator surface area water - age segment 2-6 (cm^2)	6365	U.S. EPA 2014, weighted average of mean values for children <6 years.

Symbol	Definition (units)	Default	Reference
	Ingestion and Dermal Contact Rates		
SA_{6-16}	Resident/Recreator surface area water - age segment 6-16 (cm^2)	19652	U.S. EPA 2014, weighted average of mean values for adults, male and female 21+.
SA_{16-26}	Resident/Recreator surface area water - age segment 16-26 (cm^2)	19652	U.S. EPA 2014, weighted average of mean values for adults, male and female 21+.
AF_{res-c}	Resident soil adherence factor - child (mg/cm^2)	0.2	U.S. EPA 2002 (Exhibit 1-2)
AF_{res-a}	Resident soil adherence factor - adult (mg/cm^2)	0.07	U.S. EPA 2002 (Exhibit 1-2)
AF_{out}	Outdoor Worker soil adherence factor (mg/cm^2)	0.12	U.S. EPA 2011, Table 7-20 and Section 7.2.2; arithmetic mean of weighted average of body part- specific (hands, forearms, and face) mean adherence factors for adult commercial/industrial activities
AF_{com}	Composite Worker soil adherence factor (mg/cm^2)	0.12	U.S. EPA 2011, Table 7-20 and Section 7.2.2; arithmetic mean of weighted average of body part- specific (hands, forearms, and face) mean adherence factors for adult commercial/industrial activities
AF_{con}	Construction Worker soil adherence factor (mg/cm^2)	0.3	U.S. EPA 2002 (Exhibit 5-1)
AF_{rec-c}	Recreator soil adherence factor - child (mg/cm^2)	none	U.S. EPA 2004 Exhibit 3-3 presents options
AF_{rec-a}	Recreator soil adherence factor - adult (mg/cm^2)	none	U.S. EPA 2004 Exhibit 3-3 presents options
AF_{0-2}	Resident soil adherence factor - age segment 0-2 (mg/cm^2)	0.2	U.S. EPA 2002 (Exhibit 1-2)
AF_{2-6}	Resident soil adherence factor - age segment 2-6 (mg/cm^2)	0.2	U.S. EPA 2002 (Exhibit 1-2)
AF_{6-16}	Resident soil adherence factor - age segment 6-16 (mg/cm^2)	0.07	U.S. EPA 2002 (Exhibit 1-2)
AF_{16-26}	Resident soil adherence factor - age segment 16-26 (mg/cm^2)	0.07	U.S. EPA 2002 (Exhibit 1-2)
BW_{res-c}	Resident Body Weight - child (kg)	15	U.S. EPA 1991a (pg. 15)
BW_{res-a}	Resident Body Weight - adult (kg)	80	U.S. EPA 2011, Table 8-3; weighted mean values for adults 21 - 78
BW_{rec-c}	Recreator Body Weight - child (kg)	15	U.S. EPA 1991a (pg. 15)
BW_{rec-a}	Recreator Body Weight - adult (kg)	80	U.S. EPA 2011, Table 8-3; weighted mean values for adults 21 - 78
BW_{0-2}	Resident/Recreator Body Weight - age segment 0-2 (kg)	15	U.S. EPA 1991a (pg. 15)
BW_{2-6}	Resident/Recreator Body Weight - age segment 2-6 (kg)	15	U.S. EPA 1991a (pg. 15)
BW_{6-16}	Resident/Recreator Body Weight - age segment 6-16 (kg)	80	U.S. EPA 2011, Table 8-3; weighted mean values for adults 21 - 78
BW_{16-26}	Resident/Recreator Body Weight - age segment 16-26 (kg)	80	U.S. EPA 2011, Table 8-3; weighted mean values for adults 21 - 78
BW_{out}	Outdoor Worker Body Weight (kg)	80	U.S. EPA 1991a (pg. 15)
BW_{con}	Construction Worker Body Weight (kg)	80	U.S. EPA 2011, Table 8-3; weighted mean values for adults 21 - 78
BW_{ind}	Indoor Worker Body Weight (kg)	80	U.S. EPA 2011, Table 8-3; weighted mean values for adults 21 - 78
BW_{com}	Composite Worker Body Weight (kg)	80	U.S. EPA 2011, Table 8-3; weighted mean values for adults 21 - 78
ABS	Fraction of contaminant absorbed dermally from soil (unitless)	Contaminant-specific Inorganic default = none	U.S. EPA 2004 (Exhibit 3-4 and section 3.2.2.4)

Symbol	Definition (units)	Default	Reference
Ingestion and Dermal Contact Rates			
ABS_d	Fraction of contaminant absorbed dermally from soil (unitless)	VOC default = none	U.S. EPA 2004 (Exhibit 3-4 and section 3.2.2.4)
		SVOC default = 0.1	
GIABS	Fraction of contaminant absorbed in gastrointestinal tract (unitless) Note: if the GIABS is >50% then it is set to 100% for the calculation of dermal toxicity values.	Contaminant-specific	U.S. EPA 2004 (Exhibit 4-1 and section 4.2)
		Inorganic default = 1.0	
		VOC default = 1.0	
		SVOC default = 1.0	
DA_{event}	Absorbed dose per event ($\mu g/cm^2$ - event)	Contaminant-specific	U.S. EPA 2004 (Equation 3.2 and 3.3)

Symbol	Definition (units)	Default	Reference
Exposure Frequency, Exposure Duration, and Exposure Time Variables			
EF_{res}	Resident Exposure Frequency (days/year)	350	U.S. EPA 1991a (pg. 15)
EF_{res-a}	Resident Exposure Frequency - adult (days/year)	350	U.S. EPA 1991a (pg. 15)
EF_{res-c}	Resident Exposure Frequency - child (days/year)	350	U.S. EPA 1991a (pg. 15)
EF_{com}	Composite Worker Exposure Frequency (days/year)	250	U.S. EPA 1991a (pg. 15)
EF_{ind}	Indoor Worker Exposure Frequency (days/year)	250	U.S. EPA 1991a (pg. 15)
EF_{out}	Outdoor Worker Exposure Frequency (days/year)	225	U.S. EPA 2002 (Exhibit 1-2)
EF_{con}	Construction Worker Exposure Frequency (days/year)	250	U.S. EPA 2002 Exhibit 5-1
EF_{rec}	Recreator Exposure Frequency (days/year)	Site-Specific	Site-Specific
EF_{rec-c}	Recreator Exposure Frequency - child (days/year)	Site-Specific	Site-Specific
EF_{rec-a}	Recreator Exposure Frequency - adult (days/year)	Site-Specific	Site-Specific
EF_{0-2}	Resident/Recreator Exposure Frequency - age segment 0-2 (days/year)	Resident - 350	Resident - U.S. EPA 1991a (pg. 15)
		Recreator - Site-Specific	Recreator - Site-Specific
EF_{2-6}	Resident/Recreator Exposure Frequency - age segment 2-6 (days/year)	Resident - 350	Resident - U.S. EPA 1991a (pg. 15)
		Recreator - Site-Specific	Recreator - Site-Specific
EF_{6-16}	Resident/Recreator Exposure Frequency - age segment 6-16 (days/year)	Resident - 350	Resident - U.S. EPA 1991a (pg. 15)
		Recreator - Site-Specific	Recreator - Site-Specific
EF_{16-26}	Resident/Recreator Exposure Frequency - age segment 16-26 (days/year)	Resident - 350	Resident - U.S. EPA 1991a (pg. 15)
		Recreator - Site-Specific	Recreator - Site-Specific
ED_{res}	Resident Exposure Duration (years)	26	EPA 2011, Table 16-108; 90th percentile for current residence time.
ED_{res-c}	Resident Exposure Duration - child (years)	6	U.S. EPA 1991a (pg. 15)
ED_{res-a}	Resident Exposure Duration - adult (years)	20	ED_{res} (26 years) - ED_{res-c} (6 years)
ED_{com}	Composite Worker Exposure Duration - (years)	25	U.S. EPA 1991a (pg. 15)
ED_{ind}	Indoor Worker Exposure Duration - (years)	25	U.S. EPA 1991a (pg. 15)
ED_{out}	Outdoor Worker Exposure Duration (years)	25	U.S. EPA 1991a (pg. 15)
ED_{con}	Construction Worker Exposure Duration (years)	1	U.S. EPA 2002 Exhibit 5-1
ED_{rec}	Recreator Exposure Duration (years)	26	EPA 2011, Table 16-108; 90th percentile for current residence time.
ED_{rec-c}	Recreator Exposure Duration - child (years)	6	U.S. EPA 1991a (pg. 15)
ED_{rec-a}	Recreator Exposure Duration - adult (years)	20	ED_{rec} (26 years) - ED_{rec-c} (6 years)
ED_{0-2}	Resident/Recreator Exposure Duration - age segment 0-2 (years)	2	U.S. EPA 2005 (pg. 37)
ED_{2-6}	Resident/Recreator Exposure Duration - age segment 2-6 (years)	4	U.S. EPA 2005 (pg. 37)
ED_{6-16}	Resident/Recreator Exposure Duration - age segment 6-16 (years)	10	U.S. EPA 2005 (pg. 37)
ED_{16-26}	Resident/Recreator Exposure Duration - age segment 16-26 (years)	10	U.S. EPA 2005 (pg. 37)
ET_{res-a}	Resident Exposure Time (hours/day)	24	The whole day
ET_{res-c}	Resident Exposure Time (hours/day)	24	The whole day
ET_{res}	Resident Exposure Time (hours/day)	24	The whole day
ET_{com}	Composite Worker Exposure Time (hours/day)	8	The work day

Symbol	Definition (units)	Default	Reference
Exposure Frequency, Exposure Duration, and Exposure Time Variables			
ET_{ind}	Indoor Worker Exposure Time (hours/day)	8	The work day
ET_{out}	Outdoor Worker Exposure Time (hours/day)	8	The work day
ET_{con}	Construction Worker Exposure Time (hours/day)	8	The work day
ET_{rec}	Recreator Exposure Time (hours/day)	Site-Specific	Site-Specific
ET_{rec-c}	Recreator Exposure Time - child (hours/day)	Site-Specific	Site-Specific
ET_{rec-a}	Recreator Exposure Time - adult (hours/day)	Site-Specific	Site-Specific
$ET_{event-res-c}$	Resident Water Exposure Time - child (hours/event)	0.54	U.S. EPA 2011, Table 16-28; weighted average of 90th percentile time spent bathing (birth to <6 years)
$ET_{event-res-a}$	Resident Water Exposure Time - adult (hours/event)	0.71	U.S. EPA 2011, Tables 16-30 and 16-31; weighted average of adult (21 to 78) 90th percentile of time spent bathing/ showering in a day, divided by mean number of baths/showers taken in a day.
$ET_{event-res-adj}$	Resident Water Exposure Time - age-adjusted (hours/event)	0.6708	Calculated using the age adjusted intake factors equation
$ET_{event-res-madj}$	Resident Exposure Time - age-adjusted (hours/event)	0.6708	Calculated using the age adjusted intake factors equation
$ET_{event-rec-c}$	Recreator Surface Water Exposure Time - child (hours/event)	Site-Specific	Site-Specific
$ET_{event-rec-a}$	Recreator Surface Water Exposure Time - adult (hours/event)	Site-Specific	Site-Specific
ET_{0-2}	Resident/Recreator Exposure Time - age segment 0-2 (hours/day)	Resident - 24	Resident - The whole day
		Recreator - Site-Specific	Recreator - Site-Specific
ET_{2-6}	Resident/Recreator Exposure Time - age segment 2-6 (hours/day)	Resident - 24	Resident - The whole day
		Recreator - Site-Specific	Recreator - Site-Specific
ET_{6-16}	Resident/Recreator Exposure Time - age segment 6-16 (hours/day)	Resident - 24	Resident - The whole day
		Recreator - Site-Specific	Recreator - Site-Specific
ET_{16-26}	Resident/Recreator Exposure Time - age segment 16-26 (hours/day)	Resident - 24	Resident - The whole day
		Recreator - Site-Specific	Recreator - Site-Specific
$ET_{event-rec-adj}$	Recreator Exposure Time - age-adjusted (hours/event)	Site-Specific	Calculated using the age adjusted intake factors equation
$ET_{event-rec(0-2)}$	Recreator Exposure Time - age segment 0-2 (hours/event)	Site-Specific	Site-Specific
$ET_{event-rec(2-6)}$	Recreator Exposure Time - age segment 2-6 (hours/event)	Site-Specific	Site-Specific
$ET_{event-rec(6-16)}$	Recreator Exposure Time - age segment 6-16 (hours/event)	Site-Specific	Site-Specific
$ET_{event-rec(16-26)}$	Recreator Exposure Time - age segment 16-26 (hours/event)	Site-Specific	Site-Specific
$ET_{event-res(0-2)}$	Resident Exposure Time - age segment 0-2 (hours/event)	0.54	Calculated based on the ET given for ETevent-res-c
$ET_{event-res(2-6)}$	Resident Exposure Time - age segment 2-6 (hours/event)	0.54	Calculated based on the ET given for ETevent-res-c
$ET_{event-res(6-16)}$	Resident Exposure Time - age segment 6-16 (hours/event)	0.71	Calculated based on the ET given for ETevent-res-a
$ET_{event-res(16-26)}$	Resident Exposure Time - age segment 16-26 (hours/event)	0.71	Calculated based on the ET given for ETevent-res-a
$ET_{event-rec-madj}$	Recreator Exposure Time - age-adjusted (hours/event)	Site-Specific	Calculated using the age adjusted intake factors equation
EV_{rec-c}	Recreator Events - child (events/day)	Site-Specific	Site-Specific

Symbol	Definition (units)	Default	Reference
Exposure Frequency, Exposure Duration, and Exposure Time Variables			
EV_{rec-a}	Recreator Events - adult (events/day)	Site-Specific	Site-Specific
EV_{res-c}	Resident Events - child (events/day)	1	U.S. EPA 2004; Exhibit 3-2
EV_{res-a}	Resident Events - adult (events/day)	1	U.S. EPA 2004; Exhibit 3-2
EV_{0-2}	Resident/Recreator Events - age segment 0-2 (events/day)	Resident - 1 Recreator - Site-Specific	U.S. EPA 2004; Exhibit 3-2
EV_{2-6}	Resident/Recreator Events - age segment 2-6 (events/day)	Resident - 1 Recreator - Site-Specific	U.S. EPA 2004; Exhibit 3-2
EV_{6-16}	Resident/Recreator Events - age segment 6-16 (events/day)	Resident - 1 Recreator - Site-Specific	U.S. EPA 2004; Exhibit 3-2
EV_{16-26}	Resident/Recreator Events - age segment 16-26 (events/day)	Resident - 1 Recreator - Site-Specific	U.S. EPA 2004; Exhibit 3-2

Symbol	Definition (units)	Default	Reference
Soil to Groundwater SSL Factor Variables			
C_w	Target soil leachate concentration (mg/L)	nonzero MCL or RSL × DAF	U.S. EPA. 2002 Equation 4-14
DAF	Dilution attenuation factor (unitless)	1 (or Site-Specific)	U.S. EPA. 2002 Equation 4-11
ED	Exposure duration	70	U.S. EPA. 2002 Equation 4-14
I	Infiltration Rate (m/year)	0.18	U.S. EPA. 2002 Equation 4-11
L	source length parallel to ground water flow (m)	Site-Specific	U.S. EPA. 2002 Equation 4-11
i	hydraulic gradient (m/m)	Site-Specific	U.S. EPA. 2002 Equation 4-11
K	aquifer hydraulic conductivity (m/year)	Site-Specific	U.S. EPA. 2002 Equation 4-11
θ_w	water-filled soil porosity (L_{water}/L_{soil})	0.3	U.S. EPA. 2002 Equation 4-10
θ_a	air-filled soil porosity (L_{air}/L_{soil})	$= n-\theta_w$	U.S. EPA. 2002 Equation 4-10
n	total soil porosity(L_{pore}/L_{soil})	$= 1-(\rho_b/\rho_s)$	U.S. EPA. 2002 Equation 4-10
ρ_s	soil particle density (kg/L)	2.65	U.S. EPA. 2002 Equation 4-10
ρ_b	dry soil bulk density (kg/L)	1.5	U.S. EPA. 2002 Equation 4-10
H'	Dimensionless Henry Law Constant (unitless)	Contaminant-specific	See Chemical-specific hierarchy
K_d	soil-water partition coefficient (L/kg)	$= K_{oc} \times f_{oc}$ for organics	U.S. EPA. 2002 Equation 4-10
K_{oc}	soil organic carbon/water partition coefficient (L/kg)	Contaminant-specific	See Chemical-specific hierarchy
[illegible]	fraction organic carbon in soil (g/g)	0.002	U.S. EPA. 2002 Equation 4-10
d_a	aquifer thickness (m)	Site-Specific	U.S. EPA. 2002 Equation 4-10
d_s	depth of source (m)	Site-Specific	U.S. EPA. 2002 Equation 4-10
d	mixing zone depth (m)	Site-Specific	U.S. EPA. 2002 Equation 4-12

Symbol	Definition (units)	Default	Reference
Wind Particulate Emission Factor Variables			
PEF	Particulate Emission Factor - Minneapolis (m^3/kg)	1.36 x 10^9(region-specific)	U.S. EPA 2002 Exhibit D-2
Q/C_{wind}	Inverse of the Mean Concentration at the Center of a 0.5-Acre-Square Source (g/m^2-s per kg/m^3)	93.77 (region-specific)	U.S. EPA 2002 Exhibit D-2
V	Fraction of Vegetative Cover (unitless)	0.5	U.S. EPA. 2002 Equation 4-5
U_m	Mean Annual Wind Speed (m/s)	4.69	U.S. EPA. 2002 Equation 4-5
U_t	Equivalent Threshold Value of Wind Speed at 7m (m/s)	11.32	U.S. EPA. 2002 Equation 4-5
F(x)	Function Dependent on U_m /U_t (unitless)	0.194	U.S. EPA. 2002 Equation 4-5
A	Dispersion constant unitless	PEF and region-specific	U.S. EPA 2002 Exhibit D-2
A_s	Areal extent of the site or contamination (acres)	0.5 (range 0.5 to 500)	U.S. EPA 2002 Exhibit D-2
B	Dispersion constant unitless	PEF and region-specific	U.S. EPA 2002 Exhibit D-2
C	Dispersion constant unitless	PEF and region-specific	U.S. EPA 2002 Exhibit D-2

Symbol	Definition (units)	Default	Reference
Mechanical Particulate Emission Factor Variables from Vehicle Traffic			
PEF_{sc}	Particulate Emission Factor - subchronic (m^3/kg)	Site-Specific	U.S. EPA 2002 Equation 5-5
Q/C_{sr}	Inverse of the ratio of the 1-h geometric mean concentration to the emission flux along a straight road segment bisecting a square site (g/m^2-s per kg/m^3)	23.02 (for 0.5 acre site)	U.S. EPA 2002 Equation 5-5
F_D	Dispersion correction factor (unitless)	0.185	U.S. EPA 2002 Equation E-16
T	Total time over which construction occurs (s)	Site-Specific	U.S. EPA 2002 Equation 5-5
A_R	Surface area of contaminated road segment (m^2)	($A_R = L_R \times W_R \times 0.092903 m^2/ft^2$)	U.S. EPA 2002 Equation 5-5
L_R	Length of road segment (ft)	Site-Specific	U.S. EPA 2002 Equation 5-5
W_R	Width of road segment (ft)	20	U.S. EPA 2002 Equation E-18
W	Mean vehicle weight (tons)	(number of cars x tons/car + number of trucks x tons/truck) / total vehicles)	U.S. EPA 2002 Equation 5-5
p	Number of days with at least 0.01 inches of precipitation (days/year)	Site-Specific	U.S. EPA 2002 Exhibit 5-2
∑VKT	Sum of fleet vehicle kilometers traveled during the exposure duration (km)	∑VKT = total vehicles x distance (km/day) x frequency (weeks/year) x (days/year)	U.S. EPA 2002 Equation 5-5
A	Dispersion constant unitless	12.9351	U.S. EPA 2002 Equation 5-6
A_s	Areal extent of site surface soil contamination (acres)	0.5 (range 0.5 to 500)	U.S. EPA 2002 Equation 5-6
B	Dispersion constant unitless	5.7383	U.S. EPA 2002 Equation 5-6
C	Dispersion constant unitless	71.7711	U.S. EPA 2002 Equation 5-6

Symbol	Definition (units)	Default	Reference
	Mechanical Particulate Emission Factor Variables from other than Vehicle Traffic		
PEF'_{sc}	Particulate Emission Factor - subchronic (m^3/kg)	Site-Specific	U.S. EPA 2002 Equation E-26
Q/C_{sa}	Inverse of the ratio of the 1-h. geometric mean air concentration and the emission flux at the center of the square emission source (g/m^2-s per kg/m^3)	Site-Specific	U.S. EPA 2002 Equation E-15
F_D	Dispersion correction factor (unitless)	Site-Specific	U.S. EPA 2002 Equation E-16
A	Dispersion constant unitless	2.4538	U.S. EPA 2002 Equation E-15
B	Dispersion constant unitless	17.566	U.S. EPA 2002 Equation E-15
C	Dispersion constant unitless	189.0426	U.S. EPA 2002 Equation E-15
A_e	Areal extent of site surface soil contamination (acres)	(range 0.5 to 500)	U.S. EPA 2002 Equation E-15
J'_T	Total time-averaged PM_{10} unit emission flux for construction activities other than traffic on unpaved roads (g/m^2-s)	Site-Specific	U.S. EPA 2002 Equation E-25
M^{PC}_{wind}	Unit mass emitted from wind erosion (g)	Site-Specific	U.S. EPA 2002 Equation E-20
V	Fraction of Vegetative Cover (unitless)	0	U.S. EPA 2002 Equation E-20
U_m	Mean Annual Wind Speed (m/s)	4.69	U.S. EPA 2002 Equation E-20
U_t	Equivalent Threshold Value of Wind Speed at 7m (m/s)	11.32	U.S. EPA 2002 Equation E-20
F(x)	Function Dependent on U_m/U_t (unitless)	0.194	U.S. EPA 2002 Equation E-20
A_{surf}	Areal extent of site surface soil contamination (m^2)	(range 0.5 to 500)	U.S. EPA 2002 Equation E-20
ED	Exposure duration (years)	Site-Specific	U.S. EPA 2002 Equation E-20
M_{excav}	Unit mass emitted from excavation soil dumping (g)	Site-Specific	U.S. EPA 2002 Equation E-21
0.35	PM_{10} particle size multiplier (unitless)	0.35	U.S. EPA 2002 Equation E-21
U_m	Mean annual wind speed during construction (m/s)	4.69	U.S. EPA 2002 Equation E-21
$M_{m\text{-}excav}$	Gravimetric soil moisture content (%)	12 (mean value for municipal landfill cover)	U.S. EPA 2002 Equation E-21
ρ_{soil}	In situ soil density (includes water) (mg/m^3)	1.68	U.S. EPA 2002 Equation E-21
A_{excav}	Areal extent of excavation (m^2)	(range 0.5 to 500)	U.S. EPA 2002 Equation E-21
d_{excav}	Average depth of excavation (m)	Site-Specific	U.S. EPA 2002 Equation E-21
$N_{A\text{-}dump}$	Number of times soil is dumped (unitless)	2	U.S. EPA 2002 Equation E-21
M_{doz}	Unit mass emitted from dozing operations (g)	Site-Specific	U.S. EPA 2002 Equation E-22
0.75	PM_{10} scaling factor (unitless)	0.75	U.S. EPA 2002 Equation E-22
s_{doz}	Soil silt content (%)	6.9	U.S. EPA 2002 Equation E-22
$M_{m\text{-}doz}$	Gravimetric soil moisture content (%)	7.9 (mean value for overburden)	U.S. EPA 2002 Equation E-22
$\sum VKT_{doz}$	Sum of dozing kilometers traveled (km)	Site-Specific	U.S. EPA 2002 Equation E-22
S_{doz}	Average dozing speed (kph)	11.4 (mean value for graders)	U.S. EPA 2002 Equation E-22
$N_{A\text{-}doz}$	Number of times site is dozed (unitless)	Site-Specific	U.S. EPA 2002 Equation E-22
B_s	Dozer blade length (m)	Site-Specific	U.S. EPA 2002 Page E-28
M_{grade}	Unit mass emitted from grading operations (g)	Site-Specific	U.S. EPA 2002 Equation E-23
0.6	PM10 scaling factor (unitless)	0.6	U.S. EPA 2002 Equation E-23
$\sum VKT_{grade}$	Sum of grading kilometers traveled (km)		U.S. EPA 2002 Equation E-23
S_{grade}	Average grading speed (kph)	11.4 (mean value for graders)	U.S. EPA 2002 Equation E-23
$N_{A\text{-}grade}$	Number of times site is graded (unitless)	Site-Specific	U.S. EPA 2002 Equation E-23
B_s	Grader blade length (m)	Site-Specific	U.S. EPA 2002 Page E-28
M_{till}	Unit mass emitted from tilling operations (g)	Site-Specific	U.S. EPA 2002 Equation E-24
s_{till}	Soil silt content (%)	18	U.S. EPA 2002 Equation E-24
$A_{c\text{-}till}$	Areal extent of tilling (acres)	Site-Specific	U.S. EPA 2002 Equation E-24
$A_{c\text{-}grade}$	Areal extent of grading (acres)	Site-Specific	Necessary to solve $\sum_{VKT_{grade}}$ in U.S. EPA 2002 Equation E-23
$A_{c\text{-}doz}$	Areal extent of dozinging (acres)	Site-Specific	Necessary to solve $\sum_{VKT_{grade}}$ in U.S. EPA 2002 Equation E-22
$N_{A\text{-}till}$	Number of times soil is tilled (unitless)	2	U.S. EPA 2002 Equation E-24

Symbol	Definition (units)	Default	Reference
Chronic Volatilization Factor and Soil Saturation Limit Variables			
VF_{ulim}	Volatilization Factor - Los Angeles (m^3/kg)	Contaminant-specific	U.S. EPA. 2002 Equation 4-8
C_{sat}	Soil saturation concentration (mg/kg)	Contaminant-specific	U.S. EPA. 2002 Equation 4-9
Q/C_{vol}	Inverse of the Mean Concentration at the Center of a 0.5-Acre-Square Source (g/m^2-s per kg/m^3)	68.18	U.S. EPA. 2002 Equation 4-8
A_s	Areal extent of the site contamination (acres)	0.5 (range 0.5 to 500)	U.S. EPA 2002 Equation 4-8
B	Dispersion constant unitless	18.4385 (region-specific)	U.S. EPA 2002 Exhibit D-3
C	Dispersion constant unitless	209.7845 (region-specific)	U.S. EPA 2002 Exhibit D-3
D_A	Apparent Diffusivity (cm^2/s)	Contaminant-specific	U.S. EPA. 2002 Equation 4-8
T	Exposure interval (s)	8.2×10^8 (used for unlimited source model) = 26 years	U.S. EPA. 2002 Equation 4-8
T	Exposure interval (years)	26 (used for mass-limit model)	U.S. EPA. 2002 Equation 4-13
ρ_b	Dry soil bulk density (g/cm^3)	1.5	U.S. EPA. 2002 Equation 4-8
θ_a	Air-filled soil porosity (L_{air}/L_{soil}) ($n-\theta_w$)	0.28	U.S. EPA. 2002 Equation 4-8
n	Total soil porosity (L_{pore}/L_{soil}) ($1-(\rho_b/\rho_s)$	0.43	U.S. EPA. 2002 Equation 4-8
θ_w	Water-filled soil porosity (L_{water}/L_{soil})	0.15	U.S. EPA. 2002 Equation 4-8
ρ_s	Soil particle density (g/cm^3)	2.65	U.S. EPA. 2002 Equation 4-8
S	Water Solubility Limit (mg/L)	Contaminant-specific	See Chemical-specific hierarchy
R	Universal Gas Constant (L-atm/mole-K)	0.082057	U.S. EPAFact Sheet
	Universal Gas Constant (cal/mole-K)	1.9872	U.S. EPA Fact Sheet
	Diffusivity in air (cm^2/s)	Contaminant-specific	U.S. EPA. 2001
H'	Dimensionless Henry's Law Constant	Contaminant-specific	See Chemical-specific hierarchy
D_w	Diffusivity in water (cm^2/s)	Contaminant-specific	U.S. EPA. 2001
K_d	Soil-water partition coefficient (L/kg) (Koc×foc)	Contaminant-specific	U.S. EPA. 2002 Equation 4-8
K_{oc}	Soil organic carbon-water partition coefficient (L/kg)	= $K_{oc} \times f_{oc}$ for organics	See Chemical-specific hierarchy
f_{oc}	Organic carbon content of soil (g/g)	0.006	U.S. EPA. 2002 Equation 4-8
d_s	Average source depth (m)	Site-Specific	U.S. EPA 2002 Equation 4-13

Symbol	Definition (units)	Default	Reference
Subchronic Volatilization Factor for Unlimited Source and Mass-limit Equations			
$VF_{ulim-sc}$	Subchronic Volatilization Factor (m^3/kg)	Contaminant-specific	U.S. EPA 2002 Equation 5-14
Q/C_{sa}	Inverse of the ratio of the 1-h geometric mean air concentration to the volatilization flux at the center of a square source (g/m^2-s per kg/m^3)	14.31 (for 0.5 acre site)	U.S. EPA 2002 Equation 5-14
A	Dispersion constant unitless	2.4538	U.S. EPA 2002 Equation 5-15
A_c	Areal extent of the site soil contamination (acres)	0.5 (range 0.5 to 500)	U.S. EPA 2002 Equation 5-15
B	Dispersion constant unitless	17.566	U.S. EPA 2002 Equation 5-15
C	Dispersion constant unitless	189.0426	U.S. EPA 2002 Equation 5-15
D_A	Apparent Diffusivity (cm^2/s)	Contaminant-specific	U.S. EPA 2002 Equation 5-14
T	Total time over which construction occurs (s)	Site-Specific	U.S. EPA 2002 Equation 5-14
ρ_b	Dry soil bulk density (g/cm^3)	1.5	U.S. EPA 2002 Equation 5-14
F_D	Dispersion correction factor (unitless)	0.185	U.S. EPA 2002 Equation 5-14
θ_a	Air-filled soil porosity (L_{air}/L_{soil}) ($n-\theta_w$)	0.28	U.S. EPA 2002 Equation 5-14
n	Total soil porosity (L_{pore}/L_{soil}) ($1-(\rho_b/\rho_s)$)	0.43	U.S. EPA 2002 Equation 5-14
θ_w	Water-filled soil porosity (L_{water}/L_{soil})	0.15	U.S. EPA 2002 Equation 5-14
ρ_s	Soil particle density (g/cm^3)	2.65	U.S. EPA 2002 Equation 5-14
D_{ia}	Diffusivity in air (cm^2/s)	Contaminant-specific	U.S. EPA 2001
H'	Dimensionless Henry's Law Constant	Contaminant-specific	See Chemical-specific hierarch
D_{iw}	Diffusivity in water (cm^2/s)	Contaminant-specific	U.S. EPA 2001
K_d	Soil-water partition coefficient (L/kg) (Koc×foc)	= $K_{oc} \times f_{oc}$ for organics	See Chemical-specific hierarchy
K_{oc}	Soil organic carbon-water partition coefficient (L/kg)	Contaminant-specific	See Chemical-specific hierarchy
f_{oc}	Organic carbon content of soil (g/g)	0.006 (0.6%)	U.S. EPA 2002 Equation 5-14
T	Total time over which construction occurs (year)	Site-Specific (T=ED)	U.S. EPA 2002 Equation 5-17
d_s	Average source depth (m)	Site-Specific	U.S. EPA 2002 Equation 5-17

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TOXICOLOGICAL PROFILE FOR ARSENIC

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Agency for Toxic Substances and Disease Registry

August 2007

REC 5446

TR 2131

DISCLAIMER

The use of company or product name(s) is for identification only and does not imply endorsement by the Agency for Toxic Substances and Disease Registry.

UPDATE STATEMENT

A Toxicological Profile for Arsenic, Draft for Public Comment was released in September 2005. This edition supersedes any previously released draft or final profile.

Toxicological profiles are revised and republished as necessary. For information regarding the update status of previously released profiles, contact ATSDR at:

Agency for Toxic Substances and Disease Registry
Division of Toxicology and Environmental Medicine/Applied Toxicology Branch
1600 Clifton Road NE
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Atlanta, Georgia 30333

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FOREWORD

This toxicological profile is prepared in accordance with guidelines developed by the Agency for Toxic Substances and Disease Registry (ATSDR) and the Environmental Protection Agency (EPA). The original guidelines were published in the *Federal Register* on April 17, 1987. Each profile will be revised and republished as necessary.

The ATSDR toxicological profile succinctly characterizes the toxicologic and adverse health effects information for the hazardous substance described therein. Each peer-reviewed profile identifies and reviews the key literature that describes a hazardous substance's toxicologic properties. Other pertinent literature is also presented, but is described in less detail than the key studies. The profile is not intended to be an exhaustive document; however, more comprehensive sources of specialty information are referenced.

The focus of the profiles is on health and toxicologic information; therefore, each toxicological profile begins with a public health statement that describes, in nontechnical language, a substance's relevant toxicological properties. Following the public health statement is information concerning levels of significant human exposure and, where known, significant health effects. The adequacy of information to determine a substance's health effects is described in a health effects summary. Data needs that are of significance to protection of public health are identified by ATSDR and EPA.

Each profile includes the following:

(A) The examination, summary, and interpretation of available toxicologic information and epidemiologic evaluations on a hazardous substance to ascertain the levels of significant human exposure for the substance and the associated acute, subacute, and chronic health effects;

(B) A determination of whether adequate information on the health effects of each substance is available or in the process of development to determine levels of exposure that present a significant risk to human health of acute, subacute, and chronic health effects; and

(C) Where appropriate, identification of toxicologic testing needed to identify the types or levels of exposure that may present significant risk of adverse health effects in humans.

The principal audiences for the toxicological profiles are health professionals at the Federal, State, and local levels; interested private sector organizations and groups; and members of the public.

This profile reflects ATSDR's assessment of all relevant toxicologic testing and information that has been peer-reviewed. Staff of the Centers for Disease Control and Prevention and other Federal scientists have also reviewed the profile. In addition, this profile has been peer-reviewed by a nongovernmental panel and is being made available for public review. Final responsibility for the contents and views expressed in this toxicological profile resides with ATSDR.



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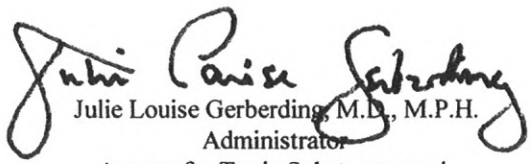

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The toxicological profiles are developed in response to the Superfund Amendments and Reauthorization Act (SARA) of 1986 (Public Law 99-499) which amended the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA or Superfund). This public law directed ATSDR to prepare toxicological profiles for hazardous substances most commonly found at facilities on the CERCLA National Priorities List and that pose the most significant potential threat to human health, as determined by ATSDR and the EPA. The availability of the revised priority list of 275 hazardous substances was announced in the *Federal Register* on December 7, 2005 (70 FR 72840). For prior versions of the list of substances, see *Federal Register* notices dated April 17, 1987 (52 FR 12866); October 20, 1988 (53 FR 41280); October 26, 1989 (54 FR 43619); October 17, 1990 (55 FR 42067); October 17, 1991 (56 FR 52166); October 28, 1992 (57 FR 48801); February 28, 1994 (59 FR 9486); April 29, 1996 (61 FR 18744); November 17, 1997 (62 FR 61332); October 21, 1999 (64 FR 56792); October 25, 2001 (66 FR 54014); and November 7, 2003 (68 FR 63098). Section 104(i)(3) of CERCLA, as amended, directs the Administrator of ATSDR to prepare a toxicological profile for each substance on the list.

QUICK REFERENCE FOR HEALTH CARE PROVIDERS

Toxicological Profiles are a unique compilation of toxicological information on a given hazardous substance. Each profile reflects a comprehensive and extensive evaluation, summary, and interpretation of available toxicologic and epidemiologic information on a substance. Health care providers treating patients potentially exposed to hazardous substances will find the following information helpful for fast answers to often-asked questions.

Primary Chapters/Sections of Interest

Chapter 1: Public Health Statement: The Public Health Statement can be a useful tool for educating patients about possible exposure to a hazardous substance. It explains a substance's relevant toxicologic properties in a nontechnical, question-and-answer format, and it includes a review of the general health effects observed following exposure.

Chapter 2: Relevance to Public Health: The Relevance to Public Health Section evaluates, interprets, and assesses the significance of toxicity data to human health.

Chapter 3: Health Effects: Specific health effects of a given hazardous compound are reported by type of health effect (death, systemic, immunologic, reproductive), by route of exposure, and by length of exposure (acute, intermediate, and chronic). In addition, both human and animal studies are reported in this section.
NOTE: Not all health effects reported in this section are necessarily observed in the clinical setting. Please refer to the Public Health Statement to identify general health effects observed following exposure.

Pediatrics: Four new sections have been added to each Toxicological Profile to address child health issues:

Section 1.6	**How Can (Chemical X) Affect Children?**
Section 1.7	**How Can Families Reduce the Risk of Exposure to (Chemical X)?**
Section 3.7	**Children's Susceptibility**
Section 6.6	**Exposures of Children**

Other Sections of Interest:

Section 3.8	**Biomarkers of Exposure and Effect**
Section 3.11	**Methods for Reducing Toxic Effects**

ATSDR Information Center

Phone: 1-800-CDC-INFO (800-232-4636) or 1-888-232-6348 (TTY) ***Fax:*** (770) 488-4178
E-mail: cdcinfo@cdc.gov ***Internet***: http://www.atsdr.cdc.gov

The following additional material can be ordered through the ATSDR Information Center:

Case Studies in Environmental Medicine: Taking an Exposure History—The importance of taking an exposure history and how to conduct one are described, and an example of a thorough exposure history is provided. Other case studies of interest include *Reproductive and Developmental*

Hazards; Skin Lesions and Environmental Exposures; Cholinesterase-Inhibiting Pesticide Toxicity; and numerous chemical-specific case studies.

Managing Hazardous Materials Incidents is a three-volume set of recommendations for on-scene (prehospital) and hospital medical management of patients exposed during a hazardous materials incident. Volumes I and II are planning guides to assist first responders and hospital emergency department personnel in planning for incidents that involve hazardous materials. Volume III—*Medical Management Guidelines for Acute Chemical Exposures*—is a guide for health care professionals treating patients exposed to hazardous materials.

Fact Sheets (ToxFAQs) provide answers to frequently asked questions about toxic substances.

Other Agencies and Organizations

The National Center for Environmental Health (NCEH) focuses on preventing or controlling disease, injury, and disability related to the interactions between people and their environment outside the workplace. Contact: NCEH, Mailstop F-29, 4770 Buford Highway, NE, Atlanta, GA 30341-3724 • Phone: 770-488-7000 • FAX: 770-488-7015.

The National Institute for Occupational Safety and Health (NIOSH) conducts research on occupational diseases and injuries, responds to requests for assistance by investigating problems of health and safety in the workplace, recommends standards to the Occupational Safety and Health Administration (OSHA) and the Mine Safety and Health Administration (MSHA), and trains professionals in occupational safety and health. Contact: NIOSH, 200 Independence Avenue, SW, Washington, DC 20201 • Phone: 800-356-4674 or NIOSH Technical Information Branch, Robert A. Taft Laboratory, Mailstop C-19, 4676 Columbia Parkway, Cincinnati, OH 45226-1998 • Phone: 800-35-NIOSH.

The National Institute of Environmental Health Sciences (NIEHS) is the principal federal agency for biomedical research on the effects of chemical, physical, and biologic environmental agents on human health and well-being. Contact: NIEHS, PO Box 12233, 104 T.W. Alexander Drive, Research Triangle Park, NC 27709 • Phone: 919-541-3212.

Referrals

The Association of Occupational and Environmental Clinics (AOEC) has developed a network of clinics in the United States to provide expertise in occupational and environmental issues. Contact: AOEC, 1010 Vermont Avenue, NW, #513, Washington, DC 20005 • Phone: 202-347-4976 • FAX: 202-347-4950 • e-mail: AOEC@AOEC.ORG • Web Page: http://www.aoec.org/.

The American College of Occupational and Environmental Medicine (ACOEM) is an association of physicians and other health care providers specializing in the field of occupational and environmental medicine. Contact: ACOEM, 25 Northwest Point Boulevard, Suite 700, Elk Grove Village, IL 60007-1030 • Phone: 847-818-1800 • FAX: 847-818-9266.

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THE PROFILE HAS UNDERGONE THE FOLLOWING ATSDR INTERNAL REVIEWS:

1. Health Effects Review. The Health Effects Review Committee examines the health effects chapter of each profile for consistency and accuracy in interpreting health effects and classifying end points.

2. Minimal Risk Level Review. The Minimal Risk Level Workgroup considers issues relevant to substance-specific Minimal Risk Levels (MRLs), reviews the health effects database of each profile, and makes recommendations for derivation of MRLs.

3. Data Needs Review. The Applied Toxicology Branch reviews data needs sections to assure consistency across profiles and adherence to instructions in the Guidance.

4. Green Border Review. Green Border review assures the consistency with ATSDR policy.

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PEER REVIEW

A peer review panel was assembled for arsenic. The panel consisted of the following members:

1. Toby Rossman, Ph.D., Professor of Environmental Medicine, New York University School of Medicine, Nelson Institute of Environmental Medicine, Tuxedo, New York;

2. Rosalind Schoof, Ph.D., DABT, Integral Consulting, Inc., Mercer Island, Washington; and

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1. Alan Hall, M.D., Toxicology Consulting and Medical Translating Services, Inc. (TCMTS, Inc.), Elk Mountain, Wyoming;

2. Gary Pascoe, Ph.D., Pascoe Environmental Consulting, Port Townsend, Washington; and

3. Toby Rossman, Ph.D., Professor of Environmental Medicine, New York University School of Medicine, Nelson Institute of Environmental Medicine, Tuxedo, New York.

These experts collectively have knowledge of arsenic's physical and chemical properties, toxicokinetics, key health end points, mechanisms of action, human and animal exposure, and quantification of risk to humans. All reviewers were selected in conformity with the conditions for peer review specified in Section 104(I)(13) of the Comprehensive Environmental Response, Compensation, and Liability Act, as amended.

Scientists from the Agency for Toxic Substances and Disease Registry (ATSDR) have reviewed the peer reviewers' comments and determined which comments will be included in the profile. A listing of the peer reviewers' comments not incorporated in the profile, with a brief explanation of the rationale for their exclusion, exists as part of the administrative record for this compound.

The citation of the peer review panel should not be understood to imply its approval of the profile's final content. The responsibility for the content of this profile lies with the ATSDR.

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1. PUBLIC HEALTH STATEMENT

This public health statement tells you about arsenic and the effects of exposure to it.

The Environmental Protection Agency (EPA) identifies the most serious hazardous waste sites in the nation. These sites are then placed on the National Priorities List (NPL) and are targeted for long-term federal clean-up activities. Arsenic has been found in at least 1,149 of the 1,684 current or former NPL sites. Although the total number of NPL sites evaluated for this substance is not known, the possibility exists that the number of sites at which arsenic is found may increase in the future as more sites are evaluated. This information is important because these sites may be sources of exposure and exposure to this substance may harm you.

When a substance is released either from a large area, such as an industrial plant, or from a container, such as a drum or bottle, it enters the environment. Such a release does not always lead to exposure. You can be exposed to a substance only when you come in contact with it. You may be exposed by breathing, eating, or drinking the substance, or by skin contact.

If you are exposed to arsenic, many factors will determine whether you will be harmed. These factors include the dose (how much), the duration (how long), and how you come in contact with it. You must also consider any other chemicals you are exposed to and your age, sex, diet, family traits, lifestyle, and state of health.

1.1 WHAT IS ARSENIC?

Arsenic is a naturally occurring element that is widely distributed in the Earth's crust. Arsenic is classified chemically as a metalloid, having both properties of a metal and a nonmetal; however, it is frequently referred to as a metal. Elemental arsenic (sometimes referred to as metallic arsenic) is a steel grey solid material. However, arsenic is usually found in the environment combined with other elements such as oxygen, chlorine, and sulfur. Arsenic combined with

these elements is called inorganic arsenic. Arsenic combined with carbon and hydrogen is referred to as organic arsenic.

Most inorganic and organic arsenic compounds are white or colorless powders that do not evaporate. They have no smell, and most have no special taste. Thus, you usually cannot tell if arsenic is present in your food, water, or air.

Inorganic arsenic occurs naturally in soil and in many kinds of rock, especially in minerals and ores that contain copper or lead. When these ores are heated in smelters, most of the arsenic goes up the stack and enters the air as a fine dust. Smelters may collect this dust and take out the arsenic as a compound called arsenic trioxide (As_2O_3). However, arsenic is no longer produced in the United States; all of the arsenic used in the United States is imported.

Presently, about 90% of all arsenic produced is used as a preservative for wood to make it resistant to rotting and decay. The preservative is copper chromated arsenate (CCA) and the treated wood is referred to as "pressure-treated." In 2003, U.S. manufacturers of wood preservatives containing arsenic began a voluntary transition from CCA to other wood preservatives that do not contain arsenic in wood products for certain residential uses, such as play structures, picnic tables, decks, fencing, and boardwalks. This phase out was completed on December 31, 2003; however, wood treated prior to this date could still be used and existing structures made with CCA-treated wood would not be affected. CCA-treated wood products continue to be used in industrial applications. It is not known whether, or to what extent, CCA-treated wood products may contribute to exposure of people to arsenic.

In the past, inorganic arsenic compounds were predominantly used as pesticides, primarily on cotton fields and in orchards. Inorganic arsenic compounds can no longer be used in agriculture. However, organic arsenic compounds, namely cacodylic acid, disodium methylarsenate (DSMA), and monosodium methylarsenate (MSMA), are still used as pesticides, principally on cotton. Some organic arsenic compounds are used as additives in animal feed. Small quantities of elemental arsenic are added to other metals to form metal mixtures or alloys with improved

properties. The greatest use of arsenic in alloys is in lead-acid batteries for automobiles. Another important use of arsenic compounds is in semiconductors and light-emitting diodes.

To learn more about the properties and uses of arsenic, see Chapters 4 and 5.

1.2 WHAT HAPPENS TO ARSENIC WHEN IT ENTERS THE ENVIRONMENT?

Arsenic occurs naturally in soil and minerals and it therefore may enter the air, water, and land from wind-blown dust and may get into water from runoff and leaching. Volcanic eruptions are another source of arsenic. Arsenic is associated with ores containing metals, such as copper and lead. Arsenic may enter the environment during the mining and smelting of these ores. Small amounts of arsenic also may be released into the atmosphere from coal-fired power plants and incinerators because coal and waste products often contain some arsenic.

Arsenic cannot be destroyed in the environment. It can only change its form, or become attached to or separated from particles. It may change its form by reacting with oxygen or other molecules present in air, water, or soil, or by the action of bacteria that live in soil or sediment. Arsenic released from power plants and other combustion processes is usually attached to very small particles. Arsenic contained in wind-borne soil is generally found in larger particles. These particles settle to the ground or are washed out of the air by rain. Arsenic that is attached to very small particles may stay in the air for many days and travel long distances. Many common arsenic compounds can dissolve in water. Thus, arsenic can get into lakes, rivers, or underground water by dissolving in rain or snow or through the discharge of industrial wastes. Some of the arsenic will stick to particles in the water or sediment on the bottom of lakes or rivers, and some will be carried along by the water. Ultimately, most arsenic ends up in the soil or sediment. Although some fish and shellfish take in arsenic, which may build up in tissues, most of this arsenic is in an organic form called arsenobetaine (commonly called "fish arsenic") that is much less harmful.

For more information on how arsenic behaves in the environment, see Chapter 6.

1.3 HOW MIGHT I BE EXPOSED TO ARSENIC?

Since arsenic is found naturally in the environment, you will be exposed to some arsenic by eating food, drinking water, or breathing air. Children may also be exposed to arsenic by eating soil. Analytical methods used by scientists to determine the levels of arsenic in the environment generally do not determine the specific form of arsenic present. Therefore, we do not always know the form of arsenic a person may be exposed to. Similarly, we often do not know what forms of arsenic are present at hazardous waste sites. Some forms of arsenic may be so tightly attached to particles or embedded in minerals that they are not taken up by plants and animals.

The concentration of arsenic in soil varies widely, generally ranging from about 1 to 40 parts of arsenic to a million parts of soil (ppm) with an average level of 3–4 ppm. However, soils in the vicinity of arsenic-rich geological deposits, some mining and smelting sites, or agricultural areas where arsenic pesticides had been applied in the past may contain much higher levels of arsenic. The concentration of arsenic in natural surface and groundwater is generally about 1 part in a billion parts of water (1 ppb), but may exceed 1,000 ppb in contaminated areas or where arsenic levels in soil are high. Groundwater is far more likely to contain high levels of arsenic than surface water. Surveys of U.S. drinking water indicate that about 80% of water supplies have less than 2 ppb of arsenic, but 2% of supplies exceed 20 ppb of arsenic. Levels of arsenic in food range from about 20 to 140 ppb. However, levels of inorganic arsenic, the form of most concern, are far lower. Levels of arsenic in the air generally range from less than 1 to about 2,000 nanograms (1 nanogram equals a billionth of a gram) of arsenic per cubic meter of air (less than 1–2,000 ng/m^3), depending on location, weather conditions, and the level of industrial activity in the area. However, urban areas generally have mean arsenic levels in air ranging from 20 to 30 ng/m^3.

You normally take in small amounts of arsenic in the air you breathe, the water you drink, and the food you eat. Of these, food is usually the largest source of arsenic. The predominant dietary source of arsenic is seafood, followed by rice/rice cereal, mushrooms, and poultry. While seafood contains the greatest amounts of arsenic, for fish and shellfish, this is mostly in an organic form of arsenic called arsenobetaine that is much less harmful. Some seaweeds may

contain arsenic in inorganic forms that may be more harmful. Children are likely to eat small amounts of dust or soil each day, so this is another way they may be exposed to arsenic. The total amount of arsenic you take in from these sources is generally about 50 micrograms (1 microgram equals one-millionth of a gram) each day. The level of inorganic arsenic (the form of most concern) you take in from these sources is generally about 3.5 microgram/day. Children may be exposed to small amounts of arsenic from hand-to-mouth activities from playing on play structures or decks constructed out of CCA-treated wood. The potential exposure that children may receive from playing in play structures constructed from CCA-treated wood is generally smaller than that they would receive from food and water. Hand washing can reduce the potential exposure of children to arsenic after playing on play structures constructed with CCA-treated wood, since most of the arsenic on the children's hands was removed with water.

In addition to the normal levels of arsenic in air, water, soil, and food, you could be exposed to higher levels in several ways, such as the following:

- Some areas of the United States contain unusually high natural levels of arsenic in rock, and this can lead to unusually high levels of arsenic in soil or water. If you live in an area like this, you could take in elevated amounts of arsenic in drinking water. Children may be taking in higher amounts of arsenic because of hand-to-mouth contact or eating soil in areas with higher than usual arsenic concentrations.

- Some hazardous waste sites contain large quantities of arsenic. If the material is not properly disposed of, it can get into surrounding water, air, or soil. If you live near such a site, you could be exposed to elevated levels of arsenic from these media.

- If you work in an occupation that involves arsenic production or use (for example, copper or lead smelting, wood treating, or pesticide application), you could be exposed to elevated levels of arsenic during your work.

- If you saw or sand arsenic-treated wood, you could inhale some of the sawdust into your nose or throat. Similarly, if you burn arsenic-treated wood, you could inhale arsenic in the smoke.

- If you live in a former agricultural area where arsenic was used on crops, the soil could contain high levels of arsenic.

- In the past, several kinds of products used in the home (rat poison, ant poison, weed killer, some types of medicines) had arsenic in them. However, most of these uses of arsenic have ended, so you are not likely to be exposed from home products any longer.

You can find more information on how you may be exposed to arsenic in Chapter 6.

1.4 HOW CAN ARSENIC ENTER AND LEAVE MY BODY?

If you swallow arsenic in water, soil, or food, most of the arsenic may quickly enter into your body. The amount that enters your body will depend on how much you swallow and the kind of arsenic that you swallow. This is the most likely way for you to be exposed near a waste site. If you breathe air that contains arsenic dusts, many of the dust particles settle onto the lining of the lungs. Most of the arsenic in these particles is then taken up from the lungs into the body. You might be exposed in this way near waste sites where arsenic-contaminated soils are allowed to blow into the air, or if you work with arsenic-containing soil or products. If you get arsenic-contaminated soil or water on your skin, only a small amount will go through your skin into your body, so this is usually not of concern.

Both inorganic and organic forms leave your body in your urine. Most of the inorganic arsenic will be gone within several days, although some will remain in your body for several months or even longer. If you are exposed to organic arsenic, most of it will leave your body within several days.

You can find more information on how arsenic enters and leaves your body in Chapter 3.

1.5 HOW CAN ARSENIC AFFECT MY HEALTH?

Scientists use many tests to protect the public from harmful effects of toxic chemicals and to find ways for treating persons who have been harmed.

One way to learn whether a chemical will harm people is to determine how the body absorbs, uses, and releases the chemical. For some chemicals, animal testing may be necessary. Animal testing may also help identify health effects such as cancer or birth defects. Without laboratory animals, scientists would lose a basic method for getting information needed to make wise decisions that protect public health. Scientists have the responsibility to treat research animals with care and compassion. Scientists must comply with strict animal care guidelines because laws today protect the welfare of research animals.

Inorganic arsenic has been recognized as a human poison since ancient times, and large oral doses (above 60,000 ppb in water which is 10,000 times higher than 80% of U.S. drinking water arsenic levels) can result in death. If you swallow lower levels of inorganic arsenic (ranging from about 300 to 30,000 ppb in water; 100–10,000 times higher than most U.S. drinking water levels), you may experience irritation of your stomach and intestines, with symptoms such as stomachache, nausea, vomiting, and diarrhea. Other effects you might experience from swallowing inorganic arsenic include decreased production of red and white blood cells, which may cause fatigue, abnormal heart rhythm, blood-vessel damage resulting in bruising, and impaired nerve function causing a "pins and needles" sensation in your hands and feet.

Perhaps the single-most characteristic effect of long-term oral exposure to inorganic arsenic is a pattern of skin changes. These include patches of darkened skin and the appearance of small "corns" or "warts" on the palms, soles, and torso, and are often associated with changes in the blood vessels of the skin. Skin cancer may also develop. Swallowing arsenic has also been reported to increase the risk of cancer in the liver, bladder, and lungs. The Department of Health and Human Services (DHHS) has determined that inorganic arsenic is known to be a human carcinogen (a chemical that causes cancer). The International Agency for Research on Cancer (IARC) has determined that inorganic arsenic is carcinogenic to humans. EPA also has classified inorganic arsenic as a known human carcinogen.

If you breathe high levels of inorganic arsenic, then you are likely to experience a sore throat and irritated lungs. You may also develop some of the skin effects mentioned above. The exposure level that produces these effects is uncertain, but it is probably above 100 micrograms of arsenic

per cubic meter ($\mu g/m^3$) for a brief exposure. Longer exposure at lower concentrations can lead to skin effects, and also to circulatory and peripheral nervous disorders. There are some data suggesting that inhalation of inorganic arsenic may also interfere with normal fetal development, although this is not certain. An important concern is the ability of inhaled inorganic arsenic to increase the risk of lung cancer. This has been seen mostly in workers exposed to arsenic at smelters, mines, and chemical factories, but also in residents living near smelters and arsenical chemical factories. People who live near waste sites with arsenic may have an increased risk of lung cancer as well.

If you have direct skin contact with high concentrations of inorganic arsenic compounds, your skin may become irritated, with some redness and swelling. However, it does not appear that skin contact is likely to lead to any serious internal effects.

Almost no information is available on the effects of organic arsenic compounds in humans. Studies in animals show that most simple organic arsenic compounds (such as methyl and dimethyl compounds) are less toxic than the inorganic forms. In animals, ingestion of methyl compounds can result in diarrhea, and lifetime exposure can damage the kidneys. Lifetime exposure to dimethyl compounds can damage the urinary bladder and the kidneys.

You can find more information on the health effects of inorganic and organic arsenic in Chapters 2 and 3.

1.6 HOW CAN ARSENIC AFFECT CHILDREN?

This section discusses potential health effects in humans from exposures during the period from conception to maturity at 18 years of age.

Children are exposed to arsenic in many of the same ways that adults are. Since arsenic is found in the soil, water, food, and air, children may take in arsenic in the air they breathe, the water they drink, and the food they eat. Since children tend to eat or drink less of a variety of foods and beverages than do adults, ingestion of contaminated food or juice or infant formula made

with arsenic-contaminated water may represent a significant source of exposure. In addition, since children often play in the soil and put their hands in their mouths and sometimes intentionally eat soil, ingestion of contaminated soil may be a more important source of arsenic exposure for children than for adults. In areas of the United States where natural levels of arsenic in the soil and water are high, or in areas in and around contaminated waste sites, exposure of children to arsenic through ingestion of soil and water may be significant. In addition, contact with adults who are wearing clothes contaminated with arsenic (e.g., with dust from copper- or lead-smelting factories, from wood-treating or pesticide application, or from arsenic-treated wood) could be a source of exposure. Because of the tendency of children to taste things that they find, accidental poisoning from ingestion of pesticides is also a possibility. Thus, although most of the exposure pathways for children are the same as those for adults, children may be at a higher risk of exposure because of normal hand-to-mouth activity.

Children who are exposed to inorganic arsenic may have many of the same effects as adults, including irritation of the stomach and intestines, blood vessel damage, skin changes, and reduced nerve function. Thus, all health effects observed in adults are of potential concern in children. There is also some evidence that suggests that long-term exposure to inorganic arsenic in children may result in lower IQ scores. We do not know if absorption of inorganic arsenic from the gut in children differs from adults. There is some evidence that exposure to arsenic in early life (including gestation and early childhood) may increase mortality in young adults.

There is some evidence that inhaled or ingested inorganic arsenic can injure pregnant women or their unborn babies, although the studies are not definitive. Studies in animals show that large doses of inorganic arsenic that cause illness in pregnant females can also cause low birth weight, fetal malformations, and even fetal death. Arsenic can cross the placenta and has been found in fetal tissues. Arsenic is found at low levels in breast milk.

In animals, exposure to organic arsenic compounds can cause low birth weight, fetal malformations, and fetal deaths. The dose levels that cause these effects also result in effects in the mothers.

You can find more information about how arsenic can affect children in Sections 3.7 and 6.6.

1.7 HOW CAN FAMILIES REDUCE THE RISK OF EXPOSURE TO ARSENIC?

If your doctor finds that you have been exposed to substantial amounts of arsenic, ask whether your children might also have been exposed. Your doctor might need to ask your state health department to investigate.

Many communities may have high levels of arsenic in their drinking water, particularly from private wells, because of contamination or as a result of the geology of the area. The north central region and the western region of the United States have the highest arsenic levels in surface water and groundwater sources, respectively. Wells used to provide water for drinking and cooking should be tested for arsenic. As of January 2006, EPA's Maximum Contaminant Level (MCL) for arsenic in drinking water is 10 ppb. If you have arsenic in your drinking water at levels higher that the EPA's MCL, an alternative source of water should be used for drinking and cooking should be considered.

If you use arsenic-treated wood in home projects, personal protection from exposure to arsenic-containing sawdust may be helpful in limiting exposure of family members. These measures may include dust masks, gloves, and protective clothing. Arsenic-treated wood should never be burned in open fires, or in stoves, residential boilers, or fire places, and should not be composted or used as mulch. EPA's Consumer Awareness Program (CAP) for CCA is a voluntary program established by the manufacturers of CCA products to inform consumers about the proper handling, use, and disposal of CCA-treated wood. You can find more information about this program in Section 6.5. Hand washing can reduce the potential exposure of children to arsenic after playing on play structures constructed with CCA-treated wood, since most of the arsenic on the children's hands was removed with water.

If you live in an area with a high level of arsenic in the water or soil, substituting cleaner sources of water and limiting contact with soil (for example, through use of a dense groundcover or thick lawn) would reduce family exposure to arsenic. By paying careful attention to dust and soil

control in the home (air filters, frequent cleaning), you can reduce family exposure to contaminated soil. Some children eat a lot of soil. You should prevent your children from eating soil. You should discourage your children from putting objects in their mouths. Make sure they wash their hands frequently and before eating. Discourage your children from putting their hands in their mouths or engaging in other hand-to-mouth activities. Since arsenic may be found in the home as a pesticide, household chemicals containing arsenic should be stored out of reach of young children to prevent accidental poisonings. Always store household chemicals in their original labeled containers; never store household chemicals in containers that children would find attractive to eat or drink from, such as old soda bottles. Keep your Poison Control Center's number by the phone.

It is sometimes possible to carry arsenic from work on your clothing, skin, hair, tools, or other objects removed from the workplace. This is particularly likely if you work in the fertilizer, pesticide, glass, or copper/lead smelting industries. You may contaminate your car, home, or other locations outside work where children might be exposed to arsenic. You should know about this possibility if you work with arsenic.

Your occupational health and safety officer at work can and should tell you whether chemicals you work with are dangerous and likely to be carried home on your clothes, body, or tools and whether you should be showering and changing clothes before you leave work, storing your street clothes in a separate area of the workplace, or laundering your work clothes at home separately from other clothes. Material safety data sheets (MSDS) for many chemicals used should be found at your place of work, as required by the Occupational Safety and Health Administration (OSHA) in the U.S. Department of Labor. MSDS information should include chemical names and hazardous ingredients, and important properties, such as fire and explosion data, potential health effects, how you get the chemical(s) in your body, how to properly handle the materials, and what to do in the case of emergencies. Your employer is legally responsible for providing a safe workplace and should freely answer your questions about hazardous chemicals. Your state OSHA-approved occupational safety and health program or OSHA can answer any further questions and help your employer identify and correct problems with hazardous substances. Your state OSHA-approved occupational safety and health program or

OSHA will listen to your formal complaints about workplace health hazards and inspect your workplace when necessary. Employees have a right to seek safety and health on the job without fear of punishment.

You can find more information about how arsenic can affect children in Sections 3.7 and 6.6.

1.8 IS THERE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO ARSENIC?

Several sensitive and specific tests can measure arsenic in your blood, urine, hair, or fingernails, and these tests are often helpful in determining if you have been exposed to above-average levels of arsenic in the past. These tests are not usually performed in a doctor's office. They require sending the sample to a testing laboratory.

Measurement of arsenic in your urine is the most reliable means of detecting arsenic exposures that you experienced within the last several days. Most tests measure the total amount of arsenic present in your urine. This can sometimes be misleading, because the nonharmful forms of arsenic in fish and shellfish can give a high reading even if you have not been exposed to a toxic form of arsenic. For this reason, laboratories sometimes use a more complicated test to separate "fish arsenic" from other forms. Because most arsenic leaves your body within a few days, analysis of your urine cannot detect if you were exposed to arsenic in the past. Tests of your hair or fingernails can tell if you were exposed to high levels over the past 6–12 months, but these tests are not very useful in detecting low-level exposures. If high levels of arsenic are detected, this shows that you have been exposed, but unless more is known about when you were exposed and for how long, it is usually not possible to predict whether you will have any harmful health effects.

You can find more information on how arsenic can be measured in your hair, urine, nails, and other tissues in Chapters 3 and 7.

1.9 WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH?

The federal government develops regulations and recommendations to protect public health. Regulations *can* be enforced by law. The EPA, the Occupational Safety and Health Administration (OSHA), and the Food and Drug Administration (FDA) are some federal agencies that develop regulations for toxic substances. Recommendations provide valuable guidelines to protect public health, but *cannot* be enforced by law. The Agency for Toxic Substances and Disease Registry (ATSDR) and the National Institute for Occupational Safety and Health (NIOSH) are two federal organizations that develop recommendations for toxic substances.

Regulations and recommendations can be expressed as "not-to-exceed" levels, that is, levels of a toxic substance in air, water, soil, or food that do not exceed a critical value that is usually based on levels that affect animals; they are then adjusted to levels that will help protect humans. Sometimes these not-to-exceed levels differ among federal organizations because they used different exposure times (an 8-hour workday or a 24-hour day), different animal studies, or other factors.

Recommendations and regulations are also updated periodically as more information becomes available. For the most current information, check with the federal agency or organization that provides it. Some regulations and recommendations for ARSENIC include the following:

The federal government has taken several steps to protect humans from arsenic. First, EPA has set limits on the amount of arsenic that industrial sources can release into the environment. Second, EPA has restricted or canceled many of the uses of arsenic in pesticides and is considering further restrictions. Third, in January 2001, the EPA lowered the limit for arsenic in drinking water from 50 to 10 ppb. Finally, OSHA has established a permissible exposure limit (PEL), 8-hour time-weighted average, of 10 $\mu g/m^3$ for airborne arsenic in various workplaces that use inorganic arsenic.

You can find more information on regulations and guidelines that apply to arsenic in Chapter 8.

1.10 WHERE CAN I GET MORE INFORMATION?

If you have any more questions or concerns, please contact your community or state health or environmental quality department, or contact ATSDR at the address and phone number below.

ATSDR can also tell you the location of occupational and environmental health clinics. These clinics specialize in recognizing, evaluating, and treating illnesses that result from exposure to hazardous substances.

Toxicological profiles are also available on-line at www.atsdr.cdc.gov and on CD-ROM. You may request a copy of the ATSDR ToxProfiles™ CD-ROM by calling the toll-free information and technical assistance number at 1-800-CDCINFO (1-800-232-4636), by e-mail at cdcinfo@cdc.gov, or by writing to:

Agency for Toxic Substances and Disease Registry
Division of Toxicology and Environmental Medicine
1600 Clifton Road NE
Mailstop F-32
Atlanta, GA 30333
Fax: 1-770-488-4178

Organizations for-profit may request copies of final Toxicological Profiles from the following:

National Technical Information Service (NTIS)
5285 Port Royal Road
Springfield, VA 22161
Phone: 1-800-553-6847 or 1-703-605-6000
Web site: http://www.ntis.gov/

2. RELEVANCE TO PUBLIC HEALTH

2.1 BACKGROUND AND ENVIRONMENTAL EXPOSURES TO ARSENIC IN THE UNITED STATES

Arsenic is widely distributed in the Earth's crust, which contains ~3.4 ppm arsenic. In nature, arsenic is mostly found in minerals and only to a small extent in its elemental form. Arsenic is mainly obtained as a byproduct of the smelting of copper, lead, cobalt, and gold ores. Arsenic trioxide is the primary form in which arsenic is marketed and consumed. There has been no domestic production of arsenic since 1985. In 2003, the world's largest producer of arsenic compounds was China, followed by Chile and Peru.

In 2003, the United States was the world's largest consumer of arsenic. Production of wood preservatives, primarily copper chromated arsenate (CCA), $CrO_3 \cdot CuO \cdot As_2O_5$, accounted for >90% of domestic consumption of arsenic trioxide. In response to consumer concerns, U.S. manufacturers of arsenical wood preservative began a voluntary transition from CCA to other wood preservatives for certain residential wood products. This phase-out was completed on December 31, 2003; wood treated prior to this date could still be used and CCA-treated wood products continue to be used in industrial applications.

Other uses for arsenic compounds include the production of agricultural chemicals, as an alloying element in ammunition and solders, as an anti-friction additive to metals used for bearings, and to strengthen lead-acid storage battery grids. High-purity arsenic (99.9999%) is used by the electronics industry for gallium-arsenide semiconductors for telecommunications, solar cells, and space research. Various organic arsenicals are still used in the United States as herbicides and as antimicrobial additives for animal and poultry feed. However, the use of inorganic arsenic compounds in agriculture has virtually disappeared beginning around the 1960s. Arsenic trioxide and arsenic acid were used as a decolorizer and fining agent in the production of bottle glass and other glassware. Arsenic compounds also have a long history of use in medicine, and have shown a re-emergence of late with the recent introduction of arsenic trioxide treatment for acute promyelocytic leukemia.

The principal route of exposure to arsenic for the general population is likely to be the oral route, primarily in the food and in the drinking water. Dietary exposures to total arsenic were highly variable, with a mean of 50.6 µg/day (range of 1.01–1,081 µg/day) for females and 58.5 µg/day (range of 0.21–1,276 µg/day) for males. U.S. dietary intake of inorganic arsenic has been estimated to range from 1 to 20 µg/day, with grains and produce expected to be significant contributors to dietary inorganic arsenic

intake. Drinking water generally contains an average of 2 µg/L of arsenic, although 12% of water supplies from surface water sources in the North Central region of the country and 12% of supplies from groundwater sources in the Western region have levels exceeding 20 µg/L. Arsenic is also widely distributed in surface water, groundwater, and finished drinking water in the United States. Surveys of arsenic concentrations in rivers and lakes indicate that most values are below 10 µg/L, although individual samples may range up to 3,400 µg/L. Arsenic released to the land at hazardous waste sites is likely to be relatively immobile due to a high capacity for soil binding, particularly to iron and manganese oxides. Exposure to arsenic from other pathways is generally small, but may be significant for areas with high levels of arsenic contamination or in occupational settings. For a more complete discussion of possible exposures to arsenic, see Chapter 6 of the profile.

2.2 SUMMARY OF HEALTH EFFECTS

Arsenic is a potent toxicant that may exist in several oxidation states and in a number of inorganic and organic forms. Most cases of arsenic-induced toxicity in humans are due to exposure to inorganic arsenic, and there is an extensive database on the human health effects of the common arsenic oxides and oxyacids. Although there may be some differences in the potency of different chemical forms (e.g., arsenites tend to be somewhat more toxic than arsenates), these differences are usually minor. An exception would be arsine, which is highly toxic. However, because arsine and its methyl derivatives are gases or volatile liquids and are unlikely to be present at levels of concern at hazardous waste sites, health effect data for these compounds are not discussed in this document. Humans may be exposed to organic arsenicals (mainly methyl and phenyl derivatives of arsenic acid) that are used in agriculture and to organic arsenicals found in fish and shellfish (arsenobetaine and arsenocholine). Although the toxicity of organic arsenicals has not been as extensively investigated as inorganic arsenicals, there are sufficient animal data to evaluate the toxicity of methyl arsenates (e.g., monomethylarsonic acid [MMA] and dimethylarsinic acid [DMA]) and roxarsone. The so-called "fish arsenic" compounds (e.g., arsenobetaine) are not thought to be toxic and health effects data are not discussed in this document.

It is generally accepted that the arsenic-carbon bond is quite strong and most mammalian species do not have the capacity to break this bond; thus, inorganic arsenic is not formed during the metabolism of organic arsenicals. In most species, including humans, ingested (or exogenous) MMA(V) and DMA(V) undergo limited metabolism, do not readily enter the cell, and are primarily excreted unchanged in the urine. This is in contrast to inorganic arsenic, which undergoes sequential reduction and methylation reactions leading to the formation of MMA and DMA. Inorganic As(V) is readily reduced to inorganic

As(III), which is taken up by the cell. Within the cell (primarily in the liver), As(III) is methylated to form MMA(V), which is reduced to MMA(III); MMA(III) subsequently undergoes oxidative methylations to form DMA(V). DMA(V) is the primary excretion product in humans. Because inorganic and organic arsenicals exhibit distinct toxicokinetic characteristics, the health effects and MRLs are considered separately.

Inorganic Arsenicals. Exposures of humans near hazardous waste sites could involve inhalation of arsenic dusts in air, ingestion of arsenic in water, food, or soil, or dermal contact with contaminated soil or water. Increased risk of lung cancer, respiratory irritation, nausea, skin effects, and neurological effects have been reported following inhalation exposure. There are only a few quantitative data on noncancer effects in humans exposed to inorganic arsenic by the inhalation route. Animal data similarly identify effects on the respiratory system as the primary noncancer effect of inhaled inorganic arsenic compounds, although only a few studies are available. Only limited data on the effects of inhaled organic arsenic compounds in humans or animals are available; these studies are generally limited to high-dose, short-term exposures, which result in frank effects.

Relatively little information is available on effects due to direct dermal contact with inorganic arsenicals, but several studies indicate that the chief effect is local irritation and dermatitis, with little risk of other adverse effects.

The database for the oral toxicity of inorganic arsenic is extensive, containing a large number of studies of orally-exposed human populations. These studies have identified effects on virtually every organ or tissue evaluated, although some end points appear to be more sensitive than others. The available data from humans identify the skin as the most sensitive noncancer target following long-term oral arsenic exposure. Typical dermal effects include hyperkeratinization of the skin (especially on the palms and soles), formation of multiple hyperkeratinized corns or warts, and hyperpigmentation of the skin with interspersed spots of hypopigmentation. Oral exposure data from studies in humans indicate that these lesions typically begin to manifest at exposure levels of about 0.002–0.02 mg As/kg/day, but one study suggests that lesions may appear at even lower levels. At these exposure levels, peripheral vascular effects are also commonly noted, including cyanosis, gangrene, and, in Taiwanese populations, the condition known as "Blackfoot Disease." Other reported cardiovascular effects of oral exposure to inorganic arsenic include increased incidences of high blood pressure and circulatory problems. The use of intravenous arsenic trioxide as therapy for acute promyelocytic leukemia has raised further concerns about the cardiovascular effects of arsenic, including alterations in cardiac QT interval and the

development of torsades de pointes. Decrements in lung function, assessed by spirometry, have been reported in subjects exposed to approximately 0.008–0.04 mg As/kg/day in the drinking water who exhibited skin lesions.

In addition to dermal, cardiovascular, and respiratory effects, oral exposure to inorganic arsenic may result in effects on other organ systems. Nausea, vomiting, and diarrhea are very common symptoms in humans following oral exposure to inorganic arsenicals, both after acute high-dose exposure and after repeated exposure to lower doses; these effects are likely due to a direct irritation of the gastrointestinal mucosa. Acute, high-dose exposure can lead to encephalopathy, with clinical signs such as confusion, hallucinations, impaired memory, and emotional lability, while long-term exposure to lower levels can lead to the development of peripheral neuropathy characterized by a numbness in the hands and feet that may progress to a painful "pins and needles" sensation. Recent studies also have reported neurobehavioral alterations in arsenic-exposed children.

Chronic exposure of humans to inorganic arsenic in the drinking water has been associated with excess incidence of miscarriages, stillbirths, preterm births, and infants with low birth weights. Animal data suggest that arsenic may cause changes to reproductive organs of both sexes, including decreased organ weight and increased inflammation of reproductive tissues, although these changes may be secondary effects. However, these changes do not result in a significant impact on reproductive ability. Animal studies of oral inorganic arsenic exposure have reported developmental effects, but generally only at concentrations that also resulted in maternal toxicity.

Arsenic is a known human carcinogen by both the inhalation and oral exposure routes. By the inhalation route, the primary tumor types are respiratory system cancers, although a few reports have noted increased incidence of tumors at other sites, including the liver, skin, and digestive tract. In humans exposed chronically by the oral route, skin tumors are the most common type of cancer. In addition to skin cancer, there are a number of case reports and epidemiological studies that indicate that ingestion of arsenic also increases the risk of internal tumors (mainly of bladder and lung, and to a lesser extent, liver, kidney, and prostate).

The Department of Health and Human Services (DHHS) has concluded that inorganic arsenic is known to be a human carcinogen. The International Agency for Research on Cancer (IARC) cites sufficient evidence of a relationship between exposure to arsenic and human cancer. The IARC classification of arsenic is Group 1. The EPA has determined that inorganic arsenic is a human carcinogen by the

inhalation and oral routes, and has assigned it the cancer classification, Group A. EPA has calculated an oral cancer slope factor of 1.5 $(mg/kg/day)^{-1}$ and a drinking water unit risk of $5x10^{-5}$ $(\mu g/L)^{-1}$ for inorganic arsenic based on human dose-response data. The inhalation unit risk for cancer is calculated to be 0.0043 $(\mu g/m^3)^{-1}$. The unit risk is the upper-bound excess lifetime cancer risk estimated to result from continuous exposure to an agent at a concentration of 1 µg/L in water or 1 $\mu g/m^3$ in air. EPA is currently revising the assessment for inorganic arsenic; a more detailed discussion of the uncertainties associated with human cancer risk levels for arsenic is presented in Section 3.2.2.7.

The following sections discuss significant effects resulting from exposure to inorganic arsenic in greater detail: dermal, cardiovascular, respiratory, gastrointestinal, neurological, and cancer. Additional information on these effects and on other effects is discussed in Section 3.2.

Dermal Effects. The most characteristic effect of long-term oral exposure to inorganic arsenic compounds is the development of skin lesions; these lesions are often used as diagnostic criteria for arsenicosis. The three lesions most often associated with chronic arsenicosis are hyperkeratinization of the skin (especially on the palms and soles), formation of multiple hyperkeratinized corns or warts, and hyperpigmentation of the skin with interspersed spots of hypopigmentation. Numerous studies of long-term, low-level exposure to inorganic arsenic in humans have reported the presence of these lesions. In general, they begin to manifest at chronic exposure levels >0.02 mg As/kg/day. Chronic oral studies of lower exposure levels, ranging from 0.0004 to 0.01 mg As/kg/day, have generally not reported dermal effects. However, in a study with detailed exposure assessment, all confirmed cases of skin lesions ingested water containing >100 µg/L arsenic (approximately 0.0037 mg As/kg/day) and the lowest known peak arsenic concentration ingested by a case was 0.115 µg/L (approximately 0.0043 mg As/kg/day). Another large study reported increased incidence of skin lesions associated with estimated doses of 0.0012 mg As/kg/day (0.023 mg As/L drinking water). The mechanism(s) by which inorganic arsenic causes dermal effects is not well-understood. Elucidating the mechanism of dermal effects has been particularly difficult because the dermal effects common in humans have not been seen in studies in animals.

Dermal effects have also been reported following inhalation exposures to inorganic arsenic, although they are not as diagnostic as for oral exposure. Several studies of arsenic-exposed workers have reported the development of dermatitis; exposure levels required to produce this condition are not well-established. Altered dermal pigmentation and hyperkeratosis have also been reported in studies of humans exposed to inorganic arsenic by inhalation, although exposure levels have varied considerably. Direct dermal contact

with inorganic arsenicals may cause irritation and contact dermatitis. Usually, the effects are mild (erythema and swelling), but may progress to papules, vesicles, or necrotic lesions in extreme cases; these conditions tend to heal without treatment if exposure ceases.

Cardiovascular Effects. A large number of studies in humans have reported cardiovascular effects following oral exposure to inorganic arsenic compounds. The cardiac effects of arsenic exposure are numerous, and include altered myocardial depolarization (prolonged QT interval, nonspecific ST segment changes), cardiac arrhythmias, and ischemic heart disease. These effects have been seen after acute and long-term exposure to inorganic arsenic in the environment, as well as side effects from intravenous therapy with arsenic trioxide for acute promyelocytic leukemia. Exposure levels for environmental exposures have not been well characterized, but intravenous doses for arsenic trioxide therapy are generally on the order of 0.15 mg As/kg/day.

Chronic exposure to inorganic arsenic has also been shown to lead to effects on the vascular system. The most dramatic of these effects is "Blackfoot Disease," a disease characterized by a progressive loss of circulation in the hands and feet, leading ultimately to necrosis and gangrene. Blackfoot Disease is endemic in an area of Taiwan where average drinking water levels of arsenic range from 0.17 to 0.80 ppm, corresponding to doses of about 0.014–0.065 mg As/kg/day. The results of a another study suggested that individuals with a lower capacity to methylate inorganic arsenic to DMA have a higher risk of developing peripheral vascular disease in the Blackfoot Disease-hyperendemic area in Taiwan. Arsenic exposure in Taiwan has also been associated with an increased incidence of cerebrovascular and microvascular diseases and ischemic heart disease. While Blackfoot Disease itself has not been reported outside of Taiwan, other vascular effects are common in areas with high arsenic exposures, and include such severe effects as increases in the incidences of Raynaud's disease and of cyanosis of fingers and toes as well as hypertension, thickening and vascular occlusion of blood vessels, and other unspecified cardiovascular conditions. However, while the majority of human studies have reported cardiovascular effects following exposure to inorganic arsenic, some have found no such effects.

Changes in cardiac rhythm and in some vascular end points have also been reported in animal studies of inorganic arsenicals, but generally only at higher exposure levels and not to the degree of severity seen in humans.

Respiratory Effects. While case reports and small cohort studies have routinely reported an increase in respiratory symptoms of humans exposed occupationally to inorganic arsenic, dose-response data for

these symptoms are generally lacking. The only study that evaluated respiratory effects (changes in chest x-ray or respiratory performance) and reported an exposure estimate did not report significant changes at an exposure level of 0.613 mg As/m^3. Exposed workers often report irritation of the mucous membranes of the nose and throat, which may lead to laryngitis, bronchitis, or rhinitis. Increased mortality due to respiratory disease has been reported in some cohort mortality studies of arsenic-exposed workers, but no conclusive evidence of an association of these diseases with arsenic exposure has been presented. It is not known whether respiratory effects following inhaled inorganic arsenic compounds are due to a direct effect of arsenic on respiratory tissues, general effects of foreign material in the lungs, or an effect of arsenic on the pulmonary vasculature. Similar responses, including rales, labored breathing, and respiratory hyperplasia, have been noted in animal studies of inhaled or instilled inorganic arsenic compounds.

Respiratory effects have also been reported following oral exposure of humans to inorganic arsenic. Acute oral exposure to ≥8 mg As/kg may result in serious respiratory effects, including respiratory distress, hemorrhagic bronchitis, and pulmonary edema; however, it is not clear whether these are primary effects or are the result of damage to the pulmonary vascular system. In general, respiratory effects have not been widely associated with long-term oral exposure to low arsenic doses. However, some studies have reported minor respiratory symptoms, such as cough, sputum, rhinorrhea, and sore throat, in people with repeated oral exposure to 0.03–0.05 mg As/kg/day. More serious respiratory effects, such as bronchitis and sequelae (bronchiectasis, bronchopneumonia) have been observed in patients chronically exposed to arsenic and at autopsy in some chronic poisoning cases. There are few animal data reporting respiratory effects of oral exposure to inorganic arsenic, and those studies generally found effects only at very high dose levels.

Gastrointestinal Effects. Both short-term and chronic oral exposures to inorganic arsenicals have been reported to result in irritant effects on gastrointestinal tissues. Numerous studies of acute, high-dose exposure to inorganic arsenicals have reported nausea, vomiting, diarrhea, and abdominal pain, although specific dose levels associated with the onset of these symptoms have not been identified. Chronic oral exposure to 0.01 mg As/kg/day generally results in similar reported symptoms. For both acute and chronic exposures, the gastrointestinal effects generally diminish or resolve with cessation of exposure. Similar gastrointestinal effects have been reported after occupational exposures to inorganic arsenicals, although it is not known if these effects were due to absorption of arsenic from the respiratory tract or from mucociliary clearance resulting in eventual oral exposure.

Neurological Effects. A common effect following both oral and inhalation exposure to inorganic is the development of peripheral neuropathy. Following occupational exposure to inorganic arsenic in pesticide plants or smelters, exposed workers have shown increased incidence of neurological changes, including altered nerve conduction velocities. One study reported that these effects were seen after 28 years of exposure to 0.31 mg As/m^3. In another study, signs and symptoms of sensory and motor polyneuropathy on both upper and lower extremities were reported in workers at a power station in Slovakia. The average length of exposure was 22.3 years (standard deviation [SD] ±8.4 years) and the average arsenic exposure in inhaled air ranged from 4.6 to 142.7 µg/m^3.

Following high-dose (>2 mg As/kg/day) acute oral exposures to inorganic arsenicals in humans, reported effects include headache, lethargy, mental confusion, hallucination, seizures, and coma. Following longer-term exposure to 0.03–0.1 mg As/kg/day, peripheral neuropathy, characterized initially by numbness of the hands and feet and a "pins and needles" sensation and progressing to muscle weakness, wrist-drop and/or ankle-drop, diminished sensitivity, and altered reflex action. Histological features of the neuropathy include a dying-back axonopathy and demyelination. Following removal from exposure, the neuropathy is only partially reversible and what recovery does occur is generally slow. Reports of neurological effects at lower arsenic levels (0.004–0.006 mg As/kg/day) have been inconsistent, with some human studies reporting fatigue, headache, depression, dizziness, insomnia, nightmare, and numbness while others reported no neurological effects. Some studies also have reported that exposure to arsenic may be associated with intellectual deficits in children. Neurological effects have also been reported in oral studies of arsenic toxicity in animals, although these were generally performed at higher doses (0.4–26.6 mg As/kg/day) than has been reported in exposed human populations. The mechanism(s) of arsenic-induced neurological changes has not been determined.

Cancer. There is clear evidence from studies in humans that exposure to inorganic arsenic by either the inhalation or oral routes increases the risk of cancer. Numerous studies of copper smelters or miners exposed to arsenic trioxide have reported an increased risk of lung cancer. Increased incidence of lung cancer has also been observed at chemical plants where exposure was primarily to arsenate. Other studies suggest that residents living near smelters or arsenical chemical plants may have increased risk of lung cancer, although the reported increases are small and are not clearly detectable in all cases. In general, studies reporting long-term exposure to 0.07 mg As/m^3 or greater have shown an increased incidence of lung cancer, while at lower exposure levels, the association has been less clear or not present.

There is convincing evidence from a large number of epidemiological studies and case reports that ingestion of inorganic arsenic increases the risk of developing skin cancer. The most common tumors seen are squamous cell carcinomas, which may develop from the hyperkeratotic warts or corns commonly seen as a dermal effect of oral inorganic arsenic exposure. Early studies of populations within the United States did not suggest an increased risk of cancer from oral inorganic arsenic exposure. Later studies have found suggestive evidence that the possibility of arsenic-induced skin cancers cannot be discounted based on an association between toenail arsenic levels and incidence of skin cancer.

There is increasing evidence that long-term exposure to arsenic can result in the development of bladder cancer, with transitional cell cancers being the most prevalent. While studies have noted statistical dose-response trends in arsenic-induced bladder cancers, reliable quantitative assessments of dose-response relationships have not been presented. Several studies have also shown that chronic oral exposure to arsenic results in the development of respiratory tumors, making lung cancer an established cause of death from exposure to arsenic in drinking water. Exposure levels in studies evaluating respiratory and bladder cancers have been comparable to those in studies evaluating skin tumors. Studies of U.S. populations have not identified an increased risk of bladder or respiratory tumors following oral exposure to inorganic arsenic.

Animal studies of both inhalation and oral exposure to inorganic arsenicals have not resulted in increased incidence of cancer formation in adult animals. However, a series of studies have shown that inorganic arsenic can induce cancer in the offspring from mice exposed to arsenic during gestation (transplacental carcinogen) and acts as a co-carcinogen with UV light and polycyclic aromatic hydrocarbons (PAHs).

Organic Arsenicals. Humans may be exposed to organic arsenicals via inhalation of dusts, ingestion of organic arsenic in water, food, soil, or dermal contact with contaminated soil, water or plants following pesticide application. There are limited data on the toxicity of organic arsenicals following inhalation exposure in humans and animals and these data do not allow for identification of critical effects. Keratosis was observed in workers exposed to 0.065 mg/m^3 arsanilic acid (i.e., 4-aminophenyl arsenic acid); no alterations in gastrointestinal symptoms or hematological alterations were observed. In animals, very high concentrations (>3,000 mg/m^3) of DMA results in respiratory distress, diarrhea, and erythematous lesions on the feet and ears. No adverse effects were observed in rats exposed to DMA concentrations as high as 100 mg DMA/m^3 for 95 days.

Similarly, the available dermal toxicity data do not allow for identification of critical effects. Contact dermatitis was observed in workers applying DMA (and its sodium salt) and mild dermal irritation was observed in a Draize test in rabbits (adverse effect level not reported). Intermediate duration (21 days) exposure studies in rabbits did not result in systemic toxicity or skin irritation following 5 day/week exposure to 1,000 mg/kg/day MMA or DMA.

The preponderance of toxicity data for organic arsenicals involves oral exposure. Human data are limited to three case reports of individuals intentionally ingesting pesticides containing organic arsenicals. Gastrointestinal irritation (vomiting, nausea, and diarrhea) were consistently reported in these cases. Animal data has primarily focused on the toxicity of MMA, DMA, and roxarsone; these data suggest that the targets of toxicity may differ between the compounds.

MMA. The gastrointestinal tract appears to be the most sensitive target of toxicity for MMA. Diarrhea and tissue damage in the large intestine have been reported in several animal species following dietary, gavage, and capsule exposure. For diarrhea, both the time of onset and incidence appear to be dose-related. In rats, diarrhea was observed in 100% of females exposed to 98.5 mg MMA/kg/day, 55% of females exposed to 33.9 mg MMA/kg/day, and 5.1% of females exposed to 3.9 mg MMA/kg/day. The increased incidence of diarrhea was observed after 3 weeks of exposure to 98.5 mg MMA/kg/day, 4 weeks at 33.9 mg MMA/kg/day, and 18 months at 3.9 mg MMA/kg/day. Histological damage consisting of squamous metaplasia of the epithelial columnar absorptive cells in the cecum, colon, and rectum was observed in rats and mice chronically exposed to 72.4 or 67.1 mg MMA/kg/day, respectively. Hemorrhagic, necrotic, ulcerated, or perforated mucosa were also observed in the large intestine of rats exposed to 67.1 mg MMA/kg/day for 2 years. In rats, the damage to the large intestine resulted in intestinal contents leaking into the abdominal cavity and the development of peritonitis. The available data provide suggestive evidence that there may be some species differences in the sensitivity to gastrointestinal damage; however, some of these differences may be due to the route of administration. The lowest adverse effect levels, regardless of duration of exposure, for gastrointestinal effects in rats, mice, rabbits, and dogs are 25.7, 67.1, 12, and 2 mg MMA/kg/day, respectively; the no adverse effect levels in rats and mice (NOAELs were not identified in rabbits and dogs) were 3.0 and 24.9 mg MMA/kg/day. However, the rabbit and dog studies involved bolus administration (gavage and capsule administration), which may have increased sensitivity; the rat and mouse studies involved dietary exposure.

The kidney also appears to be a sensitive target in rats and mice chronically exposed to MMA. An increase in the severity of progressive glomerulonephropathy was observed in female rats exposed to 33.9 mg MMA/kg/day for 2 years and an increase in the incidence of progressive glomerulonephropathy was observed in male mice exposed to 6.0 mg MMA/kg/day for 2 years. Other adverse effects that have been observed in animals exposed to MMA include hypertrophy of the thyroid follicular cells in rats exposed to 33.9 mg MMA/kg/day in the diet for 2 years, reproductive toxicity, and developmental toxicity. Decreases in pregnancy rate and male fertility index were observed in F_0 and F_1 rats exposed to 76 mg MMA/kg/day for 14 weeks prior to mating and during the mating period; the findings were not significantly different than control values but were considered treatment-related because they were outside the range found in historical controls. This study also reported a decrease in pup survival in the F_1 and F_2 offspring of rats exposed to 76 mg MMA/kg/day; as with the reproductive effects, the incidence was not statistically different from controls but was considered biologically significant because survival in the MMA pups was outside the range found in historical controls. Another study reported impaired fetal growth (decreases in fetal weights and incomplete ossification) and minor skeletal defects (an increase in the number of fetuses with supernumerary thoracic ribs and eight lumbar vertebrae) in rat and rabbit fetuses exposed to 500 or 12mg MMA/kg/day, respectively; maternal toxicity was also observed at these dose levels and the effects may be secondary to maternal stress rather than a direct effect on the developing organisms. A 2-year bioassay did not result in significant increases in the incidence of neoplastic lesions in rats and mice exposed to doses as high as 72.4 and 67.1 mg MMA/kg/day, respectively.

DMA. The most sensitive targets of DMA toxicity in rats are the urinary bladder and kidneys. In the bladder, the effects progress from cytotoxicity to cellular necrosis to regenerative proliferation and hyperplasia. At dietary doses of 11 mg DMA/kg/day, cytotoxicity is observed as early as 6 hours after exposure initiation and cellular proliferation (as evident by increased BrdU labeling) was observed after 2 weeks of exposure. After 10 weeks of exposure, necrosis and hyperplasia were also observed. The lowest adverse effect levels for urinary bladder effects following intermediate or chronic duration exposure were 5 mg DMA/kg/day for evidence of regenerative proliferation and 3.1 mg DMA/kg/day for vacuolar degeneration of urothelium and hyperplasia. Vacuolization of the superficial cells of the urothelium was observed in mice exposed to 7.8 mg DMA/kg/day and higher for 2 years. However, unlike the vacuolar degeneration observed in rats, the vacuolization observed in mice was not associated with cytotoxicity, necrosis, inflammation, or hyperplasia.

Kidney damage characterized by increased urinary calcium levels, calcification, nephrocalcinosis, and necrosis of the renal papillae have been observed in rats following intermediate- or chronic-duration exposure. Increases in urine calcium levels and corticomedullary junction calcification were observed in rats exposed to 5 or 10 mg DMA/kg/day for 10 weeks and cortical degeneration and necrosis were observed in rats exposed to 57 mg DMA/kg/day for 4 weeks. Chronic-duration exposure to 3.1 mg DMA/kg/day resulted in an increased incidence of nephrocalcinosis and necrosis of the renal papillae in rats; these lesions are typical in aged rats, although DMA exposure appeared to exacerbate them. An exacerbation of age-related kidney lesion (progressive glomerulonephropathy and nephrocalcinosis) has also been observed in male mice exposed to 37 or 94 mg DMA/kg/day, respectively, for 2 years. A consistent finding in intermediate and chronic rat studies is an increase in urine volume, which corresponds to an increase in water consumption; the toxicological significance of this finding is not known. The observed decreases in electrolyte levels and specific gravity are likely due to the higher urine volume.

Although gastrointestinal effects have been observed in animals exposed to DMA, it does not appear to be as sensitive a target compared to MMA. Diarrhea has been observed in rats exposed to a lethal dose of 190 mg DMA/kg/day for 4 weeks and in dogs administered via 16 mg DMA/kg/day. No gastrointestinal effects were observed in rats or mice chronically exposed to 7.8 or 94 mg DMA/kg/day.

Other adverse effects that have been observed in animals exposed to organic arsenicals include hypertrophy of thyroid follicular cells in rats exposed to 4.0 mg DMA/kg/day in the diet for 13 weeks and 7.8 mg DMA/kg/day in the diet for 2 years and developmental effects in rats and mice. Decreases in fetal growth and delays in ossification have been observed in rat fetuses exposed to ≥36 mg DMA/kg/day; these alterations typically occur at doses associated with decreases in maternal weight gain. Other developmental effects that have been reported include an increase in the incidences of irregular palatine rugae in rats exposed to 30 mg DMA/kg/day, diaphragmatic hernia in rats exposed to 36 mg DMA/kg/day, and cleft palate in mice exposed to 400 mg DMA/kg/day. No developmental effects were observed in rabbits exposed to 12 mg DMA/kg/day.

The available data provide strong evidence that DMA is carcinogenic in rats. A 2-year exposure to DMA resulted in significant increases in the incidence of neoplastic urinary bladder tumors in rats exposed to 7.8 mg DMA/kg/day in the diet or 3.4 mg DMA/kg/day in drinking water. No increases in neoplastic tumors were observed in mice exposed to doses as high as 94 mg DMA/kg/day for 2 years; however, a

50-week exposure to 10.4 mg DMA/kg/day did result in an increased incidence of lung tumors in A/J mice.

The available data for DMA suggest that there are species differences in terms of the critical effects and sensitivity. In rats, the urinary bladder and kidneys are the most sensitive targets with effects occurring at 5 mg DMA/kg/day following intermediate-duration exposure and 3.1 mg DMA/kg/day following chronic-duration exposure. Although the urinary bladder and kidneys are also sensitive targets in mice with LOAELs of 7.8 and 37 mg DMA/kg/day, respectively, following chronic exposure, the effects are not associated with cytotoxicity or elevated urine calcium levels. In dogs, the most sensitive effect is gastrointestinal tract irritation (diarrhea), which occurs at 16 mg DMA/kg/day.

There is concern that the rat may not be a good model to predict the human risk associated with organic arsenic exposure due to the unique toxicokinetic properties of DMA in rats. In humans and most animal species, DMA is rapidly eliminated from the body; >90% of the dose is excreted 2–3 days after dosing. In contrast, DMA is slowly eliminated in rats. One study estimated that 45% of an initial oral DMA dose was eliminated with a half-time of 13 hours; the remaining 55% of the dose DMA dose had an elimination half-time of 50 days. In rats, DMA has a strong affinity for hemoglobin resulting in an accumulation of DMA in erythrocytes. Species differences in DMA metabolism have also been found. In particular, DMA undergoes further methylation to trimethylarsine oxide (TMAO) in rats. In most animal species, almost the entire oral DMA dose is excreted in the urine unchanged; however, in rats, about half of the dose is excreted in the urine as DMA and the other half as TMAO. During the metabolism of DMA to TMAO, DMA(III) is formed as a metabolic intermediate. The formation of this highly reactive intermediate and the excretion of small amounts of DMA(III) in urine may damage the urinary bladder.

There are limited data on the mode of action of DMA for most end points. Recently, there has been considerable research on the mode of action for the development of neoplastic urinary bladder tumors in rats. Although the mechanisms have not been fully elucidated, it has been proposed that the mode of action involves cytotoxicity leading to necrosis and subsequent regeneration of the urinary bladder urothelium. There is strong evidence to suggest that DMA(III) is the causative agent for the urothelial cytotoxicity. The strongest evidence comes from the finding that urinary concentrations of DMA(III) measured in rats exhibiting urothelial cytotoxicity are equivalent to DMA(III) concentrations that are cytotoxic to urothelial cells *in vitro*. Urothelial cytotoxicity, regenerative urothelial proliferation, and urothelial tumors have not been detected in other animal species. Other animal species, including

humans, only metabolize a small percentage of ingested DMA to TMAO; thus, much lower levels of DMA(III) are produced, suggesting that rats may be very sensitive to toxicity of DMA and therefore are not an appropriate model for human risk assessment.

Roxarsone. The available data on the toxicity of roxarsone suggest that following bolus administration, the gastrointestinal tract, kidney, and nervous system are sensitive end points of roxarsone toxicity. Vomiting and gastrointestinal hemorrhage were observed in dogs receiving a single capsulized dose of 50 mg/kg roxarone; no gastrointestinal effects were observed in rats or mice administered 4 or 42 mg/kg/day roxarsone for 2 years. Kidney effects included increases in kidney weight, minimal tubular epithelial cell degeneration, and focal mineralization in rats exposed to 32 mg roxarsone/kg/day for 13 weeks; no kidney effects were observed at 16 mg/kg/day or in mice exposed to doses as high as 136 mg/kg/day for 13 weeks or 43 mg/kg/day for 2 years. Hyperexcitability, ataxia, and/or trembling were observed in rats exposed to 20 mg/kg/day for 13 weeks or 64 mg/kg/day for 13 weeks. A 14-day study in rats reported slight inactivity in rats exposed to 32 mg/kg/day, but this was not observed in longer-term studies. Neurological effects were observed in mice exposed to doses as high as 136 mg/kg/day for 13 weeks or 43 mg/kg/day for 2 years, although a slight decrease in activity at 42 mg/kg/day was reported in a 14 day study. Pigs appear to be especially sensitive to the neurotoxicity of roxarsone. Muscle tremors have been observed at doses of ≥6.3 mg roxarsone/kg/day and myelin degeneration in the spinal cord was noted at 6.3 mg/kg/day. Both the clinical signs of neuropathy and the myelin degeneration followed a time-related pattern. Mild lethargy and ataxia were observed 7 days after exposure initiation, exercise-induced muscle tremors and clonic seizures were observed at day 11, paraparesis was observed at day 22, and paraplegia was observed at day 33. At day 11, equivocal lesions were observed in the cervical spinal cord, and the severity of these lesions increased with time; myelin degeneration was observed in the peripheral nerves and optic nerve starting at day 32 (2 days after exposure termination). Equivocal evidence of carcinogenicity (a slight increase in the incidence of pancreatic tumors) was found in male rats chronically exposed to roxarsone; no increases in neoplastic tumors were observed in female rats or male and female mice.

2.3 MINIMAL RISK LEVELS (MRLs)

Estimates of exposure levels posing minimal risk to humans (MRLs) have been made for arsenic. An MRL is defined as an estimate of daily human exposure to a substance that is likely to be without an appreciable risk of adverse effects (noncarcinogenic) over a specified duration of exposure. MRLs are derived when reliable and sufficient data exist to identify the target organ(s) of effect or the most sensitive

health effect(s) for a specific duration within a given route of exposure. MRLs are based on noncancerous health effects only and do not consider carcinogenic effects. MRLs can be derived for acute, intermediate, and chronic duration exposures for inhalation and oral routes. Appropriate methodology does not exist to develop MRLs for dermal exposure.

Although methods have been established to derive these levels (Barnes and Dourson 1988; EPA 1990i), uncertainties are associated with these techniques. Furthermore, ATSDR acknowledges additional uncertainties inherent in the application of the procedures to derive less than lifetime MRLs. As an example, acute inhalation MRLs may not be protective for health effects that are delayed in development or are acquired following repeated acute insults, such as hypersensitivity reactions, asthma, or chronic bronchitis. As these kinds of health effects data become available and methods to assess levels of significant human exposure improve, these MRLs will be revised.

Inorganic Arsenicals

Inhalation MRLs. No inhalation MRLs were derived for inorganic arsenic. Human data suggest that dermal or respiratory effects may be the most prevalent (Lagerkvist et al. 1986; Mohamed 1998; Perry et al. 1948); respiratory or immunological effects appeared to be the most common following inhalation exposure to inorganic arsenic in animals (Aranyi et al. 1985; Holson et al. 1999). Adequate human studies evaluating dose-response relationships for noncancer end points were not located for inorganic arsenic, and animal data on the health effects of inorganic arsenic following inhalation exposure are limited to studies that did not evaluate a suitable range of health effects. Lacking suitable studies upon which to base the MRLs, no inhalation MRLs were derived for inorganic arsenic.

Oral MRLs

- An MRL of 0.005 mg As/kg/day has been derived for acute-duration (14 days or less) oral exposure to inorganic arsenic.

Mizuta et al. (1956) summarized findings from 220 poisoning cases associated with an episode of arsenic contamination of soy sauce in Japan. The soy sauce was contaminated with approximately 0.1 mg As/mL, probably as calcium arsenate. Arsenic intake in the cases was estimated by the researchers to be 3 mg/day (0.05 mg/kg/day, assuming 55 kg average body weight for this Asian population). The duration of exposure was 2–3 weeks in most cases. The primary symptoms were edema of the face, and gastrointestinal and upper respiratory symptoms initially, followed by skin lesions and neuropathy in

some patients. Other effects included mild anemia and leukopenia, mild degenerative liver lesions and hepatic dysfunction, abnormal electrocardiogram, and ocular lesions. For derivation of the acute oral MRL, facial edema and gastrointestinal symptoms (nausea, vomiting, diarrhea), which were characteristic of the initial poisoning and then subsided, were considered to be the critical effects. The MRL of 0.005 mg As/kg/day was calculated by applying an uncertainty factor of 10 (10 for use of a lowest-observed-adverse-effect level (LOAEL) and 1 for human variability) to the LOAEL of 0.05 mg As/kg/day (see Appendix A for MRL worksheets).

An intermediate-duration oral MRL for inorganic arsenic was not derived due to inadequacy of the database. The lowest LOAEL identified in a limited number of intermediate-duration human studies available was 0.05 mg As/kg/day in a study by Mizuta et al. (1956) (summarized above). While this study was considered appropriate to derive an acute-duration oral MRL for inorganic arsenic, there is considerable uncertainty regarding what the effects and severity might be beyond the relatively short 2–3 weeks of exposure that most subjects experienced. There are numerous studies in animals dosed for intermediate durations, but as indicated in Section 3.5.3, animals are not appropriate models for effects of inorganic arsenic in humans.

- An MRL of 0.0003 mg As/kg/day has been derived for chronic-duration (365 days or more) oral exposure to inorganic arsenic.

Tseng et al. (1968) and Tseng (1977) investigated the incidence of Blackfoot Disease and dermal lesions (hyperkeratosis and hyperpigmentation) in a large number of poor farmers (both male and female) exposed to high levels of arsenic in well water in Taiwan. A control group consisting of 17,000 people, including one group in which arsenic exposure was "undetermined" and which included those villages where arsenic-contaminated wells were no longer used or the level could not be classified, and a control population of 7,500 people who consumed water from wells almost free of arsenic (0.001–0.017 ppm) was also examined. The authors stated that the incidence of dermal lesions increased with dose, but individual doses were not provided. However, incidence data were provided based on stratification of the exposed population into low (<300 µg/L), medium (300–600 µg/L), or high (>600 µg/L) exposure levels. Doses were calculated from group mean arsenic concentrations in well water, assuming the intake parameters described by IRIS (IRIS 2007). Accordingly, the control, low-, medium-, and high-exposure levels correspond to doses of 0.0008, 0.014, 0.038, and 0.065 mg As/kg/day, respectively. The no-observed-adverse-effect level (NOAEL) identified by Tseng (1977) (0.0008 mg As/kg/day) was limited by the fact that the majority of the population was <20 years of age and the incidence of skin lesions increased as a function of age, and because the estimates of water intake and dietary arsenic intake are

highly uncertain. Schoof et al. (1998) estimated that dietary intakes of arsenic from rice and yams may have been 15–211 µg/day (mean=61 µg/day), based on arsenic analyses of foods collected in Taiwan in 1993–1995. Use of the 50 µg/day estimate would result in an approximate doubling of the NOAEL (0.0016 mg/kg/day) (see Appendix A for MRL worksheets). The MRL was derived by applying an uncertainty factor of 3 (for human variability) to the NOAEL of 0.0008 mg/kg/day.

The MRL is supported by a large number of well-conducted epidemiological studies that identify reliable NOAELs and LOAELs for dermal effects. EPA (1981b) identified a NOAEL of 0.006–0.007 mg As/kg/day for dermal lesions in several small populations in Utah. Harrington et al. (1978) identified a NOAEL of 0.003 mg As/kg/day for dermal effects in a small population in Alaska. Guha Mazumder et al. (1988) identified a NOAEL of 0.009 mg As/kg/day and a LOAEL of 0.006 mg As/kg/day for pigmentation changes and hyperkeratosis in a small population in India. Haque et al. (2003) identified a LOAEL of 0.002 mg As/kg/day for hyperpigmentation and hyperkeratosis in a case-control study in India. Cebrián et al. (1983) identified a NOAEL of 0.0004 mg As/kg/day and a LOAEL of 0.022 mg As/kg/day in two regions in Mexico. Borgoño and Greiber (1972) and Zaldívar (1974) identified a LOAEL of 0.02 mg As/kg/day for abnormal skin pigmentation in patients in Chile, and Borgoño et al. (1980) identified a LOAEL of 0.01 mg As/kg/day for the same effect in school children in Chile. Valentine et al. (1985) reported a NOAEL of 0.02 mg As/kg/day for dermal effects in several small populations in California. Collectively, these studies indicate that the threshold dose for hyperpigmentation and hyperkeratosis is approximately 0.002 mg As/kg/day. While many of these studies also identified effects on other end points at these exposure levels, including effects on gastrointestinal (Borgoño and Greiber 1972; Cebrián et al. 1983; Guha Mazumder et al. 1988; Zaldívar 1974), cardiovascular (Tseng et al. 1995, 1996), hepatic (Hernández-Zavala et al. 1998), and neurological end points (Guha Mazumder et al. 1988; Lianfang and Jianzhong 1994; Tsai et al. 2003), the overall database for dermal effects is considerably stronger than for effects on other end points.

Organic Arsenicals

Inhalation MRLs. No inhalation MRLs were derived for organic arsenic. Human data are limited to an occupational exposure study of workers exposed to 0.065 mg/m^3 ansanilic acid (Watrous and McCaughey 1945). The exposed workers more frequently complained of keratosis than nonexposed workers. A limited number of animal studies have examined the toxicity of organic arsenicals following inhalation exposure. Respiratory distress and diarrhea were observed in rats and mice exposed to high concentrations of MMA and DMA (Stevens et al. 1979); at lower concentrations (1,540–3,150 mg DMA/m^3), respiratory irritation, as evidenced by a decrease in respiration rate, was observed in animals

exposed to MMA or DMA (Stevens et al. 1979). The acute-duration studies do not clearly identify the most sensitive targets of inorganic arsenical toxicity; the available studies are of limited scope and none included a comprehensive histological examination.

One study examined the toxicity of DMA in rats following intermediate-duration exposure. This study (Whitman 1994) found an increase in intracytoplasmic eosinophilic globules in the nasal turbinates of rats exposed to 34 or 100 mg/m^3 DMA 6 hours/day, 5 days/week for 67–68 exposures; no other adverse effects were observed in this comprehensive study. As discussed in greater detail in the oral MRL section, the toxicokinetic properties of DMA in rats differ from other species and rats do not appear to be a good model for human exposure. The half-time of DMA in the body is much longer in rats compared to other species, including humans, and DMA is more extensively methylated in rats. In the absence of data to determine whether the observed effect is due to a direct interaction of DMA, derivation of an intermediate-duration MRL using rat data is not recommended at this time.

No studies examined the chronic toxicity of organic arsenicals precluding the derivation of a chronic-duration inhalation MRL.

Oral MRLs

MMA. A limited number of animal studies have examined the acute oral toxicity of MMA. These studies consisted of LD_{50} studies in rats (Gur and Nyska 1990), mice (Kaise et al. 1989), and rabbits (Jaghabir et al. 1988) and developmental toxicity studies in rats (Irvine et al. 2006) and rabbits (Irvine et al. 2006); all studies administered MMA via gavage. Adverse effects reported in the LD_{50} studies included diarrhea in rats at 2,030 mg monosodium methane arsonate (MSMA)/kg (Gur and Nyska 1990), mice at 2,200 mg MMA/kg (Kaise et al. 1989) and rabbits at 60 mg MSMA/kg (Jaghabir et al. 1988) and respiratory arrest in mice at 1,800 mg MMA/kg/day (Kaise et al. 1989). These doses were at or near the LD_{50} levels of 2,449 mg MSMA/kg, 1,800 mg MMA/kg, 100 mg MSMA/kg for the rats, mice, and rabbits, respectively. In the developmental toxicity studies (Irvine et al. 2006), maternal effects included decreases in maternal body weight gain in rats (17% less than controls) and rabbits (70% less than controls) receiving gavage doses of 100 and 12 mg MMA/kg/day, respectively, and loose feces/diarrhea in rabbit does administered 12 mg MMA/kg/day. The NOAELs for maternal effects were 10 and 7 mg MMA/kg/day in the rats and rabbits, respectively. Minor developmental effects (decreased fetal weight, incomplete ossification, and supernumerary ribs) were also observed at the maternally toxic doses in the rats and rabbits (Irvine et al. 2006); these effects were probably secondary to the maternal stress. These

data, coupled with the results of longer-term studies (Arnold et al. 2003; Waner and Nyska 1988), suggest that the gastrointestinal tract is a sensitive target of MMA toxicity. The rabbit developmental toxicity study (Irvine et al. 2006) identified the lowest LOAEL (12 mg MMA/kg/day) for gastrointestinal irritation. However, this study is not suitable for the derivation of an acute-duration oral MRL for MMA because the MMA was administered via bolus doses. It is likely that the observed gastrointestinal effect is a concentration-dependent effect; thus, at a given dose level, effects are more likely to occur following bolus administration. A marked decrease in body weight gain was also observed at this dose level.

- An MRL of 0.1 mg MMA/kg/day has been derived for intermediate-duration (15–364 days) oral exposure to MMA.

Three studies have examined the intermediate-duration toxicity of MMA; two of these are chronic-duration studies reporting diarrhea and decreases in body weight gain after MMA exposure for <1 year. Diarrhea was observed in rats exposed to 30.2 mg MMA/kg/day in the diet (Arnold et al. 2003) and in dogs exposed via a capsule to 2 mg MMA/kg/day (Waner and Nyska 1988). Decreases in body weight were observed at the next highest doses, 106.9 mg MMA/kg/day in rats and 8 mg MMA/kg/day in dogs. In the rat study (Arnold et al. 2003), diarrhea was observed in 16.7 and 40% of the males and females, respectively, exposed to 30.2/35.9 mg MMA/kg/day during the first 52 weeks of the study; diarrhea first occurred after 4 weeks of exposure. At the highest dose level (106.9 mg MMA/kg/day), diarrhea was observed in all exposed male and female rats. In dogs, the increased incidence of diarrhea first occurred during weeks 25–28; at the highest dose tested in the study (35 mg MMA/kg/day), vomiting was also observed. A NOAEL of 3.5 mg MMA/kg/day was identified in the rat study; a NOAEL was not identified in the dog study. The remaining study in the intermediate-duration database is a 2-generation study that reported reproductive (decreased pregnancy rate and male fertility index in F_0 and F_1 generations) and developmental (decreased pup survival in F_1 and F_2 generation) effects in rats exposed to 76 mg MMA/kg/day in the diet (Schroeder 1994). The lowest LOAEL identified in the intermediate-duration database is 2 mg MMA/kg/day for diarrhea in dogs (Waner and Nyska 1988). Although dogs appear to be more sensitive to the gastrointestinal effects of MMA, a direct comparison of the two studies is not possible due to the difference in the routes of exposure. It is possible that the bolus administration of MMA, in the form of a capsule, resulted in increased sensitivity of the dogs. Because the most likely route of exposure for humans would be ingestion and the critical effect appears to be irritation of the gastrointestinal tract, studies involving bolus administration (gavage or capsule) were not considered for derivation of oral MRLs. The Arnold et al. (2003) and Schroeder (1994) studies were considered as the basis for an intermediate-duration MRL. Of these two studies, Arnold et al. (2003) identified the lowest

LOAEL, 30.2 mg MMA/kg/day, for gastrointestinal effects and was selected as the principal study for the intermediate-duration oral MRL.

Arnold et al. (2003) exposed groups of 60 male and 60 female Fischer 344 rats to 0, 50, 400, or 1,300 ppm MMA in the diet for 104 weeks. Using the average doses for weeks 1–50 reported in an unpublished version of this study (Crown et al. 1990), doses of 0, 3.5, 30.2, and 106.9 mg MMA/kg/day and 0, 4.2, 35.9, and 123.3 mg MMA/kg/day were calculated for males and females, respectively. Body weights, food consumption, and water intake were monitored regularly. Blood was taken at 3, 6, and 12 months for clinical chemistry measurements, and urine samples were collected at the same interval. Mortality was increased in high-dose males and females during the first 52 weeks of the study. Body weights were decreased in the mid- and high-dose groups of both sexes; however, at 51 weeks, only the body weight for the high-dose males was <10% of the control weight (14.5%). Food and water consumption was increased in the mid- and high-dose groups. Diarrhea was observed in 100% of the high-dose males and females and in 16.7 and 40% of the mid-dose males and females during the first 52 weeks of exposure. Diarrhea first occurred after 3 weeks of exposure to the high dose and 4 weeks of exposure to the mid-dose group; the severity of the diarrhea was dose-related. The gastrointestinal system was the primary target in animals dying early; numerous macroscopic and histological alterations were observed.

A benchmark dose (BMD) analysis of the incidence data for diarrhea was conducted; details of this analysis are presented in Appendix A. Using the female incidence data, a BMD (BMD_{10}) of 16.17 mg MMA/kg/day, which corresponds to a 10% increase in the incidence of diarrhea, was calculated; the 95% lower confidence limit on the BMD ($BMDL_{10}$) was 12.38 mg MMA/kg/day. The female incidence data were selected over the male data because the females may be more sensitive than the males. Thus, the intermediate-duration oral MRL of 0.1 mg MMA/kg/day is based on the $BMDL_{10}$ of 12.38 mg MMA/kg/day in female rats and an uncertainty factor of 100 (10 to account for animal to human extrapolation and 10 for human variability).

- An MRL of 0.01 mg MMA/kg/day has been derived for chronic-duration (365 days or longer) oral exposure to MMA.

The available data on the chronic toxicity of MMA in animals (no human data are available) suggest that the gastrointestinal tract and the kidney are the most sensitive targets. Diarrhea has been observed in rats and mice exposed to MMA in the diet for 2 years (Arnold et al. 2003). The NOAEL and LOAEL values for diarrhea are 3.0 and 25.7 mg MMA/kg/day in rats, respectively, and 24.9 and 67.1 mg MMA/kg/day

in mice, respectively. At 72.4 mg MMA/kg/day, necrotic, ulcerated, or perforated mucosa and metaplasia were observed in the cecum, colon, and rectum of rats. Squamous metaplasia was also observed in the cecum, colon, and rectum of mice exposed to 67.1 mg MMA/kg/day. Diarrhea was observed in dogs exposed via capsule to 2 mg MMA/kg/day for 52 weeks (Waner and Nyska 1988). The bolus administration used in the dog study probably increased the dog's sensitivity to MMA. In both the rats and mice, chronic administration of MMA resulted in an exacerbation of chronic progressive nephropathy. In female rats, significant increases in the severity of chronic progressive nephropathy were observed at 33.9 and 98.5 mg MMA/kg/day; the NOAEL was 3.9 mg MMA/kg/day (Arnold et al. 2003). In male mice, there was an increased incidence of slight progressive nephropathy at doses ≥6.0 mg MMA/kg/day; the NOAEL was 1.2 mg MMA/kg/day (Arnold et al. 2003; incidence data reported in Gur et al. 1991). Nephrocalcinosis was also observed in male mice exposed to ≥24.9 mg MMA/kg/day (Arnold et al. 2003). Other effects that have been observed following chronic exposure MMA include decreased weight gain in male and female rats exposed to 25.7/33.9 mg MMA/kg/day and higher (Arnold et al. 2003) and hypertrophy of the thyroid follicular epithelium in female rats exposed to ≥33.9 mg MMA/kg/day (Arnold et al. 2003). A variety of other lesions including peritonitis, pancreatitis, inflammation of the ureter, uterus, prostate, testes, epididymis, and seminal vesicles, hydronephrosis, pyelonephritis, and cortical tubular cystic dilation were also observed in rats; however, these alterations were probably secondary to the ulceration and perforation of the large intestine, which resulted in leaking of gastrointestinal contents into the abdominal cavity. Hyperplasia of the urinary bladder was also observed in rats exposed to 2.1 mg MMA/kg/day as MMA in drinking water for 2 years (Shen et al. 2003). Although hyperplasia of the urinary bladder is commonly observed in rats exposed to DMA, it was not observed in the Arnold et al. (2003) study at doses as high as 72.4 mg MMA/kg/day; thus, the significance of the results of the Shen et al. (2003) study is not known.

The lowest reliable LOAEL identified in the chronic oral MMA database was 6.0 mg MMA/kg/day for an increased incidence of progressive glomerulonephropathy in mice (Arnold et al. 2003). Although the investigators noted that the kidney lesions were consistent with the normal spectrum of spontaneous renal lesions and that there was no difference in character or severity of lesions between groups, ATSDR considers the dose-related increase in glomerulonephropathy to be treatment-related.

In the Arnold et al. (2003) study (incidence data reported in Gur et al. 1991), groups of 52 male and 52 female $B6C3F_1$ mice were exposed to 0, 10, 50, 200, or 400 ppm of MMA in the diet for 104 weeks. The average doses reported in Gur et al. (1991) were 0, 1.2, 6.0, 24.9, and 67.1 mg MMA/kg/day for males and 0, 1.4, 7.0, 31.2, and 101 mg MMA/kg/day for females. Body weights, food consumption, and

water intake were monitored regularly. Blood was taken at 3, 6, 12, 18, and 24 months for white cell counts. At sacrifice, complete necropsies were performed, including histological examination of at least 13 organs. No treatment-related increases in mortality were observed. Significant decreases in body weights were observed in males and females exposed to 67.1 or 101 mg MMA/kg/day, respectively; at week 104, the males and females weighed 17 and 23%, respectively, less than controls. Food consumption was increased in females exposed to 101 mg MMA/kg/day, and water consumption was increased in 67.1 mg MMA/kg/day males and 31.2 and 101 mg MMA/kg/day females. Loose and mucoid feces were noted in mice exposed to 67.1/101 mg MMA/kg/day. No changes were seen in white cell counts of either sex. Small decreases in the weights of heart, spleen, kidney, and liver weights were observed in some animals, but the decreases were not statistically significant. Squamous metaplasia of the cecum, colon, and rectum was observed at 67.1/101 mg MMA/kg/day. The incidence of metaplasia in the cecum, colon, and rectum were 29/49, 14/49, and 39/49 in males and 38/52, 17/52, and 42/52 in females; metaplasia was not observed in other groups of male or female mice. An increased incidence of progressive glomerulonephropathy (incidence of 25/52, 27/52, 38/52, 39/52, and 46/52 in the 0, 1.2, 6.0, 24.9, and 67.1 mg MMA/kg/day males, respectively) was observed in males; the incidence was significantly higher (Fisher Exact Test) than controls at ≥6.0 mg MMA/kg/day. Significant increases in the incidence of nephrocalcinosis was observed in the males at 24.9 and 67.1 mg MMA/kg/day (Fisher Exact Test) (incidences of 25/52, 30/52, 30/52, 45/52, and 45/51 in males and 0/52, 1/52, 1/52, 2/52, and 5/52 in females). A reduction in the incidence of cortical focal hyperplasia in the adrenal gland of male mice exposed to 67.1 mg MMA/kg/day was possibly related to MMA exposure; the toxicological significance of this effect is not known. Thus, this study identifies a NOAEL of 1.2 mg MMA/kg/day and a LOAEL of 6.0 mg MMA/kg/day for progressive glomerulonephropathy in male mice.

As described in greater detail in Appendix A, BMD was applied to the incidence data for progressive glomerulonephropathy in male mice using all available dichotomous models in EPA's Benchmark Dose Software (version 1.4.1) to calculate predicted doses associated with a 10% extra risk. As assessed by the Akaike's Information Criteria (AIC), the log-logistic model provided the best fit to the data. The predicted BMD_{10} and $BMDL_{10}$ are 2.09 and 1.09 mg MMA/kg/day. The $BMDL_{10}$ was selected as the point of departure and divided by an uncertainty factor of 100 (10 for extrapolation from animals to humans and 10 for human variability) to derive a chronic-duration oral MRL of 0.01 mg MMA/kg/day.

DMA. As discussed in greater detail in Section 2.2, urinary bladder effects characterized by cytotoxicity and regenerative proliferation and hyperplase have been observed in rats, but not in other species. The LOAELs for these effects are lower than the LOAELs for sensitive effects in other species. Additionally,

rats have a much greater capacity than other species to metabolize ingested DMA to form DMA(III) (a reactive intermediate) and TMAO (Cohen et al. 2006; Marafante et al. 1987b; Yoshida et al. 1998). It is likely that DMA(III) is the causative agent for the urothelial cytoxicity observed in rats (Cohen et al. 2006). Thus, rats were not considered a suitable model for humans and these data were not considered for derivation of MRLs for DMA.

There are limited data to assess the acute toxicity of DMA in species other than rats. Diarrhea, increased startle reflex, and ataxia were observed in mice exposed to a lethal gavage dose of 1,757 mg DMA/kg (Kaise et al. 1989); vomiting and diarrhea were also observed during the second week of a 52-week study in dogs exposed via capsule to 16 mg DMA/kg/day (Zomber et al. 1989). The remaining studies in the acute database are developmental toxicity studies in mice and rabbits. Rabbits appear to be more sensitive than mice to maternal and developmental effects. Gavage exposure to 48 mg DMA/kg/day on gestational days 7–19 resulted in maternal weight loss and abortion in approximately 75% of the does; no adverse effects were observed at 12 mg DMA/kg/day (Irvine et al. 2006). In mice, decreases in maternal body weight gain were observed at gavage doses of 200 mg DMA/kg/day on gestational days 7–16 (Rogers et al. 1981), decreases in fetal body weight, delays in ossification, and increased incidence of cleft palate were observed at 400 mg DMA/kg/day on gestational days 7–16 (Rogers et al. 1981) and fetal deaths, decreases in growth, and increased incidence of malformations were observed in mice administered 1,600 mg DMA/kg on gestational day 8 (Kavlock et al. 1985). The acute-duration database for DMA was not considered adequate for derivation of an oral MRL. The database is lacking a comprehensive toxicity study, which would be useful in establishing the critical target of toxicity. In a chronic-duration study in mice (Arnold et al. 2006), vacuolization was observed in the urinary bladder at ≥7.8 mg DMA/kg/day; it is not known if these effects would also be observed after acute-duration exposure. Thus, it is not known if systemic effects would occur at lower doses than the maternal developmental effects observed in rabbits exposed to 48 mg DMA/kg/day (Irvine et al. 2006); an acute-duration oral MRL for DMA is not recommended at this time.

Excluding rat studies, the database on the toxicity of DMA following intermediate-duration oral exposure is limited to a chronic study of dogs exposed to DMA via capsule 6 days/week for 52 weeks (Zomber et al. 1989). Diarrhea and vomiting were observed at 16 and 40 mg DMA/kg/day starting after the first week of exposure. A slight decrease in erythrocyte levels and increase in total leukocyte levels were observed in males exposed to 40 mg DMA/kg/day for 51 weeks. This dog study was not selected as the basis of an MRL because it is likely that bolus administration of DMA would increase sensitivity to the gastrointestinal effects.

- An MRL of 0.02 mg DMA/kg/day has been derived for chronic-duration (365 days or longer) oral exposure to DMA.

Two studies investigated the chronic-duration toxicity of DMA in a species other than rats. In dogs, diarrhea and vomiting were observed after 52 weeks of exposure to 16 or 40 mg As/kg/day (Zomber et al. 1989); no histological alterations were observed. In mice exposed to DMA in the diet for 2 years, vacuolization of the urothelium in the urinary bladder was observed at ≥7.8 mg DMA/kg/day and progressive glomerulonephropathy was observed at ≥37 mg DMA/kg/day (Arnold et al. 2006). As noted in Section 2.2, the vacuolization was not associated with cytotoxicity or proliferation. Because the bladder effects in mice occurred at the lowest adverse effect level for the database, it was selected as the critical effect and Arnold et al. (2006) was selected as the principal study.

In the Arnold et al. (2006) study, groups of 56 male and 56 female $B6C3F_1$ mice were exposed to 0, 8, 40, 200, or 500 ppm DMA in the diet for 2 years; the results of this study were also reported in an unpublished paper (Gur et al. 1989b) submitted to EPA under Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). The investigators reported dietary doses of approximately 0, 1.3, 7.8, 37, and 94 mg DMA/kg/day. The following parameters were used to assess toxicity: clinical observations, body weight, food consumption, water consumption, differential leukocyte levels measured at 12, 18, and 24 months in mice in the control and 94 mg DMA/kg/day groups, organ weights (brain, kidneys, liver, and testes), and histopathological examination of major tissues and organs. No deaths or treatment-related clinical signs were observed. Decreases in body weight gain were observed in the male mice exposed to 94 mg DMA/kg/day; the difference was <10% and not considered adverse. An increase in water consumption was observed in males exposed to 94 mg DMA/kg/day during weeks 60–96. In the female mice exposed to 51 mg As/kg/day, a statistically significant decrease in lymphocytes and an increase in monocytes were observed at 24 months. Treatment related nonneoplastic alterations were observed in the urinary bladder and kidneys. In the urinary bladder, increases in the vacuolization of the superficial cells of the urothelium were observed in males exposed to 37 or 94 mg DMA/kg/day (0/44, 1/50, 0/50, 36/45, 48/48) and in females exposed to 7.8, 37, and 94 mg DMA/kg/day (1/45, 1/48, 26/43, 47/47, 43/43); incidence data reported in Gur et al. (1989b). An increased incidence of progressive glomerulonephropathy was observed in males at 37 mg DMA/kg/day (16/44, 22/50, 17/50, 34/45, 30/50) and an increased incidence of nephrocalcinosis was also observed in male mice at 94 mg DMA/kg/day (30/44, 25/50, 27/50, 29/50, 45/50). Neoplastic alterations were limited to an increased incidence of fibrosarcoma of the skin in females exposed to 94 mg DMA/kg/day (the incidence of 3/56, 0/55, 1/56,

1/56, and 6/56 in the 0, 1.3, 7.8, 37, and 94 mg DMA/kg/day groups, respectively); however, it was concluded that this lesion was not related to DMA exposure.

As described in detail in Appendix A, BMD analysis was applied to the incidence data for vacuolization of the urothelium in the urinary bladder of female mice using all available dichotomous models in EPA's Benchmark Dose Software (version 1.4.1) to calculate predicted doses associated with a 10% extra risk. As assessed by the AIC, the multi-stage model provided the best fit to the data. The predicted BMD_{10} and $BMDL_{10}$ are 2.68 and 1.80 mg DMA/kg/day. The $BMDL_{10}$ was selected as the point of departure and divided by an uncertainty factor of 100 (10 for extrapolation from animals to humans and 10 for human variability) to derive a chronic-duration oral MRL of 0.02 mg DMA/kg/day.

Roxarsone. A series of three National Toxicology Program (NTP) studies in rats and mice (NTP 1989b) and a study in dogs (Kerr et al. 1963) have examined the acute toxicity of roxarsone; adverse effects have also been reported within the first 2 weeks of a longer-term study in pigs (Rice et al. 1985; Kennedy et al. 1986). A single exposure study reported diarrhea and ataxia in rats and mice exposed to doses that exceeded the LD_{50} (NTP 1989b). In another study, no alterations in hematological parameters (only end point assessed) were found after 10 or 9 days of dietary exposure in rats and mice, respectively (NTP 1989b). In a 14-day study (NTP 1989b), a decrease in body weight gain and slight inactivity were observed in rats exposed to 32 mg roxarsone/kg/day and slight inactivity was observed in mice exposed to 42 mg roxarsone/kg/day; a decrease in body weight gain was also observed in mice exposed to 168 mg roxarsone/kg/day. The dog study was considered inadequate because a small number (n=3) of animals were tested and no control group was used. In a 30-day dietary exposure study in pigs (Rice et al. 1985; Kennedy et al. 1986), mild lethargy and ataxia were observed from day 7 forward and exercise-induced muscle tremors and clonic seizures were observed from day 11 forward in pigs exposed to 6.3 mg roxarsone/kg/day; equivocal evidence of myelin degeneration was also observed in pigs sacrificed after 11 days of exposure. These data clearly identify pigs as the most sensitive species following acute-duration oral exposure; in the absence of data to the contrary, it is assumed that pigs are a good model to predict the toxic potential of roxarsone in humans. Because the lowest dose tested in pigs was a serious LOAEL for neurotoxicity and a NOAEL for this effect was not identified, an acute-duration oral MRL cannot be derived for roxarsone.

As with the acute-duration database, pigs appear to be the most sensitive species; neurotoxicity has been observed at ≥6.3 mg roxarsone/kg/day. In a study reported by Rice et al. (1985) and Kennedy et al. (1986), exercise-induced muscle tremors and clonic convulsions were observed in pigs during the early

part of the study; when the pigs returned to a recumbent position, the seizures and tremors stopped. Paraparesis, evidenced by reluctance to rise and the pigs dragging their hindquarters on the ground, was observed at day 22; paraplegia was observed 2 days after exposure termination. In addition to these clinical signs of neuropathy, histological alterations consisting of myelin degeneration was observed in the spinal cord, peripheral nerves, and optic nerve. The lesions were first detected in the spinal cord on day 15 and in the peripheral nerves and optic nerve 2 days after exposure termination. The Rice et al. (1985) and Kennedy et al. (1986) studies did not identify a NOAEL. Muscle tremors were also observed in pigs exposed to 10 mg roxarsone/kg/day for 28 days (Edmonds and Baker 1986). This study was not designed to assess neurotoxicity and did not include histological examination of the spinal cord or nerves. Trembling, ataxia, and hyperexcitability were also observed in rats exposed to 64 mg roxarsone/kg/day for 13 weeks (NTP 1989b). Other effects that have been observed include tubular degeneration and focal regenerative hyperplasia in the kidney and decreased body weight in rats exposed to 32 mg roxarsone/kg/day for 13 weeks (NTP 1989b) and decreased body weight in mice at 136 mg roxarsone/kg/day for 13 weeks (NTP 1989b). The lowest identified adverse effect level is 6.3 mg roxarsone/kg/day for serious neurological effects in pigs (Kennedy et al. 1986; Rice et al. 1985) and is not suitable for the derivation of an intermediate-duration oral MRL.

The chronic toxicity of roxarsone has been examined in rats (NTP 1989b; Prier et al. 1963), mice (NTP 1989b; Prier et al. 1963), and dogs (Prier et al. 1963) in 2-year dietary exposure studies. None of these studies reported adverse effects at the highest doses tested; the highest NOAELs for each species are 10, 43, and 5 mg roxarsone/kg/day for rats, mice, and dogs, respectively. The results from shorter duration studies suggest that pigs are more sensitive to the neurotoxic effects of roxarsone than rats, mice, or dogs. Because no chronic duration pig studies were identified and deriving an MRL using a potentially less sensitive species may not be protective of human health, a chronic-duration oral MRL is not recommended at this time.

3. HEALTH EFFECTS

3.1 INTRODUCTION

The primary purpose of this chapter is to provide public health officials, physicians, toxicologists, and other interested individuals and groups with an overall perspective on the toxicology of arsenic. It contains descriptions and evaluations of toxicological studies and epidemiological investigations and provides conclusions, where possible, on the relevance of toxicity and toxicokinetic data to public health.

A glossary and list of acronyms, abbreviations, and symbols can be found at the end of this profile.

3.2 DISCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE

To help public health professionals and others address the needs of persons living or working near hazardous waste sites, the information in this section is organized first by route of exposure (inhalation, oral, and dermal) and then by health effect (death, systemic, immunological, neurological, reproductive, developmental, genotoxic, and carcinogenic effects). These data are discussed in terms of three exposure periods: acute (14 days or less), intermediate (15–364 days), and chronic (365 days or more).

Levels of significant exposure for each route and duration are presented in tables and illustrated in figures. The points in the figures showing no-observed-adverse-effect levels (NOAELs) or lowest-observed-adverse-effect levels (LOAELs) reflect the actual doses (levels of exposure) used in the studies. LOAELs have been classified into "less serious" or "serious" effects. "Serious" effects are those that evoke failure in a biological system and can lead to morbidity or mortality (e.g., acute respiratory distress or death). "Less serious" effects are those that are not expected to cause significant dysfunction or death, or those whose significance to the organism is not entirely clear. ATSDR acknowledges that a considerable amount of judgment may be required in establishing whether an end point should be classified as a NOAEL, "less serious" LOAEL, or "serious" LOAEL, and that in some cases, there will be insufficient data to decide whether the effect is indicative of significant dysfunction. However, the Agency has established guidelines and policies that are used to classify these end points. ATSDR believes that there is sufficient merit in this approach to warrant an attempt at distinguishing between "less serious" and "serious" effects. The distinction between "less serious" effects and "serious" effects is considered to be important because it helps the users of the profiles to identify levels of exposure at which major health effects start to appear. LOAELs or NOAELs should also help in determining whether or not

the effects vary with dose and/or duration, and place into perspective the possible significance of these effects to human health.

The significance of the exposure levels shown in the Levels of Significant Exposure (LSE) tables and figures may differ depending on the user's perspective. Public health officials and others concerned with appropriate actions to take at hazardous waste sites may want information on levels of exposure associated with more subtle effects in humans or animals (LOAELs) or exposure levels below which no adverse effects (NOAELs) have been observed. Estimates of levels posing minimal risk to humans (Minimal Risk Levels or MRLs) may be of interest to health professionals and citizens alike.

Levels of exposure associated with carcinogenic effects (Cancer Effect Levels, CELs) of arsenic are indicated in Tables 3-1 and 3-3 and Figures 3-1 and 3-3. Because cancer effects could occur at lower exposure levels, Figures 3-1 and 3-3 also show a range for the upper bound of estimated excess risks, ranging from a risk of 1 in 10,000 to 1 in 10,000,000 (10^{-4} to 10^{-7}), as developed by EPA.

A User's Guide has been provided at the end of this profile (see Appendix B). This guide should aid in the interpretation of the tables and figures for Levels of Significant Exposure and the MRLs.

Chemical Forms of Concern. Analysis of the toxic effects of arsenic is complicated by the fact that arsenic can exist in several different oxidation states and many different inorganic and organic compounds. Most cases of human toxicity from arsenic have been associated with exposure to inorganic arsenic, so these compounds are the main focus of this profile.

The most common inorganic arsenical in air is arsenic trioxide (As_2O_3), while a variety of inorganic arsenates (AsO_4^{-3}) or arsenites (AsO_2^-) occur in water, soil, or food. A number of studies have noted differences in the relative toxicity of these compounds, with trivalent arsenites tending to be somewhat more toxic than pentavalent arsenates (Byron et al. 1967; Gaines 1960; Maitani et al. 1987a; Sardana et al. 1981; Willhite 1981). However, these distinctions have not been emphasized in this profile, for several reasons: (1) in most cases, the differences in the relative potency are reasonably small (about 2–3-fold), often within the bounds of uncertainty regarding NOAEL or LOAEL levels; (2) different forms of arsenic may be interconverted, both in the environment (see Section 6.3) and the body (see Section 3.4); and (3) in many cases of human exposure (especially those involving intake from water or soil, which are of greatest concern to residents near wastes sites), the precise chemical speciation is not known.

Gallium arsenide (GaAs) is another inorganic arsenic compound of potential human health concern, due to its widespread use in the microelectronics industry. Available toxicokinetic data suggest that although gallium arsenide is poorly soluble, it undergoes slow dissolution and oxidation to form gallium trioxide and arsenite (Webb et al. 1984, 1986). Therefore, the toxic effects of this compound are expected to be attributable to the arsenite that is liberated, plus the additional effects of the gallium species.

It is beyond the scope of this profile to provide detailed toxicity data on other less common inorganic arsenic compounds (e.g., As_2S_3), but these are expected to be of approximately equal or lesser toxicity than the oxycompounds, depending mainly on solubility (see Section 3.4).

Although organic arsenicals are usually viewed as being less toxic than the inorganics, several methyl and phenyl derivatives of arsenic that are widely used in agriculture are of possible human health concerns based on their toxicity in animal species (Arnold et al. 2003, 2006; NTP 1989b). Chief among these are monomethylarsonic acid (MMA) and its salts (monosodium methane arsonate [MSMA] and disodium methane arsonate [DSMA]), dimethylarsinic acid (DMA, also known as cacodylic acid) and its sodium salt (sodium dimethyl arsinite, or sodium cacodylate), and roxarsone (3-nitro-4-hydroxyphenylarsonic acid). However, it should be noted that food is the largest contributor to background intakes of organic arsenicals. Estimates on the concentration of organic arsenicals in the diet were not located; Cohen et al. (2006) estimated that the intake of DMA from food and water is <1 ng/kg/day. As with the inorganic compounds, there are toxicological differences between these various organic derivatives; because of these differences, the discussion of the health effects of MMA, DMA, and roxarsone are discussed separately. As discussed below, animals do not appear to be good quantitative models for inorganic arsenic toxicity in humans, but it is not known if this also applies to toxicity of organic arsenicals.

Several organic arsenicals are found to accumulate in fish and shellfish. These derivatives (mainly arsenobetaine and arsenocholine, also referred to as "fish arsenic") have been studied by several researchers and have been found to be essentially nontoxic (Brown et al. 1990; Cannon et al. 1983; Charbonneau et al. 1978; Kaise et al. 1985; Luten et al. 1982; Siewicki 1981; Tam et al. 1982; Yamauchi et al. 1986). Thus, these compounds are not considered further here.

Arsine (AsH_3) and its methyl derivatives, although highly toxic, are also not considered in this profile, since these compounds are either gases or volatile liquids that are unlikely to be present at levels of concern at hazardous waste sites.

Use of Animal Data. An additional complexity to the analysis of arsenic toxicity is that most laboratory animals appear to be substantially less susceptible to inorganic arsenic than humans. For example, chronic oral exposure of humans to inorganic arsenic at doses of 0.05–0.1 mg/kg/day is frequently associated with neurological (Barton et al. 1992; Goddard et al. 1992; Guha Mazumder et al. 1988; Haupert et al. 1996; Hindmarsh et al. 1977; Huang et al. 1985; Sass et al. 1993; Silver and Wainman 1952; Szuler et al. 1979; Tay and Seah 1975; Valentine et al. 1981) or hematological signs of arsenic toxicity (Glazener et al. 1968; Guha Mazumder et al. 1988; Prasad and Rossi 1995; Sass et al. 1993; Tay and Seah 1975), but no characteristic neurological or hematological signs of arsenism were detected in monkeys, dogs, or rats chronically exposed to arsenate or arsenite at doses of 0.7–2.8 mg As/kg/day (Byron et al. 1967; EPA 1980f; Heywood and Sortwell 1979). This may be because the studies were not conducted for a sufficient length of time, or because too few animals were used. Moreover, while there is good evidence that inorganic arsenic is carcinogenic in humans by both oral and inhalation routes, evidence of inorganic arsenic-induced carcinogenicity in animals is mostly negative, with the exception of studies in mice demonstrating transplacental carcinogenesis. For these reasons, quantitative dose-response data from animals are not judged to be reliable for determining levels of significant human exposure, and will be considered only briefly except when human data are lacking.

3.2.1 Inhalation Exposure

Most information on human inhalation exposure to arsenic derives from occupational settings such as smelters and chemical plants, where the predominant form of airborne arsenic is arsenic trioxide dust. One limitation to this type of study is that exposure data are usually difficult to obtain, especially from earlier time periods when exposure levels were higher than in recent years. This is further complicated by the fact that significant oral and dermal exposures are also likely to occur under these conditions and co exposure to other metals and chemicals is also common. Thus, studies of this type are, like virtually all epidemiological studies, subject to some limitations and uncertainties. Table 3-1 and Figure 3-1 summarize studies that provide the most reliable quantitative data on health effects in humans, along with several studies in animals exposed to arsenic trioxide and other inorganic arsenic compounds by the inhalation route. Data for DMA are shown in Table 3-2 and Figure 3-2. All exposure data are expressed as milligrams of arsenic (as the element) per cubic meter of air (mg As/m^3). These studies and others that provide useful qualitative information on health effects of inorganic and organic arsenicals are discussed below.

Table 3-1 Levels of Significant Exposure to Inorganic Arsenic - Inhalation

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/m³)	LOAEL Less Serious (mg/m³)	LOAEL Serious (mg/m³)	Reference Chemical Form	Comments
ACUTE EXPOSURE								
Immuno/ Lymphoret								
1	Mouse (CD-1)	3 hr		0.123 F	0.271 F (decreased pulmonary bactericidal activity and increased susceptibility to streptococcal infection)		Aranyi et al. 1985 As(+3)	
2	Mouse (CD-1)	5 d 3 hr/d		0.259 F	0.519 F (decreased pulmonary bactericidal activity and increased susceptibility to streptococcal infection)		Aranyi et al. 1985 As(+3)	
Developmental								
3	Mouse (CFLP)	Gd 9-12 4 hr/d		0.2	2.2 (10% decreased average fetal body weight)	21.6 (increased fetal deaths, skeletal malformations, and retarded growth)	Nagymajtenyi et al. 1985 As(+3)	
INTERMEDIATE EXPOSURE								
Death								
4	Rat (CD)	14 pmd- Gd 19 7 d/wk 6 hr/d				20 F (5/10 dams died)	Holson et al. 1999 As(+3)	
Systemic								
5	Rat (CD)	14 pmd- Gd 19 7 d/wk 6 hr/d	Resp	2 F	8 F (rales, dried red material around nose)		Holson et al. 1999 As(+3)	
			Bd Wt	2 F	8 F (decreased body weight gain during gestation)			

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Table 3-1 Levels of Significant Exposure to Inorganic Arsenic - Inhalation (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/m³)	LOAEL Less Serious (mg/m³)	LOAEL Serious (mg/m³)	Reference Chemical Form	Comments
6	Rat (CD)	14 pmd- Gd 19 7 d/wk 6 hr/d	Resp	0.9 F	8 F (rales)	20 F (labored breathing, gasping)	Holson et al. 1999 As(+3)	
			Gastro	8 F		20 F (gross gastrointestinal lesions)		
			Bd Wt	8 F		20 F (drastic decrease body weight)		
Immuno/ Lymphoret								
7	Mouse (CD-1)	4 wk 5 d/wk 3 hr/d		0.126 F	0.245 F (decreased pulmonary bactericidal activity)		Aranyi et al. 1985 As(+3)	
Reproductive								
8	Rat (CD)	14 pmd- Gd 19 7 d/wk 6 hr/d		8 F			Holson et al. 1999 As(+3)	
9	Rat (CD)	14 pmd- Gd 19 7 d/wk 6 hr/d		20 F			Holson et al. 1999 As(+3)	
Developmental								
10	Rat (CD)	14 pmd- Gd 19 7 d/wk 6 hr/d		8			Holson et al. 1999 As(+3)	

Table 3-1 Levels of Significant Exposure to Inorganic Arsenic - Inhalation (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/m³)	LOAEL Less Serious (mg/m³)	LOAEL Serious (mg/m³)	Reference Chemical Form	Comments
11	Rat (CD)	14 pmd- Gd 19 7 d/wk 6 hr/d		8		20 (marked increase in post-implantation loss and marked decrease in viable fetuses)	Holson et al. 1999 As(+3)	
CHRONIC EXPOSURE								
Systemic								
12	Human	23 yr (avg) (occup)	Cardio			0.36 M (increased incidence of vasospasticity and clinical Raynaud's phenomenon)	Lagerkvist et al. 1986 As(+3)	
13	Human	0.5-50 yr (occup)	Resp	0.613			Perry et al. 1948 As(+3)	
			Dermal		0.078 (mild pigmentation keratosis of skin)	0.613 (gross pigmentation with hyperkeratinization of exposed areas, wart formation)		
Neurological								
14	Human	28 yr (avg) (occup)			0.31 M (decreased nerve conduction velocity)		Lagerkvist and Zetterlund 1994 As(+3)	
Cancer								
15	Human	1- >30 yr (occup)				0.213 M (CEL: lung cancer)	Enterline et al. 1987a As(+3)	
16	Human	19.5 yr (avg) (occup)				0.069 M (CEL: lung cancer)	Enterline et al. 1987b As(+3)	

REC 5512

Table 3-1 Levels of Significant Exposure to Inorganic Arsenic - Inhalation (continued)

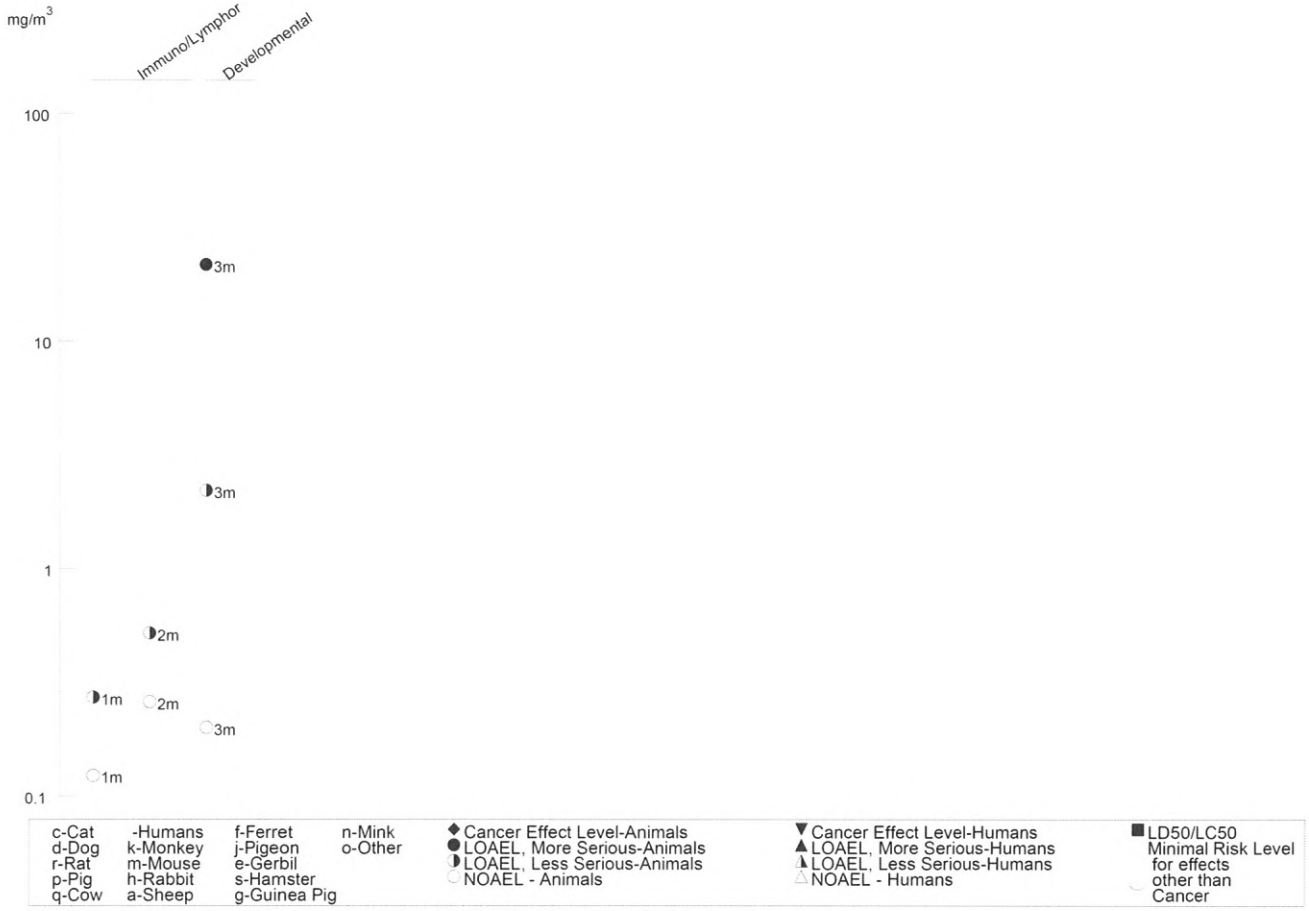
Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/m³)	LOAEL Less Serious (mg/m³)	LOAEL Serious (mg/m³)	Reference Chemical Form	Comments
17	Human	3 mo- >30 yr (occup)				0.2 M (CEL: lung cancer)	Jarup and Pershagen 1991 As(+3)	
18	Human	3 mo- >30 yr (occup)				0.05 M (CEL: lung cancer)	Jarup et al. 1989 As(+3)	
19	Human	1- >30 yr (occup)				0.38 M (CEL: lung cancer)	Lee-Feldstein 1986 As(+3)	
20	Human	>25 yr (occup)				0.29 M (CEL: lung cancer)	Lubin et al. 2000 As(+3)	
1	Human	14.8 yr (avg) (occup)				0.3 M (CEL: lung cancer)	Welch et al. 1982 As(+3)	

a The number corresponds to entries in Figure 3-1.

avg = average; Bd Wt = body weight; Cardio = cardiovascular; CEL = cancer effect level; d = day(s); F = female; Gastro = gastrointestinal; Gd = gestation day; hr = hour(s); Immuno/Lymphoret = immunological/lymphoreticular; LOAEL = lowest-observable-adverse-effect level; M = male; mo = month(s); NOAEL = no-observable-adverse-effect level; NS = not specified; occup = occupational; pmd = pre-mating day; Resp = respiratory; wk = week(s); yr = year(s)

Figure 3-1 Levels of Significant Exposure to Inorganic Arsenic - Inhalation

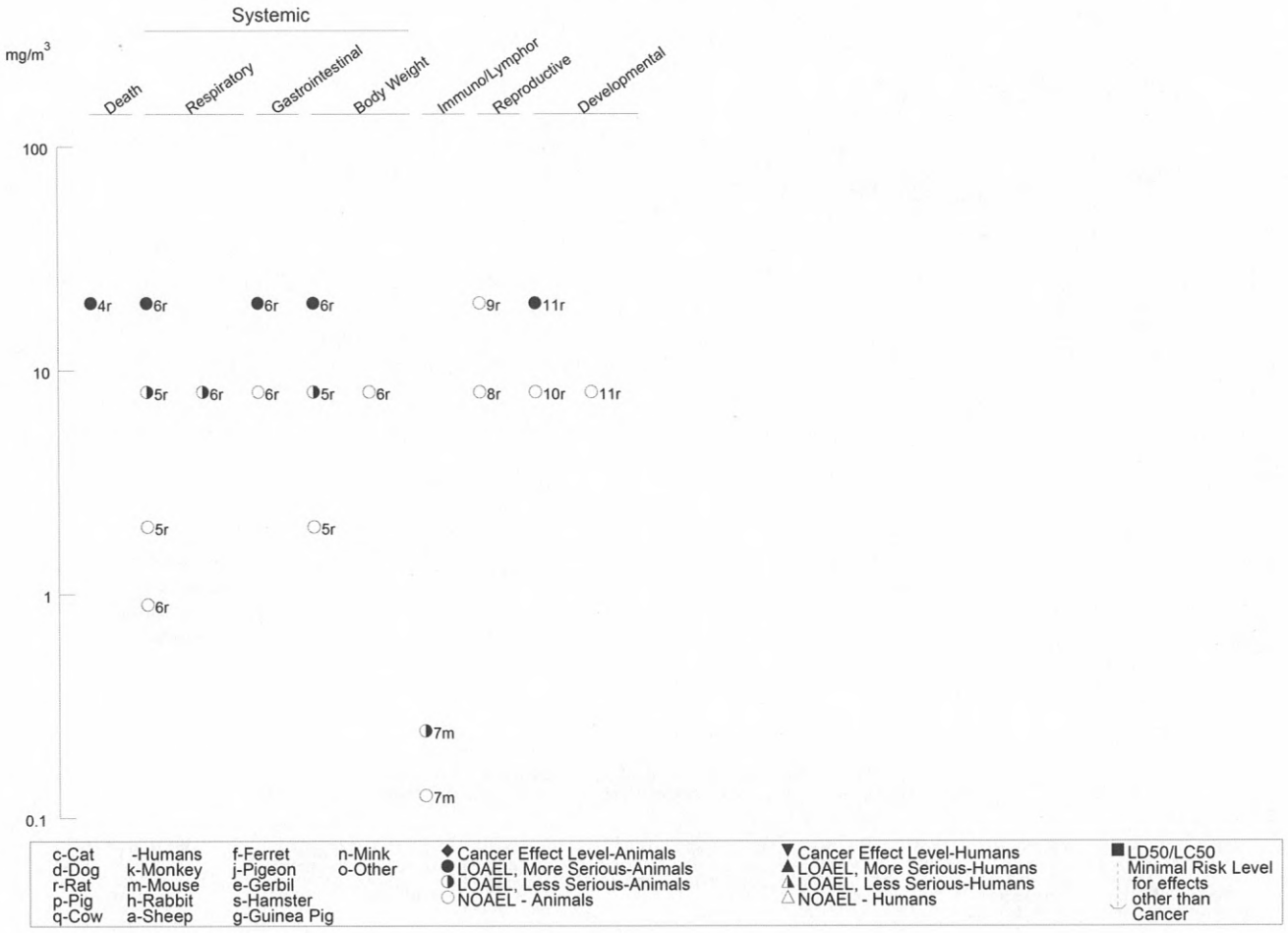
Acute (≤14 days)



REC 5514

Figure 3-1 Levels of Significant Exposure to Inorganic Arsenic - Inhalation *(Continued)*

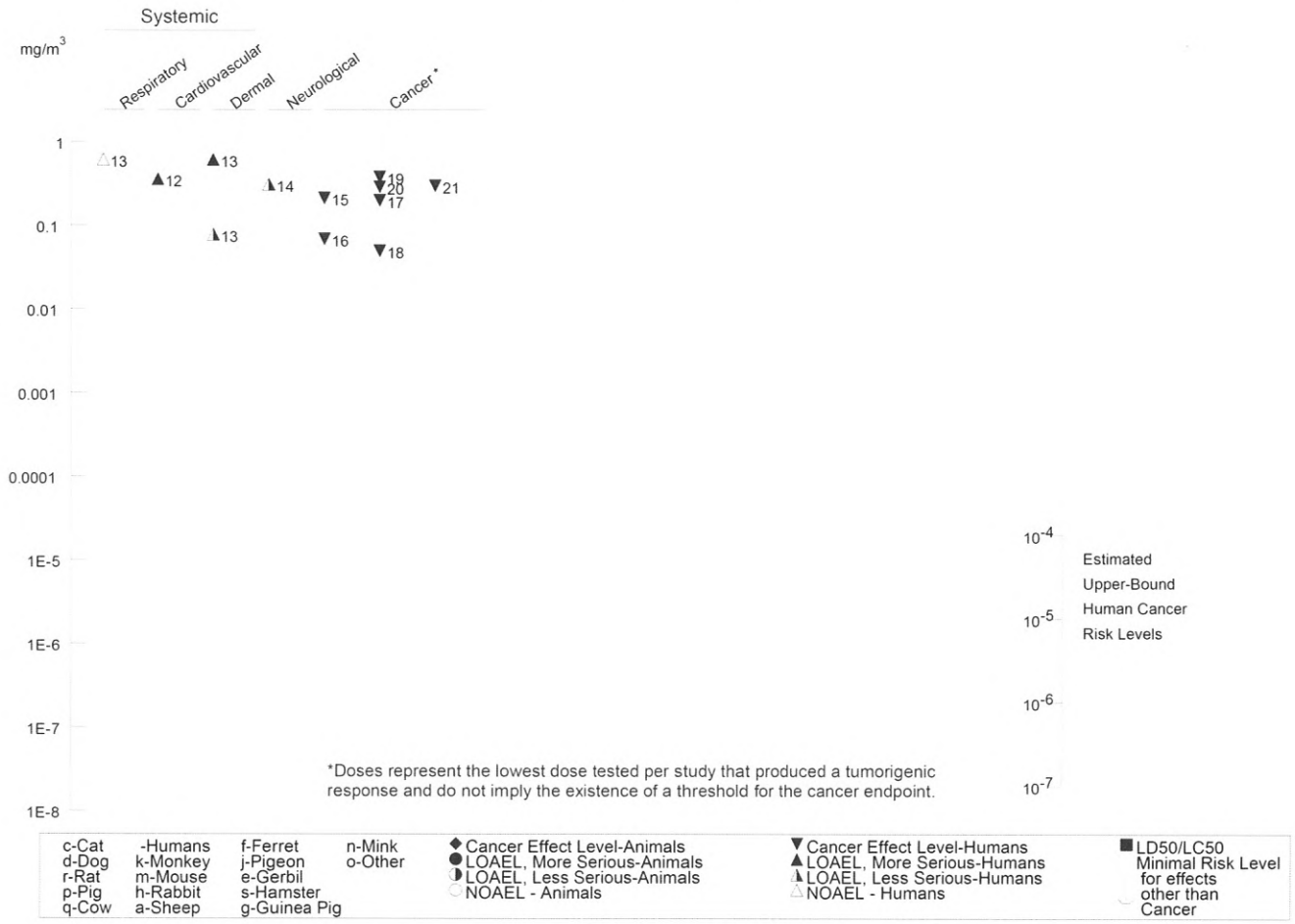
Intermediate (15-364 days)



REC 5515

Figure 3-1 Levels of Significant Exposure to Inorganic Arsenic - Inhalation *(Continued)*

Chronic (≥365 days)



REC 5516

Table 3-2 Levels of Significant Exposure to Dimethylarsinic Acid - Inhalation

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/m³)	LOAEL Less Serious (mg/m³)	LOAEL Serious (mg/m³)	Reference Chemical Form	Comments
ACUTE EXPOSURE								
Death								
1	Rat (Sherman)	2 hr				3900 F (LC50)	Stevens et al. 1979 DMA	
Systemic								
2	Rat (Sherman)	2 hr	Resp			4000 (respiratory distress)	Stevens et al. 1979 DMA	
			Gastro		4000 (diarrhea)			
			Dermal	4100	6900 F (erythematous lesions of ears and feet)			
			Ocular		4000 (eye encrustation)			
			Bd Wt		4000 (unspecified decrease in body weight)			
3	Mouse (Swiss-Webster)	5 min	Resp		3150 M (RD50)		Stevens et al. 1979 DMA	
INTERMEDIATE EXPOSURE								
Systemic								
4	Rat (Sprague-Dawley)	6 hr/d 5 d/wk 67-68 exposures	Resp	10	34 (intracytoplasmic eosinophilic globules in nasal turbinates)		Whitman 1994 DMA	
			Cardio	100				
			Gastro	100				
			Hemato	100				
			Hepatic	100				
			Renal	100				
			Endocr	100				
			Dermal	100				

Table 3-2 Levels of Significant Exposure to Dimethylarsinic Acid - Inhalation (continued)

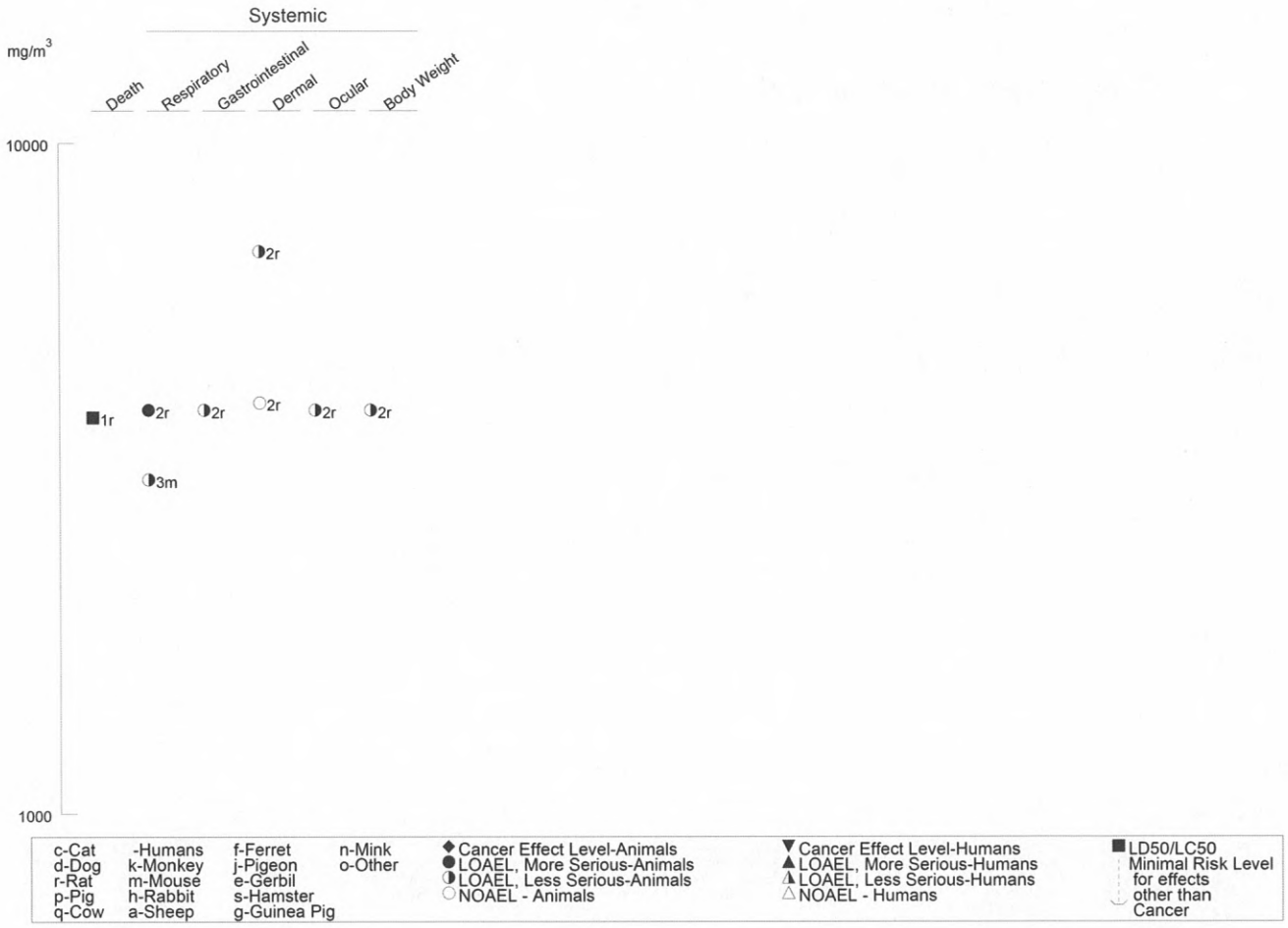
Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/m³)	LOAEL Less Serious (mg/m³)	LOAEL Serious (mg/m³)	Reference Chemical Form	Comments
			Bd Wt	100				

a The number corresponds to entries in Figure 3-2.

Bd Wt = body weight; Cardio = cardiovascular; d = day(s); DMA = dimethylarsinic acid; F = female; Gastro = gastrointestinal; Hemato = hematological; hr = hour(s); LC50 = lethal concentration, 50% kill; LOAEL = lowest-observable-adverse-effect level; M = male; min = minute(s); NOAEL = no-observable-adverse-effect level; RD50 = 50% decrease in respiration rate; Resp = respiratory; wk = week(s); yr = year(s)

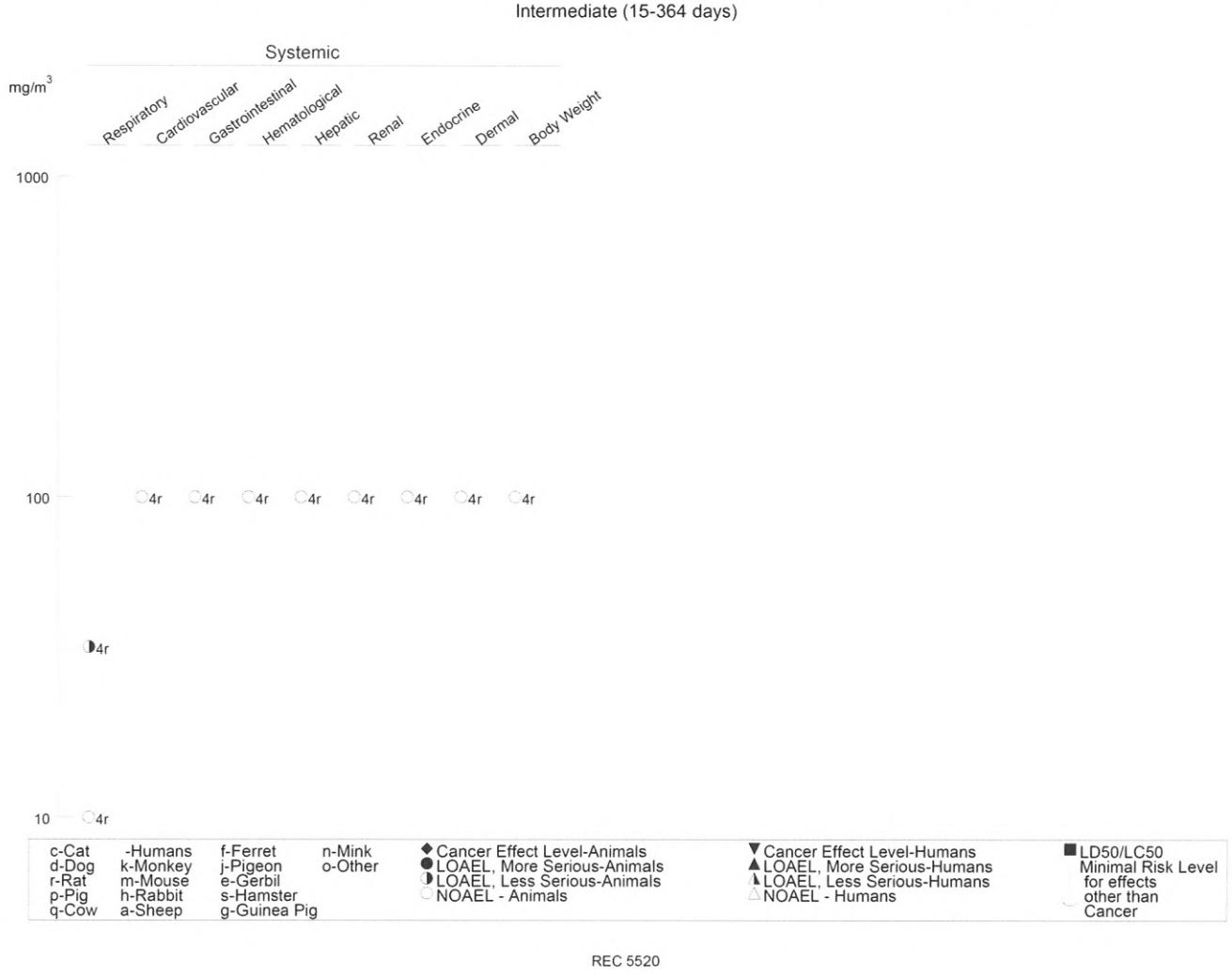
Figure 3-2 Levels of Significant Exposure to Dimethylarsinic Acid - Inhalation

Acute (≤14 days)



REC 5519

Figure 3-2 Levels of Significant Exposure to Dimethylarsinic Acid - Inhalation *(Continued)*



REC 5520

3.2.1.1 Death

Inorganic Arsenicals. Although there are many studies of humans exposed to arsenic in air, no cases of lethality from short-term exposure were located. This suggests that death is not likely to be of concern following acute exposure, even at the very high exposure levels (1–100 mg As/m^3) found previously in the workplace (e.g., Enterline and Marsh 1982; Järup et al. 1989; Lee-Feldstein 1986). Delayed lethality from chronic exposure attributable to increased risk of cardiovascular disease or lung cancer is discussed below in Sections 3.2.1.2 and 3.2.1.7, respectively. The only report of a lethal effect of inhaled inorganic arsenic in animals was a developmental toxicology study in which four of nine pregnant rats died, and one rat was euthanized in extremis, between days 12 and 19 of gestation after 30–35 days of exposure to an aerosol of arsenic trioxide at an exposure concentration of 20 mg As/m^3 (Holson et al. 1999). These animals exhibited severe hyperemia and plasma discharge into the intestinal lumen at autopsy. In this same study, there was 100% mortality in groups of 10 pregnant rats after 1 day of exposure to concentrations ≥100 mg/m^3 (76 mg As/m^3).

Organic Arsenicals. No studies were located regarding death in humans after inhalation exposure to organic arsenicals. A 2-hour LC_{50} of 3,900 mg DMA/m^3 was calculated for DMA in female rats (Stevens et al. 1979). This LC_{50} is shown in Table 3-2 and Figure 3-2. Male rats and mice of both sexes were less susceptible, with only a few deaths after 2-hour exposures as high as 6,900 mg DMA/m^3 in rats and 6,400 mg DMA/m^3 in mice (Stevens et al. 1979). The cause of death was not specified, but was probably due to lung injury (see Section 3.2.1.2). No deaths were observed among rats and mice exposed to DSMA (the disodium salt of MMA) at concentrations up to 6,100 mg DSMA/m^3 in rats and 6,900 mg DSMA/m^3 in mice (Stevens et al. 1979). Chamber atmospheres at these high concentrations were so dense that it was difficult to see the animals clearly. These data indicate that there is no significant risk of acute lethality from concentrations of DMA or MMA that might be encountered in the environment or the workplace.

3.2.1.2 Systemic Effects

The highest NOAEL values and all reliable LOAEL values for systemic effects from inhalation exposure to inorganic arsenicals in each species and duration category are recorded in Table 3-1 and plotted in Figure 3-1, while the corresponding data for DMA are shown in Table 3-2 and Figure 3-2.

Respiratory Effects.

Inorganic Arsenicals. Workers exposed to arsenic dusts in air often experience irritation to the mucous membranes of the nose and throat. This may lead to laryngitis, bronchitis, or rhinitis (Dunlap 1921; Morton and Caron 1989; Pinto and McGill 1953), and very high exposures (characteristic of workplace exposures in the past) can cause perforation of the nasal septum (Dunlap 1921; Pinto and McGill 1953; Sandstrom et al. 1989). Despite the known respiratory irritant effects of arsenic, there have been few systematic investigations of respiratory effects in humans exposed to arsenic. Perry et al. (1948) found no difference in chest x-rays or respiratory performance (vital capacity and exercise-tolerance tests) between unexposed and exposed workers in a cross-sectional study at a factory where sodium arsenite was prepared. The NOAEL of 0.613 mg As/m^3 for respiratory effects in this study is shown in Table 3-1 and plotted in Figure 3-1.

Increased mortality due to respiratory disease has been reported in some cohort mortality studies of arsenic-exposed workers, but no conclusive evidence of an association with arsenic has been produced. In studies of workers exposed to arsenic trioxide at the Anaconda copper smelter in Montana, mortality due to noncancer respiratory disease (e.g., emphysema) was significantly increased compared to the general population (Lee-Feldstein 1983; Lubin et al. 2000; Welch et al. 1982). However, the data were not adjusted for smoking (a well-known confounder for respiratory disease), and analysis of the data with respect to arsenic exposure level did not show a clear dose-response. Similarly, Enterline et al. (1995) found a significant excess of nonmalignant respiratory disease mortality in workers at the ASARCO copper smelter in Tacoma, Washington, but only a slight negative relation to cumulative arsenic exposure. Xuan et al. (1993) found an increase in the relative risk of mortality from pneumoconiosis associated with arsenic exposure in a cohort of tin miners in China. However, this finding was based on a small number of observations (n=32), a clear exposure-response relationship with arsenic was not established, and the miners experienced confounding exposures to dust (a known risk factor for pneumoconiosis) and to radon. These studies were all considered to be inconclusive as to the relationship between inhaled inorganic arsenic and respiratory disease.

Respiratory symptoms were observed in a study of developmental effects in rats. Pregnant female rats exposed to arsenic trioxide dust starting 14 days prior to mating and continuing through mating and gestation exhibited rales at 8 mg As/m^3 and labored breathing and gasping at 20 mg As/m^3, with no symptoms at 2 mg As/m^3 (Holson et al. 1999). The lungs were examined by gross necropsy and no lesions were found. Intratracheal instillation of arsenic trioxide (13 mg As/kg) or gallium arsenide (1.5–

52 mg As/kg) can cause marked irritation and hyperplasia in the lungs of rats and hamsters (Goering et al. 1988; Ohyama et al. 1988; Webb et al. 1986, 1987). Since this sort of response is produced by a number of respirable particulate materials, it is likely that the inflammatory response is not specifically due to the arsenic.

Organic Arsenicals. No studies were located regarding respiratory effects in humans exposed to organic arsenicals. Short-term exposure of rats and mice to high concentrations (≥4,000 mg/m^3) of DMA caused respiratory distress, and necropsy of animals that died revealed bright red lungs with dark spots (Stevens et al. 1979). Respiratory distress was also observed in rats and mice exposed to high levels (≥6,100 mg/m^3) of the disodium salt of MMA (Stevens et al. 1979), although none of the MMA-exposed animals died. Respiratory distress appears to be associated with inhalation of very high concentrations of organic arsenicals. In 5-minute whole-body plethysmography trials, DMA and the disodium salt of MMA had RD_{50} (concentration calculated to produce a 50% decrease in respiration rate) values of 3,150 and 1,540 mg/m^3, respectively (Stevens et al. 1979). Based on these RD_{50} values, neither DMA nor MMA is considered to be a potent respiratory irritant. At low concentrations of DMA (34 or 100 mg DMA/m^3), an increase in intracytoplasmic eosinophilic globules were found in the nasal turbinates of rats exposed to DMA 6 hours/day, 5 days/week for 67–68 exposures (Whitman 1994).

Cardiovascular Effects.

Inorganic Arsenicals. There is some evidence from epidemiological studies that inhaled inorganic arsenic can produce effects on the cardiovascular system. Cardiovascular effects following oral exposure to arsenic are well known (see Section 3.2.2.2). A cross-sectional study of workers exposed to an estimated time-weighted average of 0.36 mg As/m^3 (as arsenic trioxide) at the Ronnskar copper smelter in Sweden for an average of 23 years showed that smelter workers had significantly increased incidences of Raynaud's phenomenon (a peripheral vascular disease characterized by spasm of the digital arteries and numbness of the fingers) and showed increased vasospasticity (constriction of blood vessels) in response to cold when tested in the fingers (Lagerkvist et al. 1986). A follow-up study conducted 2–3 years later found that vasospasticity measurements in exposed workers had improved concurrent with a reduction in arsenic exposure levels, although symptoms of peripheral vascular effects (cold hands or feet, white fingers, numbness in fingers or feet) were still common (Lagerkvist et al. 1988). A cross-sectional study including 46 workers in Denmark with varying, unquantified occupational exposure to arsenic in different occupations found that systolic blood pressure was significantly increased in the arsenic workers (median=125 mmHg) compared with controls (median=117 mmHg) (Jensen and Hansen 1998). Diastolic

pressure was also increased in this study (77.9 vs. 74.7 mmHg), although the difference from controls was not statistically significant.

Cohort mortality studies of arsenic-exposed workers at the ASARCO copper smelter in Tacoma, Washington (Enterline et al. 1995), Anaconda copper smelter in Montana (Lee-Feldstein 1983; Welch et al. 1982), Ronnskar copper smelter in Sweden (Wall 1980), orchard workers in Washington state (Tollestrup et al. 1995), and tin miners in China (Qiao et al. 1997; Xuan et al. 1993) have all reported increased risk of mortality from cardiovascular disease, specifically ischemic heart disease and cerebrovascular disease, in the cohorts studied. However, none of these studies provided conclusive evidence that the observed increase in risk was due to arsenic exposure. The studies in the ASARCO and Anaconda copper smelter workers failed to find a clear dose-response relationship with arsenic (Enterline et al. 1995; Welch et al. 1982), while a follow-up study of the Ronnskar smelter workers not only found lack of a dose-response, but also that the risk of cardiovascular disease was no longer elevated in the cohort (Järup et al. 1989). The studies in orchard workers and tin miners were limited by confounding exposures to copper, lead, and radon, respectively (Qiao et al. 1997; Tollestrup et al. 1995). The risk of cardiovascular disease mortality in the tin miners not only showed no dose-response relationship with arsenic exposure, but was positively associated with radon exposure, suggesting that radon may have been responsible for the increased cardiovascular risk in this cohort (Xuan et al. 1993).

The LOAEL for Raynaud's phenomenon and vasospasticity identified by Lagerkvist et al. (1986) is shown in Table 3-1 and Figure 3-1. No studies were located regarding cardiovascular effects in animals after inhalation exposure to inorganic arsenic.

Organic Arsenicals. No studies were located regarding cardiovascular effects in humans after inhalation exposure to organic arsenicals. No histological alterations were observed in the hearts of rats exposed to 100 mg DMA/m^3 for 67–68 exposures (Whitman 1994).

Gastrointestinal Effects.

Inorganic Arsenicals. Several case studies have reported nausea, vomiting, and diarrhea in workers with acute arsenic poisoning following occupational inhalation exposure (Beckett et al. 1986; Bolla-Wilson and Bleecker 1987; Ide and Bullough 1988; Morton and Caron 1989; Pinto and McGill 1953). Although gastrointestinal effects are not typically associated with arsenic poisoning by inhalation (Pinto and McGill 1953), such effects are a common feature of oral ingestion of high doses of arsenic (see Section 3.2.2.2),

and it is possible that mucociliary transport of arsenic dust from the lungs to the gut could be responsible for the effects in these cases. Exposure levels were not reliably estimated for any of these cases.

The only report of gastrointestinal effects of inhaled inorganic arsenic in animals was a developmental toxicology study in which four of nine pregnant rats died, and one rat was euthanized *in extremis*, between days 12 and 19 of gestation after 30–35 days of exposure to an aerosol of arsenic trioxide at an exposure concentration of 20 mg As/m^3 (Holson et al. 1999). These animals exhibited severe hyperemia and plasma discharge into the intestinal lumen at autopsy. Exposure to 8 mg As/m^3 did not produce gross gastrointestinal lesions.

Organic Arsenicals. Data regarding gastrointestinal effects in people exposed to organic arsenic in the air are limited. The frequency of gastrointestinal complaints was no higher than controls in workers exposed to arsanilic acid (i.e., 4-aminophenyl arsonic acid) at mean concentrations up to 0.17 mg/m^3 in a chemical factory (Watrous and McCaughey 1945). However, this sort of data might easily be biased by workers who chose not to complain about minor symptoms, so no conclusion can be reached. Rats and mice exposed to very high levels (above 3,000 mg/m^3) of MMA (disodium salt) or DMA experienced diarrhea (Stevens et al. 1979). The diarrhea could be due to transport of inhaled particulate material from the lungs to the gastrointestinal system or to direct ingestion of the compound (e.g., from grooming of the fur). No gastrointestinal effects were observed in rats repeatedly exposed to 100 mg DMA/m^3 6 hours/day, 5 days/week for 67–68 exposures (Whitman 1994).

Hematological Effects.

Inorganic Arsenicals. Although anemia is a common feature of arsenic poisoning following oral exposure in humans (see Section 3.2.2.2), case studies of workers with arsenic poisoning from occupational inhalation exposure reported no effects on red blood cell count (Beckett et al. 1986; Bolla-Wilson and Bleecker 1987; Ide and Bullough 1988; Morton and Caron 1989). The reason for this apparent route specificity is not clear, but might simply be related to dose. No studies were located regarding hematological effects in animals after inhalation exposure to inorganic arsenicals.

Organic Arsenicals. No effect on levels of hemoglobin, red cells, or white cells was detected in the blood of manufacturing workers (323 counts in 35 workers) exposed to airborne arsanilic acid dusts at a mean concentration of 0.17 mg/m^3 in the workplace (Watrous and McCaughey 1945). Controls were an unspecified number of unexposed manufacturing workers with 221 complete blood counts. No

hematological alterations were observed in rats exposed to 100 mg DMA/m^3 for an intermediate duration (Whitman 1994).

Musculoskeletal Effects.

Inorganic Arsenicals. Few data were located regarding musculoskeletal effects associated with inhalation exposure to inorganic arsenic, and none to suggest the existence of any such effects. Electromyographic examination of the calves and feet showed no differences between control and arsenic-exposed workers in a cross-sectional study of workers at the Ronnskar copper smelter in Sweden (Blom et al. 1985). No studies were located regarding musculoskeletal effects in animals after inhalation exposure to inorganic arsenicals.

Organic Arsenicals. No studies were located regarding musculoskeletal effects in humans or animals after inhalation exposure to organic arsenicals.

Hepatic Effects.

Inorganic Arsenicals. There is no evidence that inhaled inorganic arsenic produces effects on the liver, although few data are available. Case studies of workers with inhalation arsenic poisoning that included liver function tests did not find any evidence of hepatic dysfunction (Bolla-Wilson and Bleecker 1987; Ide and Bullough 1988). No studies were located regarding hepatic effects in animals after inhalation exposure to inorganic arsenicals.

Organic Arsenicals. No studies were located regarding hepatic effects in humans after inhalation exposure to organic arsenicals. No histological alterations were observed in the livers of rats exposed to 100 mg DMA/m^3 for 67–68 exposures (Whitman 1994).

Renal Effects.

Inorganic Arsenicals. The limited data available do not suggest any relationship between inhalation of inorganic arsenic and kidney effects. A cross-sectional study of renal function parameters in glass factory workers exposed to arsenic (concentrations unknown) found no meaningful differences from controls in urinary levels of several proteins (albumin, retinol binding protein, β_2-microglobulin, brush-border antigen) used as markers of glomerular damage or tubular cell exfoliation (Foà et al. 1987). Routine

clinical urinalysis was normal when included in case studies of workers with inhalation arsenic poisoning (Ide and Bullough 1988; Morton and Caron 1989). No studies were located regarding renal effects in animals after inhalation exposure to inorganic arsenicals.

Organic Arsenicals. No studies were located regarding renal effects in humans after inhalation exposure to organic arsenicals. No renal effects were reported in rats exposed to 100 mg DMA/m^3 6 hours/day, 5 days/week for 67–68 exposures (Whitman 1994).

Dermal Effects.

Inorganic Arsenicals. Dermatitis has frequently been observed in industrial workers exposed to inorganic arsenic in the air, with the highest rates occurring in the workers with the greatest arsenic exposure (Cöl et al. 1999; Dunlap 1921; Holmqvist 1951; Lagerkvist et al. 1986; Pinto and McGill 1953). Limited quantitative information is available regarding the exposure levels that produce dermatitis, and the high likelihood of co-exposure by the dermal route makes dose-response analysis difficult. A cross-sectional study of workers at a factory where sodium arsenite was prepared found that workers with the highest arsenic exposure (mean air levels ranging from 0.384 to 1.034 mg As/m^3 and estimated to average 0.613 mg As/m^3) tended to be grossly pigmented with hyperkeratinization of exposed skin and to have multiple warts (Perry et al. 1948). In the same study, workers with lower arsenic exposure (estimated to average 0.078 mg As/m^3) were much less affected, but still had a higher incidence of pigmentation keratosis than controls. LOAEL values identified by Perry et al. (1948) and Mohamed (1998) are shown in Table 3-1 and Figure 3-1. NOAEL values for dermal irritation have not been identified. Dermal effects (hyperkeratoses, hyperpigmentation) are also very common in people exposed to inorganic arsenic by the oral route (see Section 3.2.2.2). No studies were located on dermal effects in animals after inhalation exposure to inorganic arsenicals.

Organic Arsenicals. Data regarding dermal effects in people exposed to organic arsenic in the air are limited. Complaints of keratosis were roughly 2-fold higher than unexposed controls in female packaging workers exposed to arsanilic acid at an average concentration of 0.065 mg/m^3 and in male manufacturing workers exposed to an average concentration of 0.17 mg/m^3 in a chemical factory (Watrous and McCaughey 1945). Limitations in study methodology (e.g., alternate sources of effects were not investigated, workers might choose not to report minor complaints to company officials) make the reliability of this observation uncertain. Female rats exposed to DMA at 6,900 mg/m^3 developed erythematous lesions on the feet and ears (Stevens et al. 1979); these lesions did not develop in females

exposed at lower concentrations (4,100 mg/m^3) or males. It seems likely that these effects were due to direct irritation from dermal contact with the dust. No dermal effects were observed in rats repeatedly exposed to lower levels of DMA (100 mg/m^3) (Whitman 1994).

Ocular Effects.

Inorganic Arsenicals. Chemical conjunctivitis, characterized by redness, swelling, and pain, has been observed in workers exposed to arsenic dusts in air, usually accompanied by facial dermatitis (Dunlap 1921; Pinto and McGill 1953). No information was located regarding air levels of arsenic that produce this effect. No studies were located on ocular effects in animals after inhalation exposure to inorganic arsenicals.

Organic Arsenicals. No studies were located on ocular effects in humans after inhalation exposure to organic arsenicals. Rats and mice exposed to high concentrations of DMA (≥4,000 mg/m^3) developed an encrustation around the eyes (Stevens et al. 1979). It seems likely that these effects were due to direct irritation from ocular contact with the dust.

Body Weight Effects.

Inorganic Arsenicals. No studies were located on body weight effects in humans after inhalation exposure to inorganic arsenicals. Female rats exposed to arsenic trioxide dust starting 14 days before mating and continuing through mating and gestation showed a marked decrease in body weight and food consumption at 20 mg As/m^3 (preliminary study) and a smaller decrease at 8 mg As/m^3 (definitive study), with no effect at 2 mg As/m^3 (Holson et al. 1999).

Organic Arsenicals. No studies were located on body weight effects in humans after inhalation exposure to organic arsenicals. Rats and mice exposed to high concentrations of DMA (≥4,000 mg/m^3) for 2 hours had an unspecified decrease in body weight gain during the subsequent 14 days (Stevens et al. 1979). No alterations in body weight gain were observed in rats exposed to 100 mg DMA/m^3 for 67–68 exposures (Whitman 1994).

3.2.1.3 Immunological and Lymphoreticular Effects

Inorganic Arsenicals. A single study was located regarding the immunological and lymphoreticular effects of inhaled inorganic arsenic in humans. Bencko et al. (1988) detected no abnormalities in serum levels of immunoglobins in 47 workers exposed to arsenic (exposure levels not measured) in a coal-burning power plant. However, serum levels of other proteins such as transferrin, orosomucoid, and ceruloplasmin were significantly elevated compared to levels in a group of 27 workers from a different plant in which the arsenic content in the coal was 10 times lower. The investigators suggested that the increased levels of ceruloplasmin might be related to higher cancer mortality rates found among these workers.

The immune effects of inhaled arsenic in animals were studied by Aranyi et al. (1985). Female mice exposed to arsenic trioxide aerosol for 3 hours showed a concentration-related decrease in pulmonary bactericidal activity (presumably as a result of injury to alveolar macrophages) and a corresponding concentration-related increase in susceptibility to introduced respiratory bacterial pathogens. Similar results were found when the exposure was repeated over 1- and 4-week periods. The NOAEL and LOAEL values for this study are shown in Table 3-1 and Figure 3-1.

Intratracheal studies in animals offer some support for an immune effect of inhaled inorganic arsenic. Decreases in humoral response to antigens and in several complement proteins were noted in mice given an intratracheal dose of 5.7 mg As/kg as sodium arsenite (Sikorski et al. 1989), although these changes were not accompanied by any decrease in resistance to bacterial or tumor cell challenges. Animals given an intratracheal dose of GaAs (25 mg As/kg or higher) also displayed a variety of changes in numerous immunological end points (some increased, some decreased) (Burns and Munson 1993; Sikorski et al. 1989). Whether these effects were due to a direct effect on the immune system or were secondary to the inflammatory effect of GaAs on the lung (see Section 3.2.1.2, above) is uncertain.

Organic Arsenicals. No studies were located regarding immunological and lymphoreticular effects in humans or animals after inhalation exposure to organic arsenicals.

3.2.1.4 Neurological Effects

Inorganic Arsenicals. There is evidence from epidemiological studies that inhaled inorganic arsenic can produce neurological effects. A study by Gerr et al. (2000) reported an elevated incidence of peripheral neuropathy in subjects who lived near an arsenic-using pesticide plant (13/85=15.3%; odds ratio

[OR]=5.1, p=0.004), relative to subjects who lived farther from the plant (4/118=3.4%). Concentrations of arsenic in soil and house dust were elevated (~30–300 µg As/g) for residences near the plant, according to 1993–1995 monitoring data. Studies of copper smelter workers at the ASARCO smelter in Tacoma, Washington (Feldman et al. 1979), a power station in Slovakia (Buchancová et al. 1998), and the Ronnskar smelter in Sweden (Blom et al. 1985; Lagerkvist and Zetterlund 1994) have demonstrated peripheral neurological effects in workers associated with arsenic trioxide exposure. At the ASARCO smelter, the prevalence of clinically diagnosed peripheral neuropathy was markedly higher in arsenic-exposed workers (26/61=43%) than controls (4/33=12%), and although the difference in mean nerve conduction velocities (NCV) was not statistically significant, mean peroneal motor NCV was lower in arsenic-exposed workers than controls and all 12 cases of abnormally low NCV occurred in the arsenic group (Feldman et al. 1979). In the study of 70 workers in Slovakia, the investigators described 16 cases of arsenic intoxication. Among these, 13 had signs and symptoms of sensory and motor polyneuropathy on both upper and lower extremities, 10 were diagnosed with pseudoneurasthenic syndrome, and 6 suffered from toxic encephalopathy (Buchancová et al. 1998). The average length of exposure was 22.3 years (SD ±8.4 years) and the average arsenic exposure in inhaled air ranged from 4.6 to 142.7 µg/m^3. Similar results were observed at the Ronnskar smelter, where Blom et al. (1985) reported significantly increased prevalence of workers with abnormally low NCV in the exposed group, and lower, but not statistically significant, mean NCV in five peripheral nerves. A follow-up study on the Ronnskar workers 5 years later found that the prevalence of abnormally low NCV remained significantly increased in the exposed workers, but that the decrease in mean NCV was now also statistically significant in the tibial (motor) and sural (sensory) nerves (Lagerkvist and Zetterlund 1994). Blood lead was monitored in this study as a potential confounder, but levels were low and not considered likely by the researchers to have had any influence on the results. The follow-up Ronnskar study provided enough information to estimate that mean arsenic exposure was 0.31 mg As/m^3 and lasted an average of 28 years in the exposed group, and this LOAEL is shown in Table 3-1 and Figure 3-1.

The literature also contains several case studies of workers with inhalation arsenic poisoning who developed neurological symptoms. Although these studies do not provide reliable information on exposure levels or conclusive evidence that the observed effects were related to arsenic, the findings are suggestive. Symptoms in these cases included not only indicators of peripheral neuropathy (numbness, loss of reflexes, muscle weakness, tremors) (Ide and Bullough 1988; Morton and Caron 1989), but also frank encephalopathy (hallucinations, agitation, emotional lability, memory loss) (Beckett et al. 1986; Bolla-Wilson and Bleecker 1987; Morton and Caron 1989). Both peripheral neuropathy and encephalopathy are associated with oral exposure to inorganic arsenic (see Section 3.2.2.4).

The possible association between arsenic in air and neurological effects in children has also been examined. A study by Bencko et al. (1977) reported that children of approximately 10 years of age (n=56) living near a power plant burning coal of high arsenic content showed significant hearing losses (increased threshold) compared to a control group of children (n=51) living outside the polluted area (Bencko et al. 1977). The effect was most marked at low frequencies. The precise site affected within the auditory pathway was not determined and could have been in the periphery, centrally-located, or both. A small study of children in Mexico reported a significant negative correlation between tests of verbal IQ and urinary arsenic in children (n=41) living in an urban area near a smelter complex (Calderón et al. 2001). Exposure concentrations were not available in either study.

No studies were located regarding neurological effects in animals after inhalation exposure to inorganic arsenicals. Mice given a single intratracheal dose of 200 mg/kg of GaAs displayed a decrease in overall activity 6–8 hours later, but no additional neurological evaluations were conducted on these animals (Burns and Munson 1993).

Organic Arsenicals. Data regarding neurological effects in people exposed to organic arsenic in the air are limited to a single study. The frequency of central nervous system complaints was no higher than controls in workers at a chemical factory exposed to arsanilic acid at mean concentrations up to 0.17 mg/m^3 (Watrous and McCaughey 1945). Although peripheral nerve complaints were higher in arsenic packaging workers (mean exposure=0.065 mg/m^3) than in unexposed controls, this was not the case in manufacturing workers with higher arsenic exposure (mean=0.17 mg/m^3). This suggests that the effects on the peripheral nerves in the exposed packaging workers were not due to arsenic. The reliability of these data is limited by shortcomings in the study methodology (e.g., the data might easily be biased by workers who chose not to complain about minor symptoms). No studies were located regarding neurological effects in animals after inhalation exposure to organic arsenicals.

3.2.1.5 Reproductive Effects

Inorganic Arsenicals. No studies were located regarding reproductive effects in humans after inhalation exposure to inorganic arsenicals. Reproductive performance was evaluated in female rats exposed to 0.08–20 mg As/m^3 (preliminary study) or 0.2–8 mg As/m^3 (definitive study) as As_2O_3 6 hours daily from 14 days prior to mating through gestation day 19 (Holson et al. 1999). No changes occurred in the precoital interval (time to mating), mating index (percentage of rats mated), or fertility index (percentage

of matings resulting in pregnancy). The NOAEL values for this study are shown in Table 3-1 and Figure 3-1.

Organic Arsenicals. No studies were located regarding reproductive effects in humans or animals after inhalation exposure to organic arsenicals.

3.2.1.6 Developmental Effects

Inorganic Arsenicals. Developmental effects associated with occupational and environmental exposure to airborne arsenic have been investigated in a series of studies at the Ronnskar copper smelter in northern Sweden (Nordström et al. 1978a, 1978b, 1979a, 1979b). In comparison to a northern Swedish reference population, female employees of the smelter had a significantly increased incidence of spontaneous abortion (Nordström et al. 1979a), and their children had a significantly increased incidence of congenital malformations (Nordström et al. 1979b) and significantly decreased average birth weight (Nordström et al. 1978a). Increased incidence of spontaneous abortion and decreased average birth weight of children were also found in populations living in close proximity to the smelter (Nordström et al. 1978a, 1978b, 1979b). While these data are suggestive of developmental effects associated with occupational and environmental exposure from the smelter, the reported effects are not large, the analyses include only limited consideration of potential confounders (e.g., smoking), and there are no data relating the apparent effects specifically to arsenic exposure.

Ihrig et al. (1998) conducted a case-control study of stillbirths in the vicinity of a Texas arsenic pesticide factory that included estimation of environmental arsenic exposures using atmospheric dispersion modeling and multiple regression analysis considering arsenic exposure, race/ethnicity, maternal age, median income, and parity as explanatory variables. There was a statistically significant increase in the risk of stillbirth in the highest exposure category (>100 ng As/m^3, midpoint=682 ng/m^3). Further analysis showed that this increase in risk was limited to people of Hispanic descent, who the researchers speculated may be an especially sensitive population due to a genetic impairment in folate metabolism. Interpretation of this study is limited by small numbers of cases and controls in the high exposure group, lack of data on smoking, potential confounding exposures to other chemicals from the factory, and failure to take into account previous years of deposition in the exposure estimates.

Arsenic has been shown to produce developmental effects by inhalation exposure in laboratory animals, although it is unclear whether or not the effects occur only at maternally toxic doses. Mice exposed to

22 mg As/m^3 (as As_2O_3) for 4 hours on days 9–12 of gestation had serious developmental effects (significant increases in the percentage of dead fetuses, skeletal malformations, and the number of fetuses with retarded growth), while those exposed to 2.2 mg As/m^3 had only a 10% decrease in average fetal body weight, and those exposed to 0.20 mg As/m^3 had no effects (Nagymajtényi et al. 1985). The study was limited by failure to quantify malformations on a litter basis, discuss the nature and severity of the observed malformations, or report on the occurrence of maternal effects. No increases in fetal resorptions, fetal mortality, or malformations, and no decreases in fetal body weight occurred when rats were exposed to 0.2–8 mg As/m^3 (as As_2O_3), 6 hours daily from 14 days prior to mating through gestation day 19 (Holson et al. 1999). At the 8 mg/m^3 exposure level, toxicity was observed in the dams, including rales, a dried red exudate at the nose, and lower gains in net body weight than controls. In a preliminary dose-range study, there was a marked significant increase in postimplantation loss (primarily early resorptions) and consequent marked significant decrease in viable fetuses per litter at 20 mg As/m^3, a concentration that also produced severe maternal effects including mortality (Holson et al. 1999).

The NOAEL and LOAEL values for increased risk of stillbirth in humans identified by Ihrig et al. (1998) and those for developmental effects in rodents found by Nagymajtényi et al. (1985) and Holson et al. (1999) are shown in Table 3-1 and Figure 3-1.

Organic Arsenicals. No studies were located regarding developmental effects in humans or animals after inhalation exposure to organic arsenicals.

3.2.1.7 Cancer

Inorganic Arsenicals. There is convincing evidence from a large number of epidemiological studies that inhalation exposure to inorganic arsenic increases the risk of lung cancer. Most studies involved workers exposed primarily to arsenic trioxide dust in air at copper smelters (Axelson et al. 1978; Brown and Chu 1982, 1983a, 1983b; Enterline and Marsh 1982; Enterline et al. 1987a, 1987b, 1995; Ferreccio et al. 1996; Järup and Pershagen 1991; Järup et al. 1989; Lee and Fraumeni 1969; Lee-Feldstein 1983, 1986; Lubin et al. 2000; Mazumdar et al. 1989; Pinto et al. 1977, 1978; Sandstrom et al. 1989; Viren and Silvers 1999; Wall 1980; Welch et al. 1982) and mines (Liu and Chen 1996; Qiao et al. 1997; Taylor et al. 1989; Xuan et al. 1993), but increased incidence of lung cancer has also been observed at chemical plants where exposure was primarily to arsenate (Bulbulyan et al. 1996; Mabuchi et al. 1979; Ott et al. 1974; Sobel et al. 1988). In addition, several studies suggest that residents living near smelters or arsenical chemical plants may also have increased risk of lung cancer (Brown et al. 1984; Cordier et al. 1983; Matanoski et

al. 1981; Pershagen 1985), although the increases are small and are not clearly detectable in all cases (e.g., Frost et al. 1987). The strongest evidence that arsenic is responsible for the observed lung cancer comes from quantitative dose-response data relating specific arsenic exposure levels to lung cancer risk. These data are available for arsenic-exposed workers at the ASARCO copper smelter in Tacoma, Washington (Enterline and Marsh 1982; Enterline et al. 1987a, 1995; Mazumdar et al. 1989), the Anaconda copper smelter in Montana (Lee-Feldstein 1986; Welch et al. 1982), eight other U.S. copper smelters (Enterline et al. 1987b), and the Ronnskar copper smelter in Sweden (Järup and Pershagen 1991; Järup et al. 1989). A common limitation of these studies is confounding exposure to other chemicals, such as sulfur dioxide, and cigarette smoking.

Enterline and Marsh (1982) reported a significant increase in respiratory cancer mortality (standard mortality ratio [SMR]=189.4) based on 104 observed respiratory cancer deaths and only 54.9 expected over the years 1941–1976 in a cohort of 2,802 male workers employed for ≥1 year between 1940 and 1964 at the ASARCO smelter. When the cohort was separated into low and high arsenic exposure groups, with mean estimated time-weighted average arsenic exposures of 0.054 and 0.157 mg As/m^3, respectively (based on work history, historical urinary arsenic measurements, and an experimentally derived relationship between urinary and inhaled arsenic), respiratory cancer mortality was significantly increased in both groups in a concentration-related fashion (SMR=227.7 and 291.4 in the low and high groups, respectively). Enterline et al. (1987a) re-analyzed these data using improved exposure estimates that incorporated historical measurements of arsenic in the ambient air and personal breathing zone of workers. Respiratory cancer mortality was significantly increased in a concentration-related fashion in the low (SMR=213.0), medium (SMR=312.1), and high (SMR=340.9) arsenic exposure groups, which had mean estimated time-weighted average arsenic exposures of 0.213, 0.564, and 1.487 mg As/m^3, respectively. An alternative analysis of these data by Mazumdar et al. (1989) produced similar results. Enterline et al. (1995) extended the mortality follow-up from 1976 to 1986, but reported findings similar to the earlier study in a less thorough analysis. The CEL from Enterline et al. (1987a), the most complete analysis of the ASARCO cohort with the best exposure estimates, is presented in Table 3-1 and Figure 3-1.

Respiratory cancer mortality was significantly increased (SMR=285) based on 302 observed respiratory deaths between 1938 and 1977 in a cohort of 8,045 white male workers employed for at least 1 year between 1938 and 1956 at the Anaconda smelter (Lee-Feldstein 1986). When workers were categorized according to cumulative arsenic exposure and date of hire, lung cancer mortality was significantly increased in all groups hired between 1925 and 1947. Workers in the lowest cumulative exposure group

(<10 mg-mo/m^3) were reported to have had <2 years of exposure at an average arsenic concentration of 0.38 mg/m^3. An alternative analysis of a subset of the Anaconda cohort (n=1,800, including all 277 employees with heavy arsenic exposure and 20% of the others) that included information on smoking and other occupational exposures was performed by Welch et al. (1982). This analysis showed that lung cancer mortality increased with increasing time-weighted average arsenic exposure, with a small nonsignificant increase in the low group (SMR=138) exposed to 0.05 mg/m^3 and significant increases in the medium (SMR=303), high (SMR=375), and very high (SMR=704) groups exposed to 0.3, 2.75, and 5.0 mg/m^3, respectively. Cohort members were more likely to be smokers than U.S. white males, but smoking did not differ among the arsenic exposure groups. Exposure-response analysis of smokers was similar to the analysis based on the full subcohort, while analysis of nonsmokers (limited by small group sizes) also showed a similar pattern, but with lower SMRs. In a followup analysis of the same cohort, Lubin et al. (2000) re-weighted the exposure concentrations based on duration and time of exposure and re-evaluated the effects of exposure. Relative risks for respiratory cancer increased with increasing duration in each arsenic exposure area (light, medium, and heavy) after adjustment for duration in the other two exposure areas. SMRs were significantly elevated following exposure to 0.58 mg/m^3 (medium; SMR=3.01, 95% CI=2.0–4.6) or 11.3 mg/m^3 (high; SMR=3.68, 95% CI=2.1–6.4) for 10 or more years, and following exposure to 0.29 mg/m^3 (low; SMR=1.86, 95% CI=1.2–2.9) for 25 or more years. The CELs from the analyses of the Anaconda cohort are presented in Table 3-1 and Figure 3-1.

Enterline et al. (1987b) studied the mortality experience from 1949 to 1980 of a cohort of 6,078 white males who had worked for 3 years or more between 1946 and 1976 at one of eight U.S. copper smelters in Arizona, Utah, Tennessee, and Nevada. Lung cancer mortality was significantly increased only in the Utah smelter (SMR=226.7), which had the highest average arsenic exposure concentration (0.069 mg/m^3 vs. 0.007–0.013 mg/m^3 in the other smelters) and also contributed the largest number of cohort members (n=2,288 vs. 189–965 from the other smelters). A nested case-control study showed that arsenic exposure and cigarette smoking were significant risk factors for lung cancer in the smelter workers. Smoking was lower in the Utah smelter workers than in the other smelter workers, but still higher than in the referent Utah population, suggesting that the risk attributable to arsenic in this study population is somewhat lower than indicated by the SMR reported above. The CEL from this study is presented in Table 3-1 and Figure 3-1.

Järup et al. (1989) reported significantly increased lung cancer mortality (SMR=372, 95% confidence interval [CI]=304–450) based on 106 lung cancer deaths in a cohort of 3,916 male workers employed for ≥3 months between 1928 and 1967 at the Ronnskar smelter and followed for mortality through 1981.

Workers were separated into low, medium, and high arsenic exposure groups with mean time-weighted average exposure estimates of 0.05, 0.2, and 0.4 mg/m^3, respectively. Lung cancer mortality was significantly increased in all three exposure groups in a concentration-related fashion (SMR=201, 353, and 480, respectively). A nested case-control analysis of 102 lung cancer cases and 190 controls from the cohort showed that lung cancer risk increased with increasing arsenic exposure in nonsmokers, light smokers, and heavy smokers (Järup and Pershagen 1991). The results demonstrated that arsenic is a risk factor for lung cancer in the smelter workers, but also suggested a greater-than-additive interaction between smoking and arsenic exposure. In this analysis, in contrast to the cohort study, lung cancer risk due to arsenic was increased only in the higher arsenic-exposure groups. Potential explanations for this difference between the cohort and case-control analyses include a higher proportion of smokers in the smelter workers than in the regional referent population in the cohort study, and limited power to detect increased risk in the case-control study due to small group sizes in the dose-response analysis. The CELs from both the cohort and case-control studies are presented in Table 3-1 and Figure 3-1.

Several researchers have examined the histological cell types of lung cancer (epidermoid carcinoma, small cell carcinoma, adenocarcinoma) in arsenic-exposed workers (e.g., Axelson et al. 1978; Newman et al. 1976; Pershagen et al. 1987; Qiao et al. 1997; Wicks et al. 1981). Although the incidence of the various cell types varied from population to population, all studies found an increase in several tumor types. This indicates that arsenic does not specifically increase the incidence of one particular type of lung cancer.

The studies of the ASARCO cohort (Enterline and Marsh 1982; Enterline et al. 1987a, 1995) noted a supralinear exposure-response relationship (i.e., steeper at lower doses) between arsenic exposure and lung cancer mortality. Hertz-Picciotto and Smith (1993) extended this observation to several other occupationally exposed cohorts with quantitative exposure information. The authors suggest that neither toxicokinetic mechanisms nor confounding from age, smoking, or other workplace carcinogens that differ by exposure level are likely explanations for the curvilinearity. Plausible explanations offered include: (1) synergism (with smoking), which varies in magnitude according to the level of arsenic exposure, (2) long-term survivorship at higher exposures among the healthier, less susceptible individuals, and (3) exposure estimate errors that were more prominent at higher-exposure levels as a result of past industrial hygiene sampling or worker protection practices.

Quantitative risk estimates for inhaled inorganic arsenic have been derived using the exposure-response data. EPA derived a unit risk estimate (the excess risk of lung cancer associated with lifetime exposure to

1 μg/m^3) of 4.3x10^{-3} per (μg/m^3) based on the dose-response relationships between arsenic exposure and excess lung cancer mortality in workers at the Anaconda smelter in Montana (Brown and Chu 1982, 1983a, 1983b; Lee-Feldstein 1983; and an unpublished paper by Higgins and associates) and the ASARCO smelter in Tacoma, Washington (Enterline and Marsh 1982; EPA 1984a; IRIS 2007). In some cases, calculations of exposure, as well as the procedures for generating quantitative risk estimates, are quite complex and the interested reader is referred to the EPA documents (EPA 1981c, 1984a, 1987e, 1996b; IRIS 2007) for a detailed description. Viren and Silvers (1994) re-evaluated the unit risk estimate using the same methods as EPA, but incorporating updated results from the ASARCO smelter (Enterline et al. 1987a; Mazumdar et al. 1989) and the findings from the Swedish smelter (Järup et al. 1989). Their analysis yielded a revised unit risk of 1.28x10^{-3} per (μg/m^3) that, when pooled with the earlier estimate from the Montana smelter cohort, yielded a composite unit risk of 1.43x10^{-3} per (μg/m^3). This unit risk estimate is a factor of 3 smaller than the EPA's current estimate of 4.3x10^{-3} per (μg/m^3). Figure 3-1 shows the air concentrations that correspond to excess lifetime cancer risks of 10^{-4}–10^{-7} based on the EPA unit risk estimate.

There have been occasional reports of other types of cancer (i.e., nonrespiratory cancer) potentially associated with inhalation exposure to inorganic arsenic, but there is no strong evidence for any of them. For example, Enterline et al. (1995) found significantly increased mortality due to cancer of the large intestine and bone cancer in the ASARCO cohort. However, neither cancer showed any relation to cumulative arsenic exposure, and the purported increase in bone cancer risk was based on a very small number of observations. Pesch et al. (2002) reported an increase in nonmelanoma skin cancers resulting from exposure from a Slovakian coal-burning power plant, but exposure levels associated with the lesions were not presented. Bencko et al. (2005) also reported an increase in the incidence of nonmelanoma skin cancer among workers of a power plant burning coal of a high arsenic content and in the population living in the vicinity of the power plant. Bulbulyan et al. (1996) reported an increase in risk of stomach cancer among workers exposed to the highest average arsenic concentrations at a Russian fertilizer plant, but this finding, which was based on a small number of observations and was only marginally statistically significant, was confounded by exposure to nitrogen oxides, which were more convincingly associated with stomach cancer in this study. Wingren and Axelson (1993) reported an association between arsenic exposure and stomach and colon cancer in Swedish glass workers, but this result was confounded by concomitant exposure to other metals. Lee-Feldstein (1983) observed a small, marginally significant increase in digestive tract cancer (SMR=125) in one study of the Anaconda cohort, but this was not found in other studies of this cohort (Lee and Fraumeni 1969; Lee-Feldstein 1986; Welch et al. 1982). Wulff et al. (1996) observed an apparent increase in the risk of childhood cancer (all types combined) in the

population living within 20 km of the Ronnskar smelter, but the apparent increase was based on a small number of cases (13 observed vs. 6.7 expected) and was not statistically significant, and exposure to arsenic was confounded by exposure to lead, copper, cadmium, sulfur dioxide, and possibly other emissions such as nickel and selenium. A retrospective study of deaths due to unspecified types of malignancies among workers of power plants found no significant differences in death rate between two groups whose exposure levels to arsenic had a difference of one order of magnitude (Bencko et al. 1980). However, the mean age of those deceased due to cancer in the high-exposure group was 55.9 years compared to 61.2 years in the low-exposure group, and this difference was statistically significant ($p<0.05$). Also, when the workers were stratified by exposure-duration, there was a significantly higher frequency of tumors in the high-exposure group after shorter employment periods (<5 or 6–10 years) than after a longer employment period (≥11 years). No information was provided regarding specific types of cancer. Various case reports have implicated occupational arsenic exposure as a potential contributing factor in workers who developed sinonasal cancer (Battista et al. 1996), hepatic angiosarcoma (Tsai et al. 1998a), and skin cancer (Cöl et al. 1999; Tsuruta et al. 1998), but provide no proof that inhaled arsenic was involved in the etiology of the observed tumors. Wong et al. (1992) found no evidence that environmental exposure to airborne arsenic produced skin cancer in residents living near the Anaconda smelter or an open pit copper mine.

No studies were located regarding cancer in animals after inhalation exposure to inorganic arsenicals, although several intratracheal instillation studies in hamsters have provided evidence that both arsenite and arsenate can increase the incidence of lung adenomas and/or carcinomas (Ishinishi et al. 1983; Pershagen and Björklund 1985; Pershagen et al. 1984; Yamamoto et al. 1987). These data support the conclusion that inhalation of arsenic may lead to lung cancer in humans.

Organic Arsenicals. No studies were located regarding cancer effects in humans or animals after inhalation exposure to organic arsenicals.

3.2.2 Oral Exposure

There are a large number of studies in humans and animals on the toxic effects of ingested arsenic. In humans, most cases of toxicity have resulted from accidental, suicidal, homicidal, or medicinal ingestion of arsenic-containing powders or solutions or by consumption of contaminated food or drinking water. In some cases, the chemical form is known (e.g., the most common arsenic medicinal was Fowler's solution, which contained 1% potassium arsenite or arsenic trioxide), but in many cases (e.g., exposures through

drinking water), the chemical form is not known. In these cases, it is presumed that the most likely forms are either inorganic arsenate [As(+5)], inorganic arsenite [As(+3)], or a mixture. Table 3-3 and Figure 3-3 summarize a number of studies that provide reliable quantitative data on health effects in humans and animals exposed to inorganic arsenicals by the oral route. Similar data for MMA, DMA, and roxarsone are listed in Tables 3-4, 3-5, and 3-6, and shown in Figures 3-4, 3-5, and 3-6, respectively. All exposure data are expressed as milligrams of arsenic (as the element) per kilogram body weight per day (mg As/kg/day). These studies and others that provide useful qualitative information are summarized below.

3.2.2.1 Death

Inorganic Arsenicals. There are many case reports of death in humans due to ingestion of high doses of arsenic. In nearly all cases, the most immediate effects are vomiting, diarrhea, and gastrointestinal hemorrhage, and death may ensue from fluid loss and circulatory collapse (Levin-Scherz et al. 1987; Saady et al. 1989; Uede and Furukawa 2003). In other cases, death may be delayed and result from the multiple tissue injuries produced by arsenic (Campbell and Alvarez 1989). Some accounts of fatal arsenic poisoning describe both gastrointestinal effects soon after ingestion and extensive damage to multiple organ systems prior to death (Quatrehomme et al. 1992). A precise estimate of the ingested dose is usually not available in acute poisonings, so quantitative information on lethal dose in humans is sparse. The lethal doses ranged from 22 to 121 mg As/kg in four cases where known amounts were ingested as a single bolus (Civantos et al. 1995; Hantson et al. 1996; Levin-Scherz et al. 1987; Quatrehomme et al. 1992). Two people in a family of eight died from ingestion of water containing about 110 ppm of arsenic for a week (Armstrong et al. 1984). This corresponded to a dose of about 2 mg As/kg/day. Based on a review of clinical reports in the older literature, Holland (1904) estimated the minimum lethal dose to be about 130 mg (also about 2 mg/kg). A similar estimate of 70–180 mg (about 1–3 mg/kg) was provided by Vallee et al. (1960). Death due to chronic arsenic exposure has been reported at lower concentrations. Five children between the ages of 2 and 7 years died from late sequelae of chronic arsenic poisoning after drinking contaminated water throughout their lives at estimated average doses of 0.05–0.1 mg As/kg/day (Zaldívar and Guillier 1977). A 22-year-old man with chronic arsenical dermatosis died from arsenic-related effects after lifetime exposure to an estimated average dose of 0.014 mg As/kg/day in the drinking water (Zaldívar et al. 1981). Systematic studies of lethality from chronic exposure attributable to increased risk of cardiovascular disease or cancer are discussed below in Sections 3.2.2.2 and 3.2.2.7, respectively.

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
ACUTE EXPOSURE								
Death								
1	Human	1 wk (W)				2 (death)	Armstrong et al. 1984 NS	
2	Human	once (IN)				121 M (death)	Civantos et al. 1995 As(+5)	
3	Human	once (IN)				108 M (death)	Hantson et al. 1996 As(+3)	
4	Human	once (IN)				22 M (death)	Levin-Scherz et al. 1987 As(+3)	
5	Human	once (IN)				93 M (death)	Quatrehomme et al. 1992 As(+3)	
6	Rat (wild Norway)	once (G)				104 (LD50)	Dieke and Richter 1946 As(+3)	
7	Rat (Sherman)	once (G)				112 F (LD50)	Gaines 1960 As(+5) calcium arsenate	
8	Rat (Sherman)	once (G)				44 F (LD50)	Gaines 1960 As(+3)	
9	Rat (Sherman)	once (G)				175 F (LD50)	Gaines 1960 As(+5) lead arsenate	
10	Rat (Sprague-Dawley)	once (GW)				15 M (LD50)	Harrisson et al. 1958 As(+3)	

REC 5540

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
11	Rat (Sprague-Dawley)	once (F)				145 M (LD50)	Harrisson et al. 1958 As(+3)	
12	Rat (CD)	once Gd 9 (GW)				23 F (7/25 dams died)	Stump et al. 1999 As(+3)	
13	Mouse (Swiss-Webster)	once (GW)				39 M (LD50)	Harrisson et al. 1958 As(+3)	
14	Mouse (C57H46)	once (GW)				26 M (LD50)	Harrisson et al. 1958 As(+3)	
15	Mouse (Dba2)	once (GW)				32 M (LD50)	Harrisson et al. 1958 As(+3)	
16	Mouse (C3H)	once (GW)				26 M (LD50)	Harrisson et al. 1958 As(+3)	
17	Mouse (ddY)	once (GW)				26 M (LD50)	Kaise et al. 1985 As(+3)	
18	Rabbit (New Zealand)	Gd 6-18 1 x/d (GW)				1.49 F (7/20 dams died)	Nemec et al. 1998 As(+5)	

REC 5541

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
Systemic								
19	Human	1 wk (W)	Gastro		0.2 (vomiting, diarrhea, abdominal pain)	2 M (diffuse inflammation of the GI tract)	Armstrong et al. 1984 NS	
			Hemato			0.2 (pancytopenia, leukopenia)		
			Hepatic			0.4 (hepatitis)		
			Renal			0.2 (nephropathy)		
			Ocular		0.2 (periorbital swelling)			
20	Human	once (IN)	Resp			121 M (respiratory distress, lung hemmorhage and edema)	Civantos et al. 1995 As(+5)	
			Cardio			121 M (hypotension, ventricular fibrillation, cardiac arrest)		
			Gastro			121 M (ulceration of upper gastrointestinal tract)		

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
21	Human	once (IN)	Cardio			19 F (tachycardia)	Cullen et al. 1995 As (+5)	
			Gastro			19 F (profuse vomiting and diarrhea)		
			Hemato	19 F				
			Hepatic	19 F				
			Renal	19 F				
22	Human	once (NS)	Resp			8 M (hemorrhagic bronchitis, pulmonary edema)	Fincher and Koerker 1987 As(+3)	
			Cardio			8 M (hypotension, tachycardia, massive cardiomegaly)		
			Gastro			8 M (gastrointestinal bleeding)		
			Hemato			8 M (hemolysis)		
			Musc/skel			8 M (marked atrophy of distal muscle groups)		
			Renal			8 M (acute renal failure)		
			Dermal		8 M (truncal macular rash)			
23	Human	1 or 2 x (W)	Gastro		0.05 (occasional nausea, diarrhea, and abdominal cramps)		Franzblau and Lilis 1989 As(+3) As(+5)	

REC 5543

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
24	Human	once (W)	Gastro			120 M (vomiting and diarrhea)	Goebel et al. 1990 NS	
			Renal			120 M (anuria)		
			Dermal		120 M (hyperkeratosis)			
25	Human	once (IN)	Gastro		2 F (vomiting)		Hantson et al. 1996 As(+3)	
			Hepatic		2 F (slight increase in serum bilirubin)			
			Renal		2 F (altered renal function tests)			
26	Human	once (IN)	Gastro			13 M (frequent vomiting, diarrhea)	Kamijo et al. 1998 As(+3)	
			Hepatic			13 M (large increase in serum bilirubin, ALT, AST, LDH)		
			Dermal		13 M (erythematous eruption)			
			Ocular		13 M (constricted vision)			

REC 5544

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
27	Human	once (IN)	Resp			22 M (tachypnea, respiratory failure)	Levin-Scherz et al. 1987 As(+3)	
			Cardio			22 M (cyanosis, hypotension, tachycardia, ventricular fibrillation)		
			Gastro			22 M (abdominal pain, nausea, diarrhea, massive vomiting, dysphagia, hemorrhage)		
			Hepatic			22 M (large increase in serum AST and LDH)		
			Renal			22 M (large increase in serum creatinine and BUN indicating acute renal failure)		
28	Human	once pregnancy wk 30 (IN)	Cardio			6 F (hypotension, rapid pulse)	Lugo et al. 1969 As(+3)	
			Gastro			6 F (abdominal pain, vomiting)		
			Hemato		6 F (high leukocyte count, low hematocrit)			
			Renal			6 F (acute renal failure)		

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
29	Human	2-3 wk (F)	Resp		0.05 (sore throat, rhinorrhea, cough, sputum)		Mizuta et al. 1956 As(+5)	
			Cardio			0.05 (abnormal electrocardiogram)		
			Gastro			0.05[b] (nausea, vomiting, diarrhea, occult blood in feces and gastric and duodenal juice)		
			Hemato		0.05 (mild anemia, leukopenia)			
			Musc/skel		0.05 (tender calf muscle)			
			Hepatic		0.05 (mild hepatomegaly, impaired liver function, degenerative lesions)			
			Renal	0.05				
			Dermal		0.05 (pigmentation, itching, desquamation, exanthema)			
			Ocular		0.05 (edema of eyelids, conjunctivitis, central scotoma, neuro-retinitis)			

REC 5546

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
30	Human	once (IN)	Resp	11 M		43 M (shortness of breath, decreased oxygen saturation)	Moore et al. 1994a As(+3)	
			Cardio	11 M		43 M (hypotension, asystolic cardiac arrest)		
			Gastro			11 M (profuse diarrhea and vomiting, severe abdominal pain)		
			Hemato	43 M				
			Renal		11 M (increased serum creatinine)	43 M (acute renal failure)		
31	Human	once (IN)	Resp			93 M (pulmonary edema)	Quatrehomme et al. 1992 As(+3)	
			Gastro			93 M (ulcero-necrotic hemorrhagic gastritis)		
			Hepatic			93 M (hepatomegaly, diffuse fatty degeneration)		
			Renal			93 M (glomerular congestion)		
			Dermal			93 M (dermoepidermic separation)		

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
32	Monkey (Rhesus)	13 d 1 x/d (IN)	Gastro	3		6 (vomiting, unformed stool, "loss of condition")	Heywood and Sortwell 1979 As(+5)	
			Hepatic	3	6 (decreased liver glycogen, vacuolation of hepatocytes)			
			Renal	3	6 (dilation of proximal tubules)			
33	Rat (Wistar-Barby)	4-14 d 5 d/wk 1 x/d (G)	Cardio	2 F	11 F (decreased vasoreactivity)		Bekemeier and Hirschelmann 1989 As(+3)	
			Gastro	2 F		11 F (diarrhea, bloody stools)		
34	Rat (Sprague-Dawley)	2 x (GW)	Resp	14 F			Brown and Kitchin 1996 As(+3)	
			Hepatic		0.9 F (slight increased ornithine decarboxylase and heme oxygenase activity in liver)			
			Dermal	14 F				
35	Rat (Sprague-Dawley)	2 x (GW)	Hepatic	8 F	24 F (increased heme oxygenase activity in liver)		Brown et al. 1997c As(+5)	

REC 5548

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
36	Rat (Sprague-Dawley)	1 x/d 15 d (G)	Bd Wt	10 M	20 M (20-25% decreased body weight)		Rodriguez et al. 2001 As(+3)	
37	Rat (CD)	once Gd 9 (GW)	Bd Wt	15 F	23 F (decreased body weight gain)		Stump et al. 1999 As(+3)	
38	Mouse (CD-1)	Gd 6-15 1 x/d (GW)	Bd Wt	12 F	24 F (decreased body weight gain during gestation)		Nemec et al. 1998 As(+5)	
39	Mouse (B6C3F1)	1 or 4 d 1 x/d (GW)	Hemato	3 M	6 M (decreased polychromatic erythrocytes in bone marrow)		Tice et al. 1997 As(+3)	
40	Gn Pig	1 x/d 8 d (G)	Cardio		3.8 M (prolongation of QT interval)		Chiang et al. 2002 As2O3	
41	Rabbit (New Zealand)	Gd 6-18 1 x/d (GW)	Bd Wt	0.37 F	1.49 F (loss of body weight during treatment during gestation)		Nemec et al. 1998 As(+5)	
Neurological								
42	Human	1 wk (W)				2 (encephalopathy, peripheral neuropathy)	Armstrong et al. 1984 NS	

REC 5549

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
43	Human	once (IN)				121 M (confusion, brain edema)	Civantos et al. 1995 As(+5)	
44	Human	once (IN)				19 F (lethargy)	Cullen et al. 1995 As (+5)	
45	Human	once (NS)				8 M (severe, persistent encephalopathy and peripheral neuropathy)	Fincher and Koerker 1987 As(+3)	
46	Human	once (W)				120 M (severe polyneuropathy)	Goebel et al. 1990 NS	
47	Human	once (IN)				216 M (peripheral neuropathy)	Hantson et al. 1996 As(+3)	
48	Human	once (IN)				13 M (peripheral neuropathy)	Kamijo et al. 1998 As(+3)	
49	Human	once (IN)				22 M (agitation, disorientation, paranoia, violent reactions)	Levin-Scherz et al. 1987 As(+3)	
50	Human	2-3 wk (F)				0.05 (hypesthesia in legs, abnormal patellar reflex)	Mizuta et al. 1956 As(+5)	
51	Human	once (IN)		43 M			Moore et al. 1994a As(+3)	

REC 5550

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
52	Human	once (IN)				93 M (encephalopathy)	Quatrehomme et al. 1992 As(+3)	
53	Monkey (Rhesus)	13 d 1 x/d (IN)		3		6 (marked salivation, uncontrolled head shaking)	Heywood and Sortwell 1979 As(+5)	
54	Rat (Sprague-Dawley)	1 x/d 15 d (G)		10 M	20 M (altered spontaneous locomotor activity)		Rodriguez et al. 2001 As(+3)	
55	Rabbit (New Zealand)	Gd 6-18 1 x/d (GW)		0.37 F		1.49 F (prostration, ataxia)	Nemec et al. 1998 As(+5)	
Developmental								
56	Human	once pregnancy wk 30 (IN)				6 (severe pulmonary hemorrhage that may have contributed to death in premature neonate)	Lugo et al. 1969 As(+3)	
57	Rat (CD)	once Gd 9 (GW)		15		23 (increased post-implantation loss and decreased viable fetuses)	Stump et al. 1999 As(+3)	

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)		Reference Chemical Form	Comments
58	Mouse (CD-1)	once Gd 8-15 (GW)		11		23	(increased fetal mortality, exencephaly)	Baxley et al. 1981 As(+3)	
59	Mouse (CD-1)	once Gd 7-15 (GW)				48	(increased fetal death, decreased fetal weight, gross and skeletal malformations)	Hood et al. 1978 As(+5)	
60	Mouse (CD-1)	Gd 6-15 1 x/d (GW)		12		24	(increased resorptions per litter, decreased live fetuses per litter, decreased mean fetal weight)	Nemec et al. 1998 As(+5)	
61	Hamster (Lak:LVG [SYR])	once Gd 8-12 (GW)		11		14	(increased fetal mortality, decreased fetal weight)	Hood and Harrison 1982 As(+3)	
62	Rabbit (New Zealand)	Gd 6-18 1 x/d (GW)		0.37		1.49	(increased resorptions per litter, decreased live fetuses per litter)	Nemec et al. 1998 As(+5)	

REC 5552

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
Cancer								
63	Mouse C3H	10 d (W)				9.55 M (CEL: liver and adrenal tumors)	Waalkes et al. 2003 As(+3)	
						19.13 F (CEL: ovarian and lung tumors)		
INTERMEDIATE EXPOSURE								
Systemic								
64	Human	3 mo (W)	Gastro			0.1 (severe nausea, diarrhea, pain, cramps, vomiting, traces of blood in stool)	Franzblau and Lilis 1989 As(+3) As(+5)	
			Hemato			0.1 (anemia, leukopenia)		
			Hepatic			0.1 (large increased AST and ALT)		
			Dermal		0.1 (diffuse erythematous and scaly rash)			
			Ocular		0.1 (swelling and irritation of the eyes, impaired peripheral vision)			
65	Human	0.5-14 yr (W)	Dermal			0.05 (hyperpigmentation with keratosis, possibly pre-cancerous)	Huang et al. 1985 NS	

REC 5553

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
66	Human	4 mo (W)	Gastro			0.06 F (nausea, vomiting, diarrhea)	Wagner et al. 1979 NS	
			Hemato			0.06 F (anemia, leukopenia, erythroid hyperplasia of bone marrow)		
			Dermal			0.06 F (persistent extensive hyperkeratosis of palms and soles)		
			Bd Wt			0.06 F (40 lb weight loss)		
67	Rat (Wistar-Barby)	4 wk 5 d/wk 1 x/d (GW)	Cardio		11 F (decreased vasoreactivity)		Bekemeier and Hirschelmann 1989 As(+3)	
68	Rat (Sprague-Dawley)	6 wk (W)	Renal		4.7 M (increased relative kidney weight, impaired renal mitochondrial respiration, ultrastructural changes in proximal tubule)		Brown et al. 1976 As(+5)	
			Bd Wt	9.4 M	10.9 M (decreased body weight gain)			

REC 5554

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
69	Rat (Wistar)	1 x/d 28 d (G)	Bd Wt	0.14 F			Chattopadhyay et al. 2001 As(+3)	
70	Rat (CD)	6 wk (W)	Hepatic	3 M	6 M (ultrastructural changes in hepatocytes, impaired liver mitochondrial respiration)		Fowler et al. 1977 As(+5)	
			Bd Wt	6 M		12 M (final body weight 28% lower than controls)		
1	Rat (CD)	14 pmd- Gd 19 7 d/wk 6 hr/d (GW)	Gastro	4 F		8 F (stomach adhesions, eroded luminal epithelium in the stomach)	Holson et al. 2000 As(+3)	
			Hepatic	2 F	4 F (increased liver weight)			
			Renal	4 F	8 F (increased kidney weight)			
			Bd Wt	4 F	8 F (decreased body weight gain)			
72	Rat (NS)	16 wk (W)	Hemato		0.92 M (decreased erythrocyte and leukocyte numbers)		Kannan et al. 2001 As(+3)	
			Hepatic	2.3 M				

REC 5555

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
73	Rat (Sprague-Dawley)	4 wk (W)	Hemato	0.12	0.3 (increased platelet aggregation)		Lee et al. 2002 As(+3)	
74	Rat (NS)	1 x/d 30 d (G)	Endocr		2.3 M (decreased islet cells in pancreas, increased pancreatic SOD and catalase)		Mukherjee et al. 2003 As2O3	
75	Rat (Wistar)	1 x/d 5 d/wk 12 wk (G)	Resp	19 M			Schulz et al. 2002 As(+3)	
			Renal	19 M				
			Bd Wt	9.5 M	19 M (~17% decreased body weight gain)			
76	Mouse (C57BL)	6 wk (W)	Hepatic	5 M	10 M (ultrastructural changes in hepatocytes, impaired liver mitochondrial respiration)		Fowler and Woods 1979 As(+5)	
			Bd Wt	5 M	10 M (decreased body weight gain)			

REC 5556

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
77	Mouse (C57BL/6 B6)	14 wk (W)	Hepatic	25 M			Kerkvliet et al. 1980 As(+5)	
			Renal	25 M				
78	Gn Pig (NS)	16 wk (W)	Hemato		0.69 M (decreased erythrocyte number and leukocyte number, decreased ALAD levels)		Kannan et al. 2001 As(+3)	
			Hepatic		0.69 M (increased ALAS activity)			
79	Dog (Beagle)	26 wk ad lib (F)	Hemato	1.9 F			Neiger and Osweiler 1989 As(+3)	
			Hepatic		0.8 F (mild increased serum ALT/AST)			
			Renal	1.9 F				
			Bd Wt	0.8 F	1.5 F (decreased body weight gain)	1.9 F (25% decrease in body weight)		
Immuno/ Lymphoret								
80	Mouse (C57BL/6 B6)	14 wk (W)		25 M			Kerkvliet et al. 1980 As(+5)	
Neurological								
81	Human	3 mo (W)				0.1 (paresthesia of hands and feet; confusion, disorientation and mental sluggishness)	Franzblau and Lilis 1989 As(+3) As(+5)	

REC 5557

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
82	Human	4 mo (W)				0.06 F (weakness, paresthesia)	Wagner et al. 1979 NS	
83	Rat (NS)	16 wk (W)		0.92 M	2.3 M (decreased brain neurotransmitter levels)		Kannan et al. 2001 As(+3)	
84	Rat (Wistar)	1 x/d 5 d/wk 12 wk (G)		19 M			Schulz et al. 2002 As(+3)	
85	Gn Pig (NS)	16 wk (W)		0.69 M	1.7 M (changes in brain neurotransmitter levels)		Kannan et al. 2001 As(+3)	
Reproductive								
86	Rat (Wistar)	1 x/d 28 d (G)			0.14 F (changes in uterine and ovarian weights, decreased estradiol)		Chattopadhyay et al. 2001 As(+3)	
87	Rat (CD)	14 pmd- Gd 19 7 d/wk 6 hr/d (GW)		8 F			Holson et al. 2000 As(+3)	
88	Mouse (CD)	3 gen (W)				1 (decreased litter size)	Schroeder and Mitchener 1971 As(+3)	

REC 5558

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
Developmental								
89	Rat (CD)	14 pmd- Gd 19 7 d/wk 6 hr/d (GW)		4	8 (decreased fetal body weight, increased skeletal variations)		Holson et al. 2000 As(+3)	
90	Rat (Sprague-Dawley)	Gd 15 or pnd 1-4 mo (W)			2.93 M (impaired performance in postnatal neurobehavioral tests)		Rodriguez et al. 2002 As(+3)	
91	Mouse (CD)	3 gen (W)				1 (decreased litter size)	Schroeder and Mitchener 1971 As(+3)	
CHRONIC EXPOSURE								
Death								
92	Human	2-7 yr children (W)				0.05 (death)	Zaldivar and Guillier 1977 NS	
93	Human	22 yr (W)				0.014 M (death)	Zaldivar et al. 1981 NS	Cause of death was liver tumor.
94	Monkey (Rhesus)	1 yr (IN)				3 (2/7 died)	Heywood and Sortwell 1979 As(+5)	
95	Rat (Wistar)	27 mo (F)				30 (increased mortality)	Kroes et al. 1974 As(+5) lead arsenate	
96	Mouse (CD)	2 yr (W)				1 (increased mortality, decreased life span)	Schroeder and Balassa 1967 As(+3)	

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
97	Dog (Beagle)	2 yr (F)				2.4 (6/6 died)	Byron et al. 1967 As(+3)	
98	Dog (Beagle)	2 yr (F)				2.4 (1/6 died)	Byron et al. 1967 As(+5)	
Systemic								
99	Human	NS (W)	Resp	0.032	(cough)		Ahmad et al. 1997 NS	
			Dermal			0.032 (melanosis, keratosis, hyperkeratosis, and depigmentation)		
			Ocular			0.032 (chronic conjunctivitis)		
100	Human	>8 yr (W)	Dermal	0.0012	(increased risk of premalignant skin lesions)		Ahsan et al. 2006 (NS)	
101	Human	4 yr (IN)	Dermal			0.1 F (de-pigmentation with hyperkeratosis, possibly pre-cancerous)	Bickley and Papa 1989 As(+3)	
102	Human	NS (W)	Cardio			0.014 (gangrene of feet)	Biswas et al. 1998 NS	
			Dermal			0.014 (melanosis and keratosis of hand palms and foot soles)		

REC 5560

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)		LOAEL Serious (mg/kg/day)		Reference Chemical Form	Comments
103	Human	12 yr (W)	Cardio				0.02	(Raynaud's disease, gangrene of toes)	Borgono and Greiber 1972 NS	
			Gastro		0.02	(diarrhea, abdominal pain)				
			Dermal				0.02	(abnormal pigmentation with hyperkaratosis, possibly pre-cancerous)		
104	Human	11-15 yr (W)	Dermal		0.01	(hypo- and hyperpigmentation)			Borgono et al. 1980 NS	
105	Human	NS (W)	Gastro	0.0004	0.022	(gastrointestinal irritation, diarrhea, nausea)			Cebrian et al. 1983 As(+5)	
			Dermal	0.0004			0.022	(pigmentation changes with hyperkeratosis, possibly pre-cancerous)		
106	Human	1-11 yr (W)	Hepatic		0.046	(hepatomegaly)			Chakraborty and Saha 1987 NS	
			Dermal				0.046	(pigmentation changes with keratosis, possibly pre-cancerous)		

REC 5561

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)		Reference Chemical Form	Comments
107	Human	NS (W)	Cardio			0.064	(Blackfoot disease)	Chen et al. 1988b NS	
108	Human	>10 yr (W)	Cardio	0.0008		0.022	(increased risk of ischemic heart disease mortality)	Chen et al. 1996 NS	
109	Human	NS (W)	Cardio			0.002	(increased prevalence of cerebrovascular disease and cerebral infarction)	Chiou et al. 1997 NS	
110	Human	>5 yr (W)	Hemato	0.006[c] M 0.007 F				EPA 1981b NS	
			Dermal	0.0009[c] M 0.001 F					
111	Human	3-7 yr (W)	Cardio			0.05	(Blackfoot disease)	Foy et al. 1992 NS	
			Dermal			0.05	(melanosis with hyperkeratosis, possibly pre-cancerous)		

REC 5562

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
112	Human	2-6 yr (IN)	Hepatic			0.08 M (cirrhosis, ascites)	Franklin et al. 1950 As(+3)	
			Dermal			0.08 M (pigmentation with hyperkeratosis, possibly pre-cancerous)		
113	Human	1-15 yr (W)	Hepatic		0.16 (portal fibrosis of the liver)		Guha Mazumder 2005 (NS)	
114	Human	NS (W)	Hepatic	0.004		0.014 (hepatomegaly)	Guha Mazumder et al. 1988 NS	
			Dermal	0.004		0.014 (pigmentation changes with hyperkaratosis, possibly pre-cancerous)		
115	Human	1-20 yr (W)	Gastro		0.06 (abdominal pain)		Guha Mazumder et al. 1988 NS	
			Hemato		0.06 (anemia)			
			Hepatic			0.06 (hepatomegaly, fibrosis)		
			Dermal			0.06 (hyperpigmentation with hyperkeratosis, possibly pre-cancerous)		
116	Human	NS (W)	Dermal	0.0016		0.009 (hyperpigmentation with keratosis, possibly pre-cancerous)	Guha Mazumder et al. 1998a NS	

REC 5563

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
117	Human	(W)	Dermal		0.0014 (arsenical dermatosis)		Guo et al. 2001a (NS)	
118	Human	NS (W)	Dermal		0.0043 (hyperkeratosis, hyperpigmentation)		Haque et al. 2003 (NS)	dose listed is that associated with lowest known peak As concentration ingested by a case with complete water history
119	Human	10 yr (W)	Gastro	0.0046			Harrington et al. 1978 NS	
			Hemato	0.0046				
			Dermal	0.0046				
120	Human	NS (W)	Hepatic	0.0008	0.006 (increased serum alkaline phosphatase and bilirubin)		Hernandez-Zavala et al. 1998 NS	
121	Human	lifetime (W)	Hemato		0.002 F (anemia during pregnancy)		Hopenhayn et al. 2006 (NS)	
122	Human	NS (W)	Cardio			0.067 (ischemic heart disease)	Hsueh et al. 1998b NS	

REC 5564

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
123	Human	0.5-14 yr (W)	Dermal			0.05 (hyperpigmentation with keratosis, possibly pre-cancerous)	Huang et al. 1985 NS	
124	Human	15 yr (IN)	Gastro			0.03 M (hematemesis, hemoperitoneum, melena)	Lander et al. 1975 As(+3)	
			Dermal			0.03 M (hyperkeratosis - possibly pre-cancerous)		
25	Human	NS (W)	Cardio	0.004		0.005 (cyanosis of extremities, palpitations/chest discomfort)	Lianfang and Jianzhong 1994 NS	
			Dermal	0.004		0.005 (keratosis, hyperpigmentation, depigmentation)		
126	Human	3-22 yr (IN)	Gastro			0.05 M (gastrointestinal hemorrhages)	Morris et al. 1974 As(+3)	
			Hepatic			0.05 M (vascular fibrosis, portal hypertension)		
			Dermal			0.05 M (hyperpigmentation with keratoses, possibly pre-cancerous)		

REC 5565

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
127	Human	15 yr (IN)	Hepatic			0.05 F (central fibrosis)	Piontek et al. 1989 As(+3)	
			Dermal			0.05 F (hyperkeratosis, possibly pre-cancerous)		
128	Human	NS (W)	Endocr			0.11 (diabetes mellitus)	Rahman et al. 1998 NS	
129	Human	NS (W)	Cardio	0.018	0.055 (hypertension)		Rahman et al. 1999 NS	

REC 5566

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
130	Human	28 mo (IN)	Cardio	0.06 F			Silver and Wainman 1952 As(+3)	
			Gastro		0.06 F (intermittent, progressively severe nausea, cramps, and diarrhea)			
			Hemato	0.06 F				
			Hepatic		0.06 F (hepatomegaly, fatty liver)			
			Renal	0.06 F				
			Dermal			0.06 F (melanosis with hyperkeratosis, possibly pre-cancerous)		
			Ocular		0.06 F (conjunctival injection, periocular edema)			
131	Human	55 yr (IN)	Hepatic			0.03 M (portal fibrosis and hypertension, bleeding from esophageal varices)	Szuler et al. 1979 As(+3)	
			Dermal			0.03 M (hyperpigmentation with hyperkeratosis, possibly pre-cancerous)		
132	Human	45 yr (W)	Cardio			0.014 (Blackfoot disease)	Tseng 1977 NS	

REC 5567

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
133	Human	NS (W)	Cardio			0.014 (Blackfoot disease)	Tseng 1989 NS	
134	Human	>45 yr (W)	Dermal	0.0008 M[d]	0.014 M (hyperkeratosis and hyperpigmentation)		Tseng et al. 1968 NS	
135	Human	>30 yr (W)	Cardio		0.064 M (deficits in cutaneous microcirculation of the toes)		Tseng et al. 1995 As(+3)	
136	Human	52.6 yr (avg) (W)	Cardio	0.016		0.031 (peripheral vascular disease)	Tseng et al. 1996 NS	
137	Human	16 mo (IN)	Resp	0.1 M			Wade and Frazer 1953 As(+3)	
			Cardio	0.1 M				
			Hemato	0.1 M				
			Hepatic		0.1 M (liver enlargment)			
			Dermal			0.1 M (hyperkeratosis, hyperpigmentation with hyperkeratosis, possibly pre-cancerous)		

REC 5568

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
138	Human	30-33 yr (W)	Dermal			0.015 M (hyperkeratosis of foot, possibly pre-cancerous)	Zaldivar 1974 NS	
139	Human	12 yr (W)	Resp		0.015[c] M (bronchitis, bronchiectasis)		Zaldivar 1974 NS	
					0.018 F (bronchitis, bronchiectasis)			
			Cardio			0.015[c] M (Raynaud's disease, thrombosis)		
						0.018 F		
			Gastro		0.015[c] M (diarrhea)			
					0.018 F (diarrhea)			
			Dermal		0.015[c] M (scaling of skin, hyperkeratosis, leukoderma, melanoderma)			
					0.018 F			
			Bd Wt		0.015[c] M (unspecified decreased body weight)			
					0.018 F (unspecified decreased body weight)			

REC 5569

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
140	Human	NS (W)	Dermal			0.063 (hyperpigmentation with keratoses, possibly pre-cancerous)	Zaldivar 1977 NS	
141	Human	2-7 yr children (W)	Resp			0.08 (inflammation of bronchi and larynx, bronchopneumonia)	Zaldivar and Guillier 1977 NS	
			Cardio			0.05 (vascular spasms, thrombosis, ischemia, hypotension, cardiac failure)		
			Gastro			0.05 (nause, vomiting, diarrhea, intestinal hemorrhage)		
			Hemato			0.05 (anemia)		
			Hepatic			0.08 (cirrhosis)		
			Renal		0.08 (cloudy swelling in kidneys)			
			Dermal			0.05 (hyperkeratosis of palms and soles, melanoderma, leukoderma)		
142	Human	1-39 yr (W)	Cardio			0.06 (arterial thickening, Raynaud's disease)	Zaldivar and Guillier 1977 NS	

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
143	Rat (Osborne-Mendel)	2 yr (F)	Resp	20			Byron et al. 1967 As(+3)	
			Cardio	20				
			Gastro	20				
			Hemato	9	20 (slight transient decrease in Hb and Hct values)			
			Hepatic	4		9 (enlarged bile duct, bile duct proliferation)		
			Renal	9	20 (pigmentation)			
			Bd Wt	2	4 (decreased body weight gain)			
144	Rat (Osborne-Mendel)	2 yr (F)	Resp	30			Byron et al. 1967 As(+5)	
			Cardio	30				
			Gastro	30				
			Hemato	30				
			Hepatic	9	20 (enlarged bile duct)			
			Renal	9	20 (pigmentation, cysts)			
			Bd Wt		2 (decreased body weight gain in females)			

REC 5571

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
145	Rat (Wistar)	27 mo (F)	Resp	7			Kroes et al. 1974 As(+5)	
			Cardio	7				
			Gastro	7				
			Hemato	7				
			Musc/skel	7				
			Hepatic	7				
			Renal	7				
			Endocr	7				
			Bd Wt		7 (decreased body weight gain)			

REC 5572

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
146	Rat (Wistar)	27 mo (F)	Resp	30			Kroes et al. 1974 As(+5) lead arsenate	
			Cardio	30				
			Gastro	30				
			Hemato	7	30 (slight anemia)			
			Musc/skel	30				
			Hepatic	7		30 (enlarged bile duct with extensive dilation and inflammation)		
			Renal	30				
			Endocr	30				
			Bd Wt	7	30 (decreased body weight gain)			
147	Rat (Long-Evans)	3 yr (W)	Resp	0.6			Schroeder et al. 1968 As(+3)	
			Cardio	0.6				
			Hepatic	0.6				
			Renal	0.6				
			Dermal	0.6				
			Bd Wt	0.6				

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
148	Mouse (NS)	48 wk (W)	Hepatic	11.1			Liu et al. 2000 As(+3)	
			Renal		5.6 (histological alterations of the kidney)			
			Bd Wt	11.1				
149	Mouse (NS)	48 wk (W)	Hepatic	18.5			Liu et al. 2000 As (+5)	
			Renal		18.5 (increased relative kidney weight)			
			Bd Wt	18.5				
150	Mouse (BALB/c)	15 mo (W)	Hepatic		0.7 M (increased liver weight, altered liver histopathology, decreased hepatic enzymes in serum)		Santra et al. 2000 (NS)	
			Bd Wt		0.7 M (13-17% decreased body weight)			
151	Mouse (CD)	2 yr (W)	Bd Wt		1 (decreased body weight gain after the first 6 months of the study)		Schroeder and Balassa 1967 As(+3)	

REC 5574

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
152	Dog (Beagle)	2 yr (F)	Resp	2.4			Byron et al. 1967 As(+3)	
			Cardio	2.4				
			Gastro	1		2.4 (bleeding in the gut)		
			Hemato	1	2.4 (slight to moderate anemia)			
			Hepatic	1	2.4 (hemosiderin deposits in hepatic macrophages)			
			Renal	2.4				
			Bd Wt	1		2.4 (44-61% weight loss)		
153	Dog (Beagle)	2 yr (F)	Resp	2.4			Byron et al. 1967 As(+5)	
			Cardio	2.4				
			Gastro	2.4				
			Hemato	1	2.4 (mild anemia)			
			Hepatic	1	2.4 (pigmentation in hepatic macrophages)			
			Renal	2.4				
			Bd Wt	1		2.4 (marked decreased weight gain)		

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
Neurological								
154	Human	>5 yr (W)		0.006[c] M 0.007 F			EPA 1981b NS	
155	Human	3-7 yr (W)				0.11 F (wrist weakness)	Foy et al. 1992 NS	
156	Human	1-20 yr (W)			0.06 (tingling of hands and feet)		Guha Mazumder et al. 1988 NS	
157	Human	10 yr (W)		0.0046			Harrington et al. 1978 NS	
158	Human	NS (W)		0.0014		0.04 (functional denervation)	Hindmarsh et al. 1977 NS	
159	Human	NS (W)		0.004	0.005 (fatigue, headache, dizziness, insomnia, nighmare, numbness)		Lianfang and Jianzhong 1994 NS	
160	Human	28 mo (IN)				0.06 F (paresthesia)	Silver and Wainman 1952 As(+3)	
161	Human	55 yr (IN)			0.03 M (absent ankle jerk reflex and vibration sense in legs)		Szuler et al. 1979 As(+3)	

REC 5576

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
162	Human	NS (W)			0.0017 (decreased performance in neurobehavioral tests)		Tsai et al. 2003 (NS)	
163	Human	lifetime continuous (W)			0.005 (decreased performance in neurobehavioral tests)		Wasserman et al. 2004 (NS)	
164	Human	lifetime		0.0008	0.003 (decreased score in Performance domain of an intelligence scale)		Wasserman et al. 2007 (NS)	
Reproductive								
165	Human	NS (W)				0.008 F (increased frequencies for spontaneous abortion, stillbirth, and preterm birth rates)	Ahmad et al. 2001 (NS)	98% of the exposed group drank water containing 0.1 mg As/L or more.
166	Human	lifetime (W)				0.006 F (increased incidence of spontaneous abortion)	Milton et al. 2005 (NS)	
167	Human	lifetime (W)				0.02 F (increased risk of stilbirth)	von Ehrenstein et al. 2006 (NS)	

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
Developmental								
168	Human	continuous (W)			0.002 (reduced birth weight)		Hopenhayn et al. 2003a (NS)	
169	Human	>1 yr 1 x/d (W)				0.03 (increased SMR for malignant and non-malignant lung disease)	Smith et al. 2006 (NS)	
170	Human	lifetime (W)		0.008			von Ehrenstein et al. 2006 (NS)	NOAEL is for no increase in risk of neonatal mortality or overall infant mortality.
Cancer								
171	Human	NS (W)				0.022 (CEL: skin cancer)	Cebrian et al. 1983 As(+5)	
172	Human	NS (W)				0.064 (CEL: bladder, lung and liver cancers)	Chen et al. 1986 NS	
173	Human	NS (W)				0.064 (CEL: malignant neoplasms of the bladder, skin, lung and liver)	Chen et al. 1988b NS	
174	Human	NS (W)				0.003 (CEL: bladder cancer)	Chiou et al. 2001 (NS)	

REC 5578

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
175	Human	2 wk- 12 yr (IN)				3.67 (CEL: bladder cancer risk)	Cuzick et al.1992 As(+3)	
176	Human	NS (W)				0.0011 (CEL: lung cancer)	Ferreccio et al. 1998 NS	
177	Human	NS (W)				0.0017 (CEL: lung cancers)	Ferreccio et al. 2000 (NS)	
178	Human	NS (W)				0.018 (CEL: lung cancer mortality)	Guo 2004 (NS)	
179	Human	NS (W)				0.018 (CEL: bladder cancer)	Guo and Tseng 2000 (NS)	
180	Human	NS (W)				0.052 (CEL: increased incidence of transitional cell carcinomas of the bladder, kidney, ureters, and all urethral cancer)	Guo et al. 1997 NS	
181	Human	NS (W)				0.0049[c] M (CEL: squamous cell carcinoma of the skin) 0.0094 F	Guo et al. 2001b (NS)	

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
182	Human	>1 yr (W)				0.0075 (CEL: basal or squamous skin carcinoma)	Haupert et al. 1996 NS	
183	Human	16 yr (avg) (IN)				0.04 M (CEL: basal cell and squamous cell carcinomas of the skin, small cell and squamous cell carcinoma of the lung)	Luchtrath 1983 As(+5)	
184	Human	60 yr (W)				0.038 (CEL: intraepidermal carcinoma)	Tseng 1977 NS	
185	Human	>45 yr (W)				0.014 (CEL: squamous cell carcinoma of the skin)	Tseng et al. 1968 NS	
186	Human	~5 yr (W)				0.033 (CEL: lung, urinary tract cancer)	Tsuda et al. 1995a As(+3)	

REC 5580

Table 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
187	Human	12 yr (W)				0.015[c] M (CEL: squamous cell carcinoma of the skin)	Zaldivar 1974 NS	
						0.018 F (CEL: squamous cell carcinoma of the skin)		
188	Human	22-34 yr (W)				0.014 M (CEL: basal cell and squamous cell carcinomas of the skin, hemangioendothelioma of the liver)	Zaldivar et al. 1981 NS	

a The number corresponds to entries in Figure 3-3.

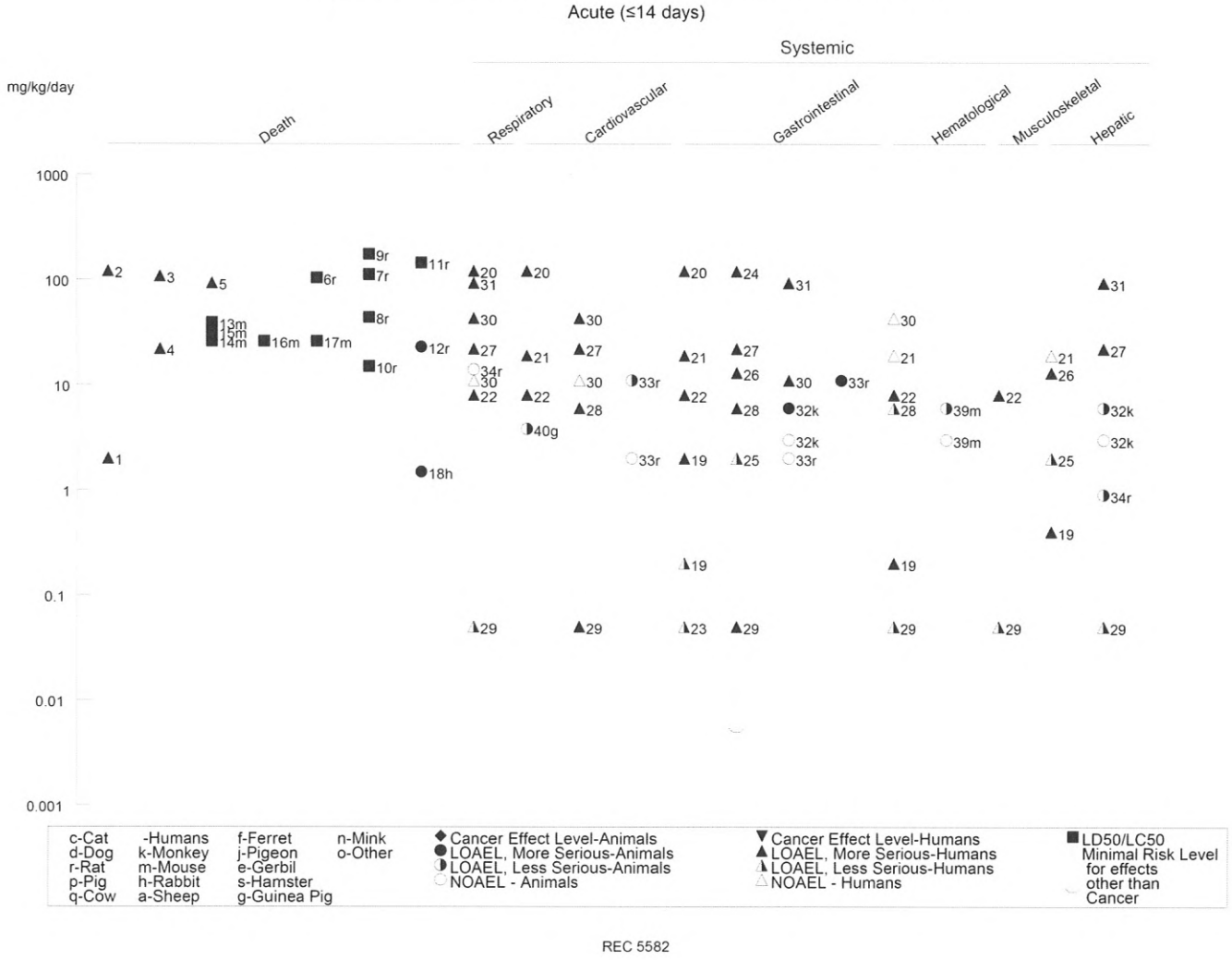
b Used to derive provisional acute oral minimal risk level (MRL) of 0.005 mg/kg/day; dose divided by an uncertainty factor of 10 (for extrapolation from a LOAEL to a NOAEL).

c Differences in levels of health effects and cancer effects between male and females are not indicated in Figure 3-3. Where such differences exist, only the levels of effect for the most sensitive gender are presented.

d Used to derive chronic oral minimal risk level (MRL) of 0.0003 mg/kg/day; dose divided by an uncertainty factor of 3 (for human variability).

avg = average; ALAD = delta-aminolevulinic acid dehydratase; ALAS = delta-aminolevulinic acid synthetase; ALT = alanine aminotransferase; AST = aspartate aminotransferase; Bd Wt = body weight; BUN = blood urea nitrogen; Cardio = cardiovascular; CEL = cancer effect level; d = day(s); Endocr = endocrine; (F) = feed; F = female; (G) = gavage; Gastro = gastrointestinal; Gd = gestational day; GI = gastrointestinal; (GW) = gavage in water; gen = generation; Gd = gestation day; Gn pig = guinea pig; Hemato = hematological; Hb = hemoglobin; Hct = hematocrit; Hemato = hematological; hr = hour(s); (IN) = ingestion; LD50 = lethal dose, 50% kill; LDH = lactate dehydrogenase; LOAEL = lowest-observable-adverse-effect level; M = male; Metab = metabolic; mo = month(s); Musc/skel = musculoskeletal; NOAEL = no-observable-adverse-effect level; NS = not specified; pmd = pre-mating day; pnd = post-natal day; Resp = respiratory; SMR =standardized mortality ratio; (W) = drinking water; wk = week(s); x = time(s); yr = year(s)

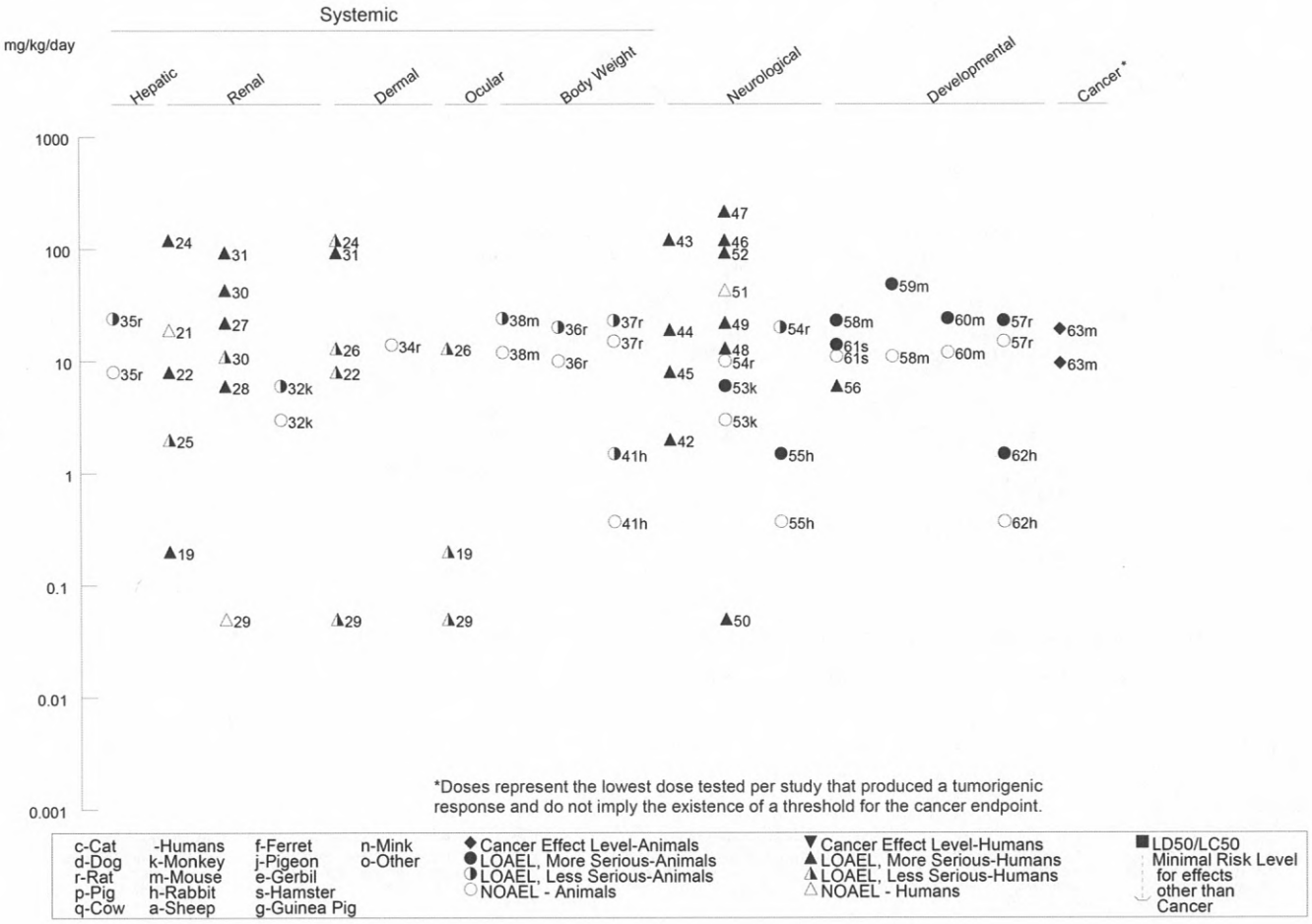
Figure 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral



REC 5582

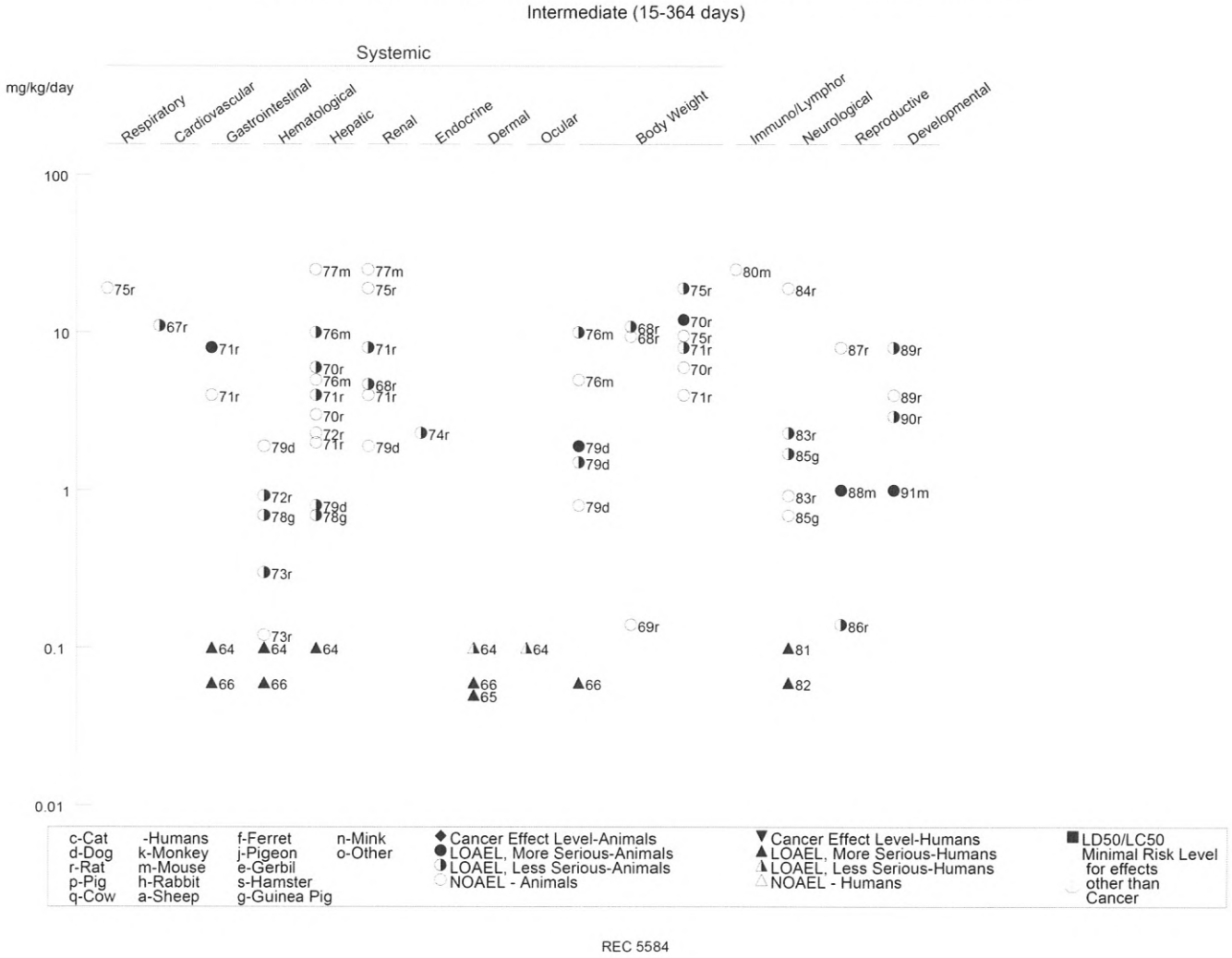
Figure 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral *(Continued)*

Acute (≤14 days)



REC 5583

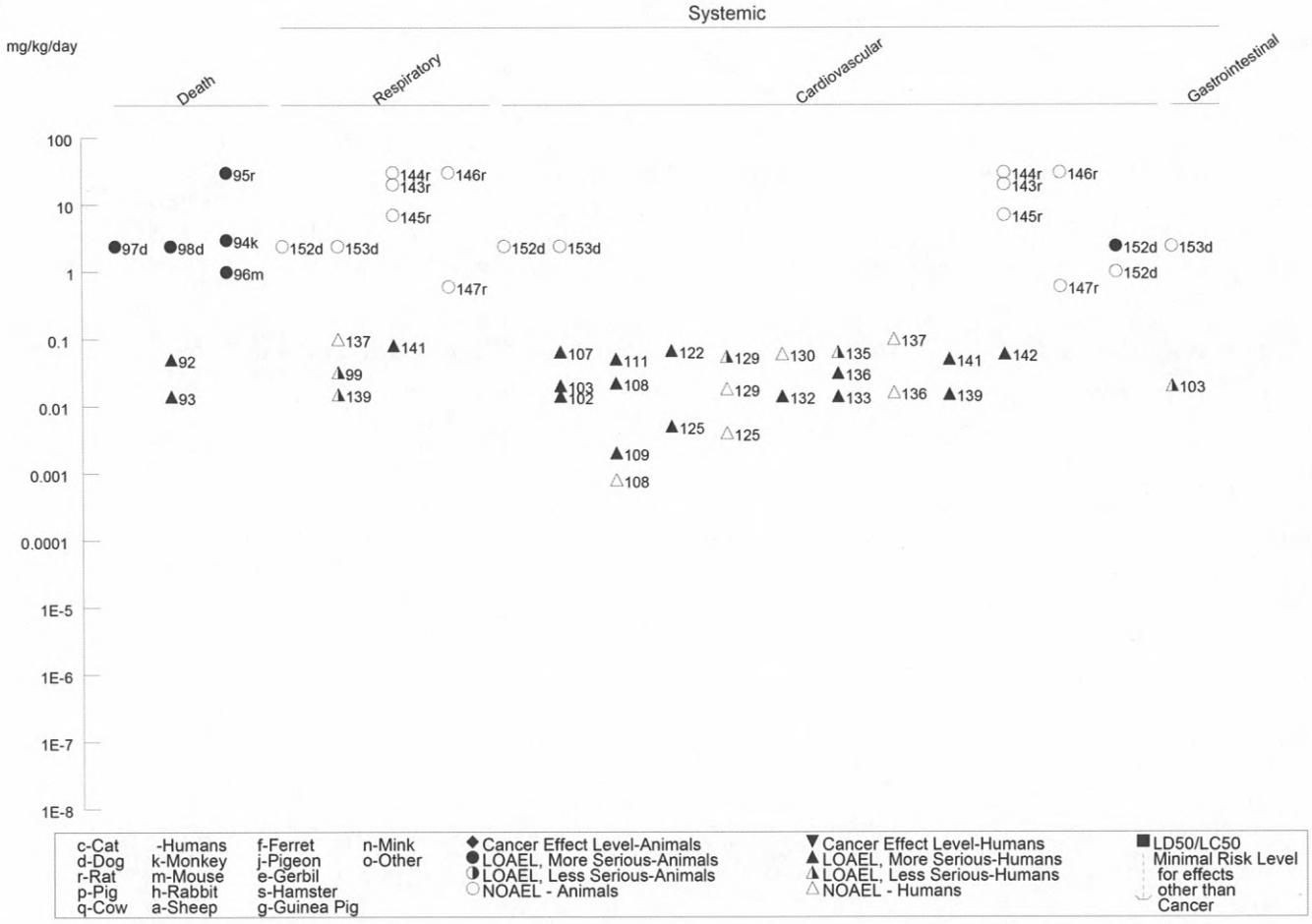
Figure 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral *(Continued)*



REC 5584

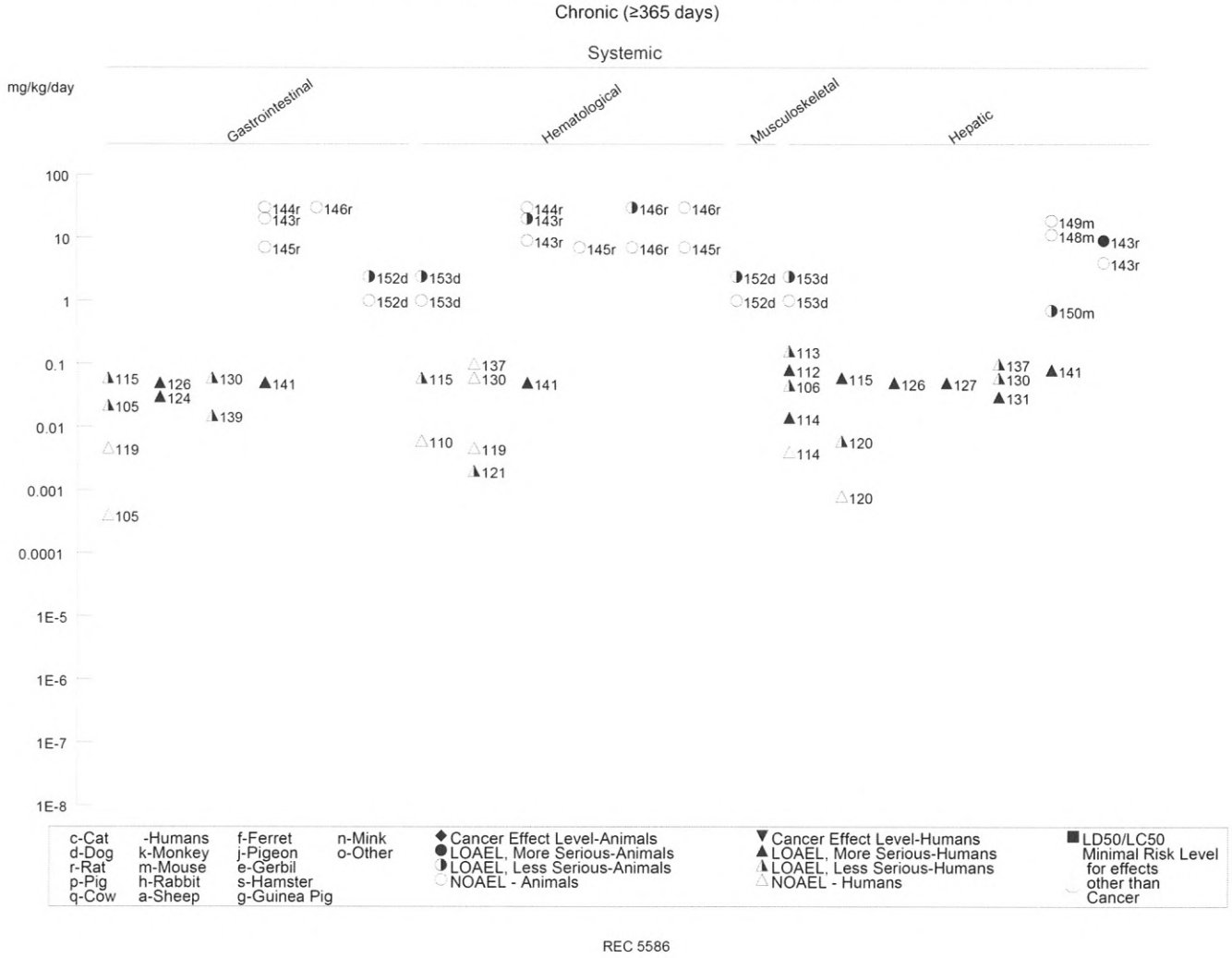
Figure 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral *(Continued)*

Chronic (≥365 days)



REC 5585

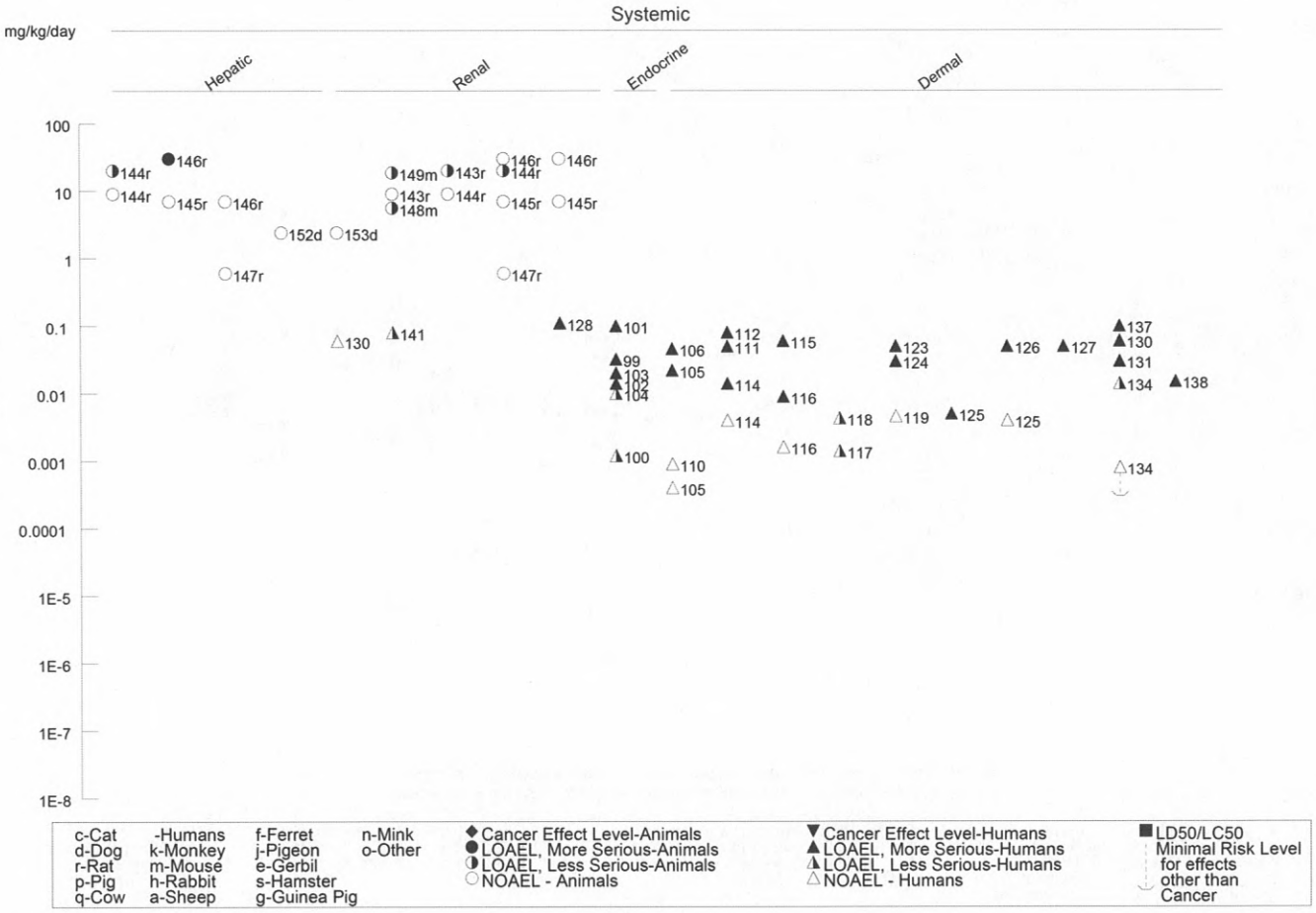
Figure 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral *(Continued)*



REC 5586

Figure 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral *(Continued)*

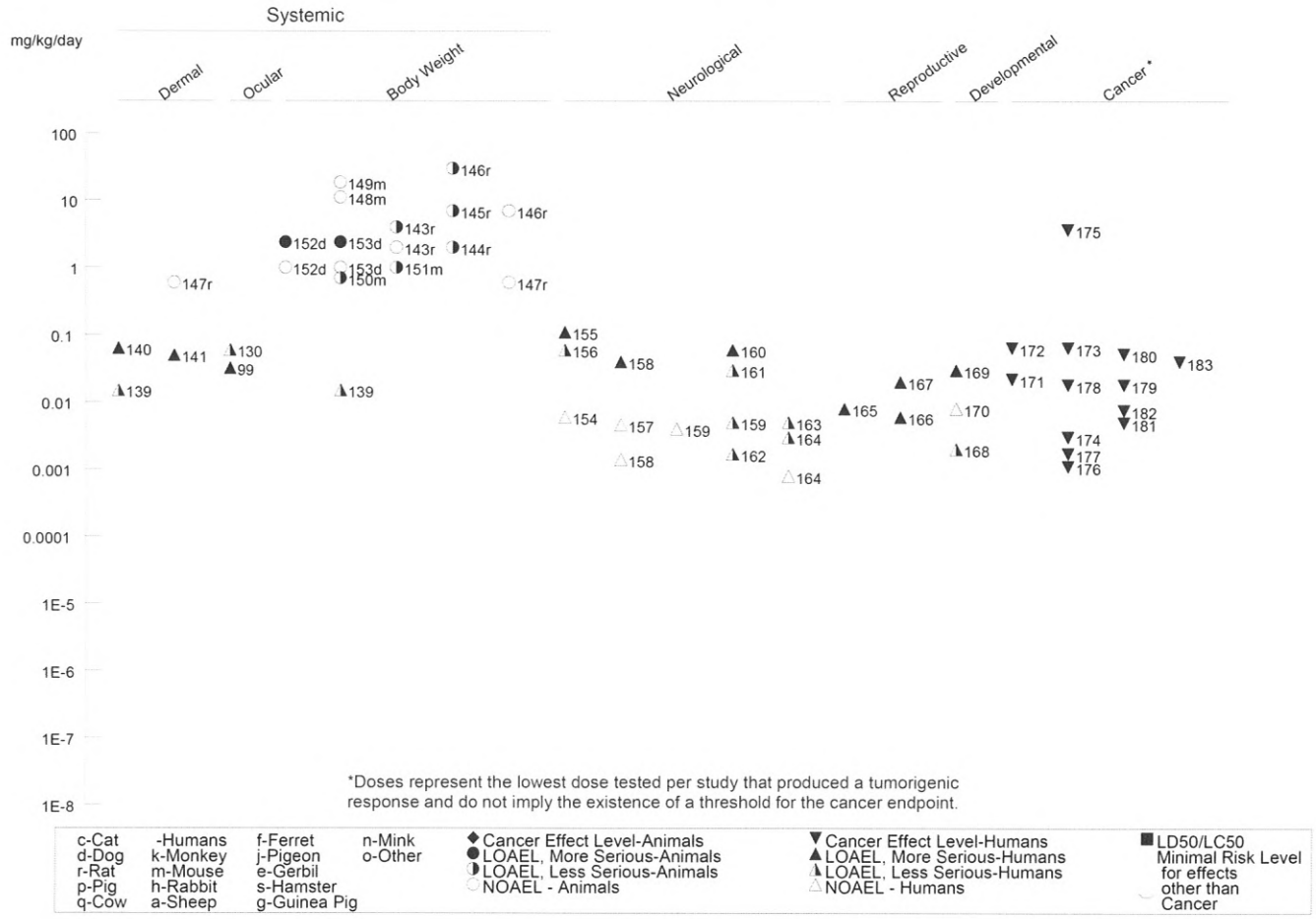
Chronic (≥365 days)



REC 5587

Figure 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral *(Continued)*

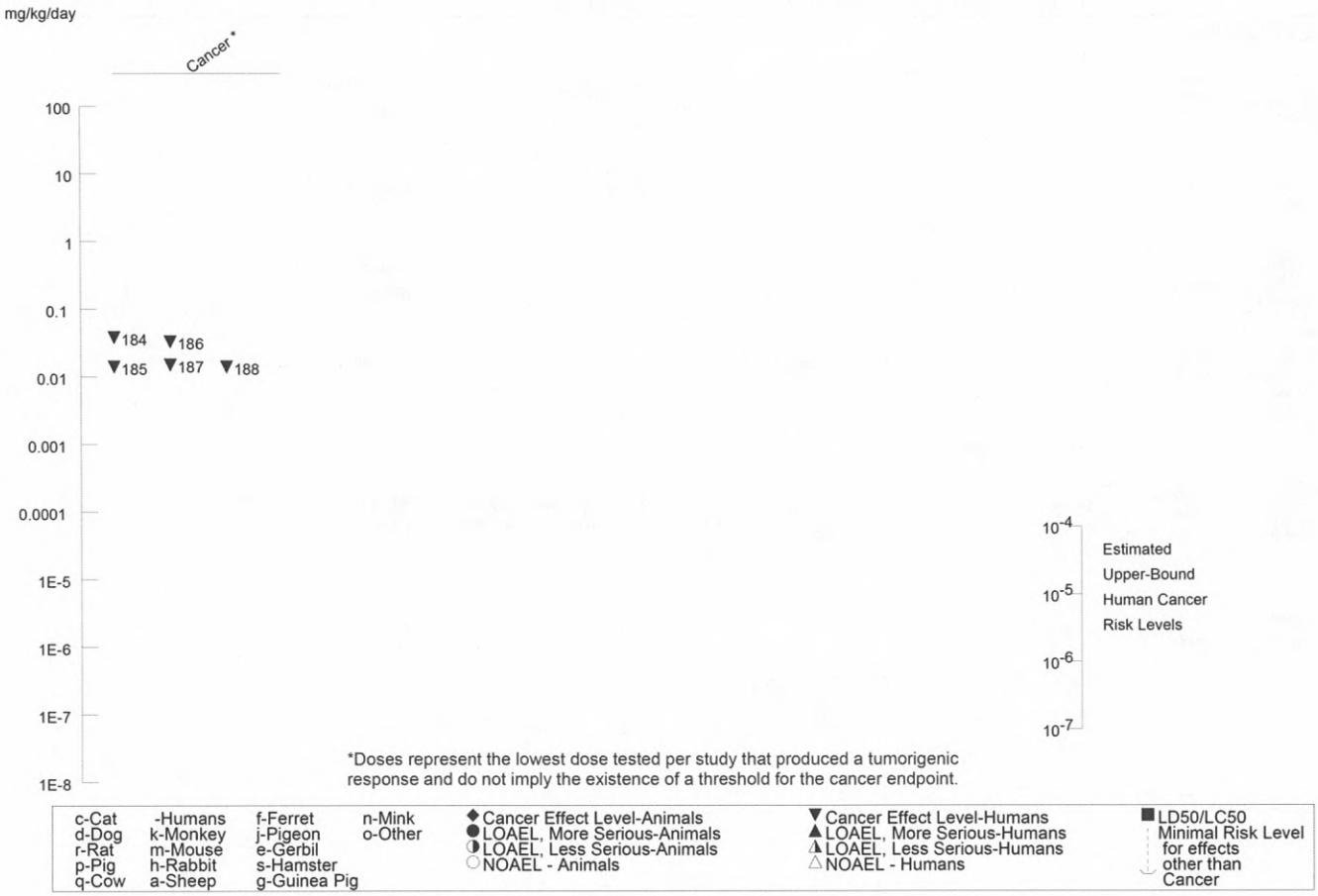
Chronic (≥365 days)



REC 5588

Figure 3-3 Levels of Significant Exposure to Inorganic Arsenic - Oral *(Continued)*

Chronic (≥365 days)



REC 5589

Table 3-4 Levels of Significant Exposure to Monomethylarsonic Acid - Oral

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
ACUTE EXPOSURE								
Death								
1	Rat (Sprague-Dawley)	once (GW)				3184 M (LD50) 2449[b] F (LD50)	Gur and Nyska 1990 MSMA	
2	Mouse (ddY)	once (GW)				1800 M (LD50)	Kaise et al. 1989 MMA	
3	Rabbit (New Zealand)	once (GW)				102 M (LD50)	Jaghabir et al. 1988 MSMA	
Systemic								
4	Rat (Sprague-Dawley)	once (GW)	Gastro		2030 (mucoid feces and diarrhea)		Gur and Nyska 1990 MSMA	
			Bd Wt	2030				
5	Rat (Sprague-Dawley)	Gd 6-15 (GW)	Bd Wt	10 F	100 F (17% decrease in maternal body weight gain)	500 F (40% decrease in maternal body weight gain)	Irvine et al. 2006 MMA	
6	Mouse (ddY)	once (GW)	Resp			1800 M (respiratory arrest)	Kaise et al. 1989 MMA	
			Gastro		2200 M (diarrhea, slight congestion of the small intestine)			

REC 5590

Table 3-4 Levels of Significant Exposure to Monomethylarsonic Acid - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
7	Rabbit (New Zealand)	Gd 7-19 (GW)	Gastro	7 F	12 F (loose feces/diarrhea in 7/14 pregnant rabbits)		Irvine et al. 2006 MMA	
			Bd Wt	7 F		12 F (67% decrease in maternal body weight gain)		
8	Rabbit (New Zealand)	once (GW)	Gastro		60 M (diarrhea)		Jaghabir et al. 1988 MSMA	
Developmental								
9	Rat (Sprague-Dawley)	Gd 6-15 (GW)		100	500 (decreased fetal weight and increased fetal incidence of imcomplete ossification of thoracic vertebrae)		Irvine et al. 2006 MMA	
10	Rabbit (New Zealand)	Gd 7-19 (GW)		7	12 (supernumerary thoracic ribs and eight lumbar vertebrae)		Irvine et al. 2006 MMA	
INTERMEDIATE EXPOSURE								
Death								
11	Rat (Fischer- 344)	52 wk (F)				106.9 M (increased mortality)	Arnold et al. 2003 MMA	

Table 3-4 Levels of Significant Exposure to Monomethylarsonic Acid - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
Systemic								
12	Rat (Fischer- 344)	52 wk (F)	Gastro	3.5[c] M	30.2 M (diarrhea)		Arnold et al. 2003 MMA	
			Bd Wt	30.2 M	106.9 M (14% decrease in body weight)			
13	Rat (Sprague-Dawley)	146-171 d pre-mating, mating, gestation, and lactation (F)	Bd Wt	76			Schroeder 1994 MMA	
14	Dog (Beagle)	52 wk (C)	Gastro		2 M (diarrhea)		Waner and Nyska 1988 MMA	
			Bd Wt	2 F	8 F (decrease in body weight)			
Reproductive								
15	Rat (Sprague-Dawley)	146-171 d pre-mating, mating, gestation, and lactation (F)		22	76 (decreased pregnancy rate and male fertility index in F0 and F1)		Schroeder 1994 MMA	
16	Mouse (Swiss)	19 d 3 d/wk (GW)			119 M (reduced fertility)		Prukop and Savage 1986 MSMA	

REC 5592

Table 3-4 Levels of Significant Exposure to Monomethylarsonic Acid - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
Developmental								
17	Rat (Sprague-Dawley)	146-171 d pre-mating, mating, gestation, and lactation (F)		22	76 (decreased pup survival F1 and F2)		Schroeder 1994 MMA	
CHRONIC EXPOSURE								
Death								
18	Rat (Fischer- 344)	104 wk (F)				72.4 M (increased mortality)	Arnold et al. 2003 MMA	

Table 3-4 Levels of Significant Exposure to Monomethylarsonic Acid - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
Systemic								
19	Rat (Fischer- 344) (F)	104 wk	Gastro	3 M	25.7 M (diarrhea)	72.4 M (necrosis, ulceration, perforation in large intestine)	Arnold et al. 2003 MMA	
			Hemato	72.4 M				
			Musc/skel	72.4 M				
			Hepatic	72.4 M				
			Renal	3.9 F	33.9 F (increased absolute kidney weight and progressive glomerulonephropathy)			
			Endocr	3.9 F	33.9 F (hypertrophy of thyroid follicular epithelium, decreased absolute thyroid weight)			
			Dermal	72.4 M				
			Ocular	72.4 M				
			Bd Wt	3 M	25.7 M (15% decrease in body weight)	33.9 F (30% decrease in body weight)		

REC 5594

Table 3-4 Levels of Significant Exposure to Monomethylarsonic Acid - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
20	Rat (Fischer- 344)	104 wk (W)	Hemato	8.4 M			Shen et al. 2003 MMA	
			Hepatic	2.1 M	8.4 M (increased GST-P-positive foci)			
			Renal		2.1 M (hyperplasia of the bladder)			
			Bd Wt	8.4 M				
21	Mouse (B6C3F1)	104 wk (F)	Cardio	67.1 M			Arnold et al. 2003 MMA	
			Gastro	24.9 M	67.1 M (loose and mucoid feces, metaplasia of the cecum and colon)			
			Musc/skel	67.1 M				
			Hepatic	67.1 M				
			Renal	1.2 M[d]	6 M (increased incidence of progressive glomeruloephropathy)			
			Dermal	67.1 M				
			Ocular	67.1 M				
			Bd Wt	24.9 M	67.1 M (17% decrease in body weight)			

Table 3-4 Levels of Significant Exposure to Monomethylarsonic Acid - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
22	Dog (Beagle)	52 wk (C)	Resp	35			Waner and Nyska 1988 MMA	
			Gastro		2 M (diarrhea)			
			Hemato	35				
			Hepatic	35				
			Renal		8 (increased urine specific gravity; increased kidney weight)			
			Ocular	35				
			Bd Wt	2 F		8 F (42% decrease in body weight)		
Neurological								
23	Dog (Beagle)	52 wk (C)		35			Waner and Nyska 1988 MMA	
Reproductive								
24	Dog (Beagle)	52 wk (C)		35 M 8 F	35 F (decrease in estrus)		Waner and Nyska 1988 MMA	Histological examination of reproductive tissues.

REC 5596

Table 3-4 Levels of Significant Exposure to Monomethylarsonic Acid - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
Cancer								
25	Rat (Fischer- 344)	104 wk (W)		8.4 M			Shen et al. 2003 MMA	

a The number corresponds to entries in Figure 3-4.

b Differences in levels of health effects and cancer effects between male and females are not indicated in Figure 3-4. Where such differences exist, only the levels of effect for the most sensitive gender are presented.

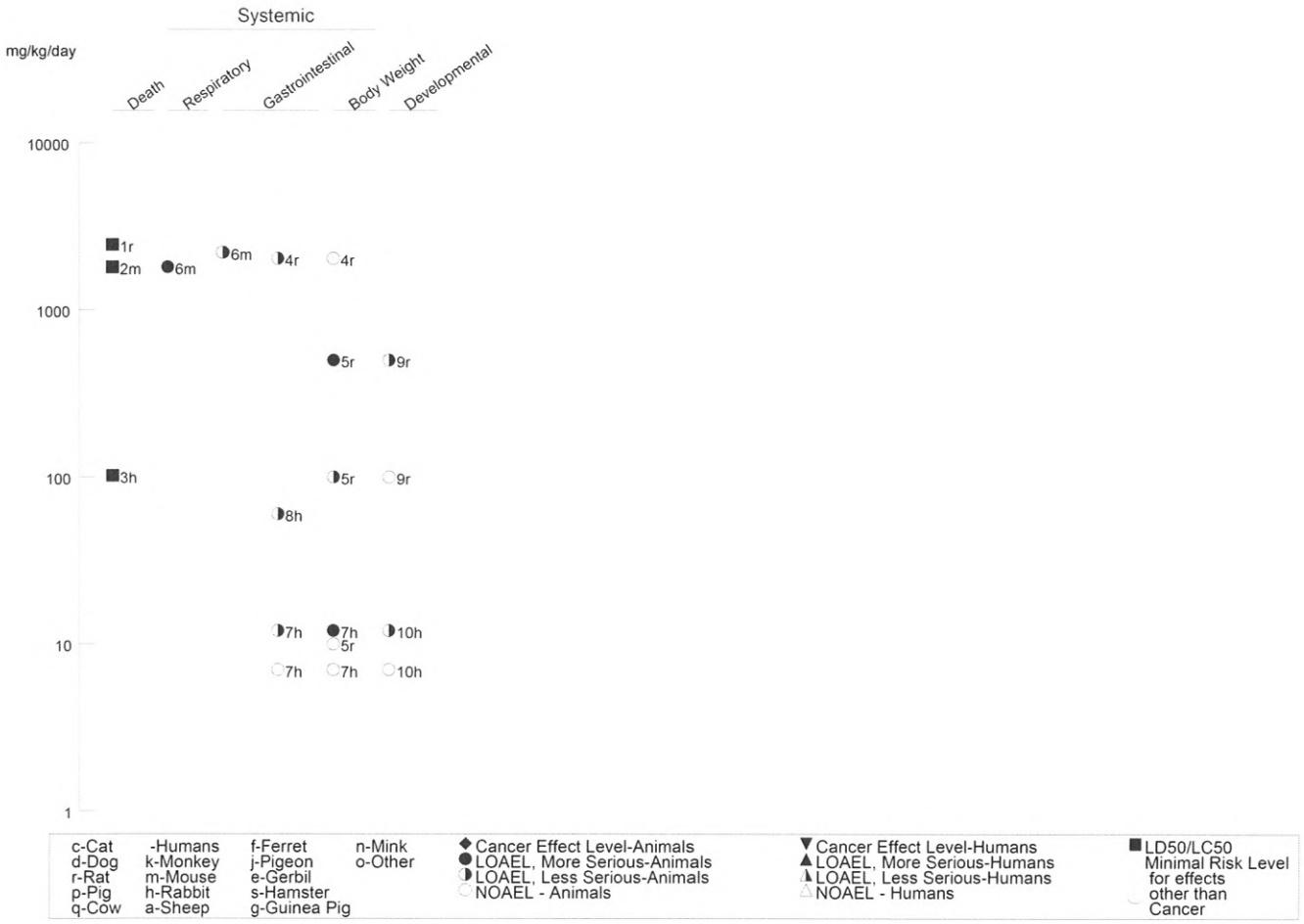
c The intermediate-duration oral MRL of 0.1 mg MMA/kg/day was calculated using a benchmark dose analysis. The BMDL10 of 12.38 mg MMA/kg/day was divided by an uncertainty factor of 100 (10 to account for extrapolation from animals to humans and 10 for human variability)

d The chronic-duration oral MRL of 0.01 mg MMA/kg/day was calculated using a benchmark dose analysis. The BMDL10 of 1.09 mg MMA/kg/day was divided by an uncertainty factor of 100 (10 to account for extrapolation from animals to humans and 10 for human variability)

Bd Wt = body weight; (C) = capsule; Cardio = cardiovascular; d = day(s); Endocr = endocrine; (F) = feed; F = female; Gastro = gastrointestinal; (GO) = gavage in oil; (GW) = gavage in water; Gd = gestation day; GST-P = glutathione S-transferase placental form; Hemato = hematological; IN = ingestion; LD50 = lethal dose, 50% kill; LOAEL = lowest-observable-adverse-effect level; M = male; MMA = monomethylarsonic acid; MSMA = monosodium methane arsonate; Musc/skel = musculoskeletal; NOAEL = no-observable-adverse-effect level; Resp = respiratory; (W) = drinking water; wk = week(s); x = time(s)

Figure 3-4 Levels of Significant Exposure to Monomethylarsonic Acid - Oral

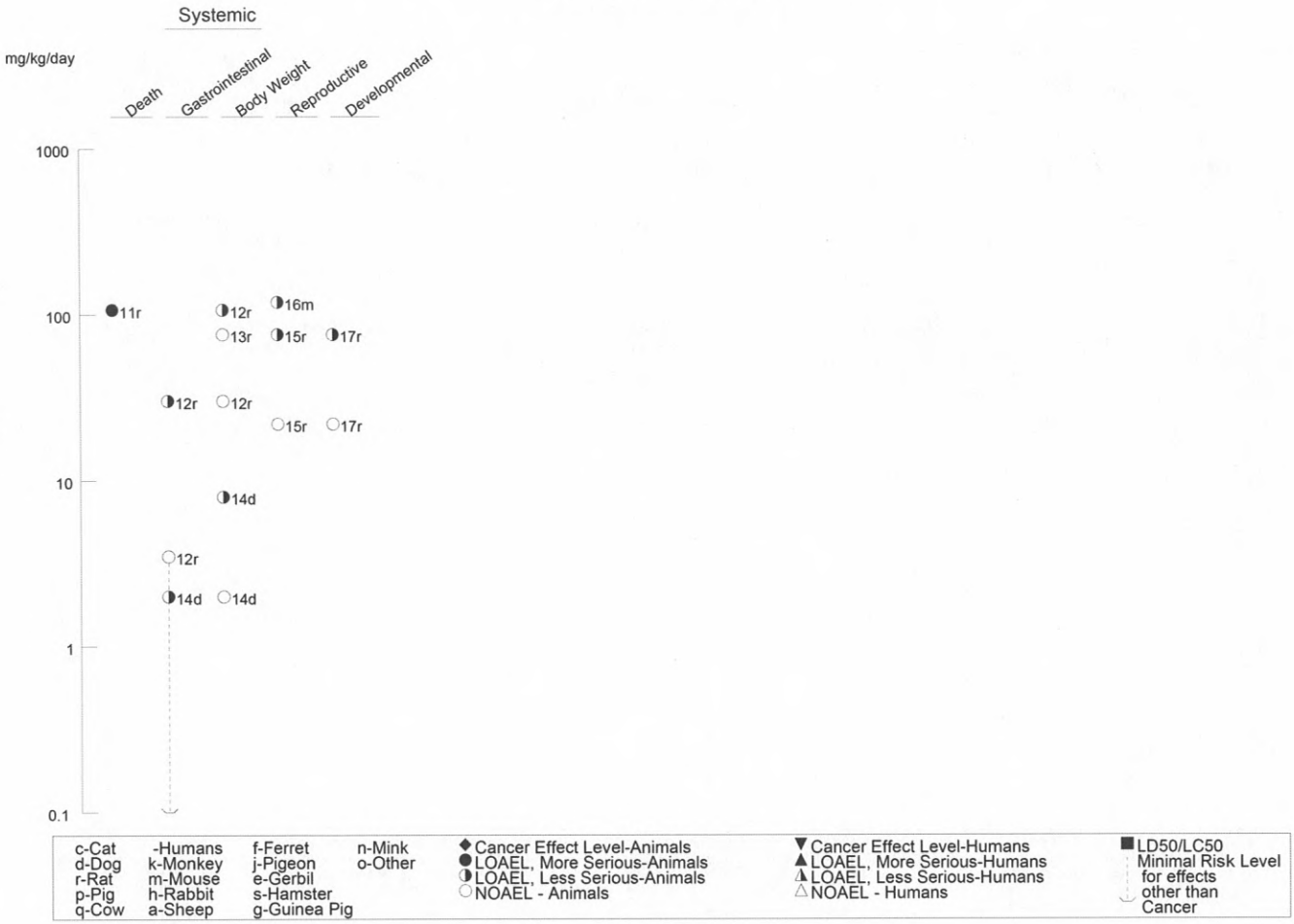
Acute (≤14 days)



REC 5598

Figure 3-4 Levels of Significant Exposure to Monomethylarsonic Acid - Oral *(Continued)*

Intermediate (15-364 days)



REC 5599

Figure 3-4 Levels of Significant Exposure to Monomethylarsonic Acid - Oral *(Continued)*

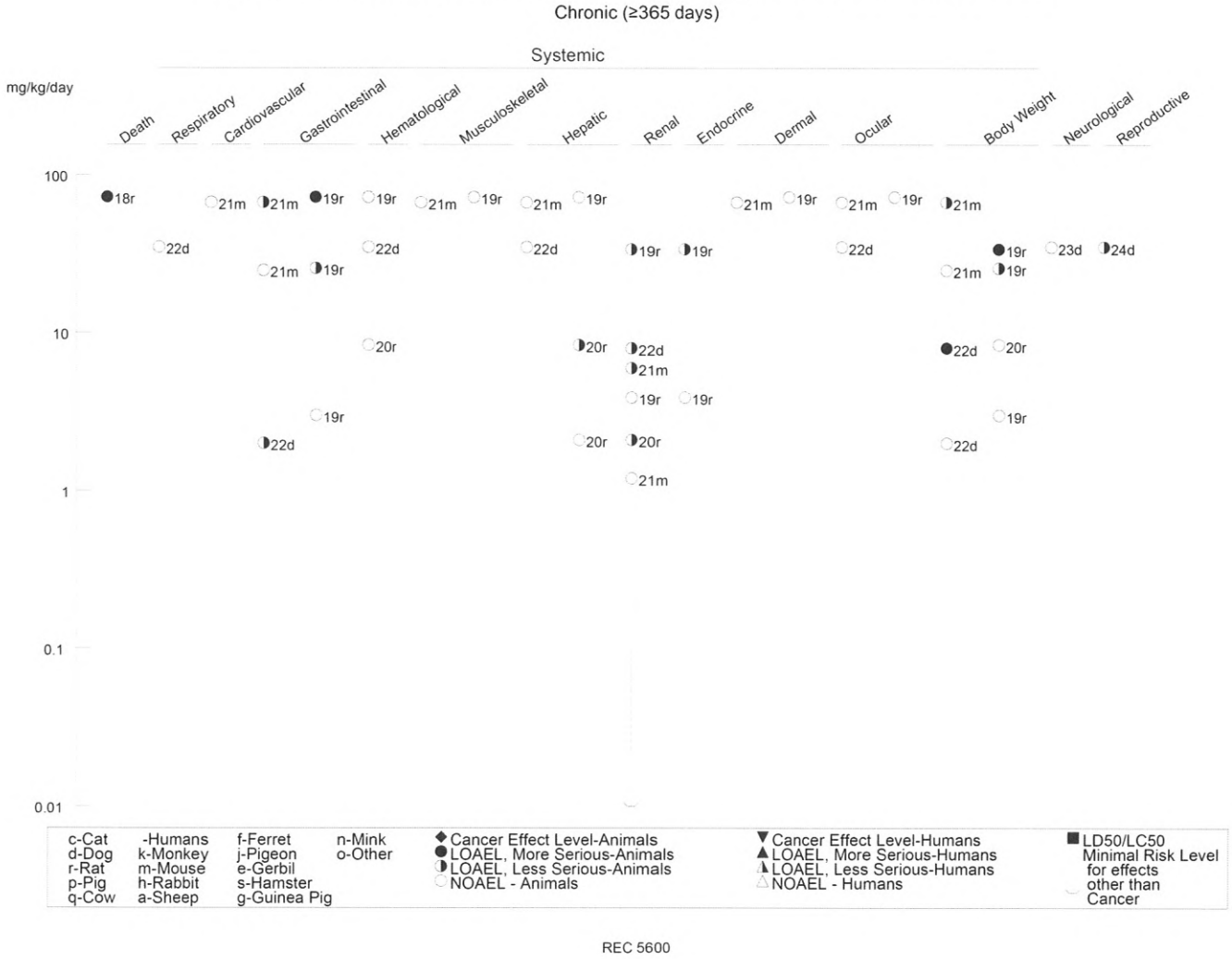


Figure 3-4 Levels of Significant Exposure to Monomethylarsonic Acid - Oral *(Continued)*

Chronic (≥365 days)

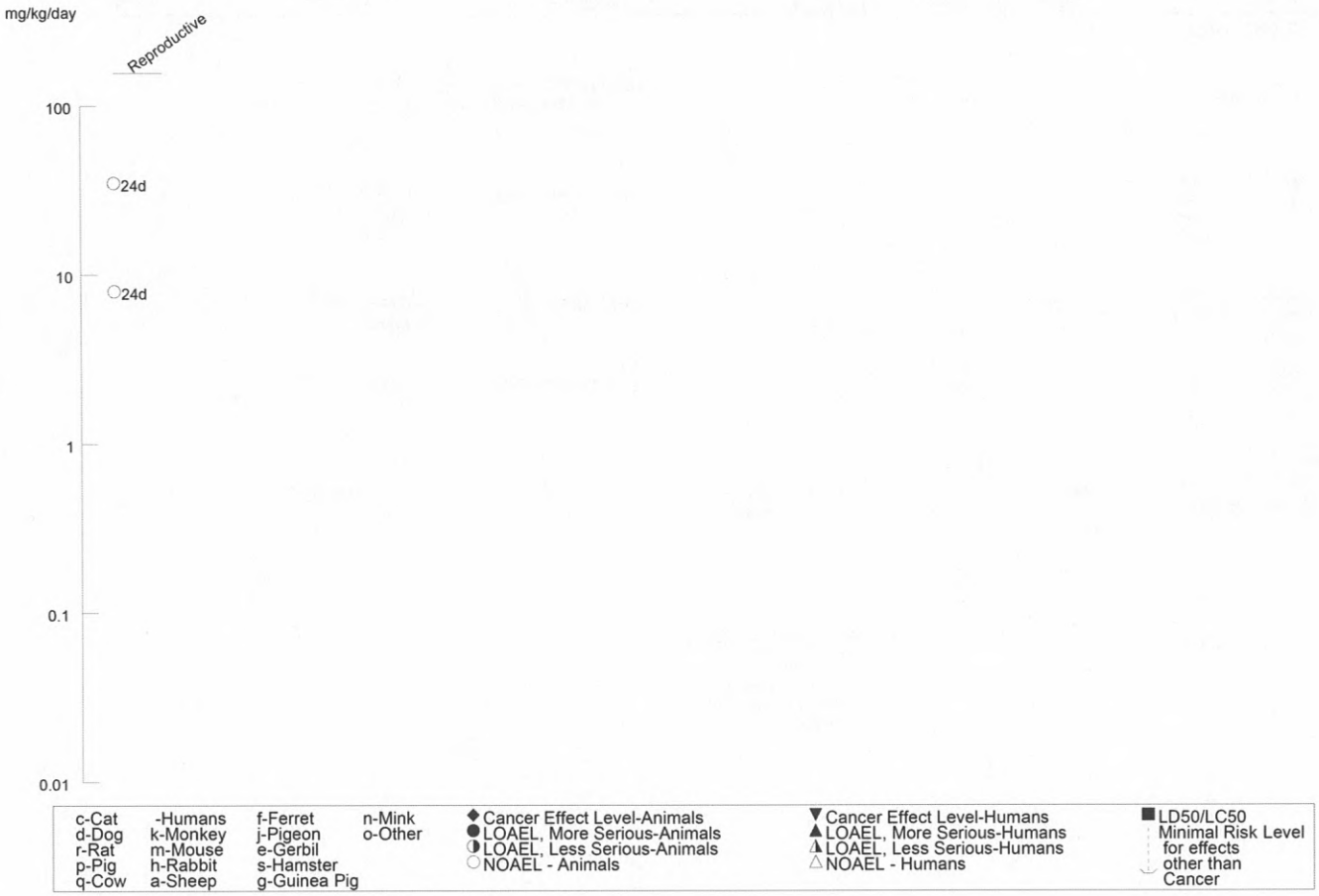


Table 3-5 Levels of Significant Exposure to Dimethylarsinic Acid - Oral

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
ACUTE EXPOSURE								
Death								
1	Rat (Fischer- 344)	13 wk (F)				475 M (100% mortality during first 2 weeks of study)	Crown et al. 1987 DMA	
2	Rat (CD)	10 d Gd 7-16 1 x/d (GW)				60 F (67% mortality)	Rogers et al. 1981 DMA	
3	Mouse (ddY)	once (GW)				1200 M (LD50)	Kaise et al. 1989 DMA	
4	Mouse (CD-1)	10 d Gd 7-16 1 x/d (GW)				600 F (59% mortality)	Rogers et al. 1981 DMA	
Systemic								
5	Rat (Fischer- 344)	2 wk (F)	Renal		11 F (altered bladder cell surface characteristics)		Cohen et al. 2001 DMA	
			Bd Wt	11 F				
6	Rat (Fischer- 344)	13 wk (F)	Gastro		475 M (diarrhea and congestion and hemorrhagic contents in gastrointestinal tract in rats dying during first 2 weeks)		Crown et al. 1987 DMA	

REC 5602

Table 3-5 Levels of Significant Exposure to Dimethylarsinic Acid - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
7	Rat (Sprague-Dawley)	Gd 6-15 (GW)	Bd Wt	12 F	36 F (decreased maternal body weight gain)		Irvine et al. 2006 DMA	
8	Rat (CD)	10 d Gd 7-16 1 x/d (GW)	Bd Wt			40 F (27% decreased maternal weight gain)	Rogers et al. 1981 DMA	
9	Mouse (B6C3F1)	24 hr 1 or 2 x (GW)	Resp		720 F (decreased lung ODC)		Ahmad et al. 1999a DMA	
			Hepatic		720 F (decreased liver GSH, GSSG, CYP-450 and ODC; increased serum ALT)			
10	Mouse (ddY)	once (GW)	Resp			900 M (respiratory arrest)	Kaise et al. 1989 DMA	
			Gastro		1757 M (diarrhea, slight congestion of the intestion)			
11	Mouse (CD-1)	10 d Gd 7-16 1 x/d (GW)	Bd Wt			200 F (26% decreased maternal weight gain)	Rogers et al. 1981 DMA	
12	Dog (Beagle)	52 wk (C)	Gastro	6.5	16 (vomiting and diarrhea)		Zomber et al. 1989 DMA	

Table 3-5 Levels of Significant Exposure to Dimethylarsinic Acid - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
13	Rabbit (New Zealand)	Gd 7-19 (GW)	Gastro	12 F	48 F (fluid gastrointestinal tract contents)		Irvine et al. 2006 DMA	
			Bd Wt	12 F		48 F (maternal weight loss)		
Neurological								
14	Mouse (ddY)	once (GW)				1757 M (increased startle reflex; ataxia)	Kaise et al. 1989 DMA	
Developmental								
15	Rat (Sprague-Dawley)	GD6-15 (GW)			40 F (decreased fetal body weight)		Chernoff et al. 1990 DMA	
16	Rat (Sprague-Dawley)	Gd 6-15 (GW)		12	36 (decreases in number of live fetuses and fetal weight; increases in fetuses with diaphragmatic hernia; delayed ossification)		Irvine et al. 2006 DMA	
17	Rat (CD)	10 d Gd 7-16 1 x/d (GW)		15		30 (malformed palates in 15%)	Rogers et al. 1981 DMA	

REC 5604

Table 3-5 Levels of Significant Exposure to Dimethylarsinic Acid - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
18	Mouse (CD-1)	Gd 8 (GW)				1600 F (fetal deaths, decreased fetal weight, delayed ossification, skeletal malformations)	Kavlock et al. 1985 DMA	
19	Mouse (CD-1)	10 d Gd 7-16 1 x/d (GW)		200		400 (18% decrease in fetal weight, delayed ossification, cleft palate in 12/28; irregular palatine rugae in 4.8%)	Rogers et al. 1981 DMA	
20	Rabbit (New Zealand)	Gd 7-19 (GW)		12			Irvine et al. 2006 DMA	
INTERMEDIATE EXPOSURE								
Death								
21	Rat (Fischer- 344)	13 wk (F)				190 M (100% mortality during first 4 weeks of study)	Crown et al. 1987 DMA	
22	Rat (Fischer- 344)	4 wk 5 d/wk 1 x/d (G)				57 (50% survival in males; 20% survival in females)	Murai et al. 1993 DMA	

Table 3-5 Levels of Significant Exposure to Dimethylarsinic Acid - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
23	Rat (Fischer- 344)	8 wk (W)				17 M (10/10 died)	Wanibuchi et al. 1996 DMA	
Systemic								
24	Rat (Fischer- 344)	10 or 20 wk (F)	Renal	1 F	10 M (necrosis in bladder epithelium)		Arnold et al. 1999 DMA	
					5 F[b] (increased kidney weight, calcification at corticomedullary junction; increased bladder weight and increased BrdU labelling in bladder epithelium)			
			Bd Wt	10				
25	Rat (Fischer- 344)	10 wk (F)	Renal		11 F (increased bladder and kidney weights, hyperplasia and necrosis of bladder epithelium)		Cohen et al. 2001 DMA	

REC 5606

Table 3-5 Levels of Significant Exposure to Dimethylarsinic Acid - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
26	Rat (Fischer- 344)	13 wk (F)	Resp	43.2 M			Crown et al. 1987 DMA	
			Cardio	43.2 M				
			Gastro	43.2 M	190 M (diarrhea and congestion and hemorrhagic contents in gastrointestinal tissues)			
			Hemato	0.44 F	4.5 F (decreased hemoglobin and erythrocyte levels)			
			Hepatic	23.5 M				
			Renal	0.4 M	4 M (increased urine volume and decreased specific gravity)			
			Endocr	0.4 M	4 M (hypertrophy of thyroid follicle epithelium)			
			Bd Wt	43.2 M				
27	Rat (Fischer- 344)	4 wk 5 d/wk 1 x/d (G)	Renal			57 (papillary necrosis and hyperplasia; cortical degeneration and necrosis)	Murai et al. 1993 DMA	
			Bd Wt		57 (decreased body weight)			

REC 5607

Table 3-5 Levels of Significant Exposure to Dimethylarsinic Acid - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
28	Rat (Sprague-Dawley)	10 wk pre-mating, gestation and lactation periods (F)	Resp	16.5			Rubin et al. 1989 DMA	
			Cardio	16.5				
			Hemato	0.34 M	2.3 M (decreased mean corpscular hemoglobin concentration)			
			Hepatic	16.5				
			Renal	16.5				
			Endocr	2.3 F	16.5 F (hypertrophy of thyroid follicle epithelium)			
			Bd Wt	16.5				
29	Rat (Sprague-Dawley)	42 d (F)	Hemato	3.7 M			Siewicki 1981 DMA	
			Hepatic	3.7 M				
			Renal	3.7 M				
			Bd Wt	3.7 M				

Table 3-5 Levels of Significant Exposure to Dimethylarsinic Acid - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
30	Dog (Beagle)	6 d/wk 52 wk (C)	Gastro	6.5	16 (vomiting and diarrhea)		Zomber et al. 1989 DMA	
			Hemato	16 M	40 M (decreased erythrocyte and increased leukocyte levels)			
Reproductive								
31	Rat (Sprague-Dawley)	10 wk pre-mating, gestation and lactation periods (F)		16.5			Rubin et al. 1989 DMA	
Cancer								
32	Mouse A/J	50 wk ad lib (W)				10.4 M (CEL: lung tumors)	Hayashi et al. 1998 DMA	

REC 5609

Table 3-5 Levels of Significant Exposure to Dimethylarsinic Acid - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
CHRONIC EXPOSURE								
Systemic								
33	Rat (Fischer- 344)	daily 2 yr (F)	Resp	7.8			Arnold et al. 2006 DMA	
			Cardio	7.8				
			Gastro	7.8				
			Hemato	7.8				
			Musc/skel	7.8				
			Hepatic	7.8				
			Renal	0.77 M	3.1 M (nephrocalcinosis)			
				0.77 F	3.1 F (urothelial vacular degeneration and hyperplasia of urothelial cells in urinary bladder)			
			Endocr	3.1	7.8 (hypertrophy of thyroid follicle epithelium)			
			Dermal	7.8				
			Ocular	7.8				
			Bd Wt	7.8				
34	Rat (Fischer- 344)	104 wk (W)	Renal	0.75 M	3.4 M (nodular or papillary hyperplasia in urinary bladder)		Wei et al. 1999, 2002 DMA	

Table 3-5 Levels of Significant Exposure to Dimethylarsinic Acid - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
35	Mouse (B6C3F1)	daily 2 yr (F)	Resp	94			Arnold et al. 2006 DMA	
			Cardio	94				
			Gastro	94				
			Hemato	94 F	94 F (decreased lymphocytes and increased monocytes)			
			Musc/skel	94				
			Hepatic	94				
			Renal	1.3[c] F	37 M (progressive glomerulonephropathy)			
					7.8[b] F (vacuolization of superficial cells of urotheliumin urinary bladder)			
			Dermal	94				
			Ocular	94				
			Bd Wt	94				

Table 3-5 Levels of Significant Exposure to Dimethylarsinic Acid - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
36	Dog (Beagle)	6 d/wk 52 wk (C)	Resp	40			Zomber et al. 1989 DMA	
			Cardio	40				
			Gastro	6.5	16 (vomiting and diarrhea)			
			Hepatic	40				
			Renal	40				
Reproductive								
37	Rat (Fischer- 344)	daily 2 yr (F)		7.8			Arnold et al. 2006 DMA	Histological examination of reproductive tissues.
38	Mouse (B6C3F1)	daily 2 yr (F)		94			Arnold et al. 2006 DMA	Histological examination of reproductive tissues.
Cancer								
39	Rat (Fischer- 344)	daily 2 yr (F)				7.8 (CEL: urothelial cell papillomas and carcinomas in urinary bladder)	Arnold et al. 2006 DMA	
40	Rat (Fischer- 344)	104 wk (W)				3.4 M (CEL: urinary bladder tumors)	Wei et al. 1999, 2002 DMA	

REC 5612

Table 3-5 Levels of Significant Exposure to Dimethylarsinic Acid - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
41	Mouse knockout	continuous 18 mo (W)				11.8 M (CEL)	Salim et al. 2003 DMA	

a The number corresponds to entries in Figure 3-5.

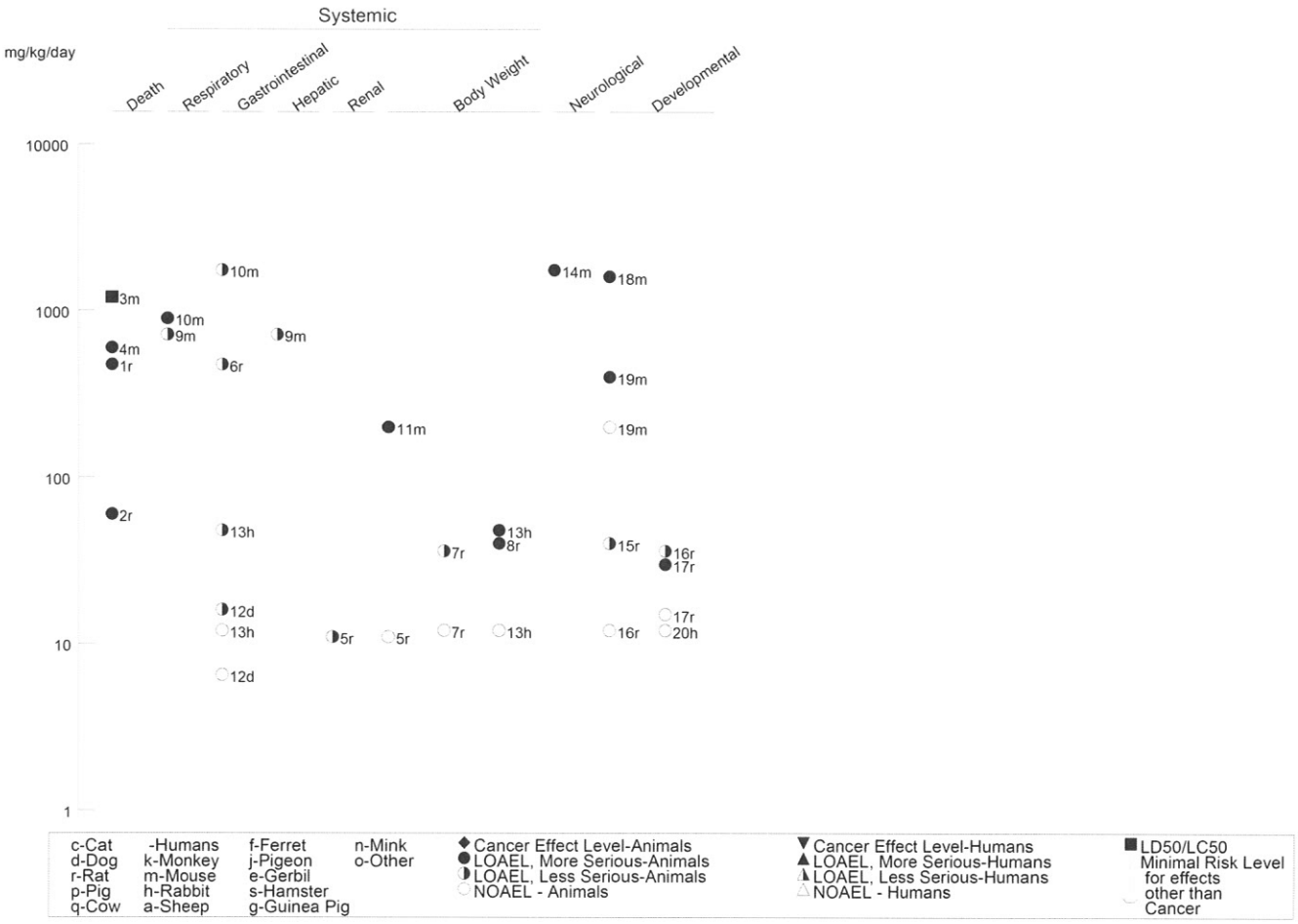
b Differences in levels of health effects and cancer effects between male and females are not indicated in Figure 3-5. Where such differences exist, only the levels of effect for the most sensitive gender are presented.

c The chronic-duration oral MRL of 0.02 mg DMA/kg/day was calculated using a benchmark dose analysis. The BMDL10 of 1.80 mg DMA/kg/day was divided by an uncertainty factor of 100 (10 to account for extrapolation from animals to humans and 10 for human variability)

ad lib = ad libitum; ALT = alanine aminotransferase; Bd Wt = body weight; BrdU = bromodeoxyuridine; (C) = capsule; Cardio = cardiovascular; CEL = cancer effect level; CYP = cytochrome p; d= day(s); DMA = dimethylarsinic acid; Endocr = endocrine; (F) = feed; F = female; (G) = gavage; Gastro = gastrointestinal; Gd = gestation day; GSH = reduced glutathione; GSSG = oxidized glutathione; (GW) = gavage in water; Hemato = hematological; hr = hour(s); LD50 = lethal dose, 50% kill; ODC = ornithine decarboxylase; LOAEL = lowest-observable-adverse-effect level; M = male; mo = month; Musc/skel = musculoskeletal; NOAEL = no-observable-adverse-effect level; Resp = respiratory; (W) = drinking water; wk = week(s); x = time(s); yr = year(s)

Figure 3-5 Levels of Significant Exposure to Dimethylarsinic Acid - Oral

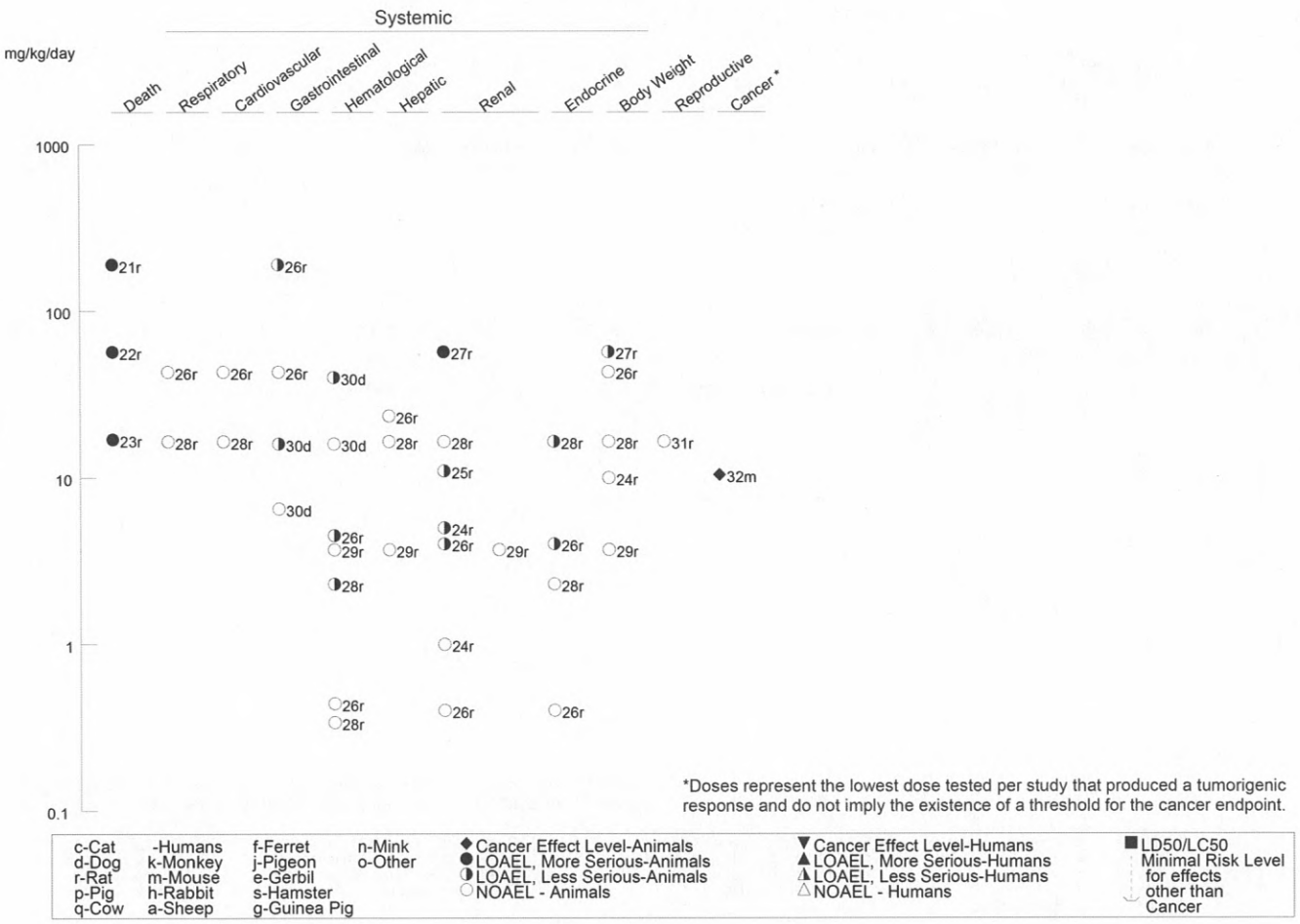
Acute (≤14 days)



REC 5614

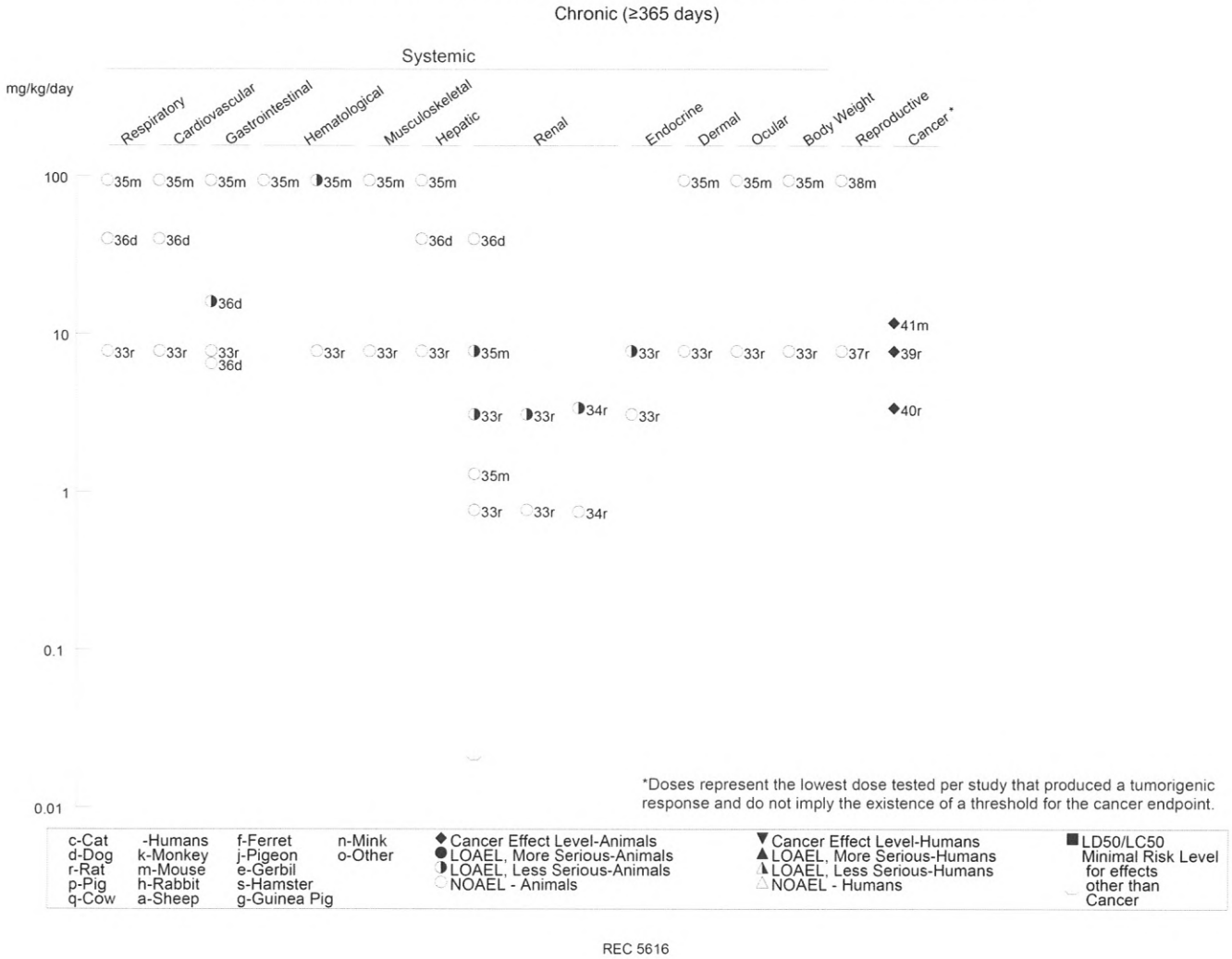
Figure 3-5 Levels of Significant Exposure to Dimethylarsinic Acid - Oral *(Continued)*

Intermediate (15-364 days)



REC 5615

Figure 3-5 Levels of Significant Exposure to Dimethylarsinic Acid - Oral *(Continued)*



REC 5616

Table 3-6 Levels of Significant Exposure to Roxarsone - Oral

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
ACUTE EXPOSURE								
Death								
1	Rat (Holtzman)	once (GW)				155 (LD50)	Kerr et al. 1963 ROX	
2	Rat (Fischer- 344)	once (GO)				150 M (5/5 died) 81[b] F (LD50)	NTP 1989b ROX	
3	Rat (Fischer- 344)	14 d (F)				128[b] M (3/5 died) 144 F (5/5 died)	NTP 1989b ROX	
4	Mouse (B6C3F1)	once (GO)				300 M (5/5 died) 244[b] F (LD50)	NTP 1989b ROX	
5	Mouse (B6C3F1)	14 d (F)				168 F (5/5 died)	NTP 1989b ROX	
Systemic								
6	Rat (Fischer- 344)	14 d (F)	Bd Wt	16 M	32 M (22% reduced body weight)		NTP 1989b ROX	
7	Mouse (B6C3F1)	14 d (F)	Bd Wt	84		168 (34% decrease in body weight)	NTP 1989b ROX	
Neurological								
8	Rat (Fischer- 344)	14 d (F)		16 M	32 M (slight inactivity)		NTP 1989b ROX	

REC 5617

Table 3-6 Levels of Significant Exposure to Roxarsone - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
9	Mouse (B6C3F1)	14 d (F)		20	42 (slight inactivity; ruffled fur)		NTP 1989b ROX	
10	Pig (Landrace)	30 d ad lib (F)				6.3 (muscle tremors and clonic convulsions)	Rice et al. 1985; Kennedy et al. 1986 ROX	
INTERMEDIATE EXPOSURE								
Death								
11	Rat (Holtzman)	13 wk (F)				20 (10/12 died)	Kerr et al. 1963 ROX	
12	Rat (Fischer- 344)	13 wk ad lib (F)				64 M (3/10 died)	NTP 1989b ROX	
13	Mouse (B6C3F1)	13 wk ad lib (F)				136 (6/10 males and 8/10 females died)	NTP 1989b ROX	

Table 3-6 Levels of Significant Exposure to Roxarsone - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
Systemic								
14	Rat (Fischer- 344)	31 or 90 d ad lib (F)	Hemato	32 M			NTP 1989b ROX	
			Hepatic	9 F	36 F (decreased absolute and relative liver weight)			
			Renal	8 M	32 M (increased kidney weight; minimal tubular degeneration)			
			Bd Wt	8 M		32 M (27% decrease in body weight)		

REC 5619

Table 3-6 Levels of Significant Exposure to Roxarsone - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
15	Rat (Fischer- 344)	13 wk ad lib (F)	Resp	64 M			NTP 1989b ROX	
			Cardio	64 M				
			Gastro	64 M				
			Musc/skel	64 M				
			Hepatic	4 M	8 M (increased relative liver weight)			
			Renal	16 M	32 M (interstitial inflammation, focal regenerative hyperplasia of tubular cell epithelium and mineralization)			
			Endocr	64 M				
			Dermal	64 M				
			Bd Wt	8 M	16 M (14% decreased body weight)	32 M (26% decreased body weight)		

REC 5620

Table 3-6 Levels of Significant Exposure to Roxarsone - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
16	Mouse (B6C3F1)	13 wk ad lib (F)	Cardio	136			NTP 1989b ROX	
			Gastro	136				
			Musc/skel	136				
			Hepatic	136				
			Renal	136				
			Endocr	136				
			Dermal	136				
			Bd Wt		136 (18% decreased body weight in males; 11% decreased body weight in females)			
17	Mouse (B6C3F1)	29 or 91 d ad lib (F)	Hemato	68			NTP 1989b ROX	
			Hepatic	68				
			Renal	68				
Neurological								
18	Rat (Fischer- 344)	13 wk ad lib (F)		32 M		64 M (trembling, ataxia, hyperexcitability, slight inactivity, ruffled fur)	NTP 1989b ROX	

REC 5621

Table 3-6 Levels of Significant Exposure to Roxarsone - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)		Reference Chemical Form	Comments
19	Pig	28 d (F)				10	(muscle tremors)	Edmonds and Baker 1986 ROX	
20	Pig (Landrace)	30 d ad lib (F)				6.3	(paraplegia, myelin degeneration in spinal cord, peripheral nerves, optic nerve)	Rice et al. 1985; Kennedy et al. 1986 ROX	
CHRONIC EXPOSURE									
Systemic									
21	Rat (Fischer- 344)	103 wk ad lib (F)	Resp	4				NTP 1989b ROX	
			Cardio	4					
			Gastro	4					
			Musc/skel	4					
			Hepatic	4					
			Renal	4					
			Endocr	4					
			Dermal	4					
			Ocular	4					
			Bd Wt	4					
22	Mouse (Fischer- 344)	103 wk ad lib (F)	Resp	43 M				NTP 1989b ROX	
			Cardio	43 M					
			Gastro	43 M					
			Musc/skel	43 M					
			Hepatic	43 M					

REC 5622

Table 3-6 Levels of Significant Exposure to Roxarsone - Oral (continued)

Key to Figure[a]	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (mg/kg/day)	LOAEL Less Serious (mg/kg/day)	LOAEL Serious (mg/kg/day)	Reference Chemical Form	Comments
			Renal	43 M				
			Endocr	43 M				
			Dermal	43 M				
			Ocular	43 M				
			Bd Wt	43 F				

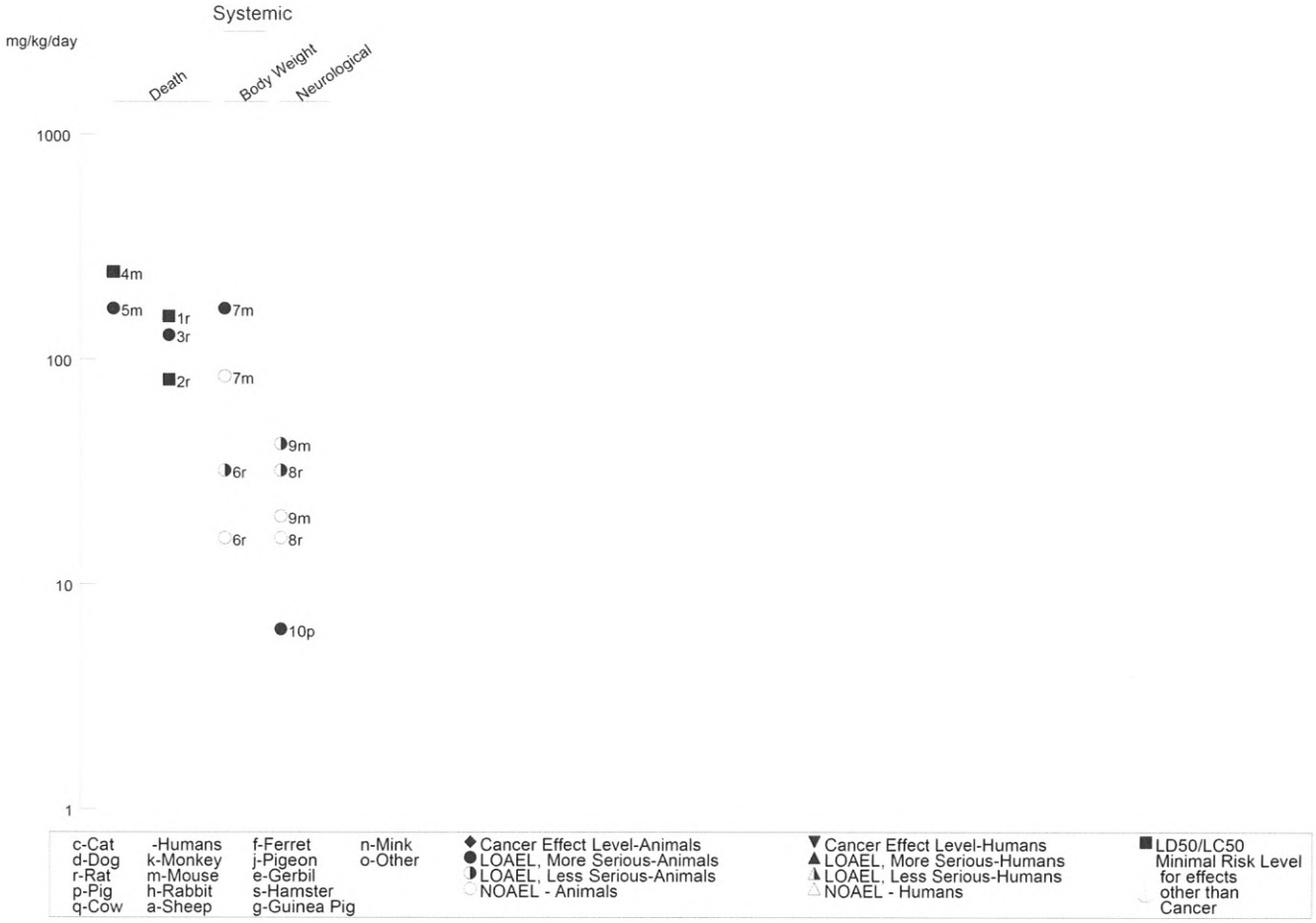
a The number corresponds to entries in Figure 3-6.

b Differences in levels of health effects and cancer effects between male and females are not indicated in Figure 3-6. Where such differences exist, only the levels of effect for the most sensitive gender are presented.

ad lib = ad libitum; Bd Wt = body weight; Cardio = cardiovascular; d = day(s); Endocr = endocrine; (F) = feed; F = Female; Gastro = gastrointestinal; (GO) = gavage in oil; (GW) = gavage in water; Hemato = hematological; LC50 = lethal concentration, 50% kill, LD50 = lethal dose, 50% kill; LOAEL = lowest-observed-adverse-effect level; M = male; Musc/skel = musculoskeletal; NOAEL = no-observed-adverse-effect level; occup = occupational; Resp = respiratory; wk = week(s)

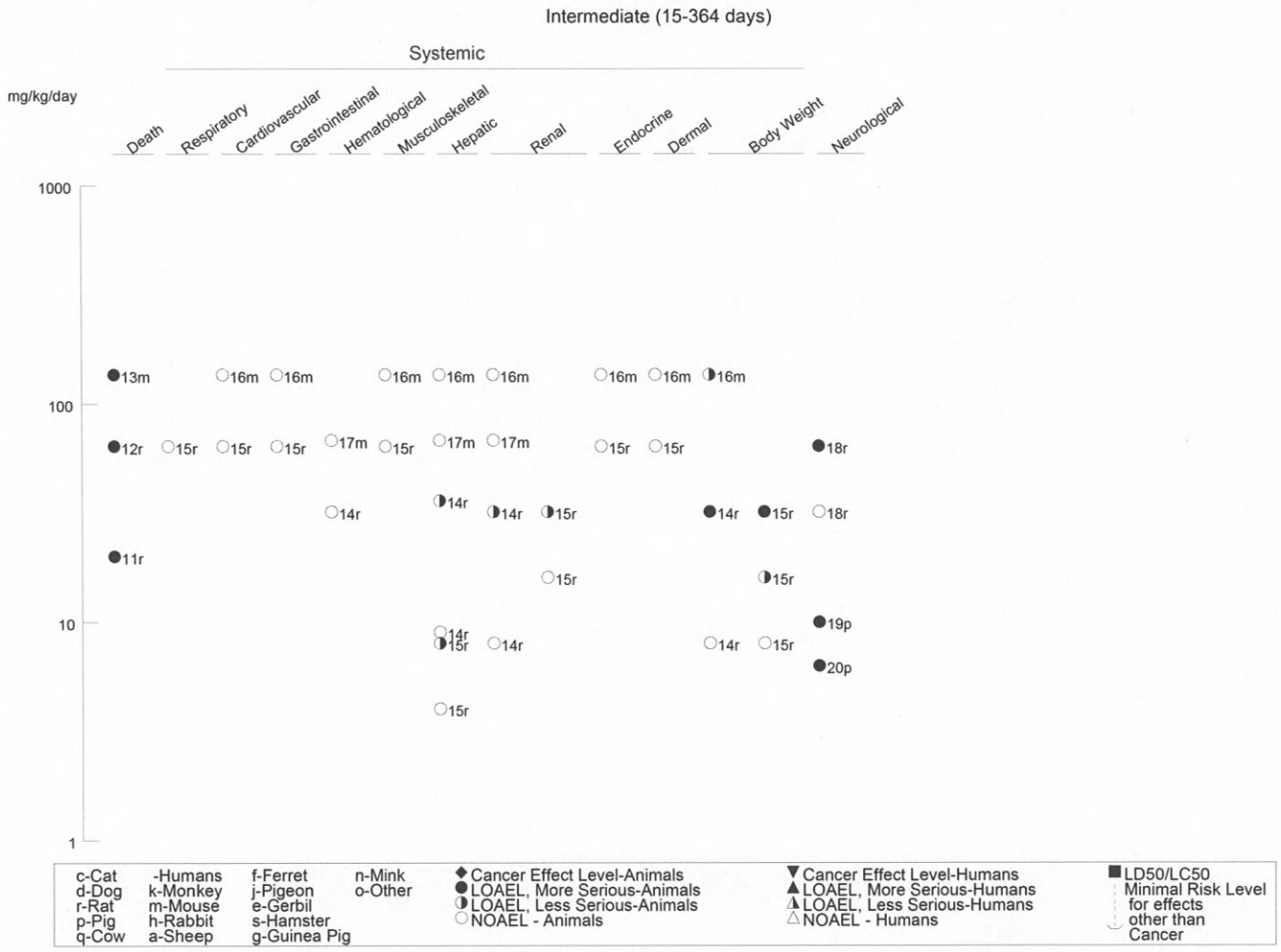
Figure 3-6 Levels of Significant Exposure to Roxarsone - Oral

Acute (≤14 days)



REC 5624

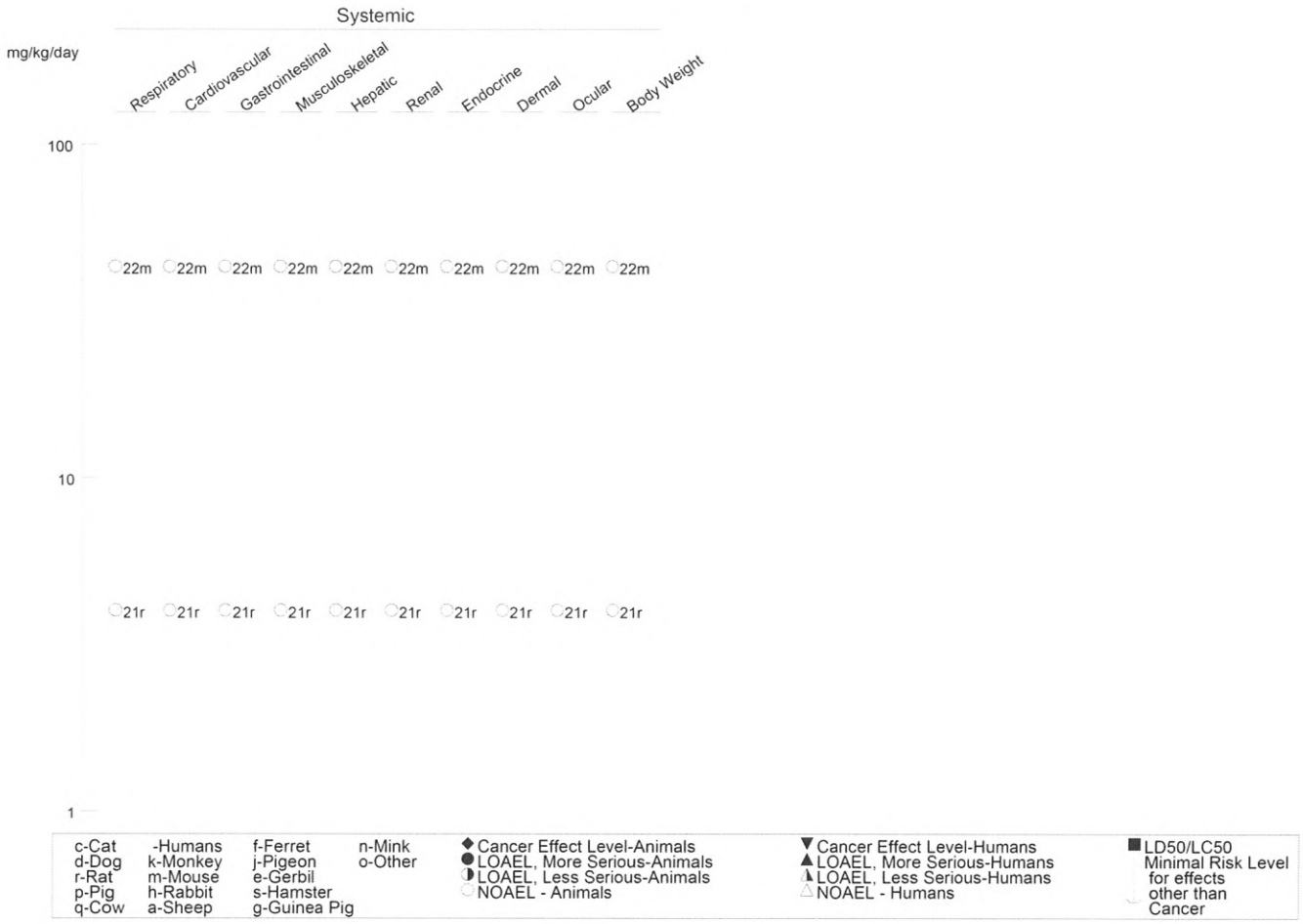
Figure 3-6 Levels of Significant Exposure to Roxarsone - Oral *(Continued)*



REC 5625

Figure 3-6 Levels of Significant Exposure to Roxarsone - Oral *(Continued)*

Chronic (≥365 days)



REC 5626

Available LD_{50} values for arsenate and arsenite in rats and mice range from 15 to 175 mg As/kg (Dieke and Richter 1946; Gaines 1960; Harrisson et al. 1958; Kaise et al. 1985). The variability can be attributed to differences based on species, strain, specific route of exposure (feed vs. gavage), specific compound tested, and testing laboratory. Most deaths occurred within 1 day of exposure, but details regarding cause of death were not generally reported. Seven of 25 pregnant rats given a single gavage dose of 23 mg As/kg as arsenic trioxide on day 9 of gestation died soon after dosing, while no deaths occurred at doses of 4–15 mg As/kg (Stump et al. 1999). Data on lethality from repeated exposure studies in animals are relatively sparse. Seven of 20 pregnant rabbits died from repeated gavage doses of 1.5 mg As/kg/day as arsenic acid during gestation, while none died at 0.1–0.4 mg As/kg/day (Nemec et al. 1998). Chronic studies observed treatment-related mortality in monkeys exposed to 3 mg As/kg/day as arsenate (Heywood and Sortwell 1979), dogs exposed to 2.4 mg As/kg/day as arsenite or arsenate (Byron et al. 1967), mice exposed to 1 mg As/kg/day as arsenite (Schroeder and Balassa 1967), and rats exposed to 30 mg As/kg/day as lead arsenate (Kroes et al. 1974).

Reliable LOAEL and LD_{50} values for lethality from oral exposure to inorganic arsenicals in each species and duration category are recorded in Table 3-3 and plotted in Figure 3-3.

Organic Arsenicals. No studies were located regarding death in humans after oral exposure to organic arsenicals, but the acute lethality of MMA, DMA, and roxarsone have been investigated in several animal studies. The LD_{50} values for MMA (including MSMA), DMA, and roxarsone are 102–3,184 mg/kg MMA or MSMA (Gur and Nyska 1990; Jaghabir et al. 1988; Kaise et al. 1989), 1,200 mg DMA/kg/day (Kaise et al. 1989), and 14.2–69.5 mg DMA/kg/day (Kerr et al. 1963; NTP 1989b), respectively. The cause of death was not investigated in any of these studies. Intermediate-duration exposure to MMA, DMA, or roxarsone resulted in increased mortality in laboratory animals exposed to 106.9 mg MMA/kg/day (Arnold et al. 2003), 17–190 mg DMA/kg/day (Crown et al. 1987; Murai et al. 1993; Wanibuchi et al. 1996) or 20–64 mg/kg/day roxarsone (Edmonds and Baker 1986; Kerr et al. 1963; NTP 1989b), respectively. Increased mortality was also observed in rats chronically exposed to 72.4 mg MMA/kg/day (Arnold et al. 2003).

3.2.2.2 Systemic Effects

The highest NOAEL values and all reliable LOAEL values for systemic effects from oral exposure in each species and duration category are recorded in Table 3-3 and plotted in Figure 3-3. Similar data for

oral exposure to MMA, DMA, and roxarsone are shown in Tables 3-4, 3-5, and 3-6, and shown in Figures 3-4, 3-5, and 3-6, respectively.

Respiratory Effects.

Inorganic Arsenicals. Serious respiratory effects, including respiratory distress, hemorrhagic bronchitis, and pulmonary edema, have been reported in some cases of acute oral arsenic poisoning at doses of 8 mg As/kg and above (e.g., Civantos et al. 1995; Fincher and Koerker 1987; Levin-Scherz et al. 1987; Moore et al. 1994b; Quatrehomme et al. 1992). These effects may be secondary to injury to the pulmonary vasculature (see Cardiovascular Effects, below). In addition, bronchitis and sequelae (bronchiectasis, bronchopneumonia) have been observed in patients and at autopsy in some chronic poisoning cases (Guha Mazumder et al. 2005; Milton and Rahman 2002; Rosenberg 1974; Tsai et al. 1999; Zaldívar 1974; Zaldívar and Guillier 1977). Bronchopneumonia secondary to arsenic-induced bronchitis was considered to be the cause of death in one young child who died after several years of exposure to an average dose of 0.08 mg As/kg/day (Zaldívar and Guillier 1977). Decrements in lung function, measured as decreased FEV_1, FVC, and FEF_{25-75} have also been reported in subjects exposed to 0.1–0.5 mg As/L in the drinking water and exhibiting skin lesions (von Ehrenstein et al. 2005). In general, however, respiratory effects have not been widely associated with repeated oral ingestion of low arsenic doses. Nevertheless, a few studies have reported minor respiratory symptoms, such as cough, sputum, rhinorrhea, and sore throat, in people with repeated oral exposure to 0.03–0.05 mg As/kg/day (Ahmad et al. 1997; Mizuta et al. 1956).

There are few data regarding respiratory effects in animals following acute oral exposure to inorganic arsenic. An infant Rhesus monkey that died after 7 days of oral exposure to a complex arsenate salt at a dose of 3 mg As/kg/day exhibited bronchopneumonia with extensive pulmonary hemorrhage, edema, and necrosis (Heywood and Sortwell 1979). Two other monkeys in this treatment group survived a 1-year exposure period and had no gross or microscopic pulmonary lesions at sacrifice. Increased relative lung weights were seen in rats exposed to 6.66 mg As/kg/day as sodium arsenite 5 days/week for 12 weeks (Schulz et al. 2002). Chronic oral studies in dogs and rats treated with arsenate or arsenite failed to find respiratory lesions (Byron et al. 1967; Kroes et al. 1974; Schroeder et al. 1968).

One study utilizing gallium arsenide included limited investigation of respiratory function. Respiration rate was significantly decreased in rats following ingestion of a single dose of gallium arsenide at 1,040 mg As/kg, but was unaffected at a dose of 520 mg As/kg (Flora et al. 1997a). Respiration rate was measured 1, 7, and 15 days after dosing, but the decrease was most noticeable after 15 days.

Organic Arsenicals. No respiratory effects were noted after acute human ingestion of 1,714 mg MSMA/kg (Shum et al. 1995). Mice exhibited respiratory arrest after a single oral dose of 1,800 mg MMA/kg (Kaise et al. 1989) or 900 mg DMA/kg (Kaise et al. 1989) and lung ornithine decarboxylase activity was reduced after ingestion of one or two doses of 720 mg DMA/kg (Ahmad et al. 1999a). Localized lung hemorrhage was observed in dogs after a single oral dose of 14.2 mg/kg roxarsone in a capsule (Kerr et al. 1963). No respiratory effects were seen after intermediate or chronic exposure of rats, mice, or dogs exposed to 35 mg MMA/kg/day (Waner and Nyska 1988), 7.8–94 mg DMA/kg/day (Arnold et al. 2006; Crown et al. 1987; Rubin et al. 1989; Zomber et al. 1989), or 4–136 mg/kg/day roxarsone (NTP 1989b).

Cardiovascular Effects.

Inorganic Arsenicals. A number of studies in humans indicate that arsenic ingestion may lead to serious effects on the cardiovascular system. Characteristic effects on the heart from both acute and long-term exposure include altered myocardial depolarization (prolonged QT interval, nonspecific ST segment changes) and cardiac arrhythmias (Cullen et al. 1995; Glazener et al. 1968; Goldsmith and From 1986; Heyman et al. 1956; Little et al. 1990; Mizuta et al. 1956; Moore et al. 1994b; Mumford et al. 2007). A significant dose-related increase in the prevalence of cardiac electrophysiologic abnormalites was observed in residents of Inner Mongolia, China; the incidences of QT prolongation were observed in 3.9, 11.1, and 20.6% of the residents with drinking water levels of <21, 110–300, and 430–690 µg/L, respectively (Mumford et al. 2007). Hypertrophy of the ventricular wall was observed at autopsy after acute exposure to 93 mg of arsenic (Quatrehomme et al. 1992). Long-term, low-level exposures may also lead to damage to the vascular system. The most dramatic example of this is "Blackfoot Disease," a condition that is endemic in an area of Taiwan where average drinking water levels of arsenic range from 0.17 to 0.80 ppm (Tseng 1977), corresponding to doses of about 0.014–0.065 mg As/kg/day (IRIS 2007). The disease is characterized by a progressive loss of circulation in the hands and feet, leading ultimately to necrosis and gangrene (Chen et al. 1988b; Ch'i and Blackwell 1968; Tseng 1977, 1989; Tseng et al. 1968, 1995, 1996). Several researchers have presented evidence that other factors besides arsenic (e.g., other water contaminants, dietary deficits) may play a role in the etiology of this disease (Ko 1986; Lu et al. 1990; Yu et al. 1984). While this may be true, the clear association between the occurrence of Blackfoot Disease and the intake of elevated arsenic levels indicates that arsenic is at least a contributing factor. The results of a recent study suggested that individuals with a lower capacity to methylate

inorganic arsenic to DMA have a higher risk of developing peripheral vascular disease in the Blackfoot Disease-hyperendemic area in Taiwan (Tseng et al. 2005).

Arsenic exposure in Taiwan has also been associated with an increased incidence of cerebrovascular and microvascular diseases (Chiou et al. 1997; Wang et al. 2002, 2003) and ischemic heart disease (Chang et al. 2004; Chen et al. 1996; Hsueh et al. 1998b; Tsai et al. 1999; Tseng et al. 2003). Moreover, effects of arsenic on the vascular system have also been reported in a number of other populations. For example, hypertension, defined as a systolic blood pressure of ≥140 mm Hg in combination with a diastolic blood pressure of ≥90 mm Hg, was associated with estimated lifetime doses of approximately 0.055 mg As/kg/day (0.25 mg/L in water) in a study of people in Bangladesh (Rahman et al. 1999); no significant association was found with estimated doses of 0.018 mg As/kg/day (0.75 mg/L in water). Wang et al. (2003) found an increased incidence of microvascular and macrovascular disease among subjects in Taiwan living in an arseniasis-endemic area in which the water of artesian wells had arsenic concentrations >0.35 mg/L (estimated doses of >0.03 mg As/kg/day). An additional study of Taiwanese subjects reported a significant increase in incidence of hypertension associated with concentrations of arsenic in the water >0.7 mg/L (estimated doses of >0.06 mg As/kg/day) (Chen et al. 1995). Studies in Chile indicate that ingestion of 0.6–0.8 ppm arsenic in drinking water (corresponding to doses of 0.02–0.06 mg As/kg/day, depending on age) increases the incidence of Raynaud's disease and of cyanosis of fingers and toes (Borgoño and Greiber 1972; Zaldívar 1974, 1977; Zaldívar and Guillier 1977). Autopsy of five children from this region who died of apparent arsenic toxicity showed a marked thickening of small and medium sized arteries in tissues throughout the body, especially the heart (Rosenberg 1974). In addition, cardiac failure, arterial hypotension, myocardial necrosis, and thrombosis have been observed in children who died from chronic arsenic ingestion (Zaldívar 1974), as well as adults chronically exposed to arsenic (Dueñas et al. 1998). Likewise, thickening and vascular occlusion of blood vessels were noted in German vintners exposed to arsenical pesticides in wine and in adults who drank arsenic-contaminated drinking water (Roth 1957; Zaldívar and Guillier 1977). A survey of Wisconsin residents using private wells for their drinking water found that residents exposed for at least 20 years to water concentrations of >10 µg As/L had increased incidences of cardiac bypass surgery, high blood pressure, and circulatory problems as compared with residents exposed to lower arsenic concentrations (Zierold et al. 2004). Similarly, Lewis et al. (1999) reported increased mortality from hypertensive heart disease in both men and women among a cohort exposed to arsenic in their drinking water in Utah, as compared with the general population of Utah. Limitations in the study included lack of evaluation of smoking as a confounder and of other dietary sources of arsenic, and the lack of a dose-response for hypertensive heart disease. Another ecological study (Engel and Smith 1994) found significant increases in deaths from

arteriosclerosis, aortic aneurysm, and all other diseases of the arteries, arterioles, and capillaries among U.S. residents with arsenic drinking waters of >20 µg/L; the increase in deaths from congenital anomalies of the heart and other anomalies of the circulatory system also observed in this subpopulation limits the interpretation of the findings.

Similar alterations in vascular reactivity have been noted in rats given repeated oral doses of arsenic trioxide (11 mg As/kg/day) for several weeks (Bekemeier and Hirschelmann 1989), although no histological effects could be detected in the hearts of rats or dogs exposed to up to 30 mg As/kg/day as arsenate or arsenite for 2 years (Byron et al. 1967; Kroes et al. 1974; Schroeder et al. 1968). Acute exposure of rats to gallium arsenide at a dose of 1,040 mg As/kg resulted in an increase in blood pressure and heart rate, while 520 mg As/kg had no effect (Flora et al. 1997a). Guinea pigs exposed to arsenic trioxide for 1 day (0, 7.6, 22.7, or 37.9 mg As/kg) or 8 days (0 or 3.8 mg As/kg/day) showed prolongation of the cardiac QT interval and action potential duration (Chiang et al. 2002).

Organic Arsenicals. No adverse cardiovascular effects were noted after acute human ingestion of 1,714 mg MSMA/kg (Shum et al. 1995). However, sinus tachycardia was noted after acute ingestion of 73 mg DMA/kg (as dimethyl arsenic acid and dimethyl arsenate) (Lee et al. 1995). No cardiovascular effects were seen after intermediate or chronic exposure of laboratory animals to 35–67.1 mg MMA/kg/day (Arnold et al. 2003; Waner and Nyska 1988), 7.8–94 mg DMA/kg/day (Arnold et al. 2006; Crown et al. 1987; Rubin et al. 1989; Zomber et al. 1989), or 4–136 mg/kg/day roxarsone (NTP 1989b).

Gastrointestinal Effects.

Inorganic Arsenicals. Clinical signs of gastrointestinal irritation, including nausea, vomiting, diarrhea, and abdominal pain, are observed in essentially all cases of short-term high-dose exposures to inorganic arsenic (e.g., Armstrong et al. 1984; Bartolome et al. 1999; Campbell and Alvarez 1989; Chakraborti et al. 2003a; Cullen et al. 1995; Fincher and Koerker 1987; Goebel et al. 1990; Kingston et al. 1993; Levin-Scherz et al. 1987; Lugo et al. 1969; Moore et al. 1994b; Muzi et al. 2001; Uede and Furukawa 2003; Vantroyen et al. 2004). Similar signs are also frequently observed in groups or individuals with longer-term, lower-dose exposures (e.g., Borgoño and Greiber 1972; Cebrián et al. 1983; Franzblau and Lilis 1989; Guha Mazumder et al. 1988, 1998a; Haupert et al. 1996; Holland 1904; Huang et al. 1985; Mizuta et al. 1956; Nagai et al. 1956; Silver and Wainman 1952; Wagner et al. 1979; Zaldívar 1974), but effects are usually not detectable at exposure levels below about 0.01 mg As/kg/day (Harrington et al. 1978; Valentine et al. 1985). These symptoms generally decline within a short time after exposure ceases.

Gastrointestinal irritation symptoms form the basis (in part) for the acute oral MRL of 0.005 mg/kg/day for inorganic arsenic, as described in footnote b in Table 3-3. More severe symptoms (hematemesis, hemoperitoneum, gastrointestinal hemorrhage, and necrosis) have been reported in some cases with acute exposure to 8 mg As/kg or more (Civantos et al. 1995; Fincher and Koerker 1987; Levin-Scherz et al. 1987; Quatrehomme et al. 1992), and also in some people with long-term ingestion of 0.03–0.05 mg As/kg/day as a medicinal preparation (Lander et al. 1975; Morris et al. 1974).

Clinical signs of gastrointestinal irritation were observed in monkeys and rats given repeated oral doses of arsenic (6 and 11 mg As/kg/day, respectively) for 2 weeks (Bekemeier and Hirschelmann 1989; Heywood and Sortwell 1979). Hemorrhagic gastrointestinal lesions have also been reported in animal studies. A monkey that died after repeated oral treatment with 6 mg As/kg/day for approximately 1 month was found to have acute inflammation and hemorrhage of the small intestine upon necropsy (Heywood and Sortwell 1979). This lesion was not found in other monkeys that died in this study, or in the survivors. Two pregnant mice that died after repeated gavage treatment with 24 mg As/kg/day as arsenic acid had hemorrhagic lesions in the stomach (Nemec et al. 1998). Gross gastrointestinal lesions (stomach adhesions, eroded luminal epithelium in the stomach) were seen frequently in rats treated by gavage with 8 mg As/kg/day as arsenic trioxide starting before mating and continuing through the end of gestation (Holson et al. 2000). The lesions were not found in rats treated with 4 mg As/kg/day in this study. No histological evidence of gastrointestinal injury was detected in rats exposed to arsenate or arsenite in the feed for 2 years at doses up to 30 mg As/kg/day, but dogs fed a diet containing 2.4 mg As/kg/day as arsenite for 2 years had some bleeding in the gut (Byron et al. 1967; Kroes et al. 1974).

Organic Arsenicals. Vomiting was noted after ingestion of 793 mg/kg arsenic (as monosodium methanearsenate) in a suicide attempt (Shum et al. 1995). Ingestion of 78 mg DMA/kg (as dimethyl arsenic acid and dimethyl arsenate) induced vomiting, abdominal pain, hyperactive bowel, and diarrhea (Lee et al. 1995).

The gastrointestinal tract appears to be the critical target of toxicity following oral exposure to MMA. Diarrhea/loose feces has been reported in mice and rabbits following a single gavage dose of 2,200 mg MMA/kg or 60 mg MSMA/kg, respectively (Jaghabir et al. 1988; Kaise et al. 1989), pregnant rabbits administered 12 mg MMA/kg/day via gavage (Irvine et al. 2006), rats exposed to 30.2 mg MMA/kg/day in the diet during the first year of a 2-year study (Arnold et al. 2003), dogs administered 2 mg MMA/kg/day via capsule for 52 weeks (Waner and Nyska 1988), rats fed diets containing 25.7 mg MMA/kg/day for 2 years (Arnold et al. 2003), and mice exposed to 67.1 mg MMA/kg/day in the diet for

2 years (Arnold et al. 2003). However, the increased incidence of diarrhea is not always accompanied by macroscopic or histological alterations in the gastrointestinal tissues. For example, in the 2-year rat study (Arnold et al. 2003; incidence data reported in Crown et al. 1990), an increased incidence of diarrhea was observed at 25.7 mg MMA/kg/day; macroscopic or histological alterations were observed in some animals, but the incidence was similar to controls. At the next highest dose level (72.4 mg MMA/kg/day), thickened wall and edema and hemorrhagic, necrotic, ulcerated, or perforated mucosa were observed in the large intestine and significant increases in the incidence of squamous metaplasia of the epithelial columnar absorptive cells were found in the cecum, colon, and rectum. Squamous metaplasia was also observed in the cecum and colon of mice chronically exposed to 67.1 mg MMA/kg/day (Arnold et al. 2003; incidence data reported in Gur et al. 1991).

There are some reports of gastrointestinal effects in rats and dogs exposed to DMA; however, the LOAELs for these effects are higher than the LOAELs for MMA and most rodent studies do not report effects at nonlethal doses. Diarrhea with congestion and hemorrhagic gastrointestinal contents were observed in rats exposed to a lethal dose of 190 mg DMA/kg/day in the diet for 4 weeks (Crown et al. 1987) and diarrhea and vomiting were reported in dogs administered 16 mg DMA/kg/day via capsule 6 days/week (Zomber et al. 1989). No gastrointestinal effects were observed in rats or mice chronically exposed to 7.8 or 94 mg DMA/kg/day, respectively (Arnold et al. 2006).

Vomiting and gastrointestinal hemorrhage were observed in dogs after a single capsulized dose of 50 mg/kg roxarsone (Kerr et al. 1963), although slightly higher doses administered for 13 weeks to rats and mice had no effect (NTP 1989b). No gastrointestinal effects were seen after chronic exposure of rats (4 mg/kg/day) or mice (43 mg/kg/day) to roxarsone (NTP 1989b).

Hematological Effects.

Inorganic Arsenicals. Anemia and leukopenia are common effects of arsenic poisoning in humans, and have been reported following acute (Armstrong et al. 1984; Goldsmith and From 1986; Mizuta et al. 1956; Muzi et al. 2001; Westhoff et al. 1975), intermediate (Franzblau and Lilis 1989; Heyman et al. 1956; Nagai et al. 1956; Wagner et al. 1979), and chronic oral exposures (Chakraborti et al. 2003a; Glazener et al. 1968; Guha Mazumder et al. 1988; Hopenhayn et al. 2006; Kyle and Pease 1965; Tay and Seah 1975) at doses of 0.002 mg As/kg/day or more. These effects may be due to both a direct cytotoxic or hemolytic effect on the blood cells (Armstrong et al. 1984; Fincher and Koerker 1987; Goldsmith and From 1986; Kyle and Pease 1965; Lerman et al. 1980) and a suppression of erythropoiesis (Kyle and

Pease 1965; Lerman et al. 1980). However, hematological effects are not observed in all cases of arsenic exposure (EPA 1981b; Harrington et al. 1978; Huang et al. 1985; Silver and Wainman 1952) or even all acute poisoning cases (Cullen et al. 1995; Moore et al. 1994b).

In an acute animal study, Tice et al. (1997) found that there was a decrease in polychromatic erythrocytes in the bone marrow of mice treated with 6 mg As/kg/day for 1 or 4 days. There was no effect at 3 mg As/kg/day. Long-term studies found mild anemia in dogs fed arsenite or arsenate for 2 years at 2.4 mg As/kg/day, but no hematological effect in dogs fed 1 mg As/kg/day for 2 years or 1.9 mg As/kg/day for 26 weeks (Byron et al. 1967; Neiger and Osweiler 1989). Chronic rat studies found little or no evidence of anemia at doses up to 30 mg As/kg/day, even with co-exposure to lead (Byron et al. 1967; Kroes et al. 1974). No hematological effects were found in monkeys exposed to arsenic doses of 3–6 mg As/kg/day for 1 year (Heywood and Sortwell 1979).

Rats exposed to arsenate for 6 weeks had decreased activities of several enzymes involved in heme synthesis, but data were not provided on whether this resulted in anemia (Woods and Fowler 1977, 1978). Exposure of rats to ≥5 ppm of arsenic (0.30 mg As/kg/day as sodium arsenite) in the drinking water for 4 weeks resulted in increased platelet aggregation, while 10 or 25 ppm (0.60 or 1.5 mg As/kg/day) was associated with increased P-selectin-positive cells and decreased occlusion time (Lee et al. 2002), representing a change in platelet function. Similarly, exposure of rats or guinea pigs to 10 or 25 ppm of arsenic as arsenite (approximate doses of 0, 0.92, or 2.3 mg As/kg/day for rats and 0, 0.69, or 1.7 mg As/kg/day for guinea pigs) in the drinking water for 16 weeks (Kannan et al. 2001) resulted in decreases in erythrocyte and leukocyte numbers (rats and guinea pigs), increased blood mean corpuscular volume and corpuscular hemoglobin mass (guinea pigs only), and decreased mean corpuscular hemoglobin concentration (rats only). Gallium arsenide also disrupts heme synthesis in rats, although the evidence suggests that this effect is due primarily to the gallium moiety (Flora et al. 1997a).

Organic Arsenicals. No adverse hematological effects were noted in a man who ingested 78 mg/kg as dimethyl arsenic acid and dimethyl arsenate (Lee et al. 1995). No hematological effects were observed in rats exposed to 8.4 or 72.4 mg MMA/kg/day for 2 years (Arnold et al. 2003; Shen et al. 2003) or dogs administered 35 mg MMA/kg/day for 52 weeks (Waner and Nyska 1988); additionally, no alterations in total or differential leukocyte levels were observed in mice exposed to 67.1 mg MMA/kg/day for 2 years (Arnold et al. 2003). Although some studies have reported hematological alterations following oral exposure to DMA, this is not a consistent finding. Observed alterations include decreased mean corpuscular hemoglobin concentration in rats exposed to 2.3 mg DMA/kg/day for 10 weeks (Rubin et al.

1989), decreased hemoglobin and erythrocyte levels in rats exposed to 4.5 mg DMA/kg/day for 13 weeks (Crown et al. 1987), decreased erythrocyte levels and increased leukocyte levels in dogs administered capsules containing 40 mg DMA/kg/day for 52 weeks (Zomber et al. 1989), and decreased lymphocyte and increased monocyte levels were observed in mice chronically exposed to 94 mg DMA/kg/day (Arnold et al. 2006). No hematological alterations have been observed in rats exposed to 7.8 mg DMA/kg/day for 2 years (Arnold et al. 2006). Similarly, no hematological effects were observed in rats (Kerr et al. 1963; NTP 1989b), mice (NTP 1989b), or dogs (Prier et al. 1963) exposed to 20–32, 68, or 5 mg/kg/day roxarsone, respectively, for intermediate or chronic durations

Musculoskeletal Effects.

Inorganic Arsenicals. No studies were located regarding musculoskeletal effects in humans or animals after oral exposure to inorganic arsenicals.

Organic Arsenicals. No studies were located regarding musculoskeletal effects in humans after oral exposure to organic arsenicals. No musculoskeletal effects were seen after intermediate or chronic exposure of rats and mice to MMA (Arnold et al. 2003), DMA (Arnold et al. 2006), or roxarsone (NTP 1989b).

Hepatic Effects.

Inorganic Arsenicals. A number of studies in humans exposed to inorganic arsenic by the oral route have noted signs or symptoms of hepatic injury. Clinical examination often reveals that the liver is swollen and tender (Chakraborty and Saha 1987; Franklin et al. 1950; Guha Mazumder et al. 1988, 1998a; Liu et al. 2002; Mizuta et al. 1956; Silver and Wainman 1952; Wade and Frazer 1953; Zaldívar 1974), and analysis of blood sometimes shows elevated levels of hepatic enzymes (Armstrong et al. 1984; Franzblau and Lilis 1989; Guha Mazumder 2005; Hernández-Zavala et al. 1998). These effects are most often observed after repeated exposure to doses of 0.01–0.1 mg As/kg/day (Chakraborty and Saha 1987; Franklin et al. 1950; Franzblau and Lilis 1989; Guha Mazumder et al. 1988; Mizuta et al. 1956; Silver and Wainman 1952; Wade and Frazer 1953), although doses as low as 0.006 mg As/kg/day have been reported to have an effect following chronic exposure (Hernández-Zavala et al. 1998). Hepatic effects have also been reported in acute bolus poisoning cases at doses of 2 mg As/kg/day or more (Hantson et al. 1996; Kamijo et al. 1998; Levin-Scherz et al. 1987; Quatrehomme et al. 1992; Vantroyen et al. 2004), although acute exposure to 19 mg As/kg did not cause hepatic effects in an infant (Cullen et al. 1995).

Histological examination of the livers of persons chronically exposed to similar doses has revealed a consistent finding of portal tract fibrosis (Guha Mazumder 2005; Guha Mazumder et al. 1988; Morris et al. 1974; Piontek et al. 1989; Szuler et al. 1979), leading in some cases to portal hypertension and bleeding from esophageal varices (Szuler et al. 1979); cirrhosis has also been reported at an increased frequency in arsenic-exposed individuals (Tsai et al. 1999). Several researchers consider that these hepatic effects are secondary to damage to the hepatic blood vessels (Morris et al. 1974; Rosenberg 1974), but this is not directly established.

Acute exposure of monkeys to 6 mg As/kg/day resulted in vacuolization of the hepatocytes (Heywood and Sortwell 1979). Studies in dogs or mice have not detected clinically significant hepatic injury following exposure to either arsenite or arsenate (Byron et al. 1967; Fowler and Woods 1979; Kerkvliet et al. 1980; Neiger and Osweiler 1989; Schroeder and Balassa 1967), although enlargement of the common bile duct was noted in rats fed either arsenate or arsenite in the diet for 2 years (Byron et al. 1967; Kroes et al. 1974) and lipid vacuolation and fibrosis were seen in the livers of rats exposed to 12 mg As/kg/day as arsenate in the drinking water for 6 weeks (Fowler et al. 1977). Similarly, fatty changes and inflammatory cell infiltration were seen in the livers of both normal and metallothionein-null mice exposed to 5.6 mg arsenic/kg/day in the drinking water for 48 weeks (Liu et al. 2000). Increases in liver zinc and copper concentrations were noted in rats receiving a single oral dose of 10 mg As/kg as sodium arsenite (Flora and Tripathi 1998) and hepatic levels of malondialdehyde were increased and glutathione levels were decreased in livers of rats receiving 200 mg As/kg as GaAs (Flora et al. 1998). An increase in indices of peroxidation was reported in rats dosed with approximately 0.02 mg As/kg/day for 60 days from drinking water containing 2.5 mg sodium arsenite/L (Bashir et al. 2006); absolute liver weight was also increased at this dose level. Elevated levels of serum aspartate aminotransferase (AST) were observed in rats administered a single oral dose of 100 mg As/kg as GaAs (Flora et al. 1998). Exposure of guinea pigs to 0.69 or 1.7 mg As/kg/day in the drinking water for 16 weeks, but not in rats exposed to 0.92 or 2.3 mg As/kg/day, resulted in increases in delta-aminolevulinic acid synthetase (ALAS) levels (Kannan et al. 2001). Exposure of BALB/C mice to 0.7 mg arsenic/kg/day in the drinking water for 15 months resulted in increased liver weights, changes in liver enzymes (glutathione S-transferase, glutathione reductase, catalase, glucose-6-phosphate dehydrogenase, glutathione peroxidase), fatty liver, and fibrosis (Santra et al. 2000).

Organic Arsenicals. No adverse hepatic effects were noted after ingestion of 1,714 mg/kg MSMA or 78 mg DMA/kg (as dimethyl arsenic acid and dimethyl arsenate) in a suicide attempt (Lee et al. 1995; Shum et al. 1995). No other studies of the hepatic effects of organic arsenicals in humans were located.

Histological examination of livers from rabbits given repeated oral doses of MMA showed diffuse inflammation and hepatocellular degeneration (Jaghabir et al. 1989), but the lesions were not severe. Male rats exposed to a time-weighted average (TWA) dose of 72.4 mg MMA/kg/day for 104 weeks showed a decrease in absolute liver weight, while females exposed to 98.5 mg MMA/kg/day showed histiocytic proliferation of the liver (Arnold et al. 2003); however, these effects were probably due to a decrease in body weight and secondary complications of perforation and ulceration of the gastrointestinal effect, respectively. Shen et al. (2003) reported increases in and the number of GST-P-positive foci in the livers of rats exposed to average concentrations of 8.4 mg MMA/kg/day in the diet for 104 weeks. No effects were observed in rats exposed to DMA (Siewicki 1981), but mice exposed to one or two oral doses of 720 mg DMA/kg had decreased liver glutathione and cytochrome P-450 content and serum ornithine decarboxylase activity (Ahmad et al. 1999a). Generalized icterus was reported in dogs after acute exposure to roxarsone (Kerr et al. 1963). Some small fluctuations in liver weight have been noted in rats and mice after intermediate oral exposure to roxarsone, but the toxicological significance of this is not clear and is not observed after chronic exposure of rats and mice to lower doses (NTP 1989b).

Renal Effects.

Inorganic Arsenicals. Most case studies of acute and chronic arsenic toxicity do not report clinical signs of significant renal injury, even when other systems are severely impaired (e.g., Cullen et al. 1995; Franzblau and Lilis 1989; Jenkins 1966; Kersjes et al. 1987; Mizuta et al. 1956; Silver and Wainman 1952). In some cases, elevated serum levels of creatinine or bilirubin have been noted (Armstrong et al. 1984; Levin-Scherz et al. 1987; Moore et al. 1994b), and mild proteinuria may occur (Armstrong et al. 1984; Glazener et al. 1968; Tay and Seah 1975). Acute renal failure in some bolus poisoning episodes (e.g., Fincher and Koerker 1987; Goebel et al. 1990; Levin-Scherz et al. 1987; Lugo et al. 1969; Moore et al. 1994b) is probably a result of fluid imbalances or vascular injury (Rosenberg 1974; Zaldívar 1974). Glomerular congestion has been observed after an acute exposure to high doses (Quatrehomme et al. 1992).

Studies in animals also indicate that the kidney is not a major target organ for inorganic arsenic (Byron et al. 1967; Schroeder and Balassa 1967; Woods and Southern 1989), although some effects have been reported at high exposure levels. Mild histological changes in the renal tubules of monkeys exposed to arsenate for 2 weeks were noted by Heywood and Sortwell (1979), and some mild alterations in renal mitochondria in rats exposed to arsenate for 6 weeks were noted by Brown et al. (1976). Mild proteinuria

(Flora et al. 1998) and an increase in kidney zinc concentration (Flora and Tripathi 1998) have also been noted in rats exposed orally to a single dose of 100 mg As/kg as GaAs or 10 mg As/kg as sodium arsenite, respectively. These data suggest that the kidney is relatively less sensitive to arsenic than most other organ systems, and renal effects are unlikely to be of concern except secondary to fluid imbalances or cardiovascular injury.

Organic Arsenicals. No adverse renal effects were noted after ingestion of 1,714 mg MSMA/kg in a suicide attempt (Shum et al. 1995). Animal studies have reported renal and urinary bladder effects following oral exposure to organic arsenicals; the available data suggest that the urinary system is a more sensitive target for DMA, than for MMA or roxarsone. A decrease in urine volume was observed in rabbits following a single gavage dose of 30 mg MSMA/kg/day (Jaghabir et al. 1988) and a decrease in urine volume (35 mg MMA/kg/day) and an increase in urine specific gravity (8 mg MMA/kg/day) were observed in dogs administered MMA via capsule for 52 weeks (Waner and Nyska 1988). However, these effects may be indicative of dehydration due to diarrhea rather than a direct effect on the kidney. In a 2-year study in rats (Arnold et al. 2003), an increase in the severity of progressive glomerulonephropathy was observed in females at 33.9 mg MMA/kg/day. Hydronephrosis, pyelonephritis, cystitis, and decreases in urine volume and pH were also observed 72.4 mg MMA/kg/day; however, the investigators noted that these lesions probably resulted from urinary tract obstruction, which was secondary to peritonitis caused by gastrointestinal tract ulcerations. An increased incidence of progressive glomerulonephropathy was also observed in male mice exposed to ≥6.0 mg MMA/kg/day in the diet for 2 years (Arnold et al. 2003; incidence data reported in Gur et al. 1991); the investigators (Gur et al. 1991) noted that the kidney lesions were consistent with the normal spectrum of spontaneous lesions and that there were no differences in character or severity of the lesions between the different groups.

Exposure to DMA has resulted in kidney effects in rats and mice exposed to at least 3.1 or 37 mg DMA/kg/day, respectively; no renal effects were observed in dogs exposed to doses as high as 40 mg As/kg/day for 52 weeks (Zomber et al. 1989). In rats, the renal damage is characterized by increased urine volume and pH, decreased urine osmolarity and electrolyte (sodium, potassium, chlorine) levels, increased urinary calcium levels, and increased organ weight, nephrocalcinosis, and necrosis in the renal papillae and/or cortex; an increase in water consumption is also typically observed. The LOAELs for these effects are 5–57 mg DMA/kg/day in intermediate-duration studies (Arnold et al. 1999; Crown et al. 1987; Murai et al. 1993) and 3.1 mg DMA/kg/day in a chronic-duration study (Arnold et al. 2006). Another study did not find renal effects in rats exposed to 16.5 mg DMA/kg/day (Rubin et al. 1989). This study involved exposure to Sprague-Dawley rats compared to Fischer 344 rats used in the studies with

positive results; it is not known if this reflects a difference in strain sensitivity. In mice, progressive glomerulonephropathy was observed at 37 mg DMA/kg/day and nephrocalcinosis was observed at 94 mg DMA/kg/day (Arnold et al. 2006).

Increased kidney weights and minimal tubular epithelial cell degeneration, tubular casts, and focal mineralization were observed in rats exposed to 32 mg/kg/day roxarsone for 13 weeks (NTP 1989b). No adverse effects were observed in rats at doses as high as 20 mg/kg/day (Kerr et al. 1963; NTP 1989b) for 13 weeks or 10 mg/kg/day for 2 years (NTP 1989b; Prier et al. 1963). No adverse renal effects have been observed in mice exposed to roxarsone doses as high as 136 mg/kg/day (NTP 1989b) or 43 mg/kg/day (NTP 1989b; Prier et al. 1963) for intermediate or chronic durations, respectively, or in dogs exposed to 5 mg/kg/day for a chronic duration (Prier et al. 1963).

Damage to the urinary bladder has been observed in several studies in which rats were exposed to DMA. The observed effects include altered bladder cell surface characteristics in rats exposed to 11 mg DMA/kg/day in the diet for 2 weeks (Cohen et al. 2001), increased bladder weight and regenerative proliferation (measured as an increase in BrdU labeling) in bladder epithelium at 5 mg DMA/kg/day for 10 weeks (Arnold et al. 1999), necrosis of bladder epithelium at 10 mg DMA/kg/day for 10 weeks (Arnold et al. 1999), nodular or papillar hyperplasia at 3.4 mg DMA/kg/day for 2 years (Wei et al. 2002), and urothelial vacuolar degeneration and hyperplasia of urothelial cells at 3.1 mg DMA/kg/day for 2 years (Arnold et al. 2006). Vacuolization of the urothelium in the urinary bladder have also been observed in mice exposed to 7.8 mg DMA/kg/day in the diet for 2 years (Arnold et al. 2006). Inconsistent results were found for MMA. Hyperplasia was observed in the bladders of rats exposed to 1 mg As/kg/day as MMA in drinking water for 2 years (Shen et al. 2003), but bladder effects were not observed in another 2-year study (Arnold et al. 2003) in which rats were exposed to doses as high as 34.8 mg As/kg/day as MMA in the diet. No urinary bladder effects were found in rats and mice exposed to 64 or 136 mg/kg/day roxarsone for 13 weeks (NTP 1989b) or 4 or 43 mg/kg/day roxarsone for 2 years (NTP 1989b).

Endocrine Effects.

Inorganic Arsenicals. Very little has been written about the effects of oral exposure to arsenic on endocrine glands. In a report of the autopsies of five children who died in Chile after chronic exposure to arsenic in the drinking water, arterial thickening in the pancreas was noted (Rosenberg 1974). An association has been demonstrated between exposure to arsenic in drinking water and an increased

incidence of diabetes mellitus (Lai et al. 1994; Rahman et al. 1998; Tsai et al. 1999; Tseng et al. 2000; Wang et al. 2003), although dose-response relationships are not available.

Exposure of rats to 2.3 mg As/kg/day as arsenic trioxide for 30 days resulted in reductions in the number of islet cells in the pancreas, as well as significant reductions in pancreatic superoxide dismutase (SOD) and catalase enzyme levels and increases in the production of nitric oxide and malondialdehyde (Mukherjee et al. 2004).

Organic Arsenicals. No studies of effects of organic arsenic compounds on endocrine glands in humans were found. Hypertrophy of thyroid epithelium was observed in rats exposed to 33.9 mg MMA/kg/day in the diet for 2 years (Arnold et al. 2003), 4.0 mg DMA/kg/day in the diet for 13 weeks (Crown et al. 1987), 16.5 mg DMA/kg/day in the diet for at least 10 weeks (Rubin et al. 1989), and 7.8 mg DMA/kg/day in the diet for 2 years (Arnold et al. 2006). No other biologically significant effects were observed in other endocrine tissues following exposure to MMA or DMA. No adverse effects were seen in the adrenal or pituitary glands, thyroid, or pancreas after intermediate or chronic exposure of rats (20–64 or 4 mg/kg/day, respectively) and mice (136 or 43 mg/kg/day, respectively) to roxarsone (NTP 1989b).

Dermal Effects.

Inorganic Arsenicals. One of the most common and characteristic effects of arsenic ingestion is a pattern of skin changes that include generalized hyperkeratosis and formation of hyperkeratotic warts or corns on the palms and soles, along with areas of hyperpigmentation interspersed with small areas of hypopigmentation on the face, neck, and back. These and other dermal effects have been noted in a large majority of human studies involving repeated oral exposure (e.g., Ahmad et al. 1997, 1999b; Ahsan et al. 2000; Bickley and Papa 1989; Borgoño and Greiber 1972; Borgoño et al. 1980; Cebrián et al. 1983; Chakraborti et al. 2003a, 2003b; Chakraborty and Saha 1987; Foy et al. 1992; Franklin et al. 1950; Franzblau and Lilis 1989; Guha Mazumder et al. 1988, 1998a, 1998b, 1998c; Guo et al. 2001a; Haupert et al. 1996; Huang et al. 1985; Lander et al. 1975; Liu et al. 2002; Lüchtrath 1983; Milton et al. 2004; Mizuta et al. 1956; Morris et al. 1974; Nagai et al. 1956; Piontek et al. 1989; Rosenberg 1974; Saha and Poddar 1986; Silver and Wainman 1952; Szuler et al. 1979; Tay and Seah 1975; Tseng et al. 1968; Wade and Frazer 1953; Wagner et al. 1979; Wong et al. 1998a, 1998b; Zaldívar 1974, 1977). In cases of low-level chronic exposure (usually from water), these skin lesions appear to be the most sensitive indication of effect, so this end point is considered to be the most appropriate basis for establishing a chronic oral MRL. This is supported by the finding that other effects (hepatic injury, vascular disease, neurological

effects) also appear to have similar thresholds. As shown in Table 3-3 and Figure 3-3, numerous studies in humans have reported dermal effects at chronic dose levels generally ranging from about 0.01 to 0.1 mg As/kg/day (Ahmad et al. 1997; Bickley and Papa 1989; Borgoño and Greiber 1972; Borgoño et al. 1980; Cebrián et al. 1983; Chakraborty and Saha 1987; Foy et al. 1992; Franklin et al. 1950; Guha Mazumder et al. 1988; Huang et al. 1985; Lüchtrath 1983; Piontek et al. 1989; Silver and Wainman 1952; Tseng et al. 1968; Zaldívar 1974, 1977). However, in a study with detailed exposure assessment, all confirmed cases of skin lesions ingested water containing >100 µg/L arsenic (approximately 0.0037 mg As/kg/day) and the lowest known peak arsenic concentration ingested by a case was 0.115 µg/L (approximately 0.0043 mg As/kg/day) (Haque et al. 2003). Another large study reported increased incidence of skin lesions associated with estimated doses of 0.0012 mg As/kg/day (0.023 mg As/L drinking water) (Ahsan et al. 2006). Several epidemiological studies of moderately sized populations (20–200 people) exposed to arsenic through drinking water have detected no dermal or other effects at average chronic doses of 0.0004–0.01 mg As/kg/day (Cebrián et al. 1983; EPA 1981b; Guha Mazumder et al. 1988; Harrington et al. 1978; Valentine et al. 1985), and one very large study detected no effects in any person at an average total daily intake (from water plus food) of 0.0008 mg As/kg/day (Tseng et al. 1968). This value has been used to calculate a chronic oral MRL for inorganic arsenic of 0.0003 mg/kg/day, as described in footnote c in Table 3-3.

Another prominent dermal effect associated with chronic ingestion of inorganic arsenic is skin cancer. As discussed in greater detail in Section 3.2.2.7 (below), some of these skin cancers may evolve from the hyperkeratotic corns or warts, while the areas of altered pigmentation are not considered to be precancerous (EPA 1988d).

Dermal lesions similar to those observed in humans have not been noted in oral exposure studies in monkeys (Heywood and Sortwell 1979), dogs (Byron et al. 1967), or rodents (Schroeder et al. 1968). However, a hyperplastic response to oral arsenic exposure was reported in arsenic-exposed mice (Rossman et al. 2004).

Organic Arsenicals. No studies were located regarding dermal effects in humans after oral exposure to organic arsenicals. No gross or histological skin alterations were observed in rats or mice following intermediate- or chronic-duration exposure to MMA (Arnold et al. 2003; as reported in Crown et al. 1990; Gur et al. 1991), DMA (Arnold et al. 2006; as reported in Gur et al. 1989a, 1989b), or roxarsone (NTP 1989b)

Ocular Effects.

Inorganic Arsenicals. Periorbital swelling was reported in people drinking contaminated well water at an approximate dose of 0.2 mg As/kg for 1 week (Armstrong et al. 1984). Facial edema, generally involving the eyelids, was a prominent feature of arsenic poisoning among 220 cases associated with an episode of arsenic contamination of soy sauce in Japan (Mizuta et al. 1956). Exposure was to an estimated dose of 0.05 mg/kg/day and lasted for up to 2–3 weeks. The edema developed soon after the initial exposure and then subsided. This effect forms the basis (in part) for the acute oral MRL of 0.005 mg/kg/day for inorganic arsenic, as described in footnote b in Table 3-3. Nemec et al. (1998) noted the appearance of dried red material around the eyes of mice receiving daily oral doses of 24 mg As/kg as arsenic acid for 10 days during gestation.

Organic Arsenicals. No studies were located regarding ocular effects in humans or animals after oral exposure to organic arsenicals. No gross or histological alterations in the eye were observed in rats or mice following intermediate- or chronic-duration exposure to MMA (Arnold et al. 2003; as reported in Crown et al. 1990; Gur et al. 1991), DMA (Arnold et al. 2006; as reported in Gur et al. 1989a, 1989b), or roxarsone (NTP 1989b).

Body Weight Effects.

Inorganic Arsenicals. A 41-year old woman exposed to arsenic in the drinking water for 4 months at an approximate dose of 0.06 mg As/kg/day reported losing 40 pounds (18 kg) of body weight before seeking treatment (Wagner et al. 1979). Weight loss was also among the effects observed in a series of 475 chronic arsenism patients hospitalized in Antofagasto, Chile after receiving approximate doses of 0.02 mg As/kg/day in the drinking water for an unspecified number of years (Zaldívar 1974).

Reductions in body weight gain are commonly seen in animal studies of ingested arsenic. In pregnant rats, body weight gain was reduced by gavage treatment with 23 mg As/kg/day as arsenic trioxide on day 9 of gestation (NOAEL=15 mg As/kg/day, Stump et al. 1999), and by repeated gavage treatment with 8 mg As/kg/day as arsenic trioxide from 2 weeks prior to mating through gestation (NOAEL=4 mg As/kg/day, Holson et al. 2000). Exposure of rats by gavage to 26.6 mg As/kg/day as sodium arsenite, but not 13.3 mg As/kg/day or lower, 5 days/week for 4 weeks resulted in a significant decrease in body weight (Schulz et al. 2002). In 6-week rat studies, body weight gain was decreased at 11–12 mg As/kg/day, but not at 6–9 mg As/kg/day (Brown et al. 1976; Fowler et al. 1977). In a 12-week oral

gavage study, rats dosed with 1.5 mg/kg/day sodium arsenite had a median final body weight 18% lower than controls Dhar et al. (2005). A 60-day rat study with sodium arsenite in the drinking water reported a 13% reduction in final body weight in rats dosed with approximately 0.02 mg As/kg/day (Bashir et al. 2006). In chronic rat studies of arsenate and arsenite, body growth decreases were found at doses as low as 2 mg As/kg/day in feeding studies (Byron et al. 1967; Kroes et al. 1974), while rats exposed to lower levels of sodium arsenite in the drinking water (0.6 mg As/kg/day) throughout their lifetimes grew normally (Schroeder et al. 1968). Rats given a single oral dose of 100 mg As/kg as GaAs exhibited a 15% reduction in body weight compared to controls 7 days after exposure (Flora et al. 1998). Body weight gain was decreased in mice at 24 mg As/kg/day in a gestation exposure study (Nemec et al. 1998), 10 mg As/kg/day in a 6-week study (Fowler and Woods 1979), and 1 mg As/kg/day in a 2-year study (Schroeder and Balassa 1967). Growth was unaffected in mice that received 12 mg As/kg/day in the gestation exposure study (Nemec et al. 1998), 5 mg As/kg/day in the 6-week study (Fowler and Woods 1979), or 0.7–0.8 mg As/kg/day in 1–3 month arsenate drinking water studies (Healy et al. 1998). Dogs chronically treated with 2.4 mg As/kg/day as sodium arsenite lost 44–61% of their starting body weight and died, while lower doses had no effect on growth (Byron et al. 1967). Weight depression was also reported in dogs chronically treated with 2.4 mg As/kg/day as sodium arsenate (Byron et al. 1967). Feed consumption and body weight gain were significantly reduced in a dose-related manner in dogs fed 1.5 or 1.9 mg As/kg/day as sodium arsenite in the diet (Neiger and Osweiler 1989). Dogs in the high-dose group lost 25% of their body weight over the 17-week study period. Pair-fed controls lost weight at the same rate as high-dose dogs, showing that the effect on body weight was due to reduced feed consumption, rather than a direct effect of arsenic.

Organic Arsenicals. No studies were located regarding body weight effects in humans after oral exposure to organic arsenicals. In animal studies of organic arsenicals, decreases in body weight gain were observed in rats and mice after acute, intermediate, and chronic duration exposure to MMA (Arnold et al. 2003; Waner and Nyska 1988), DMA (Murai et al. 1993), and roxarsone (NTP 1989b); decreases in body weight gain have also been reported in pregnant rats and rabbits exposed to MMA (Irvine et al. 2006) or DMA (Irvine et al. 2006; Rogers et al. 1981). For MMA, the decreases in body weight gain were observed following intermediate-duration exposure of rats and dogs to 106.9 or 8 mg MMA/kg/day (Arnold et al. 2003; Waner and Nyska 1988), respectively, and following chronic-duration exposure of rats, mice, and dogs to 25.7, 67.1, or 8 mg MMA/kg/day, respectively (Arnold et al. 2003; Waner and Nyska 1988). The decreases in body weight gain occurred at doses that were associated with diarrhea and histological alterations in the gastrointestinal tract (Arnold et al. 2003; Waner and Nyska 1988). One DMA study in nonpregnant animals reported decreases in body weight gain in rats administered 57 mg

DMA/kg/day via gavage 5 days/week for 4 weeks (Murai et al. 1993); other DMA studies have not reported decreases in body weight gain in rats following exposure to 11 mg DMA/kg/day for acute durations (Cohen et al. 2001), 3.7–60 mg DMA/kg/day for intermediate durations (Arnold et al. 1999; Crown et al. 1987; Rubin et al. 1989; Siewicki 1981; Wanibuchi et al. 1996; Yamamoto et al. 1995), or 0.77 mg DMA/kg/day for chronic durations (Arnold et al. 2006). No alterations in body weight gain were observed in mice exposed to 94 mg DMA/kg/day for 2 years (Arnold et al. 2006). The lowest doses of roxarsone to produce a decrease in growth were 32 and 16 mg/kg/day in rats following acute- or intermediate-duration exposure, respectively, and 168 and 136 mg/kg/day in mice following acute or intermediate exposure (NTP 1989b); at the highest dose tested in chronic studies, no significant alterations in body weight gain were observed in rats at 4 mg/kg/day or in mice at 43 mg/kg/day (NTP 1989b).

3.2.2.3 Immunological and Lymphoreticular Effects

Inorganic Arsenicals. No studies were located regarding immunological and lymphoreticular effects in humans after oral exposure to inorganic arsenicals. No evidence of immunosuppression was detected in mice exposed to arsenate at levels up to 100 ppm (20 mg As/kg/day) in drinking water (Kerkvliet et al. 1980). This NOAEL is shown in Table 3-3 and Figure 3-3. Gallium arsenide at doses of 52–260 mg As/kg/day produced significant, dose-related decreases in relative spleen weight, spleen cellularity, humoral immune response (antibody forming cell response to sheep RBC), and delayed type hypersensitivity in rats (Flora et al. 1998). However, it is not clear to what extent these effects are due to the arsenic moiety.

Organic Arsenicals. No studies were located regarding immunological and lymphoreticular effects in humans or animals after oral exposure to organic arsenicals. No histological alterations were observed in immunological or lymphoreticular tissues following intermediate-duration exposure of rats to 43.2 mg DMA/kg/day in the diet (Crown et al. 1987) or rats and mice to 18.23 or 38.7 mg As/kg/day as roxarsone, respectively (NTP 1989b) or following chronic-duration exposure of rats and mice to 72.4 or 67.1 mg MMA/kg/day (Arnold et al. 2003), 7.8 or 94 mg DMA/kg/day (Arnold et al. 2006), or 4 or 43 mg/kg/day roxarsone (NTP 1989b). No studies examined immune function following oral exposure to organic arsenicals.

3.2.2.4 Neurological Effects

Inorganic Arsenicals. A large number of epidemiological studies and case reports indicate that ingestion of inorganic arsenic can cause injury to the nervous system. Acute, high-dose exposures (2 mg As/kg/day or above) often lead to encephalopathy, with signs and symptoms such as headache, lethargy, mental confusion, hallucination, seizures, and coma (Armstrong et al. 1984; Bartolome et al. 1999; Civantos et al. 1995; Cullen et al. 1995; Danan et al. 1984; Fincher and Koerker 1987; Levin-Scherz et al. 1987; Quatrehomme et al. 1992; Uede and Furukawa 2003; Vantroyen et al. 2004). Repeated exposures to lower levels (0.03–0.1 mg As/kg/day) are typically characterized by a symmetrical peripheral neuropathy (Chakraborti et al. 2003a, 2003b; Foy et al. 1992; Franzblau and Lilis 1989; Guha Mazumder et al. 1988; Hindmarsh et al. 1977; Huang et al. 1985; Lewis et al. 1999; Mizuta et al. 1956; Muzi et al. 2001; Silver and Wainman 1952; Szuler et al. 1979; Wagner et al. 1979). This neuropathy usually begins as numbness in the hands and feet, but later may develop into a painful "pins and needles" sensation. Both sensory and motor nerves are affected, and muscle weakness often develops, sometimes leading to wrist-drop or ankle-drop (Chhuttani et al. 1967; Heyman et al. 1956). Diminished sensitivity to stimulation and abnormal patellar reflexes have also been reported (Mizuta et al. 1956). Histological examination of nerves from affected individuals reveals a dying-back axonopathy with demyelination (Goebel et al. 1990; Hindmarsh and McCurdy 1986). Some recovery may occur following cessation of exposure, but this is a slow process and recovery is usually incomplete (Fincher and Koerker 1987; Le Quesne and McLeod 1977; Murphy et al. 1981). Peripheral neuropathy is also sometimes seen following acute high-dose exposures, with or without the previously described encephalopathy (Armstrong et al. 1984; Baker et al. 2005; Fincher and Koerker 1987; Goebel et al. 1990; Hantson et al. 1996; Kamijo et al. 1998). Neurological effects were not generally found in populations chronically exposed to doses of 0.006 mg As/kg/day or less (EPA 1981b; Harrington et al. 1978; Hindmarsh et al. 1977), although fatigue, headache, dizziness, insomnia, nightmare, and numbness of the extremities were among the symptoms reported at 0.005, but not 0.004 mg As/kg/day in a study of 31,141 inhabitants of 77 villages in Xinjiang, China (Lianfang and Jianzhong 1994), and depression was reported in some Wisconsin residents exposed to 2–10 μg As/L in the drinking water for 20 years or longer (Zierold et al. 2004).

There is emerging evidence suggesting that exposure to arsenic may be associated with intellectual deficits in children. For example, Wasserman et al. (2004) conducted a cross-sectional evaluation of intellectual function in 201 children 10 years of age whose parents were part of a larger cohort in Bangladesh. Intellectual function was measured using tests drawn from the Wechsler Intelligence Scale for Children; results were assessed by summing related items into Verbal, Performance, and Full-Scale

raw scores. The mean arsenic concentration in the water was 0.118 mg/L. The children were divided into four exposure groups, representing <5.5, 5.6–50, 50–176, or 177–790 µg As/L drinking water. After adjustment for confounding factors, a dose-related inverse effect of arsenic exposure was seen on both Performance and Full-Scale subset scores; for both end points, exposure to ≥50 µg/L resulted in statistically significant differences (p<0.05) relative to the lowest exposure group (<5.5 µg/L). In a later report, the same group of investigators examined 301 6-year-old children from the same area (Wasserman et al. 2007). In this case, the children were categorized into the following quartiles based on water arsenic concentration: 0.1–20.9, 21–77.9, 78–184.9, and 185–864 µg/L. After adjustment for water Mn, blood lead, and sociodemographic features known to contribute to intellectual function, water arsenic was significantly negatively associated with both Performance and Processing speed raw scores. Analyses of the dose-response showed that compared to the first quartile, those in the second and third categories had significantly lower Performance raw scores (p<0.03 and p=0.05, respectively). Those in the fourth category had marginally significantly lower Full-Scale and Processing Speed raw scores. It should be mentioned, however, that in general, arsenic in the water explained <1% of the variance in test scores. Water arsenic made no contribution to IQ outcomes. A study of 351 children age 5–15 years from West Bengal, India, found significant associations between urinary arsenic concentrations and reductions in scores of tests of vocabulary, object assembly, and picture completion; the magnitude of the reductions varied between 12 and 21% (von Ehrenstein et al. 2007). In this cohort, the average lifetime peak arsenic concentration in well water was 0.147 mg/L. However, no clear pattern was found for increasing categories of peak arsenic water concentrations since birth and children's scores in the various neurobehavioral tests conducted. Furthermore, using peak arsenic as a continuous variable in the regression models also did not support an adverse effect on the tests results. Exposure to arsenic *in utero* also did not suggest an association with the tests scores. Von Ehrestein et al. (2007) concluded that the study provided little evidence for an effect of long-term arsenic concentrations in drinking water and that the lack of findings with past exposures via drinking water may be due to incomplete assessment of past exposure, particularly exposure originating from food. Wasserman's results are consistent with those of ecological studies in children in Taiwan (Tsai et al. 2003) and in China (Wang et al. 2007). In the former, adolescents exposed to low (0.0017–0.0018 mg As/kg/day; n=20) levels of inorganic arsenic in the drinking water showed decreased performance in the switching attention task, while children in the high exposure group (0.0034–0.0042 mg As/kg/day; n=29) showed decreased performance in both the switching attention task and in tests of pattern memory, relative to unexposed controls (n=60). In the study in China (age 8– 12 years), 87 children whose mean arsenic concentration in the drinking water was 0.190 mg/L had a mean IQ score of 95 compared with 101 for children (n=253) with 0.142 mg/L arsenic in the water and 105 for control children (n=196) with 0.002 mg/L arsenic in the drinking water (Wang et

al. 2007). The differences in IQ scores between the two exposure groups and the control group were statistically significant.

Neurological effects have also been observed in animal studies. Rodriguez et al. (2001) evaluated neurobehavioral changes in male Sprague-Dawley rats exposed to 0, 5, 10, or 20 mg As/kg/day as sodium arsenite by gavage for 2 or 4 weeks; significant effects were seen in spontaneous locomotor activity and the food pellet manipulation test in the high-dose animals, while no effects were seen in the low- or mid-dose rats. Decreased performance in open field tests were also seen in rats exposed to 26.6 mg As/kg/day, but not to 13.3 mg/kg/day or less, as sodium arsenite for 4 weeks (Schulz et al. 2002); curiously, the behavioral changes were no longer present at 8 and 12 weeks of exposure, which may suggest an adaptive response. Heywood and Sortwell (1979) reported salivation and uncontrolled head shaking in two monkeys given several doses of 6 mg As/kg/day as arsenate, while no such effects were noted in monkeys given 3 mg As/kg/day for 2 weeks. Nemec et al. (1998) observed ataxia and prostration in pregnant female rabbits treated with 1.5 mg As/kg/day repeatedly during gestation, but not in rabbits treated with 0.4 mg As/kg/day. Some changes in levels of neurotransmitters (dopamine, norepinephrine, and 5-hydroxytryptamine) were seen in rats exposed to 2.3 mg As/kg/day as sodium arsenite and guinea pigs exposed to 1.7 mg As/kg/day as sodium arsenite in the drinking water for 16 weeks (Kannan et al. 2001) or in rats exposed to 0.14 mg As/kg/day as sodium arsenite by gavage for 28 days (Chattopadhyay et al. 2001), but the functional significance of these changes is not clear.

The highest NOAEL values and all reliable LOAEL values for neurological effects from inorganic arsenic in each species and duration category are recorded in Table 3-3 and plotted in Figure 3-3.

Organic Arsenicals. Numbness and tingling of the fingertips, toes, and circumoral region were reported by a women exposed to an unspecified amount of organic arsenic in bird's nest soup. Discontinuation of exposure resulted in the disappearance of symptoms (Luong and Nguyen 1999). Decreased absolute brain weights were seen in male rats exposed to 25.7 mg MMA/kg/day and female rats exposed to ≥33.9 mg MMA/kg/day, but decreased body weight also occurred at these exposure levels, and relative brain weights were increased in the males at 25.7 mg MMA/kg/day and the females at ≥33.9 mg MMA/kg/day in this study (Arnold et al. 2003). No neurological clinical signs or brain lesions were observed following chronic exposure of rats to 72.4 mg MMA/kg/day or mice to 67.1 mg MMA/kg/day (Arnold et al. 2003). Decreased spontaneous motility, increased startle response, and ataxia were observed in mice receiving a single gavage dose of 1,757 mg DMA/kg/day (Kaise et al. 1989); no other evidence (clinical signs or histological alterations) were observed in chronic studies of DMA in which

rats and mice were exposed to 7.8 or 94 mg DMA/kg/day, respectively (Arnold et al. 2006). Two studies in pigs indicate that repeated oral doses of roxarsone (6.3–20 mg/kg/day for 1 month) can cause significant neurotoxicity (Edmonds and Baker 1986; Kennedy et al. 1986; Rice et al. 1985). The main signs were time-dependent degenerations of myelin and axons (Kennedy et al. 1986; Rice et al. 1985). Evidence of neurological effects (hyperexcitability, ataxia, trembling) was noted in some rat and mouse studies (Kerr et al. 1963; NTP 1989b). Reliable NOAELs and LOAELs are presented in Tables 3-4, 3-5, and 3-6, and Figures 3-4, 3-5, and 3-6.

3.2.2.5 Reproductive Effects

Inorganic Arsenicals. Exposure to arsenic in drinking water has been associated with adverse reproductive outcomes in some studies. For example, a study of 96 women in Bangladesh who had been drinking water containing ≥0.10 mg As/L (approximately 0.008 mg As/kg/day) for 5–10 years reported a significant increase in spontaneous abortions (p=0.008), stillbirth (p=0.046), and preterm birth (p=0.018) compared to a nonexposed group (Ahmad et al. 2001). Similar results were reported by Milton et al. (2005) who found a significant association between concentrations of arsenic in the water >0.05 mg/L (approximately 0.006 mg As/kg/day) and spontaneous abortion (odds ratio [OR]=2.5; 95% CI=1.5–4.3) in a study of 533 women, also from Bangladesh. A study of 202 women from West Bengal, India, reported that exposure to arsenic concentrations of arsenic ≥0.2 mg/L in drinking water (approximately 0.02 mg As/kg/day) during pregnancy were associated with a 6-fold increased risk of stillbirth (OR=6.1; 95% CI=1.54–24.0) after adjustment for confounders (von Ehrenstein et al. 2006). No association was found between arsenic exposure and risk of spontaneous abortion (OR=1.01; 95% CI=0.73–10.8). An earlier study of 286 women in the United States also found no significant association between arsenic in the drinking water (0.0016 mg/L; approximately 0.00005 mg As/kg/day) and spontaneous abortion (OR=1.7; 95% CI=0.7–4.2) (Aschengrau et al. 1989).

Lugo et al. (1969) reported a case of a 17-year-old mother who ingested inorganic arsenic (Cowley's Rat and Mouse Poison) at week 30 of pregnancy. Twenty-four hours after ingestion of approximately 30 mL of arsenic trioxide (0.39 mg As/kg), she was admitted for treatment of acute renal failure. She went into labor and delivered a live female infant weighing 2 pounds, 7 ounces with a 1-minute Apgar score of 4. The infant's clinical condition deteriorated and she died at 11 hours of age.

Reproductive performance was not affected in female rats that received gavage doses of 8 mg As/kg/day (as As_2O_3) from 14 days prior to mating through gestation day 19 (Holson et al. 2000). Reproductive

indices that were evaluated included the precoital interval (time to mating), mating index (percentage of rats mated), and fertility index (percentage of matings resulting in pregnancy). In a 3-generation study in mice given sodium arsenite in drinking water at an average dose of 1 mg As/kg/day, there was a significant increase in the incidence of small litters and a trend toward a decreased number of pups per litter in all three generations of the treated group (Schroeder and Mitchener 1971). This finding is consistent with the results of developmental toxicity studies reported in Section 3.2.2.6. Female rats exposed to 0.24 mg As/kg/day (as arsenite) for 28 days showed changes in several reproductive system end points, including decreases in wet weights of the ovary and uterus, inhibition of steroidogenic enzymes, decreased ovarian and uterine peroxidase activities, and decreased estradiol levels relative to controls (Chattopadhyay et al. 2001). NOAEL and LOAEL values from these studies are shown in Table 3-3 and Figure 3-3.

Organic Arsenicals. No studies were located regarding reproductive effects in humans after oral exposure to organic arsenicals. No histological alterations in male or female reproductive tissues were observed in laboratory animals following exposure to MMA (Arnold et al. 2003), DMA (Arnold et al. 2006), or roxarsone (NTP 1989b) and no alterations in sperm parameters were observed in male rats exposed to 76 mg MMA/kg/day for at least 14 weeks (Schroeder 1994). However, some functional alterations have been reported in animals exposed to MMA or DMA. A decrease in estrus was observed in dogs exposed to 35 mg MMA/kg/day for 52 weeks (Waner and Nyska 1988); decreases in body weight gain (terminal body weight was 59% lower than controls) were also observed at this dose level and the effect may have been secondary to systemic toxicity. Decreases in pregnancy rate and male fertility index were observed in F_0 and F_1 rats exposed to 76 mg MMA/kg/day for 14 weeks prior to mating and during the mating, gestation, and lactation periods (Schroeder 1994). In the F_0 animals, the pregnancy rate and male fertility index were not statistically different from controls; however, the values were below historical controls and the investigators considered the effect to be treatment-related. In the F_1 animals, the male fertility index was statistically different from controls but the pregnancy rate was not; both parameters were within the range found in historical controls, but the investigators considered the effect to be treatment-related due to the consistency of the findings in the F_0 and F_1 animals. Impaired fertility, as evidenced by a decreased number of litters, was observed in male mice dosed with MSMA (119 mg/kg/day) during a 19-day mating period with unexposed females (Prukop and Savage 1986); the poor reporting of the study protocol and results precludes drawing conclusions from this study. An increase in the number of does with aborted fetuses was observed in rabbits exposed to 48 mg DMA/kg/day as DMA (Irvine et al. 2006); severe maternal toxicity (weight loss, reduced food intake, and

diarrhea) was also observed at this dose level. No reproductive effects were observed in a 2-generation rat study in which rats were exposed to 16.5 mg DMA/kg/day (Rubin et al. 1989).

3.2.2.6 Developmental Effects

Inorganic Arsenicals. Whether ingestion of inorganic arsenic may cause developmental effects in humans has not been extensively investigated. Lugo et al. (1969) reported a case of a mother who ingested inorganic arsenic (Cowley's Rat and Mouse Poison) at 30 weeks of gestation. Twenty-four hours after ingestion, she went into labor and delivered a live female infant weighing 2 pounds, 7 ounces with a 1-minute Apgar score of 4. The infant's clinical condition deteriorated with frequent episodes of apnea and bradycardia; subsequent venous blood gas determinations documented hypoxia, hypercapnea, and acidosis. The infant died at 11 hours of age. Autopsy performed 8 hours after death showed organ immaturity, generalized petechial hemorrhages, and hyaline membrane disease. Severe intra-alveolar pulmonary hemorrhage was remarkable. High arsenic levels were found in the infant's liver, kidney, and brain, demonstrating easy passage of inorganic arsenic across the placenta. The authors considered most of the findings in the neonate to be attributable to immaturity, but suggested that arsenic may have played a role in the severe intra-alveolar hemorrhaging that contributed to death.

Chronic exposure of women to arsenic in the drinking water has been associated with infants with low birth weights in Taiwan (Yang et al. 2003) and Chile (Hopenhayn et al. 2003a). Similar associations have been made between late fetal mortality, neonatal mortality, and postneonatal mortality and exposure to high levels of arsenic in the drinking water (up to 0.86 mg/L during over a decade), based on comparisons between subjects in low- and high-arsenic areas of Chile (Hopenhayn-Rich et al. 2000). More recently, von Ehrenstein et al. (2006) reported no significant association between exposure to concentrations of ≥0.1 mg/L arsenic in drinking water (approximately 0.008 mg As/kg/day) (n=117; 29 women were exposed to ≥0.5 mg/L) and increased risk for neonatal death or infant mortality during the first year of life in a study of a population in West Bengal, India. The same group of investigators reported significantly increased SMRs for lung cancer and bronchiectasis among subjects in a city in Chile who had probable exposure *in utero* (maternal exposure) or during childhood to high levels of arsenic (near 0.9 mg/L) in the drinking water (Smith et al. 2006). For those exposed in early childhood, the SMR for lung cancer was 7.0 (95% CI=5.4–8.9, $p<0.001$) and for bronchiecstasis 12.4 (95% CI=3.3–31.7, $p<0.001$). For those born during the high-exposure period, the corresponding SMRs were 6.1 (95% CI=3.5–9.9, $p<0.001$) and 46.2 (95% CI=21.1–87.7, $p<0.001$). The mortality data analyzed were for the age range 30–49 years.

No overall association between arsenic in drinking water and congenital heart defects was detected in a case-control study in Boston (Zierler et al. 1988), although an association with one specific lesion (coarctation of the aorta) was noted (OR=3.4, 95% CI=1.3–8.9). A study of 184 women with neural tube defects in the offspring living in a Texas county bordering Mexico found that exposure to levels of arsenic in the drinking water >0.010 mg/L (range or upper limit not specified) did not significantly increase the risk for neural tube defects (OR=2.0, 95% CI=0.1–3.1) (Brender et al. 2006).

Studies in animals, however, suggest that ingested inorganic arsenic may produce developmental effects at high doses that also produce overt maternal toxicity. Rats treated with a single gavage dose of 23 mg As/kg as arsenic trioxide on day 9 of gestation had a significant increase in postimplantation loss and a decrease in viable fetuses per litter, while those treated with 15 mg As/kg showed no effects (Stump et al. 1999). Rats treated by daily gavage with 8 mg As/kg/day starting 14 days before mating and continuing through gestation had significantly reduced fetal body weights and significantly increased incidences of several skeletal variations (unossified sternebrae #5 or #6, slight or moderate sternebrae malalignment, 7th cervical ribs) that the researchers considered to be consequences of developmental growth retardation (Holson et al. 2000). No developmental effects were found at 4 mg As/kg/day in this study. Exposure of rats to 2.93–4.20 mg As/kg/day throughout gestation and for 4 months postnatally resulted in alterations in neurobehavioral parameters in the offspring, including increased spontaneous locomotor activity and number of errors in a delayed alternation task; maternal behavior was not affected (Rodriguez et al. 2002). Studies in mice found increased fetal mortality, decreased fetal body weight, a low incidence of gross malformations (primarily exencephaly), and an increase in skeletal malformations in mice given single gavage doses of 23–48 mg As/kg during gestation (Baxley et al. 1981; Hood et al. 1978), with no effects at 11 mg As/kg. Similarly, in mice treated with 24 mg As/kg/day as arsenic acid on days 6–15 of gestation, there was a significant increase in the number of resorptions per litter (42% vs. 4% in controls) and significant decreases in the number of live pups per litter (6.6 vs. 12.3 in controls) and mean fetal weight (1.0 g vs. 1.3 g in controls), while no developmental effects were found at 12 mg As/kg/day (Nemec et al. 1998). Hamsters treated with a single gavage dose of 14 mg As/kg during gestation also had increased fetal mortality and decreased fetal body weight (Hood and Harrison 1982), with no effect at 11 mg As/kg. However, the most sensitive species was the rabbit, which had increased resorptions and decreased viable fetuses per litter at 1.5 mg As/kg/day and a developmental NOAEL of 0.4 mg As/kg/day, following repeated gavage dosing with arsenic acid during gestation (Nemec et al. 1998). In each of these studies (except Hood et al. 1978, which failed to report maternal effects), overt maternal toxicity, including death in some cases, was found at the same or lower doses as the developmental

effects (Baxley et al. 1981; Holson et al. 2000; Hood and Harrison 1982; Nemec et al. 1998; Stump et al. 1999).

It is noteworthy that the effect in the 3-generation reproduction study in mice by Schroeder and Mitchener (1971), decreased pups per litter (all generations), is consistent with the findings of many of these shorter-term studies (Baxley et al. 1981; Hood and Harrison 1982; Hood et al. 1978; Nemec et al. 1998; Stump et al. 1999). The dose in this long-term study was 1 mg As/kg/day; in a 2-year study by these researchers, this dose produced effects such as decreased body weight gain and increased mortality (Schroeder and Balassa 1967).

A series of studies presented evidence that inorganic arsenic may be a transplacental carcinogen in animals. Waalkes et al. (2003, 2004a, 2004b, 2004c) exposed timed-pregnant AJ mice to 0, 42.5, or 85 ppm of sodium arsenite in the drinking water from gestation day 8 through 18 and observed the offspring for 90 weeks following birth; the study authors estimated daily doses at 9.55 and 19.3 mg As/kg/day. A dose-related increase was reported in the incidence of hepatocellular carcinomas and adrenal tumors in the male offspring from both treatment levels, while male offspring from high-dose animals showed an increase in total number of tumors. In female offspring, an increase in uterine hyperplasia was seen in the offspring of both treated groups while the offspring of high-dose animals showed increased incidence of lung carcinomas. For both exposed groups, regardless of gender, the offspring showed a significant increase in the number of malignant tumors (Waalkes et al. 2003). More recent studies from the same group of investigators have suggested that aberrant estrogen signaling, potentially through inappropriate estrogen receptor-α (ER-α), may play a role in arsenic-induced liver tumors in male offspring (Waalkes et al. 2006a) and in arsenic-induced uterine and bladder carcinoma in female offspring (Waalkes et al. 2006b). The latter was based on the observation of over-expression of ER-α and *pS*2, an estrogen-regulated gene, in the respective tissues.

These studies (shown in Table 3-3 and Figure 3-3) indicate that the fetus may be affected by ingested arsenic.

Organic Arsenicals. No studies were located regarding developmental effects in humans after oral exposure to organic arsenicals. The developmental toxicity of organic arsenicals has been investigated in rats and rabbits for MMA and in rats, mice, and rabbits for DMA. Decreased fetal weights and an increased incidence of fetuses with incomplete ossification of thoracic vertebrae were observed in the offspring of rats administered via gavage 500 mg MMA/kg/day on gestational days 6–15; no

developmental effects were observed at 100 mg MMA/kg/day (Irvine et al. 2006). Decreases in maternal body weight gain were observed at 100 and 500 mg MMA/kg/day. A decrease in pup survival was observed in F_1 and F_2 offspring of rats exposed to 76 mg MMA/kg/day (Schroeder 1994); although pup survival was not statistically different from controls, the investigators considered the effect to be biologically significant because survival in the MMA pups was outside the lower range of survival in historical controls. Increases in the number of fetuses with supernumerary thoracic ribs and eight lumbar vertebrae were observed in the offspring of rabbits administered to 12 mg MMA/kg/day on gestational days 7–19 (Irvine et al. 2006); the investigators noted that these effects were probably secondary to maternal stress.

No developmental effects were observed in the offspring of rats administered via gavage 15 mg DMA/kg/day on gestational days 7–16 (Rogers et al. 1981). At 30 mg DMA/kg/day, there was an increase in the percentage of fetuses with irregular palatine rugae; no maternal effects were observed at this dose level (Rogers et al. 1981). The investigators noted that the functional significance of aberrant rugae in rats is not known. Doses of ≥36 mg DMA/kg/day resulted in decreases in fetal weights and delays in ossification (Chernoff et al. 1990; Irvine et al. 2006; Rogers et al. 1981); decreases in maternal body weight gain were often observed at the same dose levels. Irvine et al. (2006) also reported an increase in the occurrence of diaphragmatic hernia in the offspring of rats exposed to 36 mg DMA/kg/day as DMA on gestational days 6–15. Mice appear to be less sensitive than rats to the developmental toxicity of DMA. No developmental effects were observed in the offspring of mice administered 200 mg DMA/kg/day on gestational days 7–16 (Rogers et al. 1981); at higher doses, decreases in fetal body weight, delays in ossification, and cleft palate were observed (Kavlock et al. 1985; Rogers et al. 1981). In rabbits, a NOAEL of 12 mg DMA/kg/day was identified (Irvine et al. 2006); at 48 mg DMA/kg/day, there were increased maternal deaths and abortions.

3.2.2.7 Cancer

Inorganic Arsenicals. There is convincing evidence from a large number of epidemiological studies and case reports that ingestion of inorganic arsenic increases the risk of developing skin cancer (Alain et al. 1993; Beane Freeman et al. 2004; Bickley and Papa 1989; Cebrián et al. 1983; Chen et al. 2003; Guo et al. 2001a; Haupert et al. 1996; Hsueh et al. 1995; Lewis et al. 1999; Lüchtrath 1983; Mitra et al. 2004; Morris et al. 1974; Piontek et al. 1989; Sommers and McManus 1953; Tay and Seah 1975; Tsai et al. 1998a, 1999; Tseng 1977; Tseng et al. 1968; Zaldívar 1974; Zaldívar et al. 1981). Lesions commonly observed are multiple squamous cell carcinomas, some of which appear to develop from the

hyperkeratotic warts or corns described in Section 3.2.2.2. In addition, multiple basal cell carcinomas may occur, typically arising from cells not associated with hyperkeratinization. In most cases, skin cancer develops only after prolonged exposure, but one study has reported skin cancer in people exposed for <1 year (Reymann et al. 1978). Although both types of skin cancer can be removed surgically, they may develop into painful lesions that may be fatal if left untreated (Shannon and Strayer 1989).

A number of studies that identify CELs in exposed humans are summarized in Table 3-3 and shown in Figure 3-3. The EPA reviewed the studies that provided dose-response data on the risk of skin cancer (EPA 1988d) and concluded that the most useful study for the purposes of quantitative risk assessment was the ecologic epidemiology study by Tseng et al. (1968). In this study, the incidence of skin cancer was measured as a function of exposure level in over 40,000 people residing in 37 villages in Taiwan, and compared to a control group of over 7,500 people. Beyond the very large sample size, other strengths of this study include excellent case ascertainment (physical examination), inclusion of both males and females, and lifetime exposure duration. Weaknesses and uncertainties include poor nutritional status of the exposed populations, their genetic susceptibility, their exposure to inorganic arsenic from nonwater sources, and the applicability of extrapolating data from Taiwanese to the U.S. population because of different background rates of cancer, possibly genetically determined, and differences in diet other than arsenic (e.g., low protein and fat and high carbohydrate) (EPA 1988d). Because of a lack of information on the amount of individual exposure, subjects were classified into three exposure groups (i.e., high, medium, and low). Based upon pooled data for skin cancer incidence and average well concentrations for each village in the Tseng et al. (1968) study, the EPA calculated a unit risk (the upper-bound excess cancer risk from lifetime exposure to water containing 1 µg As/L) of $5x10^{-5}$ (IRIS 2007). The average daily doses (expressed as mg As/kg/day) that correspond to excess cancer risks of $1x10^{-4}$–$1x10^{-7}$ are shown in Figure 3-3.

The use of a cancer risk estimate derived from the Tseng et al. (1968) study for a U.S. population has been the source of intense debate. Some have argued and have provided data in support of the view that there is persuasive evidence that inorganic arsenic is a cause of human cancer at several sites (i.e., Smith et al. 1992, 1995, 2002). On the other hand, a number of concerns have been raised regarding the strength, or lack of strength, of the database, including: the adequacy of the model used by EPA and the accuracy and reliability of the exposure data (Brown et al. 1997a, 1997b); a number of host and environmental factors among the Taiwanese not applicable elsewhere (Carlson-Lynch et al. 1994); a possible threshold for arsenic carcinogenicity and nonlinearities in the dose-response curve (Abernathy et al. 1996; Slayton et al. 1996); differences in health and nutrition between Taiwan and the United States

that might increase cancer risk in Taiwan (Beck et al. 1995); the possibility that lower doses of arsenic may be beneficial role in some physiological processes (EPA 1988d; FNB/IOM 2001; NRC 1999, 2001); and the possibility of significant exposure to arsenic from sources other than the well water (Chappell et al. 1997). Many of these factors were recognized by EPA (1988d). A report by NRC (2001) suggested that the risks calculated based on increases in incidence of lung and bladder cancers may be greater than those calculated by the EPA based on incidences of skin cancer.

Several early epidemiological studies performed in the United States did not report an increased frequency of skin cancer in small populations consuming water containing arsenic at levels of around 0.1–0.2 ppm (EPA 1981b; Goldsmith et al. 1972; Harrington et al. 1978; Morton et al. 1976). These early data suggested that arsenic-associated skin cancer is not a common problem in this country, but these studies lacked sufficient statistical power to detect small increases in skin cancer incidence that might have occurred at these low doses (EPA 1983g). Later studies in exposed U.S. populations from Utah (Lewis et al. 1999) and Iowa (Beane Freeman et al. 2004) have suggested that arsenic-exposed individuals within the United States may have increased incidence or risk of mortality from some skin cancers, melanoma in particular; however, exposure data from these studies are generally insufficient for dose-response analysis. Another study found a suggestion of an arsenic-induced effect on the development of skin cancer, but the association did not achieve statistical significance (Karagas et al. 2001). Therefore, the risk of arsenic-induced skin cancers in U.S. populations, while it may appear to be less than in some other evaluated populations, may be the reflection that, in most studies, exposures were lower.

In addition to the risk of skin cancer, there is mounting evidence that ingestion of arsenic may increase the risks of internal cancers as well. Many case studies have noted the occurrence of internal tumors of the liver and other tissues in patients with arsenic-induced skin cancer (Falk et al. 1981b; Kasper et al. 1984; Koh et al. 1989; Lander et al. 1975; Regelson et al. 1968; Sommers and McManus 1953; Tay and Seah 1975; Zaldívar et al. 1981). These studies are supported by large-scale epidemiological studies, where associations and/or dose response trends have been detected for tumors of the bladder, kidney, liver, lung, and prostate (Chen and Wang 1990; Chen et al. 1985, 1986, 1988a, 1988b, 1992; Chiou et al. 1995; Cuzick et al. 1992; Ferreccio et al. 1998; Guo et al. 1997; Hopenhayn-Rich et al. 1998; Kurttio et al. 1999; Lewis et al. 1999; Moore et al. 2002; Rivara et al. 1997; Smith et al. 1998; Tsuda et al. 1995a; Wu et al. 1989). The EPA has not yet calculated a unit risk value or slope factor for arsenic-induced internal tumors.

There is increasingly convincing evidence that long-term exposure to arsenic can result in the development of bladder cancer (Bates et al. 2004; Chen et al. 1992, 2003; Chiou et al. 1995, 2001; Cuzick et al. 1992; Guo et al. 2001b; Karagas et al. 2004; Lamm et al. 2004; Michaud et al. 2004; Steinmaus et al. 2003), with transitional cell cancers being the most prevalent. Chiou et al. (1995) reported a dose-response relationship between long-term arsenic exposure from drinking artesian well water and the incidence of lung cancer, bladder cancer, and cancers of all sites combined (after adjustment for age, sex, and cigarette smoking) in four townships in Taiwan exposed to inorganic arsenic in drinking water (0–1.14 mg/L). In a later followup study of the same cohort, the increase in bladder cancer was found to be statistically significant only in subjects exposed for 40 years or longer (Chiou et al. 2001). Cuzick et al. (1992) evaluated a cohort treated with Fowler's solution (potassium arsenite) in Lancashire, England, during the period 1945–1969 and followed through 1991; the cohort of 478 patients showed a significant excess of bladder cancer, but no excess for other causes of death. Of a subcohort of 142 patients examined for signs of arsenicism around 1970 (Cuzick et al. 1992), all 11 subsequent cancer deaths occurred in those with signs of arsenicism (p=0.0009). Hopenhayn-Rich et al. (1996a) investigated bladder cancer mortality for the years 1986–1991 in the 26 counties of Cordoba, Argentina, and reported that bladder cancer SMRs were consistently higher in counties with documented arsenic exposure; a later case-control study by the same authors (Bates et al. 2004) did not report statistically significant increases in bladder cancers resulting from arsenic exposure, except in individuals exposed for 50 years or longer. Guo et al. (2001a) reported significantly increased rate differences for bladder cancer in men and women in Taiwan exposed to 0.64 mg arsenic/L in the drinking water, but not at lower exposure levels. The arsenic-induced bladder tumors do not appear to be histologically different than similar bladder tumor types of nonarsenic origin (Chow et al. 1997), although they tended to be more pronounced. In contrast, Michaud et al. (2004) reported no correlation between arsenic levels in toenails and the incidence of bladder cancers in Finnish workers. Among evaluated U.S. cohorts, there has generally been no association between arsenic exposure (~60–100 µg As/L) and the incidence of mortality from bladder cancers (Lamm et al. 2004; Steinmaus et al. 2003), although it is possible that smoking may render individuals more susceptible to arsenic-induced bladder tumors (Karagas et al. 2004; Steinmaus et al. 2003).

Studies have also suggested that chronic oral exposure to arsenic may result in the development of respiratory tumors and increased incidence of lung cancer (Ferreccio et al. 2000; Guo 2004; Nakadaira et al. 2002; Smith et al. 1998; Viren and Silvers 1999). A study of arsenic-exposed individuals in northern Chile reported significantly increased odds ratios for lung cancer among subjects with ≥30 µg As/L of drinking water (Ferreccio et al. 2000), although when adjusted for socioeconomic status, smoking, and

other factors, the increase was only significant at 60 µg As/L or greater. Guo (2004) reported significantly increased rates differences (RD) for lung cancer for Taiwanese men and women exposed to 0.64 mg As/L or greater, with those subjects >50 years of age being particularly at risk. Nakadaira et al. (2002) suggested that even comparatively short exposure durations (≤5 years) may be sufficient for the development of arsenic-induced lung cancer.

Studies in U.S. populations exposed to arsenic in drinking water (EPA 1981b; Lamm et al. 2004; Lewis et al. 1999; Morton et al. 1976; Steinmaus et al. 2003; Valentine et al. 1992) have not yielded the cancer incidences and health effects noted in Taiwan, Mexico, and Chile. Whether this difference is due to a smaller population of subjects compared to Taiwan, to overall lower doses in exposed U.S. populations, or to differences in nutritional or socioeconomic conditions has not been resolved. It should be noted that exposed populations in Mexico and Chile are also smaller than those in Taiwan.

Most studies of animals exposed to arsenate or arsenite by the oral route have not detected any clear evidence for an increased incidence of skin cancer or other cancers (Byron et al. 1967; Kroes et al. 1974; Schroeder et al. 1968). Arsenic has sometimes been called a "paradoxical" human carcinogen because of this lack of animal data (Jager and Ostrosky-Wegman 1997). The basis for the lack of tumorigenicity in animals is not known, but could be related to species-specific differences in arsenic distribution, and induction of cell proliferation (Byrd et al. 1996) (see Section 3.5). As discussed in Section 3.5 below, the carcinogenic effects of arsenic may partially result from its function as a cocarcinogen, which would not manifest in most animal carcinogenicity studies.

One mouse study using transgenic mice (which carry the v-Ha-ras oncogene) administered 48 mg As/kg/day as sodium arsenite in drinking water for 4 weeks followed by dermal application of 12-O-tetradecanoylphorbol-13-acetage (TPA) to shaved back skin twice a day for 2 weeks showed an increase in the incidence of skin papillomas when compared to transgenic mice receiving only TPA treatment, only arsenic, or to wild-type mice receiving both TPA and arsenic (Germolec et al. 1998); arsenic treatment alone did not result in increased papilloma incidence. Increases in mRNA transcripts for the growth factors transforming growth factor-α (TGF-α) and granulocyte/ macrophage-colony stimulating factor (GM-CSF) were detected in the epidermis of the arsenic-treated mice.

A few studies in mice have noted that arsenic ingestion may actually decrease the incidence of some tumor types. For example, arsenic exposure caused decreased incidence of urethane-induced pulmonary tumors (Blakley 1987), spontaneous mammary tumors (Schrauzer and Ishmael 1974; Schrauzer et al.

1976), and tumors resulting from injection of mouse sarcoma cells (Kerkvliet et al. 1980). However, arsenic also increased the growth rate of the tumors that did occur, resulting in a net decrease in survival time in tumor-bearing animals (Kerkvliet et al. 1980; Schrauzer and Ishmael 1974). These observations suggest that arsenic may affect different types of neoplastic cells differently, perhaps acting mainly as a tumor promoter (Schrauzer and Ishmael 1974; Shirachi et al. 1983), although some studies have suggested that arsenic's actions are not consistent with tumor promotion (Baroni et al. 1963; Boutwell 1963).

There is evidence suggesting that inorganic arsenic can induce cancer in the offspring from mice exposed to arsenic during gestation (transplacental carcinogen) (Waalkes et al. 2003, 2004a, 2004b, 2004c, 2006a, 2006b). These studies are summarized in Section 3.2.2.6, Developmental Effects.

Organic Arsenicals. No studies were located regarding cancer in humans after oral exposure to organic arsenicals. Two lifetime carcinogenicity studies with MMA did not find significant increases in tumors in rats exposed to 72.4 mg MMA/kg/day in the diet for 2 years (Arnold et al. 2003) or 8.4 mg MMA/kg/day in drinking water for 2 years (Shen et al. 2003). No significant increases in neoplastic lesions were observed in mice exposed to 67.1 mg MMA/kg/day in the diet for 2 years (Arnold et al. 2003).

In contrast, significant increases in the incidence of urinary bladder tumors have been observed in rats exposed for 2 years to 7.8 mg DMA/kg/day in the diet (Arnold et al. 2006) or 3.4 mg DMA/kg/day in drinking water (Wei et al. 1999, 2002). The incidence of bladder tumors was similar to controls in the rats exposed to 0.77 mg DMA/kg/day (Arnold et al. 2006) or 0.75 mg DMA/kg/day (Wei et al. 1999, 2002). Neither study reported significant increases in the incidence of neoplastic lesions in other tissues. Arnold et al. (2006) did not find increases in the incidence of neoplastic lesions in mice exposed to doses as high as 94 mg DMA/kg/day in the diet for 2 years. Hayashi et al. (1998) reported that exposure of A/J mice (a strain susceptible to lung tumorigenesis) to 10.4 mg DMA/kg/day (but not 1.3 or 5.2 mg DMA/kg/day) in drinking water for 50 weeks resulted in an increased incidence of papillary adenomas and/or adenocarcinomas and an increased number of lung tumors per mouse.

The incidence of basophilic foci (believed to be a precancerous lesion) in the liver of rats initiated with diethylnitrosamine was increased by subsequent 6-month drinking water exposure to 11 mg DMA/kg/day, suggesting that this compound could act as a cancer promoter (Johansen et al. 1984). Additional evidence for the possible role of DMA as a promoter comes from Yamamoto et al. (1995), who reported that 15 or 60 mg DMA/kg/day in the drinking water for 24 weeks significantly enhanced the tumor induction in the

urinary bladder, kidney, liver, and thyroid gland in male F344 rats treated with a series of initiators. Wanibuchi et al. (1996) reported that treatment of F344 rats for 32 weeks with up to 14.3 mg DMA/kg/day DMA in the drinking water did not result in increased incidences of urinary bladder papillomas or carcinomas, but that incidence of these tumors was elevated if the animals were first pretreated with an initiating compound (BBN). A later study by Li et al. (1998) reported that NBR rats (which do not synthesize $\alpha_{2\mu}$-globulin) exposed to an initiator for 4 weeks followed by DMA for 32 weeks, similar to the Wanibuchi et al. (1996) study, showed a statistically significant increase in simple hyperplasia and papillary or nodular hyperplasia of the bladder. A study by Salim et al. (2003) suggested that DMA primarily exerts its carcinogenic effects on spontaneous tumor development.

No increases in tumor incidence were observed in rats, mice, or dogs exposed to 10, 13, or 5 mg/kg/day roxarsone, respectively, in the diet for 2 years (Prier et al. 1963). Similarly, no evidence of carcinogenicity was observed in female rats or male or female mice exposed to 4 or 43 mg/kg/day as roxarsone in the diet for 2 years (NTP 1989b). However, a slight increase in pancreatic tumors was noted in male rats exposed to 4 mg/kg/day (NTP 1989b); this was considered to constitute equivocal evidence of carcinogenicity.

3.2.3 Dermal Exposure

Adverse effects from dermal exposure to inorganic or organic arsenicals have not been extensively investigated. Table 3-7 summarizes studies in animals and humans that provide quantitative data on dermal exposure-effect relationships for inorganic arsenicals. No quantitative data on dermal exposure to organic arsenicals were located. Available quantitative and qualitative data are discussed in greater detail below.

3.2.3.1 Death

Inorganic Arsenicals. No studies were located regarding death in humans after dermal exposure to inorganic arsenicals. In rats, no deaths resulted from dermal exposure to arsenate or arsenite at doses up to 1,000 mg As/kg (Gaines 1960). These data indicate that dermal exposure to inorganic arsenic compounds is very unlikely to result in death.

Organic Arsenicals. No studies were located regarding death in humans after dermal exposure to organic arsenicals. No deaths were observed in rabbits receiving daily dermal applications of 540 mg As/kg as

Table 3-7 Levels of Significant Exposure to Inorganic Arsenic - Dermal

Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL	LOAEL Less Serious	LOAEL Serious	Reference Chemical Form	Comments
ACUTE EXPOSURE							
Immuno/ Lymphoret							
Gn Pig (Hartley)	once		580 mg/L			Wahlberg and Boman 1986 As(+3)	
Gn Pig (Hartley)	once		4000 mg/L			Wahlberg and Boman 1986 As(+5)	
INTERMEDIATE EXPOSURE							
Systemic							
Mouse (Rockland)	30 wk 11 x/wk	Dermal		6 F mg/kg/day (gross hyperplasia, ulceration)		Boutwell 1963 As(+3)	

F = female; Gn pig = guinea pig; Immuno/Lymphoret = immunological/lymphoreticular; wk = week(s); x = time(s)

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MMA 5 days/week for 21 days (Margitich and Ackerman 1991b) or 1,000 mg DMA/kg/day 5 days/week for 21 days (Margitich and Ackerman 1991a).

3.2.3.2 Systemic Effects

No studies were located that have associated respiratory, cardiovascular, gastrointestinal, hematological, musculoskeletal, hepatic, renal, endocrine, ocular, or body weight effects in humans or animals with dermal exposure to inorganic arsenicals.

Respiratory Effects. No studies were located regarding respiratory effects in humans after dermal exposure to organic arsenicals. No histological effects were observed in the respiratory tracts of rabbits following dermal application of 1,000 mg/kg/day MMA or DMA 5 days/week for 21 days (Margitich and Ackerman 1991a, 1991b).

Cardiovascular Effects. No studies were located regarding cardiovascular effects in humans after dermal exposure to organic arsenicals. No histological effects were observed in the hearts of rabbits following dermal application of 1,000 mg/kg/day MMA or DMA 5 days/week for 21 days (Margitich and Ackerman 1991a, 1991b).

Hematological Effects. No studies were located regarding hematological effects in humans after dermal exposure to organic arsenicals. No treatment-related hematological alterations were observed in rabbits receiving dermal applications of 1,000 mg MMA/kg/day (Margitich and Ackerman 1991a) or 1,000 mg DMA/kg/day 5 days/week for 21 days (Margitich and Ackerman 1991b).

Hepatic Effects. No studies were located regarding hepatic effects in humans after dermal exposure to organic arsenicals. No significant alterations in blood clinical chemistry, liver weights, or histopathology were observed in rabbits dermally exposed to 1,000 mg/kg/day MMA or DMA 5 days/week for 21 days (Margitich and Ackerman 1991a, 1991b).

Renal Effects. No studies were located regarding renal effects in humans after dermal exposure to organic arsenicals. No significant alterations in urinalysis, kidney weights, or histopathology were observed in rabbits following dermal exposure to 1,000 mg MMA/kg/day (Margitich and Ackerman 1991a) or 1,000 mg DMA/kg/day 5 days/week for 21 days (Margitich and Ackerman 1991b).

Endocrine Effects. No studies were located regarding endocrine effects in humans after dermal exposure to organic arsenicals. No alterations in adrenal gland weight or histopathology of the adrenal glands, pancreas, pituitary gland, thyroid gland, and parathyroid gland were observed in rabbits following dermal application of 1,000 mg/kg/day MMA or DMA 5 days/week for 21 days (Margitich and Ackerman 1991a, 1991b).

Dermal Effects.

Inorganic Arsenicals. Several studies of humans exposed to arsenic dusts in the workplace have reported that inorganic arsenic (usually arsenic trioxide) can cause contact dermatitis (Holmqvist 1951; Pinto and McGill 1953). Typical responses included erythema and swelling, with papules and vesicles in more severe cases (Holmqvist 1951). The dermal contact rates that cause these effects in humans have not been quantified, but a similar direct irritation of the skin has been noted in mice exposed to 4 mg As/kg/day as potassium arsenite for 30 weeks (Boutwell 1963). In contrast, no significant dermal irritation was noted in guinea pigs exposed to aqueous solutions containing 4,000 mg As/L as arsenate or 580 mg As/L as arsenite (Wahlberg and Boman 1986). These studies indicate that direct contact may be of concern at high exposure levels, but do not suggest that lower levels are likely to cause significant irritation.

Studies on possible dermal sensitization by inorganic arsenicals are discussed in Section 3.2.3.3 below.

Organic Arsenicals. Contact dermatitis was reported in workers involved in the application of an organic arsenical herbicide, which is a mixture of DMA and its sodium salt (Peoples et al. 1979).

Application of an unspecified amount of MMA to the skin of rabbits was reported to result in mild dermal irritation in a Draize test (Jaghabir et al. 1988). No dermal irritation was reported in rabbits repeatedly exposed to 1,000 mg MMA/kg/day (Margitich and Ackerman 1991a) or 1,000 mg DMA/kg/day 5 days/week for 21 days (Margitich and Ackerman 1991b).

Ocular Effects. No studies were located regarding ocular effects in humans or animals after dermal exposure to organic arsenicals.

Body Weight Effects. No studies were located regarding body weight effects in humans after dermal exposure to organic arsenicals. No significant alterations in body weight gain were observed in rabbits

following a 5 day/week exposure to 1,000 mg/kg/day MMA or DMA for 21 days (Margitich and Ackerman 1991a, 1991b).

3.2.3.3 Immunological and Lymphoreticular Effects

Inorganic Arsenicals. Examination of workers exposed to arsenic trioxide dusts in a copper smelter led Holmqvist (1951) to suspect that repeated dermal contact could lead to dermal sensitization. In support of this, Holmqvist (1951) found a positive patch test in 80% of the exposed workers compared to 30% in a control population. These data do suggest that workers may be sensitized to arsenic, but the high response rate in controls seems unusual. A much lower response rate (0.5%) was noted in another patch test study of dermal sensitization (Wahlberg and Boman 1986), and the few positive responses seemed to be due to a cross-reactivity with nickel. Mohamed (1998) evaluated 11 male workers at a tin smelting factory where arsenic trioxide levels ranged from 5.2 to 14.4 mg/m^3. The workers experienced symptoms of generalized itch, dry and hyperpigmented skin, folliculitis, and superficial ulcerations. The authors concluded that arsenic-containing dust collected on the sweat on the workers' skin, causing contact dermatitis. Studies in guinea pigs did not yield evidence of a sensitization reaction to inorganic arsenic (Wahlberg and Boman 1986).

Organic Arsenicals. Support for sensitization to DMA is provided in a case report of a 26-year-old woman who was occupationally exposed to DMA and experienced eczema on her face (Bourrain et al. 1998). Patch testing confirmed an allergic reaction to DMA, and avoidance of DMA resulted in disappearance of the symptoms. No studies were located regarding immunological or lymphoreticular effects in animals after dermal exposure to organic arsenicals.

No studies were located that have associated any of the following effects in humans or animals with dermal exposure to inorganic or organic arsenicals:

3.2.3.4 Neurological Effects

3.2.3.5 Reproductive Effects

3.2.3.6 Developmental Effects

3.2.3.7 Cancer

Inorganic Arsenicals. No studies were found that have associated cancer in humans with dermal exposure to arsenic. Application of arsenic acid to the skin of mice pretreated with dimethylbenz-

anthracene did not result in any skin tumors (Kurokawa et al. 1989), suggesting that arsenic does not act as a promoter in this test system.

Organic Arsenicals. No studies were located regarding cancer in humans or animals after dermal exposure to organic arsenicals.

3.3 GENOTOXICITY

Inorganic Arsenicals. There have been a large number of studies of the genotoxic effects of arsenic. Tables 3-8 and 3-9 summarize a number of reports on the *in vitro* and *in vivo* genotoxicity of inorganic arsenicals, respectively. In general, *in vitro* studies in prokaryotic organisms have been negative for gene mutations (Lantzsch and Gebel 1997; Löfroth and Ames 1978; Nishioka 1975; Rossman et al. 1980; Ulitzur and Barak 1988). Studies in human fibroblasts, lymphocytes, and leukocytes, mouse lymphoma cells, Chinese hamster ovary cells, and Syrian hamster embryo cells demonstrate that *in vitro* arsenic exposure can induce chromosomal aberrations and sister chromatid exchange (see Table 3-8 for citations). *I vitro* studies in human, mouse, and hamster cells have also been positive for DNA damage and repair and enhancement or inhibition of DNA synthesis.

Studies of humans have detected a higher-than-average incidence of chromosomal aberrations in peripheral lymphocytes, both after inhalation exposure (Beckman et al. 1977; Nordenson et al. 1978) and oral exposure (Burgdorf et al. 1977; Nordenson et al. 1979). These studies must be interpreted with caution, since in most cases, there were only a small number of subjects and a number of other chemical exposures were possible (EPA 1984a). Human and animal data are available indicating that inhaled inorganic arsenic is clastogenic. Workers exposed to unspecified concentrations of arsenic trioxide at the Ronnskar copper smelter in Sweden were found to have a significant increase in the frequency of chromosomal aberrations in peripheral lymphocytes (Beckman et al. 1977; Nordenson et al. 1978). This result is supported by an animal study that found increased chromosomal aberrations in the livers of fetuses from pregnant mice exposed to 22, but not 2.2 or 0.20, mg As/m^3 as arsenic trioxide on days 9–12 of gestation (Nagymajtényi et al. 1985). Workers in the arsenic-based glass making industry in southern India had a significantly increased frequency of micronuclei in buccal cells and increased DNA damage in leukocytes compared to a control group (Vuyyuri et al. 2006). Exposure levels were not available, but the concentration of arsenic in the blood from workers was approximately 5 times higher than in the reference group.

Table 3-8. Genotoxicity of Inorganic Arsenic *In Vitro*

Valence	Species (test system)	End point	Results: With activation	Results: Without activation	Reference
Prokaryotic organisms:					
As^{+3}	*Escherichia coli*	Reverse mutation	No data	+	Nishioka 1975
As^{+3}	*E. coli* PQ37	Gene mutation	No data	–	Lantzsch and Gebel 1997
As^{+3}	*E. coli* (six strains)	Reverse mutation	No data	–	Rossman et al. 1980
As^{+3}	*Salmonella typhimurium*	Gene mutation	No data	–	Löfroth and Ames 1978
As^{+3}	*Photobacterium fischeri*	Gene mutation	No data	–	Ulitzur and Barak 1988
As^{+5}	*S. typhimurium*	Gene mutation	No data	–	Löfroth and Ames 1978
As^{+5}	*P. fischeri*	Gene mutation	No data	+	Ulitzur and Barak 1988
Eukaryotic organisms:					
Fungi:					
As^{+3}; As^{+5}	*Saccharomyces cerevisiae*	Gene mutation	No data	–	Singh 1983
	Mammalian cells:				
As^{+3}	Human fibroblasts	DNA repair inhibition	No data	+	Okui and Fujiwara 1986
As^{+3}	Human fibroblasts	DNA repair and mutant frequencies	+	+	Wiencke et al. 1997
As^{+3}	Human fibroblasts	DNA repair inhibition	+	+	Hartwig et al. 1997
As^{+3}	Human fibroblasts (MRC5CV1)	DNA migration	No data	+	Hartmann and Speit 1996
As^{+3}	Human fibroblasts (HFW cells)	Cytotoxicity	No data	+	Lee and Ho 1994
As^{+3}	Human skin fibroblasts (HFW)	Chromosome endoreduplication	No data	+	Huang et al. 1995
As^{+3}	Human skin fibroblasts	Chromosomal aberrations	No data	+	Yih et al. 1997
As^{+3}	Human fetal lung fibroblasts	DNA strand breaks	No data	+	Dong and Luo 1993
As^{+3}	Human fetal lung fibroblasts (2BS cells)	DNA damage and repair	No data	+	Dong and Luo 1994
As^{+3}; As^{+5}	Human umbilical cord fibroblasts	Chromosomal aberrations	No data	+	Oya-Ohta et al. 1996
As^{+3}	Diploid human fibroblasts	Morphological transformation	No data	+	Landolph 1994

Table 3-8. Genotoxicity of Inorganic Arsenic *In Vitro*

Valence	Species (test system)	End point	Results		Reference
			With activation	Without activation	
As^{+3}	Human leukocytes	Chromosomal aberration	No data	+	Nakamuro and Sayato 1981
As^{+3}	Human lymphocytes	DNA protein cross-links	–	–	Costa et al. 1997
As^{+3}; As^{+5}	Human lymphocytes	Enhancement or inhibition on DNA synthesis	No data	+	Meng 1993a
As^{+3}; As^{+5}	Human lymphocytes	Enhancement or inhibition on DNA synthesis	No data	+	Meng 1993b
As^{+3}; As^{+5}	Human lymphocytes	Enhancement or inhibition on DNA synthesis	No data	+	Meng 1994
As^{+3}	Human lymphocytes	Hyperdiploidy and chromosomal breakage	No data	(+)	Rupa et al. 1997
As^{+3}	Human lymphocytes	Hyperdiploid nuclei	No data	+	Ramirez et al. 1997
As^{+3}	Human lymphocytes	Chromosomal aberration	No data	+	Beckman and Nordenson 1986
As^{+3}	Human lymphocytes	Chromosomal aberrations and sister chromatid exchange	No data	+	Nordenson et al. 1981
As^{+3}	Human lymphocytes	Chromosomal aberration	No data	+	Sweins 1983
As^{+3}	Human lymphocytes	Chromosomal aberrations	No data	+	Yager and Wiencke 1993
As^{+3}	Human lymphocytes	Chromosomal aberrations	No data	+	Vega et al. 1995
As^{+3}	Human lymphocytes	Chromosomal aberrations	No data	+	Wan et al. 1982
As^{+3}	Human lymphocytes	Chromosomal aberrations and sister chromatic exchange	No data	+	Wiencke and Yager 1992
As^{+3}	Human lymphocytes	Chromosome aberrations and sister chromatid exchanges	No data	+	Larramendy et al. 1981
As^{+3}	Human lymphocytes	Sister chromatid exchange	No data	+	Gebel et al. 1997
As^{+5}	Human lymphocytes	Sister chromatid exchange	No data	–	Gebel et al. 1997
As^{+3}	Human lymphocytes	Sister chromatid exchange	No data	+	Hartmann and Speit 1994
As^{+3}	Human lymphocytes	Sister chromatid exchange	No data	+	Jha et al. 1992
As^{+3}	Human lymphocytes	Sister chromatid exchange	No data	+	Rasmussen and Menzel 1997

Table 3-8. Genotoxicity of Inorganic Arsenic *In Vitro*

Valence	Species (test system)	End point	Results: With activation	Results: Without activation	Reference
As^{+3}; As^{+5}	Human T-cell lymphoma-derived cell line (Molt-3)	PARP activity inhibition	No data	+	Yager and Wiencke 1997
As^{+3}	Human cervix carcinoma HeLa and cisplatin-resistant HeLa/CPR variant cells	DNA repair modification	+	+	Chao 1996
As^{+3}	Human cervix carcinoma cells (HeLa)	DNA damage recognition	No data	-	Hartwig et al. 1998
As^{+3}	Human osteosarcoma cells (HOS)	DNA repair	No data	+	Hu et al. 1998
As^{+3}	Human osteosarcoma cells (HOS)	Cell transformation	No data	+	Mure et al. 2003
As^{+3}	Human-hamster hybrid A_1 cells	DNA adducts	No data	+	Kessel et al. 2002
As^{+3}	Mouse lymphoma cells	Enhanced viral forward mutation	No data	(+)	Oberly et al. 1982
As^{+3}; As^{+5}	Mouse lymphoma cells [L5178Y/$TK^{+/-}$ (-3.7.2C)]	Chromosomal mutations	No data	+	Moore et al. 1997a
As^{+3}	Mouse lymphoma cells [L5178Y $tk^{+/-}$ (3.7.sc)]	Mutagenicity	No data	+	Oberly et al. 1996
As^{+3}; As^{+5}	Mouse lymphoma cells	Chromosomal aberrations	No data	+	Moore et al. 1994a
As^{+3}	Mouse lymphoma cells	Chromosomal aberrations	No data	+	Sofuni et al. 1996
As^{+3}	Mouse 3T6 cells	Gene amplification	No data	+	Lee et al. 1988
As^{+3}	Mouse embryo fibroblasts (C3H/10T/2 Cl8)	Morphological transformation	No data	+	Landolph 1994
As^{+3}	Chinese hamster V79 cells	Gene mutation	No data	–	Li and Rossman 1991
As^{+3}	Chinese hamster V79 cells	Gene mutation	No data	–	Rossman et al. 1980
As^{+3}	Chinese hamster V79 cells	DNA damage, DNA-protein cross-linking, micronucleus induction	No data	+	Gebel et al. 1998a
As^{+3}	Chinese hamster V79 cells	DNA repair and mutant frequencies	No data	+	Li and Rossman 1991
As^{+3}	Chinese hamster V79 cells	Intrachromosomal homologous recombination	No data	+	Helleday et al. 2000
As^{+3}	Chinese hamster ovary cells (CHO-AL)	Gene mutation	No data	+	Hei et al. 1998
As^{+3}	Chinese hamster ovary cells (CHO-AS52)	Mutagenicity	No data	+	Meng and Hsie 1996

Table 3-8. Genotoxicity of Inorganic Arsenic *In Vitro*

Valence	Species (test system)	End point	Results		Reference
			With activation	Without activation	
As^{+3}	Chinese hamster ovary cells	Gene mutation	No data	+	Yang et al. 1992
As^{+3}	Chinese hamster ovary cells	DNA repair inhibition	No data	+	Lee-Chen et al. 1993
As^{+3}	Chinese hamster ovary cells	DNA repair inhibition	No data	–	Lee-Chen et al. 1992
As^{+3}	Chinese hamster ovary cells (CHO-K1)	DNA strand breaks	+	+	Lee-Chen et al. 1994
As^{+3}	Chinese hamster ovary cells (CHO-K1)	DNA strand breaks	No data	+	Lynn et al. 1997
As^{+3}	Chinese hamster ovary cells	Aberrant metaphases	No data	+	Jan et al. 1986
As^{+3}	Chinese hamster ovary cells	Aberrant metaphases	No data	+	Lee et al. 1986
As^{+3}	Chinese hamster ovary cells	Chromosomal aberrations	+	+	Huang et al. 1992
As^{+3}	Chinese hamster ovary cells (CHO-K1)	Chromosomal aberrations	No data	+	Huang et al. 1993
As^{+3}; As^{+5}	Chinese hamster ovary cells (CHO-K1)	Chromosomal aberrations and sister chromatid exchange	No data	+	Kochhar et al. 1996
As^{+3}	Chinese hamster ovary cells	Chromosomal aberrations and sister chromatid exchange	+	+	Lin and Tseng 1992
As^{+3}	Chinese hamster ovary cells	Chromosomal aberrations and sister chromatid exchange	No data	+	Wan et al. 1982
As^{+3}	Chinese hamster ovary cells	Sister chromatid exchange and micronucleus induction	No data	+	Fan et al. 1996
As^{+3}	Chinese hamster ovary cells	Cell-killing and micronucleus induction	No data	+	Wang and Huang 1994
As^{+3}	Chinese hamster ovary cells	Micronuclei	No data	+	Liu and Huang 1997
As^{+3}	Chinese hamster ovary cells	Micronuclei formation	No data	+	Yee-Chien and Haimei 1996
As^{+3}	Chinese hamster ovary cells	Micronuclei induction	No data	+	Wang et al. 1997
As^{+3}	Chinese hamster ovary cells	Cytotoxicity	No data	–	Lee and Ho 1994
As^{+3}	Syrian hamster embryo cells	Gene mutation	No data	–	Lee et al. 1985

Table 3-8. Genotoxicity of Inorganic Arsenic *In Vitro*

Valence	Species (test system)	End point	Results: With activation	Results: Without activation	Reference
As^{+3}	Syrian hamster embryo cells	Chromosome aberrations and sister chromatid exchanges	No data	+	Larramendy et al. 1981
As^{+3}	Syrian hamster embryo cells	Chromosomal aberration	No data	+	Lee et al. 1985
As^{+3}	Syrian hamster embryo cells	Sister chromatid exchange	No data	+	Lee et al. 1985
As^{+3}	Syrian hamster embryo cells	Micronuclei induction	No data	–	Gibson et al. 1997
As^{+3}	Syrian hamster embryo cells	Micronuclei induction	No data	–	Gibson et al. 1997
As^{+3}	Syrian hamster embryo cells	Morphological transformation	No data	+	Kerckaert et al. 1996
As^{+3}	Syrian hamster embryo cells	Morphological transformation	No data	+	Lee et al. 1985
As^{+3}	Syrian hamster embryo cells	Morphological transformation	No data	+	Casto et al. 1979
As^{+5}	Human fibroblasts	DNA repair inhibition	No data	–	Okui and Fujiwara 1986
As^{+5}	Human leukocytes	Chromosomal aberrations	No data	(+)	Nakamuro and Sayato 1981
As^{+5}	Human lymphocytes	Chromosomal aberrations	No data	–	Nordenson et al. 1981
As^{+5}	Human lymphocytes	Chromosome aberrations and sister chromatid exchanges	No data	+	Larramendy et al. 1981
As^{+5}	Human lymphocytes	Sister chromatid exchange	No data	–	Rasmussen and Menzel 1997
As^{+5}	Human peripheral lymphocytes	Sister chromatid exchange	No data	+	Zanzoni and Jung 1980
As^{+5}	Human keratinocyte line SCC-9 cells	Keratinocyte programming and transcriptional activity	No data	+	Kachinskas et al. 1997
As^{+5}	Mouse lymphoma cells	Gene mutation	No data	–	Amacher and Paillet 1980
As^{+5}	Mouse lymphoma cells	Gene mutation	No data	–	Amacher and Paillet 1980
As^{+5}	Chinese hamster ovary cells	Chromosomal aberrations	No data	+	Wan et al. 1982
As^{+5}	Syrian hamster embryo cells	Gene mutation	No data	–	Lee et al. 1985
As^{+5}	Syrian hamster embryo cells	Chromosome aberrations and sister chromatid exchanges	No data	+	Larramendy et al. 1981

Table 3-8. Genotoxicity of Inorganic Arsenic *In Vitro*

Valence	Species (test system)	End point	Results		Reference
			With activation	Without activation	
As^{+5}	Syrian hamster embryo cells	Chromosomal aberrations	No data	+	Lee et al. 1985
As^{+5}	Syrian hamster embryo cells	Sister chromatid exchange	No data	+	Lee et al. 1985
As^{+5}	Syrian hamster embryo cells	Morphological transformation	No data	+	Lee et al. 1985
As^{+5}	Syrian hamster embryo cells	Morphological transformation	No data	+	DiPaolo and Casto 1979

(+) = weakly positive or marginal result; – = negative result; + = positive result; DNA = deoxyribonucleic acid

Table 3-9. Genotoxicity of Inorganic Arsenic *In Vivo*

Valence	Exposure route	Species (test system)	End point	Results	Reference
Nonmammalian					
As^{+3} As^{+5}	Injection	*Drosophila melanogaster*	Somatic mutations and mitotic recombination	+	Ramos-Morales and Rodriguez-Arnaiz 1995
As^{+3} As^{+5}	Larval feeding	*D. melanogaster*	Somatic mutations and mitotic recombination	+	Ramos-Morales and Rodriguez-Arnaiz 1995
As^{+5}	Larvae	*D. melanogaster*	Mitotic recombinations	+	de la Rosa et al. 1994
Mammalian					
As^{+3}	Inhalation	Human (lymphocytes)	Chromosomal aberrations	–	Beckman et al. 1977
As^{+3}	Inhalation	Human (lymphocytes)	Chromosomal aberrations	+	Nordenson et al. 1978
As^{+3}	Oral	Human (lymphocytes)	Chromosomal aberrations	–	Burgdorf et al. 1977
No data	Oral	Human (lymphocytes)	Chromosomal aberrations	–	Vig et al. 1984
No data	Oral	Human (skin)	DNA adducts	+	Matsui et al. 1999
As^{+3}	Oral	Human (lymphocytes)	Sister chromatid exchange	–	Burgdorf et al. 1977
As^{+3}	Oral	Human (lymphocytes)	Sister chromatid exchange	+	Hsu et al. 1997
No data	Oral	Human (lymphocytes)	Sister chromatid exchange	+	Lerda 1994
No data	Oral	Human (lymphocytes)	Sister chromatid exchange	+	Liou et al. 1999
No data	Oral	Human (lymphocytes)	Sister chromatid exchange	+	Mahata et al. 2003
As^{+3}	Oral	Human (lymphocytes)	Sister chromatid exchange	–	Nordenson et al. 1978
No data	Oral	Human (lymphocytes)	Sister chromatid exchange	–	Vig et al. 1984
No data	Oral	Human skin carcinoma	Mutation and overexpression of p53	+	Hsu et al. 1999
As^{+3}	Oral	Exfoliated human epithelial cells	Micronuclei	+	Moore et al. 1996
As^{+3}	Oral	Exfoliated human epithelial cells	Micronuclei	+	Tian et al. 2001
No data	Oral	Human (bladder cells)	Micronuclei	+	Moore et al. 1995
No data	Oral	Human (lymphocytes)	Micronuclei	+	Martínez et al. 2004
No data	Oral	Human (lymphocytes)	Micronuclei	+	Basu et al. 2004
No data	Oral	Human (oral mucosa cells)	Micronuclei	+	Basu et al. 2004

Table 3-9. Genotoxicity of Inorganic Arsenic *In Vivo*

Valence	Exposure route	Species (test system)	End point	Results	Reference
No data	Oral	Human (urothelial cells)	Micronuclei	+	Basu et al. 2004
As^{+5}	Oral	Rat (bone marrow cells)	Chromosomal aberrations	+	Datta et al. 1986
As^{+3}	Inhalation	Mouse (fetal liver)	Chromosomal aberrations	(+)	Nagymajtényi et al. 1985
As^{+3}	Oral	Mouse (bone marrow cells)	Chromosomal aberrations	+	Das et al. 1993
As^{+3}	Oral	Mouse (bone marrow cells)	Chromosomal aberrations	+	Poddar et al. 2000
As^{+3}	Oral	Mouse (bone marrow cells)	Chromosomal breaks, exchanges	–	Poma et al. 1987
As^{+3}	Oral	Mouse (spermatogonia)	Chromosomal aberrations	–	Poma et al. 1987
As^{+3}	Oral	Mouse (leukocytes)	Chromosomal breaks	+	McDorman et al. 2002
As^{+3}	Intraperitoneal	Mouse (bone marrow cells)	Chromosomal breaks, exchanges	–	Poma et al. 1981
As^{+3}	Intraperitoneal	Mouse (bone marrow cells)	Micronuclei	+	DeKnudt et al. 1986
As^{+3}	Intraperitoneal	Mouse (spermatogonia)	Spermatongonia	–	Poma et al. 1981
As^{+3}	Intraperitoneal	Mouse (spermatogonia)	Sperm morphology	–	DeKnudt et al. 1986
As^{+3}	Intraperitoneal	Mouse (spermatogenesis)	Dominant lethal mutations	–	DeKnudt et al. 1986

(+) = weakly positive or marginal result; – = negative result; + = positive result; DNA = deoxyribonucleic acid

Investigations of genotoxic effects of ingested arsenic have yielded mixed results possibly due to the different types of cells examined and the different exposure levels experienced by the populations studied. A study of p53 mutations in arsenic-related skin cancers from patients in Taiwan exposed to arsenic from drinking water found a high rate of p53 mutations and different types of p53 mutations compared with those seen in UV-induced skin cancers (Hsu et al. 1999); similar results have been found in mice (Salim et al. 2003). In humans exposed to Fowler's solution (potassium arsenite, usually taken at a dose of about 0.3 mg As/kg/day [Holland 1904]), increased sister chromatid exchanges, but no increase in chromosomal aberrations, was reported in one study (Burgdorf et al. 1977), while just the converse (increased aberrations but no increase in sister chromatid exchange) was reported in another (Nordenson et al. 1979). Moore et al. (1997a) reported an exposure-dependent increase in the occurrence of micronucleated cells in epithelial cells from the bladder in a male population in northern Chile chronically exposed to high and low arsenic levels in their drinking water (average concentrations, 600 and 15 µg As/L, respectively), and noted that chromosome breakage was the major cause of micronucleus (MN) formation. Similar results were reported by Martínez et al. (2004) who evaluated micronuclei formation in peripheral lymphocytes from people in northern Chile exposed to up to 0.75 mg As/L in their drinking water. In contrast, Martínez et al. (2005) did not find a significant increase in micronuclei in buccal cells from subjects from the same area relative to a low exposure group. Vig et al. (1984) found no significant differences in the frequency of chromosomal aberrations or sister chromatid exchanges between two populations in Nevada with differing levels of arsenic in their drinking water (mean concentrations of 5 and 109 µg/L). In animal studies, an increased incidence of chromosomal abnormalities was detected in rats given oral doses of sodium arsenate (4 mg As/kg/day) for 2–3 weeks (Datta et al. 1986), but no consistent increase in chromosomal aberrations was detected in bone marrow cells or spermatogonia from mice given sodium arsenite (about 50 mg As/kg/day) for up to 8 weeks (Poma et al. 1987). These studies suggest that ingested arsenic may cause chromosomal effects, but these data are too limited to draw a firm conclusion.

Organic Arsenicals. The genotoxicity of the organic arsenicals has been investigated in a number of studies (see Table 3-10). Several tests indicate that DMA and roxarsone may be able to cause chromosome aberrations, mutations, and deoxyribonucleic acid (DNA) strand breaks; *in vitro* studies with MMA did not find significant increases in the occurrence of chromosome aberrations, forward or reverse mutations, unscheduled DNA synthesis (Chun and Killeen 1989a, 1989b, 1989c, 1989d). An increased number of DNA strand breaks were detected in lung and other tissues of mice and rats given oral doses of ~1,500 mg/kg DMA (Okada and Yamanaka 1994; Yamanaka et al. 1989a); this effect appeared to be related to the formation of some active oxygen species. These breaks were largely repaired within 24 hours, so the relevance with respect to health risk is uncertain.

Table 3-10. Genotoxicity of Organic Arsenic

Chemical form	Species (test system)	End point	Results: With activation	Results: Without activation	Reference
Prokaryotic organisms (*in vitro*):					
MMA	*Salmonella typhimurium*	Gene mutation	–	–	Chun and Killeen 1989c
DMA	*Escherichia coli*	Gene mutation	No data	+	Yamanaka et al. 1989b
Roxarsone	*S. typhimurium*	Gene mutation	–	–	NTP 1989b
Eukaryotic organisms (*in vitro*):					
MMA	Chinese hamster ovary cells	Chromosome aberrations	–	–	Chun and Killeen 1989a
MMA	Mouse lymphoma cells (L5178Y/TK$^{+/-}$)	Forward mutation	–	–	Chun and Killeen 1989b
MMA	Rat heptocytes	Unscheduled DNA synthesis	No data	–	Chun and Killeen 1989d
DMA	Human peripheral lymphocytes	Mitogenesis inhibited	No data	–	Endo et al. 1992
DMA	Human lymphocytes	Sister chromatid exchange	No data	–	Rasmussen and Menzel 1997
DMA	Human alveolar (L-132) cells	Lung-specific DNA damage	No data	+	Kato et al. 1994
DMA	Human alveolar type II (L-132) cells	DNA single-strand breaks	+	+	Kawaguchi et al. 1996
DMA	Human diploid L-132 epithelial cells	DNA single-strand breaks	No data	+	Rin et al. 1995
DMA	Human alveolar type II (L-132) cells	DNA strand breaks	No data	+	Tezuka et al. 1993
DMA	Human embryonic cell line of type II alveolar epithelial cells (L-132)	DNA single-strand breaks and DNA-protein crosslinks	No data	+	Yamanaka et al. 1993
DMA	Human alveolar epithelial (L-132) cells	DNA single-strand breaks and DNA-protein crosslinks	No data	+	Yamanaka et al. 1995
DMA	Human pulmonary epithelial (L-132) cells	DNA single-strand breaks	No data	+	Yamanaka et al. 1997
DMA	Human umbilical cord fibroblasts	Chromosomal aberrations	No data	+	Oya-Ohta et al. 1996
DMA	Mouse lymphoma cells (L5178Y/TK$^{+/-}$ -3.7.2C)	Chromosomal mutations	No data	+	Moore et al. 1997a
DMA	Chinese hamster lung and diploid cells (V79)	Mitotic arrest and tetraploid formation	No data	+	Endo et al. 1992

Table 3-10. Genotoxicity of Organic Arsenic

Chemical form	Species (test system)	End point	Results: With activation	Results: Without activation	Reference
DMA	Chinese hamster V79 cells	Chromosomal aberrations	No data	+	Ueda et al. 1997
DMA	Chinese hamster lung and diploid cells (V79)	Chromosomal aberrations	No data	+	Kitamura et al. 2002
DMA	Chinese hamster lung and diploid cells (V79)	Chromosomal aberrations	+	+	Kuroda et al. 2004
DMA	Chinese hamster V79 cells	Tetraploids and mitotic arrest	No data	+	Eguchi et al. 1997
MMA	Human umbilical cord fibroblasts	Chromosomal aberrations	No data	+	Oya-Ohta et al. 1996
MMA	Chinese hamster V79 cells	Tetraploids and mitotic arrest	No data	+	Eguchi et al. 1997
Roxarsone	*Drosophila melanogaster*	Sex linked recessive	No data	–	NTP 1989b
Roxarsone	Rat hepatocyte	DNA double-strand breaks	No data	+	Storer et al. 1996
Roxarsone	A31-1-13 clone of BALB/c-3T3 cells	Transformation response and mutagenicity	No data	–	Matthews et al. 1993
Roxarsone	Mouse lymphoma (L5178Y) cells	Trifluorothymidine resistance	No data	+	NTP 1989b
Eukaryotic organisms (*in vivo*):					
DMA	Rat (oral exposure)	DNA single-stand breaks in lung	No data	+	Yamanaka and Okada 1994
DMA	Mouse (oral exposure)	DNA strand breaks in tissues	No data	+	Yamanaka et al. 1989b
DMA	Mouse (oral exposure)	DNA single-stand breaks in lung	No data	+	Yamanaka et al. 1993
DMA	Mouse (oral exposure)	DNA single-strand breaks in lung	No data	–	Yamanaka et al. 1989a
DMA	Mouse (oral exposure)	DNA adduct formation	No data	+	Yamanaka et al. 2001
DMA	Mouse (injection)	Aneuploidy in bone marrow cells	No data	+	Kashiwada et al. 1998

– = negative result; + = positive result; DMA = dimethylarsinic acid; DNA = deoxyribonucleic acid; MMA = monomethylarsonic acid

3.4 TOXICOKINETICS

There is an extensive database on the toxicokinetics of inorganic arsenic. Most studies have been performed in animals, but there are a number of studies in humans as well. These studies reveal the following main points:

- Both arsenate and arsenite are well absorbed by both the oral and inhalation routes. Absorption by the dermal route has not been well characterized, but is low compared to the other routes. Inorganic arsenic in soil is absorbed to a lesser extent than solutions of arsenic salts.
- The rate of absorption of arsenic in highly insoluble forms (e.g., arsenic sulfide, lead arsenate) is much lower than that of more soluble forms via both oral and inhalation routes.
- Once absorbed, arsenites are oxidized to arsenates and methylated. This process may then be repeated to result in dimethylated arsenic metabolites.
- Distribution of arsenic in the rat is quite different from other animal species, suggesting that the rat is probably not an appropriate toxicokinetic model for distribution, metabolism, or excretion of arsenic by humans.
- The As(+3) form undergoes enzymic methylation primarily in the liver to form MMA and DMA. The rate and relative proportion of methylation production varies among species. The rate of methylation varies considerably among tissues.
- Most arsenic is promptly excreted in the urine as a mixture of As(+3), As(+5), MMA, and DMA; DMA is usually the primary form in the urine. Smaller amounts are excreted in feces. Some arsenic may remain bound to tissues, depending inversely on the rate and extent of methylation.

Less information is available for the organic arsenicals. It appears that both MMA and DMA are well absorbed, but are rapidly excreted in the urine and feces. MMA may be methylated to DMA, but neither MMA nor DMA are demethylated to yield inorganic arsenic.

A review of the evidence that supports these conclusions is presented below.

3.4.1 Absorption

3.4.1.1 Inhalation Exposure

Inorganic Arsenicals. Since arsenic exists in air as particulate matter, absorption across the lung involves two processes: deposition of the particles onto the lung surface, and absorption of arsenic from the deposited material. In lung cancer patients exposed to arsenic in cigarette smoke, deposition was

estimated to be about 40% and absorption was 75–85% (Holland et al. 1959). Thus, overall absorption (expressed as a percentage of inhaled arsenic) was about 30–34%. In workers exposed to arsenic trioxide dusts in smelters, the amount of arsenic excreted in the urine (the main route of excretion; see Section 3.4.4) was about 40–60% of the estimated inhaled dose (Pinto et al. 1976; Vahter et al. 1986). Absorption of arsenic trioxide dusts and fumes (assessed by measurement of urinary metabolites) correlated with time weighted average arsenic air concentrations from personal breathing zone air samplers (Offergelt et al. 1992). Correlations were best immediately after a shift and just before the start of the next shift. Although the percent deposition was not measured in these cases, it seems likely that nearly all of the deposited arsenic was absorbed. This conclusion is supported by intratracheal instillation studies in rats and hamsters, where clearance of oxy compounds of arsenic (sodium arsenite, sodium arsenate, arsenic trioxide) from the lung was rapid and nearly complete (60–90% within 1 day) (Marafante and Vahter 1987; Rhoads and Sanders 1985). In contrast, arsenic sulfide and lead arsenate were cleared more slowly (Marafante and Vahter 1987), indicating that the rate of absorption may be lower if the inhaled arsenic is in a highly insoluble form. There are no data to suggest that absorption of inhaled arsenic in children differs from that in adults.

Organic Arsenicals. No studies were located regarding absorption of organic arsenicals in humans or animals after inhalation exposure. However, DMA instilled in the lungs of rats was absorbed very rapidly (half-time of 2.2 minutes) and nearly completely (at least 92%) (Stevens et al. 1977). This indicates that organic arsenicals are likely to be well absorbed by the inhalation route.

3.4.1.2 Oral Exposure

Inorganic Arsenicals. Several studies in humans indicate that arsenates and arsenites are well absorbed across the gastrointestinal tract. The most direct evidence is from a study that evaluated the 6-day elimination of arsenic in healthy humans who were given water from a high-arsenic sampling site (arsenic species not specified) and that reported approximately 95% absorption (Zheng et al. 2002). A similar absorption efficiency can be estimated from measurements of fecal excretion in humans given oral doses of arsenite, where <5% was recovered in the feces (Bettley and O'Shea 1975). This indicates absorption was at least 95%. These results are supported by studies in which urinary excretion in humans was found to account for 55–87% of daily oral intakes of arsenate or arsenite (Buchet et al. 1981b; Crecelius 1977; Kumana et al. 2002; Mappes 1977; Tam et al. 1979b). In contrast, ingestion of arsenic triselenide (As_2Se_3) did not lead to a measurable increase in urinary excretion (Mappes 1977), indicating that

gastrointestinal absorption may be much lower if highly insoluble forms of arsenic are ingested. There are no data to suggest that absorption of arsenic from the gut in children differs from that in adults.

These observations in humans are supported by a number of studies in animals. Fecal excretion of arsenates and arsenites ranged from 2 to 10% in monkeys and mice, with 70% or more appearing in urine (Charbonneau et al. 1978; Roberts et al. 2002; Vahter 1981; Vahter and Norin 1980). Oral absorption of [^{73}As] labeled sodium arsenate in mice was unaffected by dose (0.0005–5 mg/kg) as reflected in percentage of dose excreted in feces over 48 hours (Hughes et al. 1994). Absorption ranged from 82 to 89% at all doses. Gonzalez et al. (1995) found that the percentage of arsenate that was absorbed in rats decreased as the dose increased from 6 to 480 µg, suggesting saturable, zero-order absorption of arsenate in this species. Hamsters appear to absorb somewhat less than humans, monkeys, and mice, since fecal excretion usually ranges from 10 to 40% (Marafante and Vahter 1987; Marafante et al. 1987a; Yamauchi and Yamamura 1985). Rabbits also appear to absorb less arsenate than humans, monkeys, or mice after oral exposure (Freeman et al. 1993). After a gavage dose of 1.95 mg/kg sodium arsenate, 45% of the arsenate was recovered in feces in males and 52% in females. As in humans, when highly insoluble arsenic compounds are administered (arsenic trisulfide, lead arsenate), gastrointestinal absorption is reduced 20–30% (Marafante and Vahter 1987).

Bioavailability of arsenic was measured in rabbits ingesting doses of smelting soils that contained arsenic primarily in the form of sulfides (Freeman et al. 1993). Bioavailability was assessed by comparing the amounts of arsenic that was excreted after ingestion of the soil to that excreted after an intravenous dose of sodium arsenate. The bioavailability of the arsenic in the ingested soil was 24±3.2% and that of sodium arsenate in the gavage dose was 50±5.7%. Approximately 80% of the arsenic from ingested soil was eliminated in the feces compared with 50% of the soluble oral dose and 10% of the injected dose. In another study, rabbits dosed with sodium arsenite (0.8 mg As/kg) had 5 times greater blood arsenic concentrations than rabbits dosed with arsenic-containing soil (2.8 mg As/kg), suggesting a lower bioavailability of the arsenic in soil (Davis et al. 1992).

Studies of the bioavailability of arsenic suggest that absorption of arsenic in ingested dust or soil is likely to be considerably less than absorption of arsenic from ingested salts (Davis et al. 1992, 1996; EPA 1997g; Freeman et al. 1993, 1995; Pascoe et al. 1994; Roberts et al. 2002, 2007; Rodriguez et al. 1999). Oral absorption of arsenic in a group of three female Cynomolgus monkeys from a soluble salt, soil, and household dust was compared with absorption of an intravenous dose of sodium arsenate (Freeman et al. 1995). Mean absolute percentage bioavailability based on urine arsenic excretion was reported at

67.6±2.6% (gavage), 19.2±1.5% (oral dust), and 13.8±3.3% (oral soil). Mean absolute percentage bioavailability based on blood arsenic levels was reported at 91.3±12.4% (gavage), 9.8±4.3% (oral dust), and 10.9±5.2% (oral soil). The arsenic in the dust and soil was approximately 3.5–5-fold (based on levels in the urine) and 8–9-fold (based on levels in the blood) less bioavailable than arsenic in solution. Two other studies in monkeys reported relative bioavailability of arsenic in soil from a number of locations (electrical substation, wood preserving sites, pesticide sites, cattle-dip sites, volcanic soil, and mining sites) ranged from 5 to 31% (Roberts et al. 2002, 2007). A study in beagle dogs fed with soil containing As_2O_5 or treated with intravenous soluble arsenic found that compared to injection the bioavailability of arsenic from ingested soil was 8.3±2.0% (Groen et al. 1993). The bioavailability of arsenic in soil has been studied in juvenile swine that received daily oral doses of soil or sodium arsenate (in food or by gavage) for 15 days (EPA 1997g). The soils were obtained from various mining and smelting sites and contained, in addition to arsenic at concentrations of 100–300 µg/g, lead at concentrations of 3,000–14,000 µg/g. The arsenic doses ranged from 1 to 65.4 µg/kg/day. The fraction of the arsenic dose excreted in urine was measured on days 7 and 14 and the relative bioavailability of the soil-borne arsenic was estimated as the ratio of urinary excretion fractions, soil arsenic:sodium arsenate. The mean relative bioavailability of soil-borne arsenic ranged from 0 to 98% in soils from seven different sites (mean±SD, 45%±32). Estimates for relative bioavailability of arsenic in samples of smelter slag and mine tailings ranged from 7 to 51% (mean±SD, 35%±27). Rodriguez et al. (1999) used a similar approach to estimate the relative bioavailability of arsenic in mine and smelter wastes (soils and solid materials) in juvenile swine. Samples included iron slag deposits and calcine deposits and had arsenic concentrations that ranged from 330 to 17,500 µg/g. Relative bioavailability (waste:sodium arsenate) ranged from 3 to 43% for 13 samples (mean, 21%) and was higher in iron slag wastes (mean, 25%) than in calcine wastes (mean, 13%).

Bioavailability of arsenic from soil is reduced by low solubility and inaccessibility due to the presence of secondary reaction products or insoluble matrix components (Davis et al. 1992). This is supported by studies conducted with *in vitro* simulations of the gastric and/or intestinal fluids (Hamel et al. 1998; Pouschat and Zagury 2006; Rodriguez et al. 1999; Ruby et al. 1996, 1999; Williams et al. 1998). When soils containing arsenic are incubated in simulated gastrointestinal fluids, only a fraction of the arsenic becomes soluble. Estimates of the soluble, or bioaccessible, arsenic fraction have ranged from 3 to 50% for various soils and mining and smelter waste materials (Pouschat and Zagury 2006; Rodriguez et al. 1999; Ruby et al. 1996); these estimates are similar to *in vivo* estimates of the relative bioavailability of arsenic in these same materials (Ruby et al. 1999).

Organic Arsenicals. Based on urinary excretion studies in volunteers, it appears that both MMA and DMA are well absorbed (at least 75–85%) across the gastrointestinal tract (Buchet et al. 1981a; Marafante et al. 1987b). This is supported by studies in animals, where at least 75% absorption has been observed for DMA (Marafante et al. 1987b; Stevens et al. 1977; Vahter et al. 1984; Yamauchi and Yamamura 1984) and MMA (Hughes et al. 2005; Yamauchi et al. 1988). In mice, the relative bioavailability of MMA appears to be dose-dependent; 81% was absorbed following a single gavage dose of 0.4 mg MMA/kg/day compared to 60% following administration of 4 mg MMA/kg/day (Hughes et al. 2005).

3.4.1.3 Dermal Exposure

Inorganic Arsenicals. No quantitative studies were located on absorption of inorganic arsenicals in humans after dermal exposure. Percutaneous absorption of [^{73}As] as arsenic acid (H_3AsO_4) alone and mixed with soil has been measured in skin from cadavers (Wester et al. 1993). Labeled arsenic was applied to skin in diffusion cells and transit through the skin into receptor fluid measured. After 24 hours, 0.93% of the dose passed through the skin and 0.98% remained in the skin after washing. Absorption was lower with [^{73}As] mixed with soil: 0.43% passed through the skin over 24 hours and 0.33% remained in the skin after washing.

Dermal absorption of arsenic has been measured in Rhesus monkeys (Lowney et al. 2005; Wester et al. 1993). After 24 hours, 6.4% of [^{73}As] as arsenic acid was absorbed systemically, as was 4.5% of [^{73}As] mixed with soil (Wester et al. 1993). Similarly, 2.8% of soluble arsenic in water was detected in the urine 24 hours after exposure (Lowney et al. 2005). However, arsenic from soil was poorly absorbed; 0.12% was detected in the urine after 24 hours. Differences between the Wester et al. (1993) and Lowney et al. (2005) studies in terms of uptake from soil may be due to the differences in forms of arsenic in the soil. In the Wester et al. (1993) study, soil was mixed with radiolabelled arsenic acid in water; Lowney et al. (2005) used soil samples from a pesticide manufacturing facility that historically manufactured arsenical pesticides (the arsenic was primarily in the iron oxide and iron silicate mineral phases). Lowney et al. (2005) also measured urinary levels of arsenic following dermal application of CCA residues and found that the levels did not increase from background. Uptake of arsenic into blood or tissues was undetectable for up to 24 hours in rats whose tails were immersed in solutions of sodium arsenate for 1 hour. However, arsenic began to increase in blood, liver, and spleen over the next 5 days (Dutkiewicz 1977). The rate of uptake was estimated to be 1–33 μg/cm^2/hour. These findings suggest that dermal exposure leads initially to arsenic binding to skin, and that the bound arsenic may slowly be taken up into the blood, even after exposure ends.

Organic Arsenicals. No studies were located on absorption of organic arsenicals in humans or animals after dermal exposure.

3.4.2 Distribution

3.4.2.1 Inhalation Exposure

Inorganic Arsenicals. No studies were located on the distribution of arsenic in humans or animals after inhalation exposure, but intratracheal administration of arsenic trioxide to rats resulted in distribution of arsenic to the liver, kidney, skeleton, gastrointestinal tract, and other tissues (Rhoads and Sanders 1985). This is consistent with data from oral and parenteral studies (below), which indicate that absorbed arsenic is distributed throughout the body.

Organic Arsenicals. No studies were located regarding the distribution of organic arsenicals in humans or animals after inhalation exposure. However, DMA administered to rats by the intratracheal route was distributed throughout the body (Stevens et al. 1977), suggesting that inhalation of organic arsenicals would also lead to widespread distribution.

3.4.2.2 Oral Exposure

Inorganic Arsenicals. Analysis of tissues taken at autopsy from people who were exposed to background levels of arsenic in food and water revealed that arsenic is present in all tissues of the body (Liebscher and Smith 1968). Most tissues had about the same concentration level (0.05–0.15 ppm), while levels in hair (0.65 ppm) and nails (0.36 ppm) were somewhat higher. This indicates that there is little tendency for arsenic to accumulate preferentially in any internal organs. However, exposure levels may not have been high enough to cause elevated levels in tissues. Arsenic exposure may have been low enough that the methylation process in the body resulted in limited accumulation in internal organs. Tissue analysis of organs taken from an individual following death from ingestion of 8 g of arsenic trioxide (about 3 g of arsenic) showed a much higher concentration of arsenic in liver (147 µg/g) than in kidney (27 µg/g) or muscle, heart, spleen, pancreas, lungs, or cerebellum (11–12 µg/g) (Benramdane et al. 1999a). Small amounts were also found in other parts of the brain (8 µg/g), skin (3 µg/g), and hemolyzed blood (0.4 µg/g). Many studies have been performed where arsenic levels in hair and nails have been measured and correlations with exposure analyzed. Some of these studies are discussed in Section 3.8, Biomarkers of Exposure.

Inorganic arsenic passes easily through the placenta. High levels of arsenic were found in the liver, kidney, and brain during autopsy of an infant prematurely born to a young mother who had ingested inorganic arsenic at week 30 of gestation (Lugo et al. 1969). Arsenic was detected in human breast milk at concentrations of 0.00013–0.00082 ppm in a World Health Organization study (Somogyi and Beck 1993). Arsenic concentrations were 0.0001–0.0044 ppm in human milk sampled from 88 mothers on the Faroe Islands whose diets were predominantly seafood (Grandjean et al. 1995). Exposures to arsenic from the seafood diet in this population was most likely to organic "fish arsenic." In a population of Andean women exposed to high concentrations (about 200 ppb) of inorganic arsenic in drinking water, concentrations of arsenic in breast milk ranged from about 0.0008 to 0.008 ppm (Concha et al. 1998b).

Studies in mice and hamsters given oral doses of arsenate or arsenite have found elevated levels of arsenic in all tissues examined (Hughes et al. 2003; Vahter and Norin 1980; Yamauchi and Yamamura 1985), including the placenta and fetus of pregnant females (Hood et al. 1987, 1988). Inorganic arsenic crosses the placental barrier and selectively accumulates in the neuroepithelium of the developing animal embryo (Hanlon and Ferm 1977; Lindgren et al. 1984). In mice, radiolabel from orally administered 74-As was widely distributed to all tissues, with the highest levels in skin, kidney, and liver (Hughes et al. 2003). No obvious differences between As(+3) and As(+5) were found, although residual levels after 24 hours tended to be higher for As(+3) than As(+5) (Vahter and Norin 1980). However, *in vitro* studies have found that the cellular uptake of As(+3) was higher than that of As(+5) (Bertolero et al. 1987; Dopp et al. 2004); in mouse cells, the difference was 4-fold (Bertolero et al. 1987). In hamsters, increases in tissue levels were noted after oral treatment with As(+3) for most tissues (hair, kidney, liver, lung, skin, muscle), with the largest increases in liver and lung (Yamauchi and Yamamura 1985). Liver and kidney arsenic concentrations increased with dose in dogs fed arsenite in the diet for 6 months (Neiger and Osweiler 1992). A study examining the speciation of arsenic following a single dose exposure to sodium arsenate to mice (Kenyon et al. 2005) found that the levels of inorganic arsenic and DMA were similar in the blood, liver, and kidney; much lower levels of MMA were found in these tissues. The concentration of DMA in the lungs exceeded inorganic arsenic and the levels of inorganic arsenic and MMA were similar; the DMA concentration was about 6 times higher than that of inorganic arsenic.

Inorganic arsenic crosses the placental barrier and selectively accumulates in the neuroepithelium of the developing animal embryo (Hanlon and Ferm 1977; Lindgren et al. 1984). Following maternal exposure to arsenite or arsenate throughout gestation and lactation, inorganic arsenic and DMA were detected in the

newborn mouse brains (Jin et al. 2006). The levels of inorganic arsenic in the brain were similar to those in the newborn livers; however, the levels of DMA in the brain were about twice as high as in the liver.

Organic Arsenicals. No studies were located on the distribution of organic arsenicals in humans following oral exposure. Studies in animals found MMA and DMA distributed to all tissues after acute oral doses (Hughes et al. 2005; Stevens et al. 1977; Vahter et al. 1984; Yamauchi and Yamamura 1984; Yamauchi et al. 1988). In mice, MMA is rapidly distributed throughout the body with peak tissue concentrations occurring between 0.25 and 4 hours after administration of a single gavage dose of 0.4 or 4 mg MMA/kg (Hughes et al. 2005). The peak levels of MMA in the bladder, kidneys, and lungs were higher than blood, with the highest levels occurring in the bladder. The terminal half-lives of MMA were 4.2–4.9 hours in the liver, lung, and blood, 9.0 hours in the urinary bladder, and 15.9 hours in the kidney in mice dosed with 0.4 mg MMA/kg; similar half-lives were measured in the 4.0 mg MMA/kg mice. Two hours after dosing, most of the methylated arsenic in the tissues was in the form of MMA. In rats exposed to 100 mg/kg DMA in the diet for 72 days, high levels of arsenic was detected in the blood (Lu et al. 2004a). The arsenic was primarily found in the erythrocyte; the concentration in the erythrocyte was 150 times higher than the arsenic concentration in the plasma.

3.4.2.3 Dermal Exposure

No studies were located regarding distribution of inorganic or organic arsenicals in humans or animals after dermal exposure.

3.4.2.4 Other Routes of Exposure

Inorganic Arsenicals. Studies in mice, rabbits, and monkeys injected intravenously with solutions of arsenite or arsenate confirm that arsenic is widely distributed throughout the body (Lindgren et al. 1982; Marafante and Vahter 1986; Vahter and Marafante 1983; Vahter et al. 1982). Shortly after exposure, the concentration of arsenic tends to be somewhat higher in liver, kidney, lung, and gastrointestinal epithelium (Hughes et al. 2000; Lindgren et al. 1982; Vahter and Marafante 1983; Vahter et al. 1982), but levels tend to equilibrate over time. Arsenate shows a tendency to deposit in skeletal tissue that is not shared by arsenite (Lindgren et al. 1982, 1984), presumably because arsenate is an analog of phosphate.

The distribution of arsenic in the rat is quite different from other animal species. Following intramuscular injection of carrier-free radio-arsenate in rats, most of the injected arsenic became bound to hemoglobin in red blood cells, and very little reached other tissues (Lanz et al. 1950). However, similar experiments

in dogs, mice, guinea pigs, rabbits, and chicks found very little uptake of arsenic into the blood in these species (cats gave intermediate results).

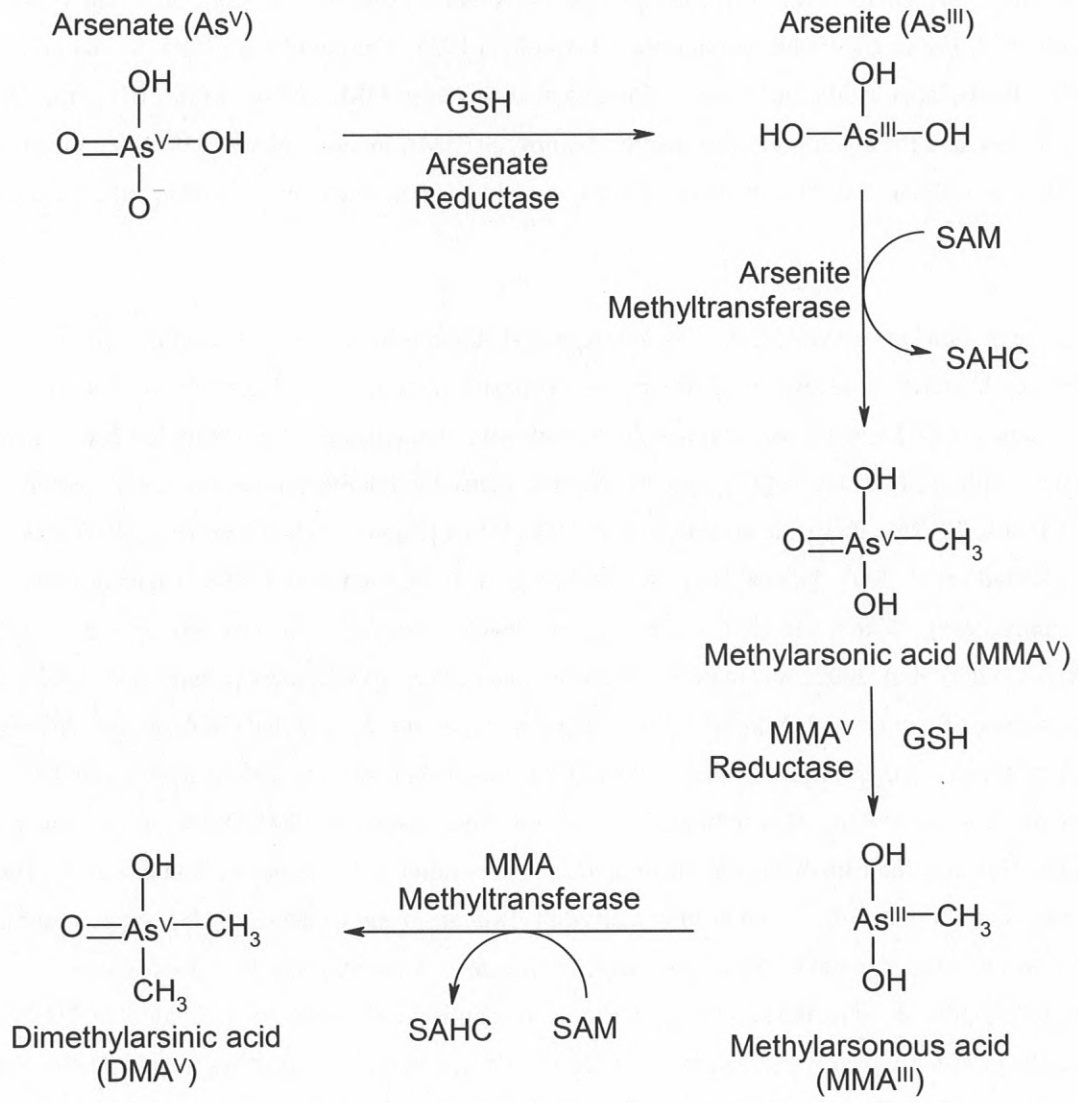
Organic Arsenicals. Following intravenous administration of DMA in mice, DMA is rapidly distributed throughout the body (Hughes et al. 2000). In the blood, the DMA was initially detected in the plasma, but fairly rapidly equilibrated between the plasma and erythrocytes. Blood, plasma, erythrocyte, liver, and kidney distribution and elimination of DMA did not differ in groups of mice administered 1.11 or 111 mg DMA/kg. However, a significant difference in DMA elimination from the lungs was observed; the elimination half-time increased from 91 minutes in the 1.11 mg DMA/kg group to 6,930 minutes in the 111 mg DMA/kg group.

3.4.3 Metabolism

Inorganic Arsenicals. The metabolism of inorganic arsenic has been extensively studied in humans and animals, and is diagrammed in Figure 3-7. Two basic processes are involved: (1) reduction/oxidation reactions that interconvert As(III) and As(V), and (2) methylation reactions, which convert arsenite to MMA and DMA. The resulting series of reactions results in the reduction of inorganic arsenate to arsenite (if necessary), methylation to MMA(V), reduction to MMA(III), and methylation to DMA(V). These processes appear to be similar whether exposure is by the inhalation, oral, or parenteral route. The human body has the ability to change inorganic arsenic to organic forms (i.e., by methylation) that are more readily excreted in urine. In addition, inorganic arsenic is also directly excreted in the urine. It is estimated that by means of these two processes, >75% of the absorbed arsenic dose is excreted in the urine (Marcus and Rispin 1988), although this may vary with the dose and exposure duration. This mechanism is thought to have an upper-dose limit which, when overwhelmed, results in a higher incidence of arsenic toxicity. This is supported by a case report of an individual who died 3 days after ingesting 8 g of arsenic trioxide (about 3 g of arsenic) (Benramdane et al. 1999a). Only 20% of the total arsenic in all tissues analyzed was methylated (14% MMA, 6% DMA), while 78% remained as arsenite and 2% as arsenate.

The majority of the evidence characterizing the metabolic pathways of arsenic is derived from analysis of urinary excretion products. Exposure of humans to either arsenates or arsenites results in increased levels of inorganic As(+3), inorganic As(+5), MMA, and DMA in urine (Aposhian et al. 2000a, 2000b; Buchet et al. 1981a, 1981b; Concha et al. 1998a, 1998b; Crecelius 1977; Kurttio et al. 1998; Lovell and Farmer

Figure 3-7. Inorganic Arsenic Biotransformation Pathway



SAHC = S-adenosylhomocysteine; SAM = S-adenosylmethionine

Source: adapted from Aposhian et al. 2000b

1985; Smith et al. 1977; Tam et al. 1979b; Vahter 1986). Similar results are obtained from studies in mice (Vahter 1981; Vahter and Envall 1983), hamsters (Hirata et al. 1988; Marafante and Vahter 1987; Takahashi et al. 1988), and rabbits (Maiorino and Aposhian 1985; Marafante et al. 1985; Vahter and Marafante 1983). Historically, little distinction was made between MMA(V) and MMA(III) in the urine in most studies, and the assumption was that the majority of MMA in the urine was MMA(V); however, Aposhian et al. (2000a, 2000b) demonstrated that the methylated arsenic atom may be in either valance state.

The relative proportions of As(+3), As(+5), MMA, and DMA in urine can vary depending upon the chemical administered, time after exposure, route of exposure, dose level, and exposed species. In general, however, DMA is the principal metabolite following long-term exposure, with lower levels of inorganic arsenic [As(+3) and As(+5)] and MMA. In humans, the relative proportions are usually about 40–75% DMA, 20–25% inorganic arsenic, and 15–25% MMA (Buchet et al. 1981a; Hopenhayn et al. 2003b; Loffredo et al. 2003; Mandal et al. 2001; Smith et al. 1977; Tam et al. 1979b; Tokunaga et al. 2002; Vahter 1986). With relatively constant exposure levels, these metabolic proportions remain similar over time (Concha et al. 2002), and appear to be similar among family members (Chung et al. 2002). One study of groups of women and children in two villages in Argentina showed that children ingesting large amounts of arsenic in their drinking water (200 µg/L) excreted about 49% inorganic arsenic and 47% DMA (Concha et al. 1998b). This compared to 32% inorganic arsenic and 66% DMA for the women in the study. This may indicate that metabolism of arsenic in children is less efficient than in adults. The rabbit has a ratio of metabolites similar to human adults (Maiorino and Aposhian 1985), suggesting that this may be a good animal model for toxicokinetics in humans. Mice may also be a good human toxicokinetic model based on the similarity of arsenic metabolism and deposition (Vahter et al. 2002). In contrast, the guinea pig, marmoset, and tamarin monkey do not methylate inorganic arsenic (Healy et al. 1998; Vahter and Marafante 1985; Vahter et al. 1982; Zakharyan et al. 1996); thus, they may be poor models for humans.

Reduction of arsenate to arsenite can be mediated by glutathione (Menzel et al. 1994). Scott et al. (1993) showed that glutathione forms complexes with both arsenate and arsenite *in vitro*, and that glutathione is oxidized (and arsenate reduced) in the glutathione-arsenate reaction. Studies *in vitro* indicate that the substrate for methylation is As(+3), and that As(+5) is not methylated unless it is first reduced to As(+3) (Buchet and Lauwerys 1985, 1988; Lerman et al. 1983). The main site of methylation appears to be the liver, where the methylation process is mediated by enzymes that utilize S-adenosylmethionine as cosubstrate (Buchet and Lauwerys 1985, 1988). Under normal conditions, the availability of methyl

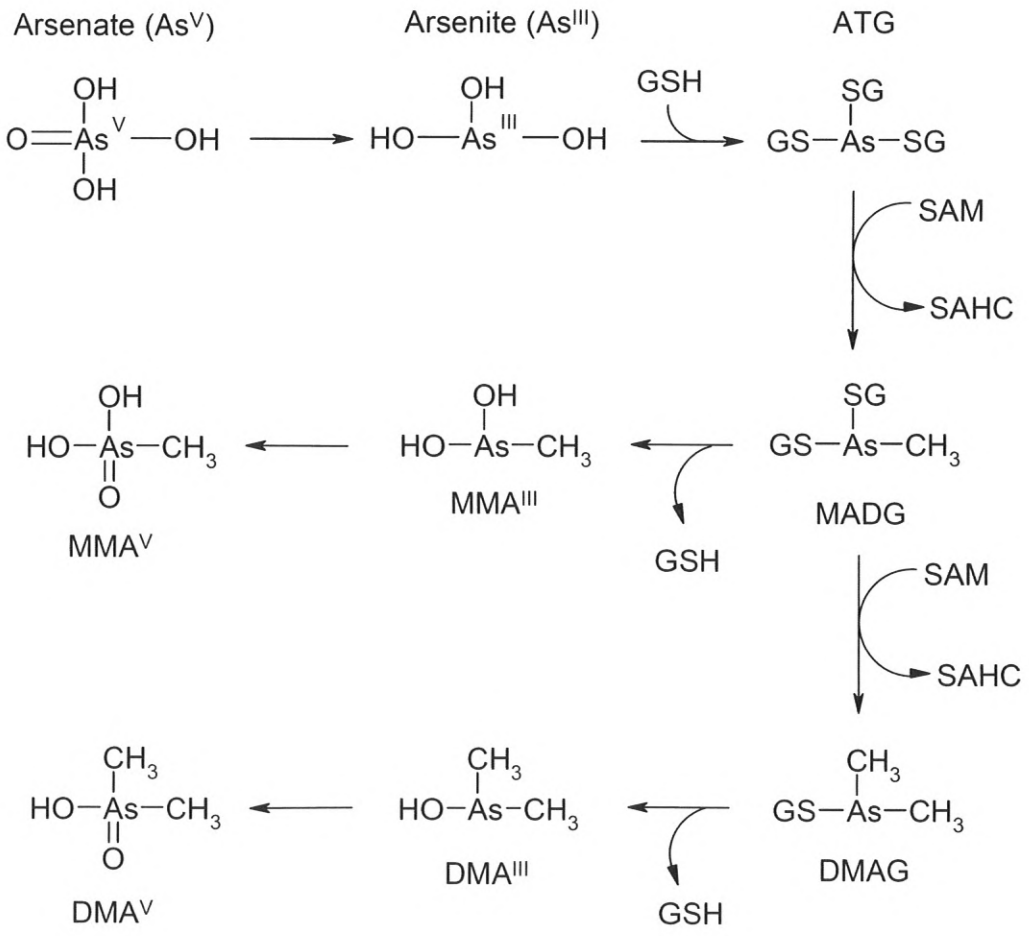
donors (e.g., methionine, choline, cysteine) does not appear to be rate limiting in methylating capacity, either in humans (Buchet et al. 1982) or in animals (Buchet and Lauwerys 1987; Buchet et al. 1981a). However, severe dietary restriction of methyl donor intake can result in significant decreases in methylating capacity (Buchet and Lauwerys 1987; Vahter and Marafante 1987).

Arsenic methyltransferase and MMA methyltransferase activities have been purified to homogeneity from cytosol of rabbit liver (Zakharyan et al. 1995), Rhesus monkey liver (Zakharyan et al. 1996), and rat liver (Thomas et al. 2004). It appears that a single protein catalyzes both activities. This activity transfers a methyl group from S-adenosylmethionine to As(+3) yielding MMA, which is then further methylated to DMA. Reduced glutathione is probably a co-factor *in vivo*, but other thiols can substitute *in vitro* (L-cysteine, dithiothreitol). The substrate saturation concentration for rabbit arsenite methyltransferase is 50 μM, for MMA methyltransferase it is 1,000 μM. The purified activity is specific for arsenite and MMA; selenite, selenate, selenide, and catechols do not serve as substrates. Thomas et al. (2004) reported cloning the gene for an S-adenosylmethionine-dependent methyltransferase from rat liver cytosol that catalyzes the conversion of arsenic to methylated and dimethylated species. It bears a high similarity to translations of *cyt19* genes in both the mouse and the human; both this gene and protein are now termed arsenic (+3 oxidation state) methyltransferase (AS3MT).

Studies in mice indicate that exposure to arsenic does not induce arsenic methylation activity (Healy et al. 1998). Mice receiving up to 0.87 mg As/kg/day as sodium arsenate in drinking water for 91 days had the same arsenic methylating activity as unexposed controls. Specific activities were highest in testis (1.45 U/mg) followed by kidney (0.70 U/mg), liver (0.40 U/mg), and lung (0.20 U/mg). None were affected by arsenic exposure.

An alternative biotransformation pathway (Figure 3-8) has recently been proposed for arsenic (Hayakawa et al. 2005) based on the nonenzymatic formation of glutathione complexes with arsenite resulting in the formation of arsenic triglutathione. The arsenic triglutathione is subsequently methylated by AS3MT to form monomethyl arsenic glutathione. At low glutathione levels (1 mM), the monomethyl arsenic glutathione is hydrolyzed to form MMA(III). At high glutathione levels (5 mM), the monomethyl arsenic glutathione is methylated to dimethylarsinic glutathione by AS3MT. Dimethylarsinic glutathione is quickly hydrolyzed to form DMA(III) (Hayakawa et al. 2005; Thomas et al. 2007). In the classical inorganic arsenic biotransformation pathway (Figure 3-7), MMA(V) is converted to the more toxic MMA(III); in contrast, in the alternative pathway, MMA(III) is converted to the less toxic MMA(V).

Figure 3-8. Alternative Inorganic Arsenic Biotransformation Pathway



ATG = arsenic triglutathione; DMAG = dimethylarsinic glutathione; GSH = glutathione; MADG = monomethyl arsenic glutathione; SAHC = S-adenosylhomocysteine; SAM = S-adenosylmethionine

Source: Hayakawa et al. 2005; Thomas et al. 2007

Since methylation tends to result in lower tissue retention of inorganic arsenic (Marafante and Vahter 1984, 1986; Marafante et al. 1985; Vahter and Marafante 1987), the methylation process is usually viewed as a detoxification mechanism. However, several studies showing an elevated toxicity of MMA(III) relative even to As(III) in cultured human liver cells (Petrick et al. 2000, 2001) have called this assumption into question. Because methylation is an enzymic process, an important issue is the dose of arsenic that saturates the methylation capacity of an organism, resulting in a possible increased level of the more toxic As(III) in tissues, or whether or not such a dose exists. Limited data from studies in humans suggest that methylation may begin to become limiting at doses of about 0.2–1 mg/day (0.003–0.015 mg/kg/day) (Buchet et al. 1981b; Marcus and Rispin 1988). However, these observations are relatively uncertain since they are based on data from only a few subjects, and the pattern of urinary excretion products in humans who ingested high (near lethal) oral doses or were exposed to elevated levels in the workplace is not much different from that in the general population (Lovell and Farmer 1985; Vahter 1986). Furthermore, the nutrient intakes reported by Engel and Receveur (1993) were sufficient to accommodate the body stores of methyl groups needed for arsenic biomethylation. At the highest arsenic level reported in the endemic area, the biomethylation process required only a few percent of the total daily methyl intake (Mushak and Crocetti 1995). Thus, the dose rate at which methylation capacity becomes saturated cannot be precisely defined with current data.

Organic Arsenicals. With the exception of arsenosugars, which may undergo extensive metabolism, organic arsenicals appear to undergo little metabolism. Humans who ingested a dose of MMA converted a small amount (about 13%) to DMA (Buchet et al. 1981a). Similarly, in mice and hamsters, DMA and MMA are primarily excreted unchanged in the urine (Hughes et al. 2005; Marafante et al. 1987b; Vahter et al. 1984). In mice, a small percentage of MMA is methylated to DMA and some is further methylated to trimethylarsine oxide (TMAO) (Hughes et al. 2005). In contrast, administration of MMA(III) to mice resulted in the excretion of mostly DMA(V) and smaller amounts of MMA(V), MMA(III), and DMA(III) (Hughes et al. 2005). As with MMA, only a small percentage (<10%) of the DMA is methylated to TMAO (Hughes et al. 2005; Marafante et al. 1987b; Yamauchi and Yamamura 1984; Yamauchi et al. 1988).

MMA and DMA are more extensively methylated in rats compared to other animal species. After 1 week of exposure to 100 mg As/kg/day as MMA in drinking water, rats excreted 50.6% of the total arsenic in urine as MMA, 19.0% as DMA, 6.9% as TMAO, and 0.4% as tetramethylarsonium (Yoshida et al. 1998). In contrast, mice exposed to a single dose of 40 mg As/kg as MMA excreted 89.6% of the dose as MMA, 6.2% as DMA, and 1.9% as TMAO (Hughes et al. 2005). Similarly, 24 hours after administration of a

single oral dose of 50 mg As/kg as MMA in hamsters, 26.9% was excreted in urine as MMA, 1.43% as DMA, and 0.07% as trimethylarsenic compound (Yamauchi et al. 1988). As with MMA, oral exposure of mice and hamsters to DMA results in most of the dose being excreted in the urine in the form of DMA (or DMA complex) (Marafante et al. 1987b); in rats, the levels of DMA and TMAO are about equal (Yoshida et al. 1998).

The available data suggest that the methylarsenates are not demethylated to inorganic arsenic either in humans (Buchet et al. 1981a; Marafante et al. 1987b) or in animals (rats and hamsters) (Stevens et al. 1977; Yamauchi and Yamamura 1984; Yoshida et al. 2001).

3.4.4 Elimination and Excretion

3.4.4.1 Inhalation Exposure

Inorganic Arsenicals. As noted previously (see Section 3.4.1.1), urinary excretion of arsenic appears to account for 30–60% of the inhaled dose (Holland et al. 1959; Pinto et al. 1976; Vahter et al. 1986). Since the deposition fraction usually ranges from about 30 to 60% for most respirable particles (EPA 1989b), this suggests that nearly all arsenic that is deposited in the lung is excreted in the urine. The time course of excretion in humans exposed by inhalation has not been thoroughly investigated, but urinary arsenic levels in workers in a smelter rose within hours after they came to work on Monday and then fell over the weekend (Vahter et al. 1986). This implies that excretion is fairly rapid, and this is supported by intratracheal studies in rats (Rhoads and Sanders 1985) and hamsters (Marafante and Vahter 1987), where whole-body clearance of administered arsenate or arsenite occurred with a half-time of 1 day or less. However, the study in rats (Rhoads and Sanders 1985) found that the clearance of arsenic trioxide was biphasic, with 95% cleared with a half-time of 29 minutes and the remaining arsenic cleared with a half-time of 75 days. For sodium arsenate and sodium arsenite, <0.1% of the dose was retained in the lung 3 days after exposure of hamsters; 1.3% of the arsenic trisulfide dose was retained after 3 days (Marafante and Vahter 1987). The Marafante and Vahter (1987) study suggested that lung clearance was influenced by compound solubility. The primary forms of arsenic found in the urine of inhalation-exposed humans are DMA and MMA, with inorganic arsenic comprising <25% of the total urinary arsenic (Apostoli et al. 1999).

Organic Arsenicals. No studies were located regarding the excretion of organic arsenicals by humans or animals after inhalation exposure. However, rats that were given a single intratracheal dose of DMA

excreted about 60% in the urine and about 8% in the feces within 24 hours (Stevens et al. 1977). This indicates that organic arsenicals are likely to be promptly excreted after inhalation exposure.

3.4.4.2 Oral Exposure

Inorganic Arsenicals. Direct measurements of arsenic excretion in humans who ingested known amounts of arsenite or arsenate indicate that very little is excreted in the feces (Bettley and O'Shea 1975), and that 45–85% is excreted in urine within 1–3 days (Apostoli et al. 1999; Buchet et al. 1981a; Crecelius 1977; Mappes 1977; Tam et al. 1979b). At low exposure levels, urinary arsenic levels generally increase linearly with increasing arsenic intake (Calderon et al. 1999). During lactation, a very small percent of ingested arsenic may also be excreted in the breast milk (Concha et al. 1998a). A similar pattern of urinary and fecal excretion is observed in hamsters (Marafante and Vahter 1987; Yamauchi and Yamamura 1985) and mice (Vahter and Norin 1980); this pattern is typically modeled as a biphasic process (e.g., Hughes et al. 2003). Generally, whole body clearance is fairly rapid, with half-times of 40–60 hours in humans (Buchet et al. 1981b; Mappes 1977). Clearance is even more rapid in mice and hamsters, with 90% removed in 2 days (Hughes et al. 2003; Marafante and Vahter 1987; Vahter 1981; Vahter and Norin 1980).

A study in pregnant women exposed to elevated levels of inorganic arsenic in drinking water found that most of the ingested arsenic was excreted in the urine as DMA (79–85%), with smaller amounts excreted as inorganic arsenic (8–16%) or MMA (5–6%) (Christian et al. 2006). Similarly, in mice, arsenate is primarily excreted in the urine as DMA, with lesser amounts of inorganic arsenic and MMA (Kenyon et al. 2005). Following a single oral dose of 10 µmol/kg sodium arsenate, 78.4% was excreted as DMA, 20.2% as inorganic arsenic, and 1.45% as MMA; at a 10-fold higher dose, the ratio of DMA to inorganic arsenic decreased (57.7% DMA, 39.8% inorganic arsenic, and 2.59% MMA).

Arsenic is also excreted in the bile via the formation of two arsenic-glutathione complexes (arsenic triglutathione and methylarsenic diglutathione) (Kala et al. 2000). In rats administered 5.0 mg/kg sodium arsenite, equal amounts of arsenic triglutathione and methylarsenic diglutathione were found in the bile 18–20 minutes after exposure. At a lower arsenic dose (0.5 mg/kg), only methylarsenic diglutathione was found. As discussed in Section 3.4.4.4, biliary excretion of arsenic has also been detected in mice, hamsters, guinea pigs, and rabbits following parenteral exposure (Csanaky and Gregus 2002).

Organic Arsenicals. Studies in humans indicate that ingested MMA and DMA are excreted mainly in the urine (75–85%), and this occurs mostly within 1 day (Buchet et al. 1981a; Marafante et al. 1987b). This is supported by studies in rats, mice, and hamsters, although in animals, excretion is more evenly distributed between urine and feces (Hughes et al. 2005; Marafante et al. 1987b; Stevens et al. 1977; Yamauchi and Yamamura 1984; Yamauchi et al. 1988). In mice administered 40 mg As/kg as DMA, 56.4% was excreted in the urine as DMA, 7.7% as a DMA complex, and 3.5% as TMAO during a 48-hour period after dosing; in the feces, 24.3% was DMA and 4.9% as DMA complex (Marafante et al. 1987b). In hamsters, 38.7% was DMA, 11.2% as DMA complex, and 6.4% as TMAO in the urine; in the feces, 37.3% as DMA and 4.9% as DMA complex. As with DMA, most MMA is excreted in the urine and feces as parent compound. In the urine of mice administered 0.4 mg As/kg as MMA, 98.2% of the urinary arsenicals was in the form of MMA(V) and 1.8% as MMA(III) (Hughes et al. 2005); at a 10-fold higher dose, 89.6% was excreted as MMA(V), 1.2% as MMA(III), 6.2% as DMA(V), 1.1% as DMA(III), and 1.9% as TMAO. As discussed previously, exposure of rats to MMA or DMA results in the excretion of a higher percentage of metabolites. After 1 week exposure to MMA, 50.6% of the dose was excreted as MMA, 19.0% as DMA, and 6.9% of TMAO (Yoshida et al. 1998). A 1-week exposure to DMA, 44.9% was excreted as DMA in the urine and 40.0% as TMAO (Yoshida et al. 1998). A longer-term exposure to DMA (>7 months) resulted in a higher percentage of the amount of parent compound excreted; 56–65% as DMA and 23–35% as TMAO (Li et al. 1998; Wanibuchi et al. 1996; Yoshida et al. 1998).

In mice and hamsters, DMA and MMA are rapidly cleared from the body (Hughes et al. 2005; Marafante et al. 1987b; Vahter et al. 1984). In mice, 85% of the initial oral dose of DMA was eliminated from the body with a half-life of 2.5 hours (Vahter et al. 1984). In contrast to the mouse data, 45% on the initial DMA dose to rats was eliminated with a half-time of 13 hours and the remaining 55% had an elimination half-time of 50 days (Vahter et al. 1984).

3.4.4.3 Dermal Exposure

Inorganic Arsenicals. No studies were located regarding excretion of inorganic arsenicals in humans or animals following dermal exposure. In rats, arsenic absorbed through the tail was excreted approximately equally in urine and feces, similar to the excretion pattern following oral exposure (Dutkiewicz 1977).

Organic Arsenicals. No studies were located regarding excretion of organic arsenicals in humans or animals following dermal exposure.

3.4.4.4 Other Routes of Exposure

Inorganic Arsenicals. Excretion of arsenate and arsenite following parenteral exposure of animals is similar to that seen following oral exposure. In rabbits and mice, urinary excretion within 8 hours usually accounts for about 50–80% of the dose (Maehashi and Murata 1986; Maiorino and Aposhian 1985; Vahter and Marafante 1983). Somewhat lower levels (30–40%) are excreted in the urine of marmoset monkeys (Vahter and Marafante 1985; Vahter et al. 1982), probably because of the absence of methylation in this species. Whole-body clearance studies in mice indicate that arsenate is over 65% removed within 24 hours, while arsenite is about 86% removed at 24 hours (Lindgren et al. 1982). A relatively small proportion of an injected dose of arsenic V (10% for rats, 4% for mice, and <2% for hamsters, guinea pigs, and rabbits) was found to be excreted into the bile within the first 2 hours postinjection (Csanaky and Gregus 2002). Following arsenic III injection, a much greater percentage (92% for guinea pigs and 75% for rats) of the arsenic was found in the bile in the first 2 hours after administration (Csanaky and Gregus 2002). Similarly, approximately 40% of an intravenous dose of sodium arsenite was excreted into the bile of rats, most of it occurring during the first hour after exposure (Kala et al. 2000). Kala et al. (2000) determined that the biliary transport of arsenic was dependent on the formation of arsenic-glutathione complexes, which were transported out of hepatocytes by multidrug resistance associated protein 2 (MRP2/cMOAT); most of the arsenic in bile was in the form of arsenic triglutathione or methylarsenic diglutathione.

3.4.5 Physiologically Based Pharmacokinetic (PBPK)/Pharmacodynamic (PD) Models

Physiologically based pharmacokinetic (PBPK) models use mathematical descriptions of the uptake and disposition of chemical substances to quantitatively describe the relationships among critical biological processes (Krishnan et al. 1994). PBPK models are also called biologically based tissue dosimetry models. PBPK models are increasingly used in risk assessments, primarily to predict the concentration of potentially toxic moieties of a chemical that will be delivered to any given target tissue following various combinations of route, dose level, and test species (Clewell and Andersen 1985). Physiologically based pharmacodynamic (PBPD) models use mathematical descriptions of the dose-response function to quantitatively describe the relationship between target tissue dose and toxic end points.

PBPK/PD models refine our understanding of complex quantitative dose behaviors by helping to delineate and characterize the relationships between: (1) the external/exposure concentration and target tissue dose of the toxic moiety, and (2) the target tissue dose and observed responses (Andersen and

Krishnan 1994; Andersen et al. 1987). These models are biologically and mechanistically based and can be used to extrapolate the pharmacokinetic behavior of chemical substances from high to low dose, from route to route, between species, and between subpopulations within a species. The biological basis of PBPK models results in more meaningful extrapolations than those generated with the more conventional use of uncertainty factors.

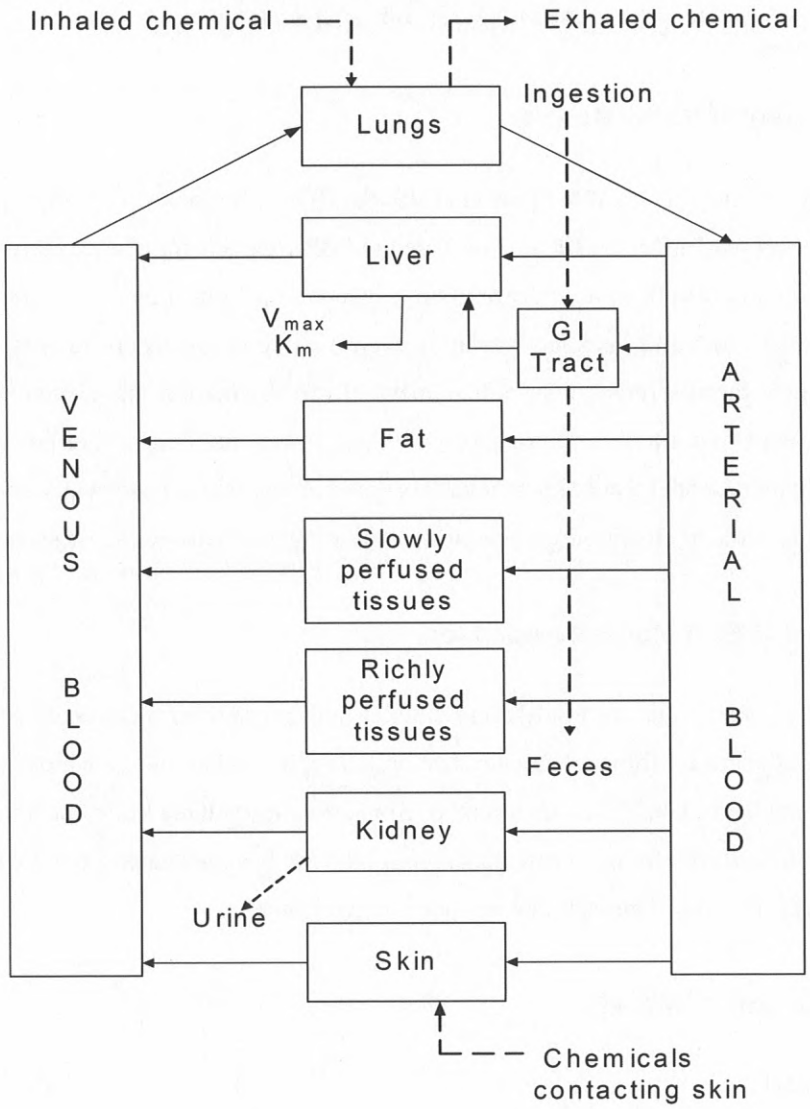
The PBPK model for a chemical substance is developed in four interconnected steps: (1) model representation, (2) model parameterization, (3) model simulation, and (4) model validation (Krishnan and Andersen 1994). In the early 1990s, validated PBPK models were developed for a number of toxicologically important chemical substances, both volatile and nonvolatile (Krishnan and Andersen 1994; Leung 1993). PBPK models for a particular substance require estimates of the chemical substance-specific physicochemical parameters, and species-specific physiological and biological parameters. The numerical estimates of these model parameters are incorporated within a set of differential and algebraic equations that describe the pharmacokinetic processes. Solving these differential and algebraic equations provides the predictions of tissue dose. Computers then provide process simulations based on these solutions.

The structure and mathematical expressions used in PBPK models significantly simplify the true complexities of biological systems. If the uptake and disposition of the chemical substance(s) are adequately described, however, this simplification is desirable because data are often unavailable for many biological processes. A simplified scheme reduces the magnitude of cumulative uncertainty. The adequacy of the model is, therefore, of great importance, and model validation is essential to the use of PBPK models in risk assessment.

PBPK models improve the pharmacokinetic extrapolations used in risk assessments that identify the maximal (i.e., the safe) levels for human exposure to chemical substances (Andersen and Krishnan 1994). PBPK models provide a scientifically sound means to predict the target tissue dose of chemicals in humans who are exposed to environmental levels (for example, levels that might occur at hazardous waste sites) based on the results of studies where doses were higher or were administered in different species. Figure 3-9 shows a conceptualized representation of a PBPK model.

If PBPK models for arsenic exist, the overall results and individual models are discussed in this section in terms of their use in risk assessment, tissue dosimetry, and dose, route, and species extrapolations.

Figure 3-9. Conceptual Representation of a Physiologically Based Pharmacokinetic (PBPK) Model for a Hypothetical Chemical Substance



Note: This is a conceptual representation of a physiologically based pharmacokinetic (PBPK) model for a hypothetical chemical substance. The chemical substance is shown to be absorbed via the skin, by inhalation, or by ingestion, metabolized in the liver, and excreted in the urine or by exhalation.

Source: adapted from Krishnan and Andersen 1994

Several PBPK models have been developed for inorganic arsenic; the Mann, Yu, and Menzel models are discussed below. A joint research effort between the Chemical Industry Institute of Toxicology (CIIT) Centers for Health Research, EPA, ENVIRON International, and the Electric Power Research Institute (EPRI) is underway to develop a biologically based dose response model of carcinogenicity. Part of this effort involves refining the existing PBPK models (Clewell et al. 2007).

3.4.5.1 Summary of PBPK Models

The Mann model (Gentry et al. 2004; Mann et al. 1996a, 1996b), Yu model (Yu 1998a, 1998b; Yu 1999a, 1999b), and Menzel model (Menzel et al. 1994) are the PBPK models for arsenic currently available. The Mann model simulates the absorption, distribution, metabolism, elimination, and excretion of As(+3), As(+5), MMA, and DMA after oral and inhalation exposure in mice, hamsters, rabbits, and humans. The Yu model simulates the absorption, distribution, metabolism, elimination, and excretion of As(+3), As(+5), MMA, and DMA after oral exposure to inorganic arsenic in mice, rats, or humans. The Menzel model is a preliminary model that predicts internal organ burden of arsenic during specific oral exposures, simulating the metabolism, distribution to organs and binding to organs in mice, rats, and humans.

3.4.5.2 Arsenic PBPK Model Comparison

The Mann model is a well-derived model, consisting of multiple compartments and metabolic processes, and modeling four chemical forms of arsenic (two organic and two inorganic), which has been validated using experimental data. The Yu model has more compartments than the Mann model, also models metabolism and fate of four forms of arsenic, and has likewise been validated using experimental data. The Menzel model is still preliminary and has not been validated.

3.4.5.3 Discussion of Models

The Mann Model

Risk assessment. The Mann model was not used for risk assessment.

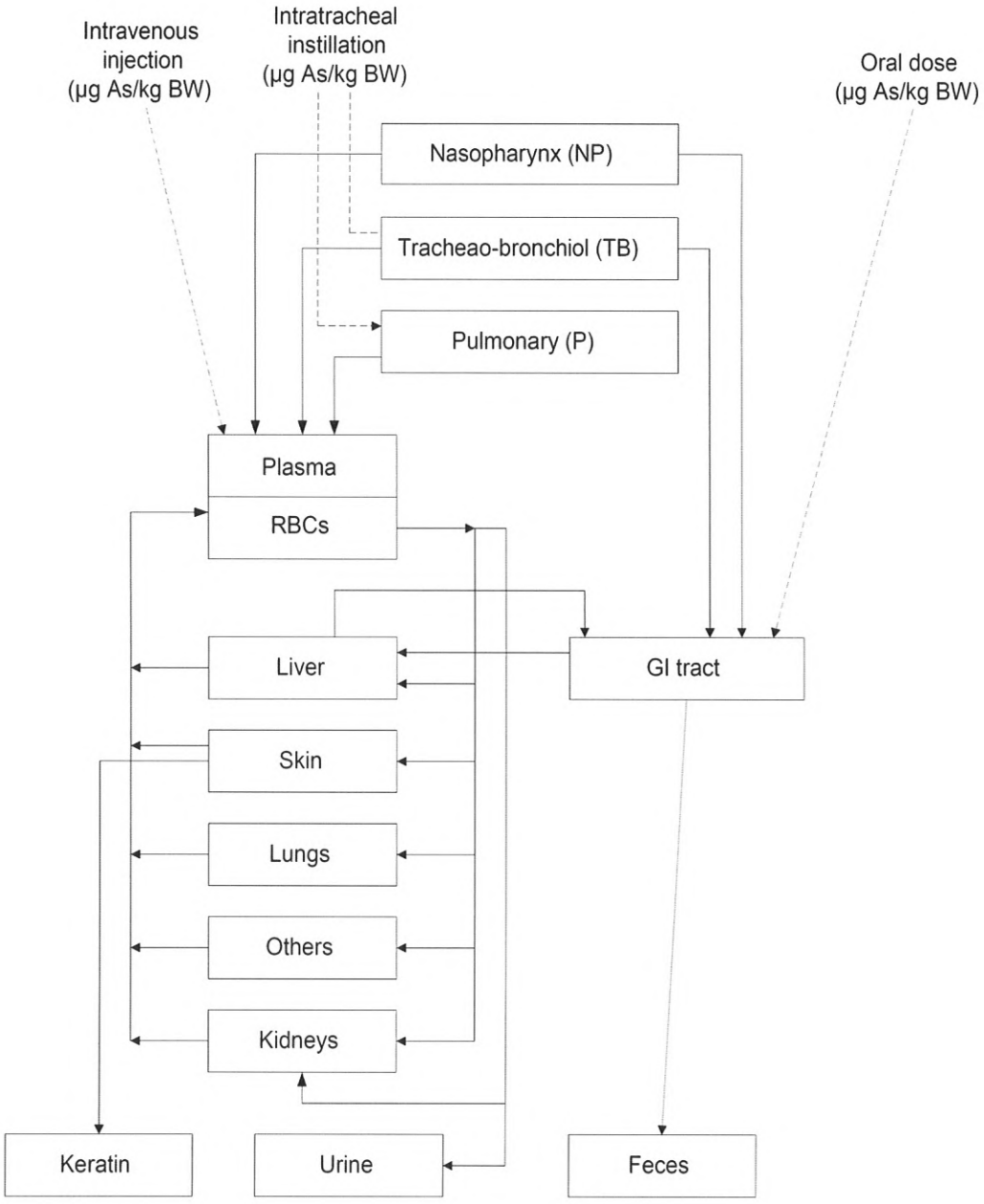
Description of the model. The Mann model was initially developed to simulate oral, intratracheal, and intravenous exposure to arsenic in rabbits and hamsters (Mann et al. 1996a). In a companion paper, the model was expanded to include inhalation exposure and extrapolated and applied to humans (Mann et al. 1996b). A subsequent paper further expanded the model to include mice (Gentry et al. 2004).

The model consists of six tissue compartments: blood, liver, kidneys, lungs, skin, and other tissues. The blood compartment is divided into plasma and red blood cell subcompartments, considered to be at equilibrium. Three routes of exposure are considered in the model. Oral exposure is considered to enter the liver from the gastrointestinal tract via first-order kinetics. Intratracheal exposure results in deposition into the pulmonary and tracheo-bronchial regions of the respiratory tract. Uptake into blood from the pulmonary region is considered to be via first order kinetics into plasma, uptake from the tracheo-bronchial region is by both transfer into plasma and transport into the gastrointestinal tract. Intravenous injection results in a single bolus dose into the plasma compartment.

Metabolism in the model consists of oxidation/reduction and two methylation reactions. The oxidation/reduction of inorganic arsenic was modeled as a first order process in the plasma, with reduction also included in the kidneys. Methylation of As(+3) was modeled as a two-step process occurring in the liver according to Michaelis-Menton kinetics.

Most physiological parameters were derived by scaling to body weight. In cases where parameters were not available (absorption rates, tissue affinity, biotransformation), estimates were obtained by fitting. This was done by duplicating the initial conditions of published experiments in the model, varying the unknown parameters and comparing the results of the simulation to the reported results. Tissue affinity constants were estimated using reported arsenic levels in tissues at various times after exposure. Metabolic rate constants and absorption rate constants were estimated using data for excretion of arsenic metabolites in urine and feces. Figure 3-10 shows the animal model and Tables 3-11, 3-12, 3-13, and 3-14 provide the parameters used in the animal model. The human model is similar to the animal models with adjustments for body weight and absorption and metabolic rates. A naso-pharynx compartment is included in the human model, which was not present in the animal models. Penetration and deposition in the respiratory tract are based on the log-normal particle size distribution of the aerosol. Metabolic and absorption rate constants were fitted using experimental data on urinary excretion of arsenic following a single oral dose of As(+3) (Buchet et al. 1981a) or As(+5) (Tam et al. 1979b) in volunteers. The lung absorption rate constant was obtained by fitting the total urinary excretion of arsenic as predicted with the model to experimental data obtained from occupational exposure to arsenic trioxide (Offergelt et al. 1992). Figure 3-11 shows the human model, and Tables 3-15 and 3-16 provide the data and constants used in the human model.

Figure 3-10. Parameters Used in the Mann PBPK Model for Animals



Source: Mann et al. 1996b

Table 3-11. Parameters Used in the Mann PBPK Model for Animals

Physiological parameter	Rabbit (body weight=3.5 kg)	Hamster (body weight=0.100 kg)
Blood volume (mL)	253	7.0
Organ weight (g)		
Liver	121	4.8
Kidneys	25	1.2
Lungs	31	1.0
Skin	420	17.1
Organ volume (mL)		
Others	2,386	62.0
Lumen volume (mL)		
Stomach	15	0.5
Small intestine	20	0.6
Blood flow (mL/minute)		
Cardiac output	556	38.3
Liver, hepatic	25	1.2
Liver, splanchic	98	6.0
Kidneys	100	7.0
Lungs	13	0.7
Skin	38	2.6
Others	282	20.8
Clearance (mL/minute)		
Glomerular Filtration Rate	10	0.6
Small intestine length (cm)	180	56.0
Total capillary surface area (cm^2)	93,835	2,681.0

PBPK = physiologically based pharmacokinetic

Source: Mann et al. 1996a

Table 3-12. Tissue Affinity Constants (K_{ij}) Obtained for the Mann PBPK Model for Animals by Fitting for Rabbits and Hamsters

	K_{ij} (unitless)			
Tissue (*i*)	As(V)	As(III)	MMA	DMA
Liver	1	200	10	1
Kidneys	40	20	100	5
Lungs	1	1	1	20
Skin	1	60	50	1
Others	10	40	1	1

DMA = dimethylarsinic acid; MMA = monomethylarsonic acid; PBPK = physiologically based pharmacokinetic

Source: Mann et al. 1996a

Table 3-13. Metabolic Rate Constants for the Mann PBPK Model for Animals Obtained by Fitting for Rabbits and Hamsters

Oxidation/reduction	First order	Rabbit	Hamster
Reduction	(1/hour)	3,000.00	100.00
Oxidation	(1/hour)	6,000.00	400.00
Kidney reduction	(1/hour)	30.00	1.00
Methylation	Michaelis–Menten		
1st step	$K_{M_{MMA}}$ (µmol/mL)	0.05	0.12
	$V_{MAX_{MMA}}$ (µmol/mL-hour)	4.00	0.12
2nd step	$K_{M_{DMA}}$ (µmol/mL)	0.90	0.08
	$V_{MAX_{DMA}}$ (µmol/mL-hour)	1.50	0.12

DMA = dimethylarsinic acid; MMA = monomethylarsonic acid; PBPK = physiologically based pharmacokinetic

Source: Mann et al. 1996a

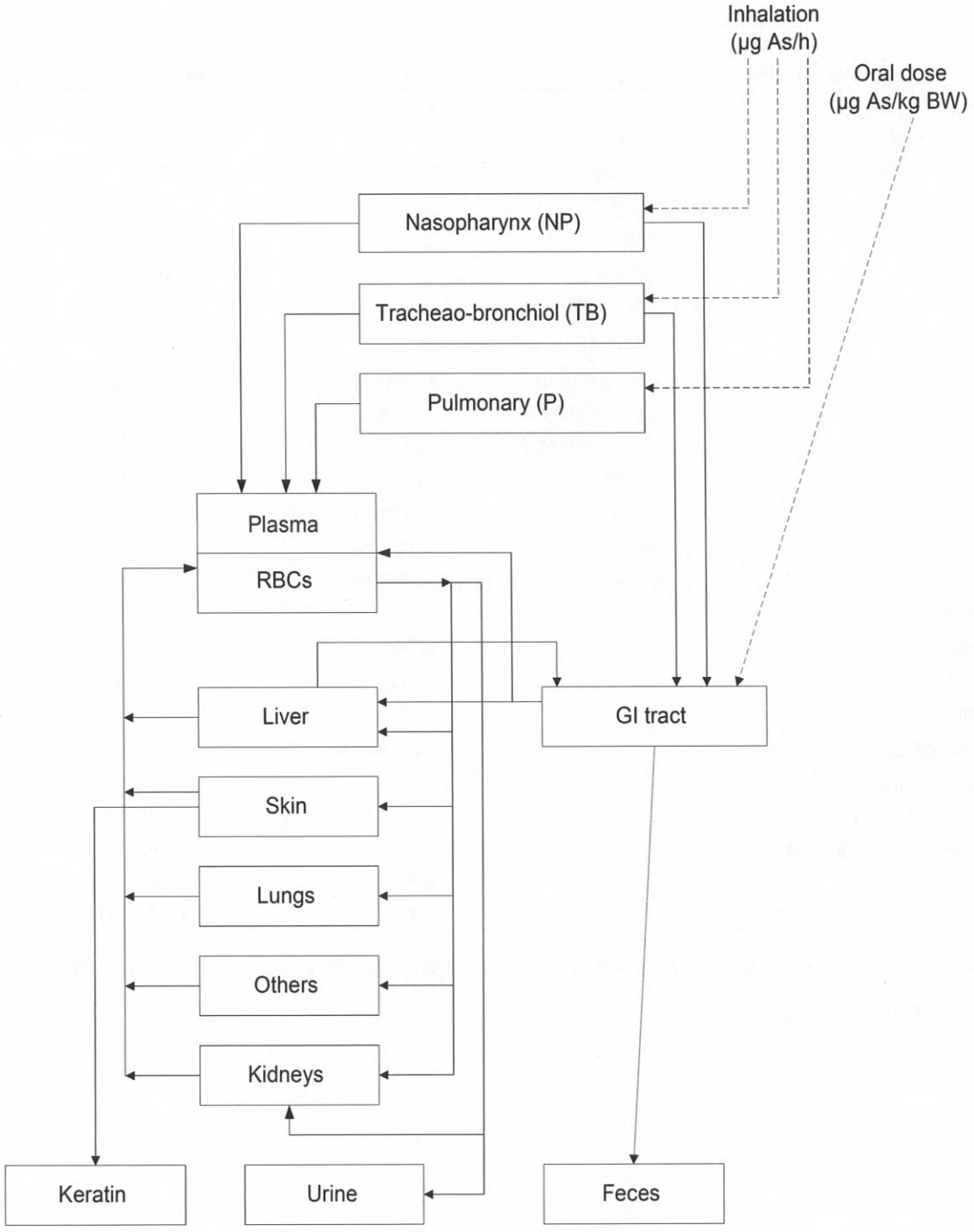
Table 3-14. Fitted Gastrointestinal Tract and Lung Absorption Half-time for the Hamster for the Mann PBPK Model

	Absorption, half-time (hour)	
Arsenic compound	Gastrointestinal tract	Lung
As(V)		
$Na_3(AsO_4)$	0.08	12
$Pb_3(AsO_4)$	0.39	690
As_2O_5	0.28	—
As(III)		
$NaAsO_2$	0.08	12
As_2S_3	0.48	12
As_2O_3	0.02	—
DMA	0.09	—

DMA = dimethylarsinic acid; PBPK = physiologically based pharmacokinetic

Source: Mann et al. 1996a

Figure 3-11. Parameters Used in the Mann PBPK Model for Humans



Source: Mann et al. 1996b

Table 3-15. Physiological Data Used in the Mann PBPK Model for Humans

Physiological parameter	Organ	Units	Human (body weight=70 kg)
Blood volume		mL	5,222
Organ weight	Liver	g	1,856
	Kidneys	g	314
	Lungs	g	584
	Skin	g	6,225
	Others	g	55,277
Lumen volume	Stomach	mL	274
	Small intestine	mL	393
Blood flow	Cardiac output	L/minute	5.29
	Liver, hepatic	L/minute	0.32
	Liver, splanchic	L/minute	1.02
	Kidneys	L/minute	0.95
	Lungs	L/minute	0.16
	Skin	L/minute	0.35
	Others	L/minute	2.49
Creatinine			
Male		g/day	1.7
Female		g/day	1.0
Clearance			
Glomerular filtration rate		mL/minute	156
Small intestine length		cm	481
Nasopharynx area		cm^2	177
Tracheobronchial area		cm^2	5,036
Pulmonary area		cm^2	712,471
Total capillary surface area		cm^2	$1,877x10^6$

DMA = dimethylarsinic acid; MMA = monomethylarsonic acid; PBPK = physiologically based pharmacokinetic

Source: Mann et al. 1996b

Table 3-16. Tissue Affinity Constants (K_{ij}) Obtained by Fitting the Mann PBPK Animal Model for Use with Humans

	K_{ij} (unitless)			
Tissue (i)	As(V)	As(III)	MMA	DMA
Liver	1	200	10	1
Kidneys	40	20	100	5
Lungs	1	1	1	20
Skin	1	60	50	1
Red blood cells	0.2	1.5	0.2	0.2
Others	10	40	1	1

DMA = dimethylarsinic acid; MMA = monomethylarsonic acid; PBPK = physiologically based pharmacokinetic

Source: Mann et al. 1996b

Validation of the model. The model was generally successful in describing the disposition of an intravenous dose of sodium arsenate in rabbits over a 24-hour period (Marafante et al. 1985). Discrepancies included a 6–7-fold overestimation of levels in skin at 24 hours and underestimation of As(+5) in plasma in the hour following injection. A statistical assessment of how well the model fit the empirical data was not presented. In hamsters, the model was also generally predictive of oral and intratracheal exposures (Marafante and Vahter 1987). Generally, predictions were better for the exposures to As(+5) than for those to As(+3).

The human model was validated using data from studies of repeated oral intake of sodium arsenite in volunteers (Buchet et al. 1981b), occupational exposure to arsenic trioxide and elemental arsenic (Vahter et al. 1986), and community exposure to As(+5) via drinking water (Harrington et al. 1978; Valentine et al. 1979). Simulations were generally in good agreement with the experimental data.

The predictions of tissue distribution, metabolism, and elimination of arsenic compounds from the mouse model were compared with experimental data, and showed generally good agreement. The model tended to overpredict the concentration of organic arsenicals in the lungs, and to a lesser extent in the kidneys and liver, while for inorganic arsenic, the model overpredicted the levels of arsenic (V) present in the urine of acutely-exposed mice.

Target tissues. Levels in skin were not well predicted by this model in animals. Results for the lung were not presented, except for the mouse model, which tended to overpredict lung levels. The human model was only used to predict urinary metabolites.

Species extrapolation. Species extrapolation was not attempted in this model. However, tissue affinities derived for the rabbit and hamster models were used in the human model.

Interroute extrapolation. Interroute extrapolation was not attempted in this model.

The Menzel Model

Risk assessment. The Menzel model was not used for risk assessment.

Description of the model. The Menzel model was developed to simulate oral exposure to arsenic from drinking water and food. Inhalation of arsenic in the particulate phase or as arsine gas is not considered. The chemical species in drinking water is assumed to be As(+5).

The model consists of two sets of compartments: those in which the pools of arsenic are not influenced by blood perfusion, and those in which blood perfusion does determine arsenic burden. The former set of compartments includes the gut, feces, hair, bladder, and urine. The latter set of compartments included lung, liver, fat, skin, kidney, and other tissues. Oral exposure is considered to enter the liver from the gastrointestinal tract.

The model followed that of Andersen and coworkers (Andersen et al. 1987; Ramsey and Andersen 1984). Data from mice were used to test predictions of absorption. Excretion is considered to be rapid and complete into the urine, with no reabsorption from the kidney. Fecal arsenic content accounts for unabsorbed arsenic excreted in the bile, and complex arsenic species from food. Metabolism includes reduction by glutathione and methylation. Arsenic accumulation in the skin, hair and nails was included by assuming that arsenic binds irreversibly to protein sulfide groups in hair and nails.

Validation of the model. The model was preliminary and has not been validated.

Target tissues. Target tissues have not yet been modeled.

Species extrapolation. Species extrapolation was not attempted in this model.

Interroute extrapolation. Interroute extrapolation was not attempted in this model.

The Yu Model

Risk assessment. The Yu model was not used for risk assessment.

Description of the model. The Yu model was developed to simulate oral exposure to arsenic in mice and rats (Yu 1998a, 1998b), and was later adapted for oral exposures in humans (Yu 1999a, 1999b). Inhalation of arsenic in the particulate phase or as arsine gas is not considered. As(+3), As(+5), MMA, and DMA were all considered in the model, though the movements of MMA and DMA were not considered.

The model consists of eight tissue compartments: intestine, skin, muscle, fat, kidney, liver, lung, and vessel-rich group (VRG, e.g., brain); in the human model, the VRG and kidney compartments were combined. Only oral exposure was considered. Absorption is based on absorption to the stomach, which then passes the arsenic to the gastrointestinal tract. From the gastrointestinal tract, arsenic is either transferred to the blood or excreted in the feces.

The physiological parameters for the model were obtained from published values in the literature. Tissue/blood partition coefficients were based on the postmortem blood and tissue concentrations from a fatal human poisoning case study (Saady et al. 1989). Tissue volumes and blood flow rates were based on published values from a number of sources (EPA 1988e; Reitz et al. 1990). Absorption and excretion rate constants were based on experimental observations of blood concentrations and urinary and fecal excretion following oral administration of inorganic arsenic (Odanaka et al. 1980; Pomroy et al. 1980). Metabolic rate constants for the methylation and dimethylation of inorganic arsenic were also based on experimental observations (Buchet et al. 1981a; Crecelius 1977). Figure 3-12 shows the model and Table 3-17 provides the parameters used for each species.

Validation of the model. The model was generally successful at predicting the urinary excretion 48 hours after administration of 5 mg/kg inorganic arsenic in both rats and mice. After 48 hours, the observed/predicted ratios associated with excreted doses ranged from 0.78 to 1.11 for the mouse and from 0.85 to 0.93 for the rat. However, the model overpredicted the amount of inorganic arsenic found in the feces of mice at 24 and 48 hours, and overpredicted the amount of DMA formed by exposed mice at 48 hours. In rats, the model overestimated the urinary and fecal excretion of inorganic arsenic at 24 hours postexposure, though at 48 hours, measured values all fell within the predicted ranges. The human model was also generally successful at predicting the urinary excretion of arsenic compounds following oral exposure, based on results of controlled human exposure studies (Buchet et al. 1981a; Vahter 1983). In general, however, the model underpredicts excretion at early time points and overpredicts at later time points, with 24 hours being the time at which its predictive capabilities agreed most strongly with available data.

The ability of the model to predict tissue burdens was not compared to actual data for any species.

Figure 3-12. Parameters Used in the Yu PBPK Model for Animals

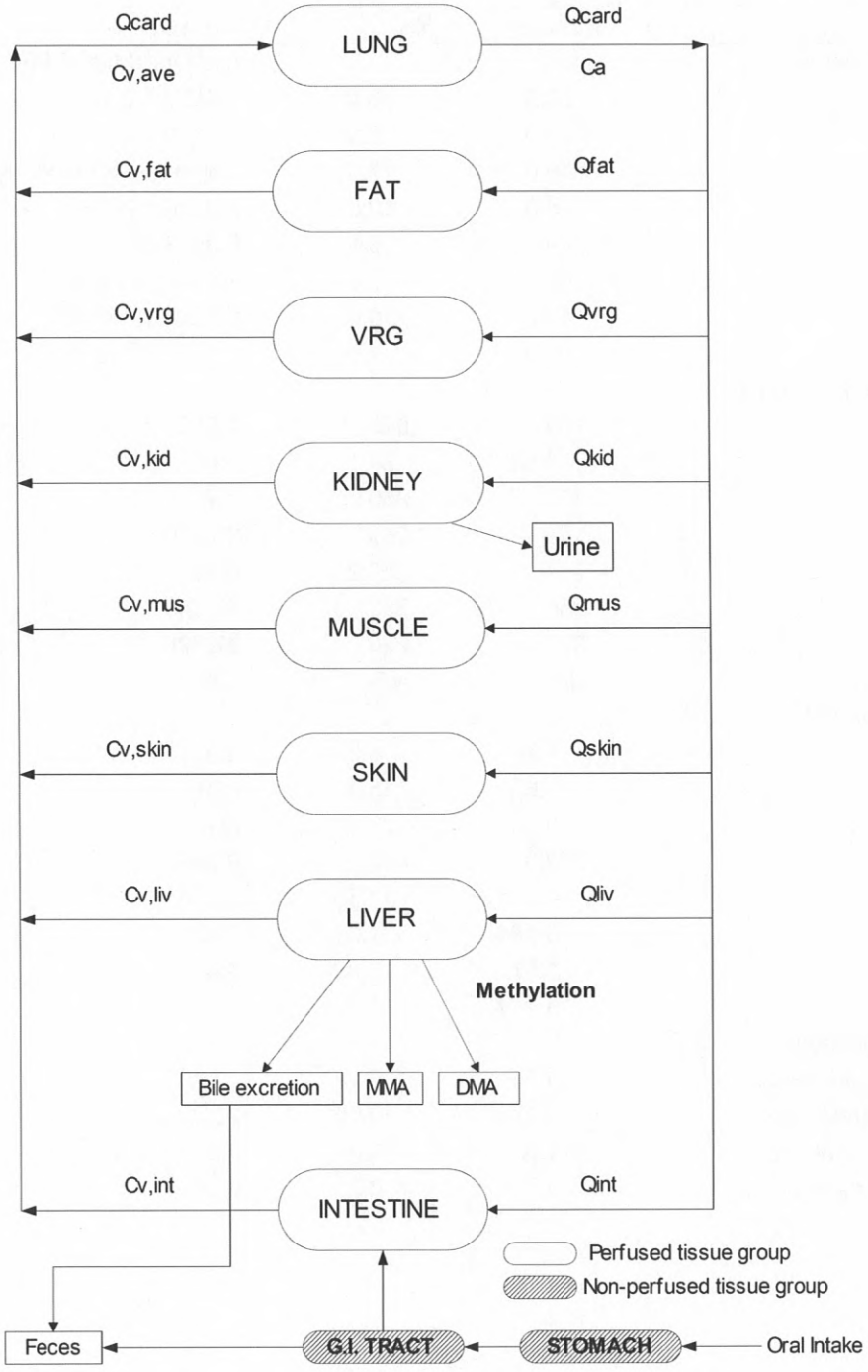


Table 3-17. Parameters Used in the Yu PBPK Model

	Mouse	Rat	Human
Partition coefficients			(As^{III}/As^{V}/MMA/DMA)
Intestine	6.0	6.0	2.8/2.8/1.2/1.4
Skin	5.0	5.0	2.5/2.5/1.25/1.25
VRG	6.0	6.0	Combined with kidney
Muscle	5.0	10.0	2.6/2.6/1.8/2.8
Fat	—	0.5	0.3/0.3/0.3/0.3
Kidney	8.5	7.5	4.15/4.15/1.8/2.075
Liver	10.0	10.0	5.5/5.3/2.35/2.65
Lung	4.0	4.0	4.15/4.15/1.8/2.075
Blood flow rate (mL/hour)			
Intestine	100	528	1,810
Skin	7.68	37.8	130
VRG	157	960	N/A
Muscle	153	1,260	25,850
Fat	—	253.2	6,467
Kidney	255	255	45,240
Liver	255	1,260	32,320
Lung	N/R	N/R	129,000
Tissue volume (mL)			
Intestine	1.94	6.9	558
Skin	1.83	15.4	606
VRG	0.81	23.0	N/A
Muscle	19.9	162	6,989
Fat	—	14.5	2,328
Kidney	0.484	1.63	248
Liver	1.67	5.82	422
Lung	0.124	1.0	400
Metabolism constants			
$Vmax_{(MMA)}$ (µmol/hour)	0.45	0.15	11.25
$Vmax_{(DMA)}$ (µmol/hour)	0.375	0.06	22.25
$Km_{(MMA)}$ (µmol/hour)	1.0	0.2	0.01
$Km_{(DMA)}$ (µmol/hour)	0.2	0.2	0.01

Table 3-17. Parameters Used in the Yu PBPK Model

	Mouse	Rat	Human
First-order rate constants			(As^{III}/As^{V}/MMA/DMA)
K_{SI} ($hour^{-1}$)	0.3	0.3	-/1.2/-/-
K_{AI} ($hour^{-1}$)	1.5	3.6	-/1.2/-/-
K_{fecal} ($hour^{-1}$)	0.33	0.048	-/0.0012/0.0/0.0
$K_{urinary}$ ($hour^{-1}$)	1.32	0.9	0.05/0.075/0.07/0.04
$K_{biliary}$ ($hour^{-1}$)	0.33	0.3	-/0.018/-/-

DMA = dimethylarsinic acid; MMA = monomethylarsonic acid; N/A = not applicable; N/R = not reported

Source: Yu 1998a, 1998b, 1999a, 1999b

Target tissues. Model predictions of tissue burdens were not compared to actual data. The model accurately predicted, with a few exceptions, the urinary and fecal excretion of inorganic arsenic and its metabolites in rats, mice, and humans.

Species extrapolation. Species extrapolation beyond rats and mice was not attempted using this model. The human model has not been compared to, or linked with, either of the rodent models.

Interroute extrapolation. Interroute extrapolation was not attempted using this model.

3.5 MECHANISMS OF ACTION

3.5.1 Pharmacokinetic Mechanisms

Arsenic absorption depends on its chemical form. In humans, As(+3), As(+5), MMA, and DMA are orally absorbed ≥75%. Arsenic is also easily absorbed via inhalation. Absorption appears to be by passive diffusion in humans and mice, although there is evidence (Gonzalez et al. 1995) for a saturable carrier-mediated cellular transport process for arsenate in rats (for review, see Rosen 2002). Dermal absorption appears to be much less than by the oral or inhalation routes. Bioavailability of arsenic from soil appears to be lower via the oral route than it is for sodium salts of arsenic. Arsenic in soil may form water insoluble compounds (e.g., sulfides), which are poorly absorbed.

Arsenic and its metabolites distribute to all organs in the body; preferential distribution has not been observed in human tissues at autopsy or in experiments with animal species other than rat (in which arsenic is concentrated in red blood cells). Since the liver is a major site for the methylation of inorganic arsenic, a "first-pass" effect is possible after gastrointestinal absorption; however, this has not been investigated in animal models.

Arsenic and its metabolites are largely excreted via the renal route. This excretion mechanism is not likely to be saturated within the dose range expected from human exposure. Excretion can also occur via feces after oral exposure; a minor excretion pathway is nails and hair. The methylation of inorganic arsenic is the major metabolism pathway. The proportion of metabolites recovered in urine (As(+3), As(+5), MMA, DMA) are roughly consistent in humans regardless of the exposure scenario. However, interindividual variation is great enough that it cannot be determined if capacity limitation may occur in some individuals.

The manifestation of arsenic toxicity depends on dose and duration of exposure. Single oral doses in the range of 2 mg As/kg and higher have caused death in humans. Doses as low as 0.05 mg As/kg/day over longer periods (weeks to months) have caused gastrointestinal, hematological, hepatic, dermal, and neurological effects. These effects appear to be a result of direct cytotoxicity. Long-term exposure (years) to drinking water at levels as low as 0.001 mg As/kg/day have been associated with skin diseases and skin, bladder, kidney, and liver cancer. Long-term inhalation exposure to arsenic has also been associated with lung cancer at air levels as low as 0.05–0.07 mg/m^3. It is not clear at this time why long-term toxicity is different between the oral and inhalation routes, given that arsenic is easily absorbed into the systemic circulation by both routes.

Studies in mice and rats have shown that arsenic compounds induce metallothionein, a metal-binding protein thought to detoxify cadmium and other heavy metals, *in vivo* (Albores et al. 1992; Hochadel and Waalkes 1997; Kreppel et al. 1993; Maitani et al. 1987a). The potency of arsenic compounds in inducing metallothionein parallels their toxicity (i.e., As(+3) > As(+5) > MMA > DMA). For cadmium, it is thought that metallothionein binds the metal, making it biologically inactive. For arsenic, however, only a small percentage of the administered arsenic is actually bound to metallothionein (Albores et al. 1992; Kreppel et al. 1994; Maitani et al. 1987a). *In vitro* studies have shown that affinity of arsenic for metallothionein is much lower than that of cadmium or zinc (Waalkes et al. 1984). It has been proposed that metallothionein might protect against arsenic toxicity by acting as an antioxidant against oxidative injury produced by arsenic (NRC 1999).

3.5.2 Mechanisms of Toxicity

Mechanisms of arsenic-induced toxicity and carcinogenicity have not been clearly identified. However, recent efforts to elucidate mechanisms of arsenic toxicity and carcinogenicity have resulted in numerous *in vitro* and *in vivo* reports. Whereas these mechanistic studies typically employed relatively high arsenic exposure levels, some of the most recent studies were performed using more environmentally-relevant exposure levels. Due to the extremely large amount of mechanistic data for arsenic, it is not feasible to include all pertinent primary studies that address issues concerning proposed mechanisms of arsenic toxicity and carcinogenicity. Therefore, the following discussion of mechanisms of arsenic toxicity represents a summary of information from several recent review articles (Chen et al. 2004, 2005; Florea et al. 2005; Hughes 2002; Kitchin 2001; Lantz and Hays 2006; Navas-Acien et al. 2005; Rossman 2003; Roy and Saha 2002; Thomas et al. 2007; Vahter 2002).

It is becoming increasingly evident that the toxicity and carcinogenicity of arsenic is likely to be closely associated with metabolic processes. Absorbed pentavalent arsenic (AsV) is rapidly reduced to trivalent arsenic (AsIII) at least partially in the blood. Much of the formed AsIII is distributed to tissues and taken up by cells (particularly hepatocytes). Many cell types appear to accumulate AsIII more rapidly than AsV. Because AsIII (as arsenite) is known to be more highly toxic than AsV (as arsenate), the reduction step may be considered bioactivation rather than detoxification. Glutathione appears to play a role in the reduction of AsV to AsIII, which is required prior to methylation. Methylation of arsenic ultimately forms relatively less toxic MMA and DMA; this process is accomplished by alternating between the reduction of AsV to AsIII and the addition of a methyl group; S-adenosylmethionine is considered to be the source of the methyl group. Both MMA and DMA are less reactive with tissue constituents than inorganic arsenic and both are readily excreted in the urine. The methylation process appears to include multiple intermediates, some of which are more reactive than inorganic arsenic. For example, reactive trivalent metabolites, MMAIII and DMAIII, have been detected in the urine of human subjects chronically exposed to arsenic in drinking water, and *in vitro* studies have demonstrated MMAIII to be more toxic than arsenite or arsenate to human hepatocytes, epidermal keratinocytes, and bronchial epithelial cells. Additional *in vitro* studies have demonstrated genotoxic and DNA damaging properties of both MMAIII and DMAIII.

AsV (as arsenate) has been demonstrated to: (1) replace phosphate in glucose-6-phosphate and 6-phosphogluconate *in vitro*, (2) replace phosphate in the sodium pump and the anion exchange transport system of human red blood cells, (3) diminish the *in vitro* formation of adenosine-t′-triphosphate (ATP) by replacing phosphate in enzymatic reactions, and (4) deplete ATP in some cellular systems, but not in human erythrocytes. However, it is becoming more apparent that the major source of arsenic toxicity and carcinogenicity is related to its reduction to arsenite.

AsIII (as arsenite) is known to react with thiol-containing molecules such as glutathione and cysteine *in vitro*. Methylated trivalent arsenics such as MMAIII are potent inhibitors of glutathione reductase and thioredoxin reductase. It has been suggested that binding of arsenite and methylated trivalent arsenicals to critical thiol groups could lead to the inhibition of essential biochemical reactions, alteration of cellular redox status, and eventual cytotoxicity. Binding of MMAIII and DMAIII to protein has also been demonstrated *in vitro*. Arsenite inhibits pyruvate dehydrogenase (PDH), a complex that oxidizes pyruvate to acetyl-CoA, a precursor to intermediates of the citric acid cycle that provides reducing equivalents to the electron transport system for ATP production. This property may explain the depletion of carbohydrates in arsenite-treated rats.

Evidence that arsenic may induce alterations in nitric oxide metabolism and endothelial function includes findings that persons exposed to high levels of arsenic in drinking water had decreased serum and urine concentrations of nitric oxide metabolites, which was reversed upon intervention with drinking water containing lower levels of arsenic. Urinary arsenic levels have been inversely associated with nitric oxide production in activated monocytes. Arsenite concentrations of 1–25 μM inhibited endothelial nitric oxide synthase activity and resulting decreased cell growth in human endothelial cells, although lower concentrations up-regulated the expression of constitutive nitric oxide synthase 3, which might serve as an explanation for observed arsenic-induced cell growth and angiogenesis.

Although epidemiological studies demonstrate the carcinogenicity of arsenic in humans, early animal cancer bioassays failed to demonstrate a carcinogenic effect following lifetime exposure to inorganic arsenic. However, more recent focus has resulted in the development of animal models that exhibit carcinogenic activity in skin, urinary bladder, liver, and lung, tissues implicated in arsenic-induced cancer in humans. This concordance in target sites among animal models and humans indicates that common mechanisms of action may be applicable to humans and laboratory animals.

Several modes of action have been proposed to explain, at least in part, the carcinogenicity of arsenic. It is likely that multiple mechanisms are involved, some of which may relate to noncancer effects as well.

Oxidative Stress. Mechanistic studies of arsenic toxicity have suggested a role of the generation of reactive oxygen species in the toxicity of inorganic arsenic. Results of both *in vivo* and *in vitro* studies of arsenic-exposed humans and animals suggest the possible involvement of increased lipid peroxidation, superoxide production, hydroxyl radical formation, blood nonprotein sulfhydrals, and/or oxidant-induced DNA damage. Reduction of cellular oxidant defense by treatment with glutathione-depleting agents results in an increased sensitivity of cells to arsenic toxicity. Support for mechanisms of toxicity that involves arsenic-induced oxidative stress includes findings that inhaled arsenic can predispose the lung to oxidative damage, chronic low-dose arsenic alters genes and proteins that are associated with oxidative stress and inflammation, and major transcriptional regulators of altered genes are redox sensitive.

Genotoxicity. Collectively, *in vitro* and *in vivo* genotoxicity assays have demonstrated that arsenics cause single strand breaks, formation of apurinic/apyrimidinic sites, DNA base and oxidative base damage, DNA-protein crosslinks, chromosomal aberrations, aneuploidy, sister chromatid exchanges, and micronuclei. Chromosomal aberrations, characterized by chromatid gaps, breaks and fragmentation,

endoreduplication, and chromosomal breaks, are dose-dependent and arsenite is more potent than arsenate. Both MMAIII and DMAIII are directly genotoxic and are many times more potent than arsenite at inducing DNA damage. Inorganic arsenic can potentiate the mutagenicity observed with other chemicals, although arsenic itself does not appear to induce point mutations. Arsenic-induced genotoxicity may involve oxidants or free radical species.

Altered Growth Factors→Cell Proliferation→Promotion of Carcinogenesis. Increased concentrations of growth factors can lead to cell proliferation and eventual promotion of carcinogenesis. Arsenic-induced cell death can also lead to compensatory cell regeneration and carcinogenesis. Altered growth factors, cell proliferation, and promotion of carcinogenesis have all been demonstrated in one or more systems exposed to arsenics. Altered growth factors and mitogenesis were noted in human keratinocytes. Cell death was observed in human hepatocytes and rat bladder epithelium. Cell proliferation was demonstrated in human keratinocytes and intact human skin and rodent bladder cells. Promotion of carcinogenesis was noted in rat bladder, kidney, liver, and thyroid, and mouse skin and lung.

Additional Mechanisms of Toxicity Data. Inorganic arsenic exposure has been shown to modify the expression of a variety of genes related to cell growth and defense, including the tumor suppressor gene p53, as well as to alter the binding of nuclear transcription factors. Carcinogenic effects of arsenic may result from a cocarcinogenic effect. Whereas arsenic exposure alone did not elicit skin tumors in mice, co-exposure to arsenic and ultraviolet light resulted in skin tumors that were greater in number and larger in size than those produced by ultraviolet light alone. Arsenate and arsenite enhanced the amplification of a gene that codes for the enzyme dihydrofolate reductase, arsenate being more potent than arsenite. Furthermore, inhibition of DNA repair has been demonstrated in arsenic-treated cells.

3.5.3 Animal-to-Human Extrapolations

The usefulness of animal models for toxicity studies with arsenic is significantly limited by two major factors. First and most importantly, no animal model exists for the health effect of greatest concern for human exposure: carcinogenicity in skin and other organs after oral exposure. Second, the pattern of metabolism in humans (significant excretion of the methylated forms of arsenic) is unlike that of most other mammalian species (the mouse and rabbit may be exceptions). The ratios of inorganic to organic arsenic excreted also vary between species. The rat sequesters arsenic in its erythrocytes and is not a suitable model for human toxicity.

3.6 TOXICITIES MEDIATED THROUGH THE NEUROENDOCRINE AXIS

Recently, attention has focused on the potential hazardous effects of certain chemicals on the endocrine system because of the ability of these chemicals to mimic or block endogenous hormones. Chemicals with this type of activity are most commonly referred to as *endocrine disruptors*. However, appropriate terminology to describe such effects remains controversial. The terminology *endocrine disruptors*, initially used by Thomas and Colborn (1992), was also used in 1996 when Congress mandated the EPA to develop a screening program for "...certain substances [which] may have an effect produced by a naturally occurring estrogen, or other such endocrine effect[s]...". To meet this mandate, EPA convened a panel called the Endocrine Disruptors Screening and Testing Advisory Committee (EDSTAC), and in 1998, the EDSTAC completed its deliberations and made recommendations to EPA concerning *endocrine disruptors*. In 1999, the National Academy of Sciences released a report that referred to these same types of chemicals as *hormonally active agents*. The terminology *endocrine modulators* has also been used to convey the fact that effects caused by such chemicals may not necessarily be adverse. Many scientists agree that chemicals with the ability to disrupt or modulate the endocrine system are a potential threat to the health of humans, aquatic animals, and wildlife. However, others think that endocrine-active chemicals do not pose a significant health risk, particularly in view of the fact that hormone mimics exist in the natural environment. Examples of natural hormone mimics are the isoflavinoid phytoestrogens (Adlercreutz 1995; Livingston 1978; Mayr et al. 1992). These chemicals are derived from plants and are similar in structure and action to endogenous estrogen. Although the public health significance and descriptive terminology of substances capable of affecting the endocrine system remains controversial, scientists agree that these chemicals may affect the synthesis, secretion, transport, binding, action, or elimination of natural hormones in the body responsible for maintaining homeostasis, reproduction, development, and/or behavior (EPA 1997h). Stated differently, such compounds may cause toxicities that are mediated through the neuroendocrine axis. As a result, these chemicals may play a role in altering, for example, metabolic, sexual, immune, and neurobehavioral function. Such chemicals are also thought to be involved in inducing breast, testicular, and prostate cancers, as well as endometriosis (Berger 1994; Giwercman et al. 1993; Hoel et al. 1992).

There is little evidence to suggest that arsenic functions as an endocrine disruptor. An association has been demonstrated between exposure to arsenic in drinking water and increased incidence of diabetes mellitus (Rahman et al. 1998; Tsai et al. 1999; Tseng et al. 2000; Wang et al. 2003), although dose-response relationships are not available and the mechanism of action for this response has not been characterized. Studies by Waalkes and coworkers (Waalkes et al. 2006a, 2006b) have suggested that in

mice, arsenic may interact with estrogens to enhance production of female urogenital cancers and male hepatocellular cancer following exposure to arsenic *in utero*. The mechanism by which this might happen has not been elucidated. No other relevant data were located in humans or animals. Data on general effects of arsenic compounds on the endocrine system are presented in Sections 3.2.1.2 and 3.2.2.2 above.

In vitro studies provide suggestive evidence that arsenic may act as an endocrine disruptor. Studies by Bodwell et al. (2004, 2006) and Davey et al. (2007) demonstrate that arsenic can alter gene regulation of steroid hormone receptors for glucocorticoids, mineralocorticoids, progesterone, and estrogen.

3.7 CHILDREN'S SUSCEPTIBILITY

This section discusses potential health effects from exposures during the period from conception to maturity at 18 years of age in humans, when all biological systems will have fully developed. Potential effects on offspring resulting from exposures of parental germ cells are considered, as well as any indirect effects on the fetus and neonate resulting from maternal exposure during gestation and lactation. Relevant animal and *in vitro* models are also discussed.

Children are not small adults. They differ from adults in their exposures and may differ in their susceptibility to hazardous chemicals. Children's unique physiology and behavior can influence the extent of their exposure. Exposures of children are discussed in Section 6.6, Exposures of Children.

Children sometimes differ from adults in their susceptibility to hazardous chemicals, but whether there is a difference depends on the chemical (Guzelian et al. 1992; NRC 1993). Children may be more or less susceptible than adults to health effects, and the relationship may change with developmental age (Guzelian et al. 1992; NRC 1993). Vulnerability often depends on developmental stage. There are critical periods of structural and functional development during both prenatal and postnatal life, and a particular structure or function will be most sensitive to disruption during its critical period(s). Damage may not be evident until a later stage of development. There are often differences in pharmacokinetics and metabolism between children and adults. For example, absorption may be different in neonates because of the immaturity of their gastrointestinal tract and their larger skin surface area in proportion to body weight (Morselli et al. 1980; NRC 1993); the gastrointestinal absorption of lead is greatest in infants and young children (Ziegler et al. 1978). Distribution of xenobiotics may be different; for example, infants have a larger proportion of their bodies as extracellular water, and their brains and livers are proportionately larger (Altman and Dittmer 1974; Fomon 1966; Fomon et al. 1982; Owen and Brozek

1966; Widdowson and Dickerson 1964). The infant also has an immature blood-brain barrier (Adinolfi 1985; Johanson 1980) and probably an immature blood-testis barrier (Setchell and Waites 1975). Many xenobiotic metabolizing enzymes have distinctive developmental patterns. At various stages of growth and development, levels of particular enzymes may be higher or lower than those of adults, and sometimes unique enzymes may exist at particular developmental stages (Komori et al. 1990; Leeder and Kearns 1997; NRC 1993; Vieira et al. 1996). Whether differences in xenobiotic metabolism make the child more or less susceptible also depends on whether the relevant enzymes are involved in activation of the parent compound to its toxic form or in detoxification. There may also be differences in excretion, particularly in newborns who all have a low glomerular filtration rate and have not developed efficient tubular secretion and resorption capacities (Altman and Dittmer 1974; NRC 1993; West et al. 1948). Children and adults may differ in their capacity to repair damage from chemical insults. Children also have a longer remaining lifetime in which to express damage from chemicals; this potential is particularly relevant to cancer.

Certain characteristics of the developing human may increase exposure or susceptibility, whereas others may decrease susceptibility to the same chemical. For example, although infants breathe more air per kilogram of body weight than adults breathe, this difference might be somewhat counterbalanced by their alveoli being less developed, which results in a disproportionately smaller surface area for alveolar absorption (NRC 1993).

Arsenic has been recognized as a human toxicant for many centuries, and the symptoms of acute poisoning are well known. Children who are exposed to high levels of arsenic exhibit symptoms similar to those seen in adults, including respiratory, cardiovascular, dermal, and neurological effects, and vomiting if the arsenic is ingested (Borgoño et al. 1980; Foy et al. 1992; Kersjes et al. 1987; Muzi et al. 2001; Rosenberg 1974; Zaldívar 1974; Zaldívar and Guillier 1977). Arterial thickening of the pancreas was observed in five children who died in Chile after chronic exposure to arsenic (Rosenberg 1974). Foy et al. (1992) described systemic effects of chronic arsenic exposure in children in a village near a tin and tungsten mining operation in Thailand. The arsenic concentration in water samples from 35 shallow wells averaged 0.82 mg As/L (range, 0.02–2.7 mg As/L). Piped water (available in some homes) had a concentration of 0.07 mg As/L. A survey of skin manifestations of arsenic poisonings was conducted in the autumn of 1987. The case reports of four children were presented. All of the children had hyperkeratosis and hyperpigmentation of the extremities, including tibia, palms, and soles. In addition, one child had developed weakness 3 years previously and had anorexia and a chronic cough for 1 year. She had been held back twice in school as a slow learner. On examination, she had a runny nose and

weakness of her wrist joints. The liver was about 4 finger-breadths below the right costal margin with a sharp but tender edge. Blood arsenic levels ranged from 0.087 to 0.46 µg/mL and the arsenic level in hair ranged from 14.4 to 20 µg/g. The authors concluded that the finding of typical skin manifestations of chronic arsenic poisoning suggests that it may take a considerably shorter period of time to develop these manifestations than previously thought. However, it is not known what effect co-exposure to tin and tungsten might have had on skin manifestations in these children. Exposure to high arsenic levels during gestation and/or during early childhood also was associated with significant increases in SMRs for lung cancer and bronchiectasis during adulthood in a study of residents in a city in Chile with high arsenic levels in the drinking water (near 0.9 mg/L) during several years (Smith et al. 2006).

As previously mentioned in Sections 3.2.1.4 and 3.2.2.4, exposure of children to arsenic also has been associated with neurological deficits in children. Studies by Wasserman et al. (2004, 2007) of 6- and 10-year-old children from Bangladesh reported small but significant decreases in some tests of cognitive function associated with levels of arsenic in the water ≥0.05 mg/L. A study of pre-school age children in West Bengal, India, reported an association between current urinary arsenic concentrations, but not long-term water arsenic, and small decrements in intellectual tests (von Ehrenstein et al. 2007). Similar results were reported in a study of children in Taiwan (Tsai et al. 2003) and in China (Wang et al. 2007). Neurological effects have also been associated with elevated levels of arsenic in the air. For example, Bencko et al. (1977) reported that children of approximately 10 years of age living near a power plant burning coal of high arsenic content showed significant hearing losses (increased threshold) compared to a control group of children living outside the polluted area (Bencko et al. 1977). Also, in a study of Mexican children, Calderón et al. (2001) reported that children living near a smelter complex had poor performance on tests evaluating verbal IQ than children who lived farther from the smelter. Thus, the limited data available suggest that exposure of children to inorganic arsenic may result in detrimental effects on neurobehavioral parameters.

Wulff et al. (1996) conducted a retrospective study of a cohort of children born between 1961 and 1990 in the municipality of Skelleftea, Sweden, where a smelter released arsenic and other pollutants including lead, copper, cadmium, and sulfur dioxide. Childhood cancer incidences among children born in the vicinity of the smelter (i.e., within 20 km) and distant from the smelter (>20 km) were compared with expected incidences based on Swedish national statistics. There appeared to be an increased risk of childhood cancer (all types combined) among children born in the vicinity of the smelter (SIR=195, 95% CI=88–300, based on 13 cases observed and 6.7 expected), but the increase was not statistically significant, and in any event, the role of arsenic in any finding from this study is confounded by the

presence of other metals. The number of cases (n=42) was very close to the expected number (n=41.8) among children born distant from the smelter. Similar results were reported in a study by Moore et al. (2002), which did not find increased incidence ratios for all childhood cancers or for childhood leukemias in children from an area of Nevada with high arsenic exposures.

Inorganic arsenic has been characterized as a developmental toxicant. It is known to cross the placental barrier and selectively accumulate in the neuroepithelium of the developing animal embryo (Hanlon and Ferm 1977; Lindgren et al. 1984). Studies in animals have also revealed that various fetal malformations occur after embryonic exposure to arsenic *in vitro*; neural tube defects are the predominant and consistent malformation in these studies (Chaineau et al. 1990; Mirkes and Cornel 1992; Morrissey and Mottet 1983; Mottet and Ferm 1983; Tabacova et al. 1996; Willhite and Ferm 1984; Wlodarczyk et al. 1996). *In vivo* studies have shown that high doses of ingested arsenic can produce developmental effects (fetal mortality, skeletal defects), but generally only at maternally toxic doses (Baxley et al. 1981; Holson et al. 1999, 2000; Hood and Harrison 1982; Hood et al. 1978; Nemec et al. 1998; Stump et al. 1999). A series of studies showed an increased incidence of tumors in the offspring of mice exposed to arsenic from gestational day 8 through day 18(Waalkes et al. 2003, 2004a, 2004b, 2004c, 2006a, 2006b) (see Section 3.2.2.6 for further details). In humans, acute prenatal exposure to high doses of inorganic arsenic can result in miscarriage and early neonatal death (Bolliger et al. 1992; Lugo et al. 1969). Although several studies have reported marginal associations between prolonged low-dose human arsenic exposure and adverse reproductive outcomes, including spontaneous abortion, stillbirth, developmental impairment, and congenital malformation (Ahmad et al. 2001; Aschengrau et al. 1989; Chakraborti et al. 2003c; Hopenhayn-Rich et al. 2000; Nordström et al. 1978a, 1979b; Yang et al. 2003; Zierler et al. 1988), none of these studies have provided convincing evidence for such effects or information concerning possible dose-response relationships.

There is no evidence for differences in absorption of arsenic in children and adults. Ingestion of arsenic in dirt may be an important route of exposure for young children. A study that used a synthetic gastric juice designed to mimic gastric conditions in a 2-year-old child found that absorption of arsenic from contaminated soil was likely to be up to 5 times lower than the total concentration of arsenic in the soil (Williams et al. 1998). As previously mentioned, arsenic crosses the placenta and preferentially accumulates in the embryonic neuroepithelium. In addition, arsenic is known to be present in breast milk at low concentrations. Arsenic concentrations were low in human milk sampled from 88 mothers in the Faroe Islands (0.0001–0.0044 ppm), where the diet is predominantly seafood (exposures were primarily to "fish arsenic" [Grandjean et al. 1995]), in a population of Andean women (0.0008–0.008 ppm) exposed

to high concentrations of inorganic arsenic in drinking water (Concha et al. 1998b), and in a World Health Organization survey (0.00013–0.00082 ppm) (Somogyi and Beck 1993). There is no information in the literature describing storage of arsenic in maternal tissues. There is some evidence that metabolism of arsenic in children is less efficient than in adults. Children in two villages in Argentina ingesting large amounts of arsenic in their drinking water (200 µg/L) excreted about 49% inorganic arsenic and 47% DMA, compared to 32% inorganic arsenic and 66% DMA for the women in the study (Concha et al. 1998b). No PBPK models specifically targeted at fetuses, infants, or children, or pregnant or lactating women were found in the literature. There are no biomarkers that have been specifically identified for children exposed to arsenic. In addition, no unique interactions of arsenic with other chemicals have been identified in children.

The mechanism of toxic action of arsenic in the mammalian cell may involve inhibition of proliferation of cells (Dong and Luo 1993; Jha et al. 1992; Petres et al. 1977). In addition, high-dose arsenic impairs assembly and disassembly of microtubules, thus interfering with mitotic spindle formation and embryonal cell division (Léonard and Lauwerys 1980; Li and Chou 1992; Mottet and Ferm 1983). Arsenic compounds also cause chromosomal aberrations (Jha et al. 1992; Léonard and Lauwerys 1980), which may disrupt cell cycling. The direct toxic effects of high levels of arsenic in the developing embryo result not from a difference in the mechanism of toxicity during development, but rather from the existence of a unique target tissue, the neuroepithelium. The process of neurulation involves cell shape changes, cytokinesis, and cell adhesion, which are dependent upon cytoskeletal elements that are functionally affected by arsenic (Dallaire and Béliveau 1992; Edelman 1992; Gunn et al. 1992; Li and Chou 1992; Moriss-Kay et al. 1994; Schoenwolf and Smith 1990; Taubeneck et al. 1994). However, since arsenic is known to affect vasculature, and since altered placental and/or embryonal vasculature has been suggested as a mechanism leading to neural tube defects, the embryo may be sensitive to this manifestation of arsenic toxicity.

3.8 BIOMARKERS OF EXPOSURE AND EFFECT

Biomarkers are broadly defined as indicators signaling events in biologic systems or samples. They have been classified as markers of exposure, markers of effect, and markers of susceptibility (NAS/NRC 1989).

Due to a nascent understanding of the use and interpretation of biomarkers, implementation of biomarkers as tools of exposure in the general population is very limited. A biomarker of exposure is a xenobiotic

substance or its metabolite(s) or the product of an interaction between a xenobiotic agent and some target molecule(s) or cell(s) that is measured within a compartment of an organism (NAS/NRC 1989). The preferred biomarkers of exposure are generally the substance itself, substance-specific metabolites in readily obtainable body fluid(s), or excreta. However, several factors can confound the use and interpretation of biomarkers of exposure. The body burden of a substance may be the result of exposures from more than one source. The substance being measured may be a metabolite of another xenobiotic substance (e.g., high urinary levels of phenol can result from exposure to several different aromatic compounds). Depending on the properties of the substance (e.g., biologic half-life) and environmental conditions (e.g., duration and route of exposure), the substance and all of its metabolites may have left the body by the time samples can be taken. It may be difficult to identify individuals exposed to hazardous substances that are commonly found in body tissues and fluids (e.g., essential mineral nutrients such as copper, zinc, and selenium). Biomarkers of exposure to arsenic are discussed in Section 3.8.1.

Biomarkers of effect are defined as any measurable biochemical, physiologic, or other alteration within an organism that, depending on magnitude, can be recognized as an established or potential health impairment or disease (NAS/NRC 1989). This definition encompasses biochemical or cellular signals of tissue dysfunction (e.g., increased liver enzyme activity or pathologic changes in female genital epithelial cells), as well as physiologic signs of dysfunction such as increased blood pressure or decreased lung capacity. Note that these markers are not often substance specific. They also may not be directly adverse, but can indicate potential health impairment (e.g., DNA adducts). Biomarkers of effects caused by arsenic are discussed in Section 3.8.2.

A biomarker of susceptibility is an indicator of an inherent or acquired limitation of an organism's ability to respond to the challenge of exposure to a specific xenobiotic substance. It can be an intrinsic genetic or other characteristic or a preexisting disease that results in an increase in absorbed dose, a decrease in the biologically effective dose, or a target tissue response. If biomarkers of susceptibility exist, they are discussed in Section 3.10, Populations That Are Unusually Susceptible.

3.8.1 Biomarkers Used to Identify or Quantify Exposure to Arsenic

Arsenic levels in blood, urine, hair, and nails have all been investigated and used as biological indicators of exposure to arsenic. Since arsenic is cleared from blood within a few hours (Tam et al. 1979b; Vahter 1983), measurements of blood arsenic reflect exposures only within the very recent past. Typical values in nonexposed individuals are <1 µg/L (Heydorn 1970; Hindmarsh and McCurdy 1986; Valentine et al.

1979). Consumption of medicines containing arsenic is associated with blood values of 100–250 µg/L, while blood levels in acutely toxic and fatal cases may be 1,000 µg/L or higher (Driesback 1980).

However, blood levels do not appear to be reliable indicators of chronic exposure to low levels of arsenic. For example, there was no correlation between the level of arsenic in blood of residents and the level of arsenic in drinking water in several U.S. communities where water levels ranged from about 6 to 125 µg/L (Valentine et al. 1979, 1981). Consequently, measurement of blood arsenic is not generally considered to be a reliable means of monitoring human populations for arsenic exposure.

As discussed in Section 3.4.4, most arsenic that is absorbed from the lungs or the gastrointestinal tract is excreted in the urine, mainly within 1–2 days. For this reason, measurement of urinary arsenic levels is generally accepted as the most reliable indicator of recent arsenic exposure, and this approach has proved useful in identifying above-average exposures in populations living near industrial point sources of arsenic (e.g., Milham and Strong 1974; Polissar et al. 1990). By the inhalation route, several researchers have found that there is a good quantitative correlation between the concentration of arsenic in workplace air (C_{air}, µg/m^3) and the concentration in the urine (C_{urine}, µg/L) of exposed workers. For example, Pinto et al. (1976) found a linear relationship for exposures ranging up to 150 µg/m^3, given by the following equation:

$$C_{air}=0.3\ C_{urine}$$

Enterline et al. (1987a) reinvestigated this relationship over a wider range of exposures (up to 3,500 µg/m^3), and found that the curve tended to be concave upward, as given by the following equation:

$$C_{air}=0.0064\ (C_{urine})^{1.94}$$

This indicates that at higher exposure levels, a higher fraction of the dose is excreted in urine, although the toxicokinetic basis for this is not certain. Numerous studies have used above-average urinary levels (i.e., higher than about 100 µg/L) as evidence of recent arsenic ingestion (e.g., Borgoño et al. 1980; Fincher and Koerker 1987; Franzblau and Lilis 1989; Goldsmith and From 1986; Kyle and Pease 1965; Valentine et al. 1981). Calderon et al. (1999) found a quantitative correlation between the log of the mean total urinary arsenic concentration/creatinine (TAs/c, µg/mg) of people living in areas with arsenic-contaminated drinking water sources and the log of the inorganic arsenic concentration in the drinking water (InAs, µg/L). The equation for the regression line is:

$$TAs/c=10^{-2.57} \times (InAs)^{0.63}$$

where -2.57 and 0.63 are the intercept and slope, respectively, for the regression of the log10-transformed data. Mixed model regression analysis showed that the log of estimated arsenic intake from drinking water (µg/day) is also a good predictor of TAs/c excretion (Calderon et al. 1999).

There is some indication that speciation of urinary arsenic may indicate the extent of past cumulative exposure to arsenic. Hsueh et al. (1998a) reported higher levels of DMA and MMA in the urine of individuals with higher cumulative past exposure to inorganic arsenic. Speciated urinary arsenic is also a recommended biomarker for recent inorganic arsenic exposure. Walker and Griffin (1998) used the EPA Exposure Assessment Model and a number of site-specific data covering environmental and biological factors to predict total and speciated urinary arsenic concentrations for children living near high levels of arsenic-contaminated soil. There was reasonable agreement between the measured and predicted speciated urinary arsenic concentrations.

An important limitation to the use of total urinary arsenic as a biomarker of exposure is that arsenobetaine is excreted (unmetabolized) in urine after ingestion of certain seafoods (Brown et al. 1990; Kalman 1987; Tam et al. 1982). Since "fish arsenic" is essentially nontoxic, analytical methods based on total urinary arsenic content may overestimate exposures to arsenic species that are of health concern. As discussed in Section 7.1, there are adequate methods for distinguishing arsenobetaine from other forms of arsenic in urine (inorganic, MMA, DMA), although these are not convenient to use as a routine screening method.

Arsenic tends to accumulate in hair and nails, and measurement of arsenic levels in these tissues may be a useful indicator of past exposures. Normal levels in hair and nails are 1 ppm or less (Choucair and Ajax 1988; Franzblau and Lilis 1989). These values may increase from several-fold to over 100-fold following arsenic exposure (Agahian et al. 1990; Bencko 2005; Bencko et al. 1986; de Peyster and Silvers 1995; EPA 1977a, 1981b; Karagas et al. 1996; Milham and Strong 1974; Valentine et al. 1979; Yamauchi et al. 1989) and remain elevated for 6–12 months (Choucair and Ajax 1988). Minimum exposure levels that produce measurable increases in arsenic levels in hair and nails have not been precisely defined. For hair, ingestion of 50–120 ppb of arsenic in drinking water produced only a marginal effect, but a clear increase was noted at 393 ppb (Valentine et al. 1979). A study of children living in a region polluted with arsenic derived from a power plant burning coal with a high arsenic content found a significant correlation between arsenic levels in hair and distance from the source of emission (Bencko and Symon 1977).

Inhalation exposure of workers to about 0.6 μg/m^3 of arsenic in air significantly increased average levels in nails (Agahian et al. 1990), although there was wide variation between individuals.

Analysis of hair may yield misleading results due to the presence of arsenic adsorbed to the external surface, but this can be minimized by collecting samples from close to the scalp or from unexposed areas and by washing the hair before analysis (e.g., Paschal et al. 1989). Similarly, extensive washing of nails is required to remove exogenous contamination (Agahian et al. 1990). The relationship between consumption of food items and levels of arsenic in toenails has been evaluated by MacIntosh et al. (1997) using standard multivariate regression models. This approach does not appear to be highly reliable, but may be sufficient for exploring associations between diet and disease. Kurttio et al. (1998) used linear regression models to show that there is a good association between arsenic concentration in hair (mg/kg) and total arsenic concentration in urine (μg/L), arsenic concentration in drinking water (μg/L) or daily intake of arsenic (μg/day). A 10 μg/L increase in the drinking water concentration or a 10–20 μg/day increase in daily arsenic intake corresponded to a 0.1 mg/kg increase in the arsenic concentration in hair. It is also important to note that the measurement of arsenic in hair and fingernails is a process not readily accessible to many clinical offices.

3.8.2 Biomarkers Used to Characterize Effects Caused by Arsenic

As discussed in Section 3.2, the characteristic pattern of skin changes caused by arsenic (hyperkeratinization, hyperpigmentation) is probably the most sensitive and diagnostic clinical indicator of chronic exposure to arsenic. However, no means has been developed for detecting these effects except by routine dermatological examination.

Peripheral neuropathy is another characteristic effect of arsenic exposure, and several researchers have investigated decreased nerve conduction velocity or amplitude as a biomarker for peripheral neuropathy. While effects can usually be detected in individuals with clinical signs of neuropathy (e.g., Goebel et al. 1990; Jenkins 1966; Le Quesne and McLeod 1977; Morton and Caron 1989; Murphy et al. 1981), effects are only marginal (EPA 1977a; Hindmarsh et al. 1977; Valentine et al. 1981) or undetectable (EPA 1981b; Kreiss et al. 1983) in exposed populations without obvious clinical signs of toxicity. This indicates that this approach is probably not sufficiently sensitive to detect neurological effects earlier than by standard neurological examination (Hindmarsh and McCurdy 1986). Also, decreases in nerve conduction velocity or amplitude are not specific for arsenic-induced neuropathy.

Arsenic is known to affect the activity of a number of enzymes, and some of these may have potential as biomarkers of effect. Most promising is the spectrum of effects caused by arsenic on the group of enzymes responsible for heme synthesis and degradation, including inhibition of coproporphyrinogen oxidase and heme synthetase (Woods and Fowler 1978; Woods and Southern 1989) and activation of heme oxygenase (Sardana et al. 1981). Menzel et al. (1998) has examined the *in vitro* induction of human lymphocyte heme oxygenase 1(HO1) as a biomarker of arsenite exposure. Arsenite did induce *de novo* synthesis of HO1 in human lymphoblastoid cells, but it has not been determined if the same response is induced *in vivo*. It has been shown in animals that these arsenic-induced enzymic changes result in increased urinary levels of uroporphyrin, coproporphyrin, and bilirubin (Albores et al. 1989; Woods and Fowler 1978), and it has been shown that these effects can be detected in the urine of arsenic-exposed humans (García-Vargas and Hernández-Zavala 1996). Therefore, altered urinary levels of these heme-related compounds could serve as a biomarker of effect. However, it is known that numerous other toxic metals also have similar effects on heme metabolism (Albores et al. 1989; Sardana et al. 1981; Woods and Southern 1989), so it is likely that these effects would not be specific for arsenic.

For more information on biomarkers for renal and hepatic effects of chemicals, see ATSDR/CDC Subcommittee Report on Biological Indicators of Organ Damage (Agency for Toxic Substances and Disease Registry 1990b) and for information on biomarkers for neurological effects, see OTA (1990).

3.9 INTERACTIONS WITH OTHER CHEMICALS

A number of researchers have found that arsenic compounds tend to reduce the effects of selenium (Hill 1975; Howell and Hill 1978; Kraus and Ganther 1989; Levander 1977; Miyazaki et al. 2003; Moxon et al. 1945; Schrauzer 1987; Schrauzer et al. 1978). Likewise, selenium can decrease the effects of arsenic, including clastogenicity (Beckman and Nordenson 1986; Biswas et al. 1999; Sweins 1983), delayed mutagenesis (Rossman and Uddin 2004), cocarcinogenesis (Uddin et al. 2005), cytotoxicity (Babich et al. 1989; Rössner et al. 1977; Styblo and Thomas 2001), and teratogenicity (Holmberg and Ferm 1969). The mechanism of this mutual inhibition of effects is not known, but may be related to the formation of a selenium-arsenic complex (seleno-bis [S-gluthionyl] arsinium ion; Gailer et al. 2002) that is excreted more rapidly than either arsenic or selenium alone (Cikrt et al. 1988; Hill 1975; Levander 1977; Levander and Baumann 1966) or due to selenium-induced changes in arsenic methylation (Styblo and Thomas 2001; Walton et al. 2003). There is little direct evidence that variations in selenium exposure in humans lead to significant increases or decreases in arsenic toxicity, although copper smelter workers who developed lung cancer had lower tissue levels of selenium than workers who did not develop lung tumors

(Gerhardsson et al. 1985, 1988). This suggests that selenium deficiency could significantly increase the risk of lung cancer following inhalation exposure to arsenic, but it is difficult to distinguish cause from effect in such a study. However, there is evidence that administration of selene can facilitate recovery from arsenic poisoning. In residents living in an area of Inner Mongolia with high levels of arsenic in drinking water, administration of 100–200 µg selenium/day in the form of selenium yeast and exposure to arsenic-free water for 14 months resulted in a greater improvement in clinical signs and symptoms, liver function, and EKG readings as compared to residents administered arsenic-free water only (Wuyi et al. 2001; Yang et al. 2002). An improvement in skin lesions was observed in 67 and 21% of the subjects in the selenium-supplemented and control groups (Yang et al. 2002). Additionally, the levels of arsenic in blood, hair, and urine were significantly lower after the 14-month period only in the selenium supplemented group.

The interaction between cigarette smoking, inhalation of arsenic, and the risk of lung cancer has not been extensively investigated. Smoking appeared to increase lung cancer risk synergistically (multiplicatively) in one study of smelter workers (Pershagen et al. 1981), although the data are not adequate to exclude a simple additive interaction (Thomas and Whittemore 1988). Cigarette smoking has been shown to increase the occurrence of lung cancer in people with high levels of arsenic in the drinking water (Chiou et al. 1995; Tsuda et al. 1995a). Suggestive evidence of a positive interaction between arsenic and benzo(a)pyrene has also been noted for induction of lung adenocarcinomas in hamsters (Pershagen et al. 1984).

Co-exposure to ethanol and arsenic may exacerbate the toxic effects of arsenic. Simultaneous exposure of rats to ethanol (10% in drinking water) and arsenic (dose not stated) for 6 weeks produced a significant increase in the concentration of arsenic in the kidney, a nonsignificant increase of arsenic in the liver and a significant increase in the concentration of glutathione in the liver, compared to rats treated with either ethanol or arsenic alone (Flora et al. 1997a, 1997b). Histological damage to the liver, but not the kidneys, was increased in rats treated with both ethanol and arsenic compared to those receiving only arsenic.

Studies of rats exposed to arsenic, lead, and cadmium, alone or in combination, have revealed mainly additive or subadditive effects on body weight, hematological parameters, and enzymes of heme synthesis (Mahaffey and Fowler 1977; Mahaffey et al. 1981). Similarly, studies of the tissue levels of arsenic in rats fed arsenic with or without lead or cadmium revealed only limited evidence of any toxicokinetic interactions (Mahaffey et al. 1981). Pretreatment of rats with a nontoxic dose of cadmium had no effect on the lethality of a high dose of arsenic and did not reduce arsenic-induced hepatotoxicity (Hochadel and

Waalkes 1997). These data do not suggest that arsenic toxicity is likely to be significantly influenced by concomitant exposure to these metals. However, supplementation with zinc or chromium may be useful in reducing chronic arsenism. Arsenic has been shown to cause an increase in total plasma cholesterol; co-administration of chromium(III) counteracts this effect (Aguilar et al. 1997). Pretreatment of mice with zinc, at least 24 hours before injection with arsenic-73, reduced arsenic retention compared to controls that did not receive the zinc pretreatment or received it only a short time before the administration of arsenic (Kreppel et al. 1994). Zinc is an inducer of metallothionein, but this induction does not appear to be the mechanism that reduces arsenic toxicity because other inducers of metallothionein did not reduce arsenic toxicity and arsenic elimination was increased by the zinc pretreatment.

Since methylation of arsenic is a detoxification mechanism, it is possible that chemicals that interfere with the methylation process could increase toxicity. This is supported by studies in animals in which reagents that inhibit methylation enzymes (e.g., periodate-oxidized adenosine) caused an increase in tissue levels of inorganic arsenic (Marafante and Vahter 1986; Marafante et al. 1985). Similarly, cellular glutathione levels appear to play a role in the methylation process, and treatment with reagents (e.g., phorone) that decrease glutathione levels increases arsenic toxicity (Buchet and Lauwerys 1987). Inadequate dietary intake of methionine, choline, or protein may also exacerbate arsenic toxicity. Rabbits pretreated with diets low in choline, methionine, or protein showed a significant increase in tissue retention of arsenic and a significant decrease in the excretion of dimethylarsinic acid (Vahter and Marafante 1987). The increased retention of arsenic in rabbits fed these deficient diets is likely to be due to a reduction in arsenic methylation. Thus, the toxic effects of chronic arsenic ingestion may be increased in populations that are also subject to malnutrition.

3.10 POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE

A susceptible population will exhibit a different or enhanced response to arsenic than will most persons exposed to the same level of arsenic in the environment. Reasons may include genetic makeup, age, health and nutritional status, and exposure to other toxic substances (e.g., cigarette smoke). These parameters result in reduced detoxification or excretion of arsenic, or compromised function of organs affected by arsenic. Populations who are at greater risk due to their unusually high exposure to arsenic are discussed in Section 6.7, Populations with Potentially High Exposures.

No studies were located that identified an unusual susceptibility of any human subpopulation to arsenic. Several studies have evaluated possible sex-related differences in arsenic toxicity and carcinogenesis (Aposhian et al. 2000a, 2000b; Calderon et al. 1999; Loffredo et al. 2003; Mandal et al. 2001; Watanabe et al. 2001), but have not consistently identified differences. However, since the degree of arsenic toxicity may be influenced by the rate and extent of its methylation in the liver (see Section 3.4.3), it seems likely that some members of the population might be especially susceptible because of lower than normal methylating capacity. Studies of exposed humans in Taiwan suggested that subjects with lower secondary methylation indices have an increased risk of bladder cancer (Chen et al. 2003) and peripheral vascular disease (Tseng et al. 2005), particularly in subjects with high exposure levels. Reduced hepatic methylation could result from dietary deficiency of methyl donors such as choline or methionine (Buchet and Lauwerys 1987; Vahter and Marafante 1987), although this is unlikely to be a concern for most people in the United States. There is evidence that methylation capacity can vary greatly among individuals (e.g., Buchet et al. 1981a; Foà et al. 1984; Hopenhayn-Rich et al. 1996b; Tam et al. 1979b), but the basis of this variation and its impact on human susceptibility have not been fully established. There is some evidence that low dietary protein intake and possibly other nutritional deficiencies can decrease arsenic methylation (Steinmaus et al. 2005a). Recently, Heck et al. (2007) examined whether the capacity to methylate arsenic differs by nutrient intake in a cohort of 1,016 Bangladeshi adults exposed to arsenic in drinking water. The results showed that higher intakes of cysteine, methionine, calcium, protein, and vitamin B-12 were associated with lower percentages of inorganic arsenic and higher ratios of MMA to inorganic arsenic in urine. In addition, higher intakes of niacin and choline were associated with higher DMA/MMA ratios, after adjustment for sex, age, smoking, total urinary arsenic, and total energy intake. The issue of increased susceptibility to arsenic due to poor nutrition was discussed by NRC (2001), it was concluded that, with regard to skin effects, studies of cohorts from India, Bangladesh, and Taiwan suggest that nutrition plays an important role in arsenic toxicity. On the other hand, studies in other regions of the world (i.e., Chile) involving populations with much better nutrition argue against poor nutrition having a major impact on arsenic toxicity.

Various genetic polymorphisms also seem to play a role in arsenic-induced toxicity. For example, a study of 85 lung cancer patients and 108 healthy controls in northern Chile reported that there was a nonstatistically significant difference for the frequency of the GSTM1 null genotype between the healthy and lung cancer patients stratified by gender and smoking status. The same results were observed for the MspI CYP450 1A1 polymorphism (Adonis et al. 2005). Hsueh et al. (2005) examined the association of four polymorphisms: NAD(P)H oxidase, manganese superoxide dismutase (MnSOD), catalase, and endothelial nitric oxide synthase (eNOS) with arsenic related hypertension risk among 79 hypertensive

cases and 213 controls in an arseniasis-hyperendemic area in Taiwan. The results showed that MnSOD polymorphism significantly increased the risk of hypertension regardless of exposure to arsenic. NAD(P)H oxidase and eNOS polymorphisms were significantly associated with increased risk of hypertension in subjects with higher cumulative arsenic exposure (≥10.5 mg/L x year), whereas catalase polymorphism was not associated with hypertension. The results also showed that the association between MnSOD, NAD(P)H oxidase, and eNOS polymorphisms and risk of hypertension were more pronounced in subjects with high triglyceride level. A study of a population of West Bengal, India, exposed to arsenic via drinking water reported that the frequencies of null genotype in GSTT1 were 13.52 and 12.92% in skin-symptomatic and skin-asymptomatic individuals, and GSTM1 null genotype were 13.90 and 22.47% in skin-symptomatic and skin-asymptomatic individuals, respectively (Ghosh et al. 2006). Compared to those with GSTM1 null genotype, subjects with GST1-positive (at least one allele) had significantly higher risk of arsenic-induced skin lesions. Recently, Steinmaus et al. (2007) investigated urinary arsenic methylation patterns and genetic polymorphisms in methylenetetrahydrofolate reductase (MTHFR) and GST in 170 subjects (139 males) from an arsenic-exposed region in Argentina. MTHFR is a key enzyme in the metabolism of folate and has been linked to arsenic metabolism and toxicity (NRC 1999). Steinmaus et al. (2007) found that subjects with the TT/AA variant of MTHFR 677/1298 (associated with lower MTHFR activity) excreted a significantly higher proportion on ingested arsenic as inorganic arsenic and a smaller proportion as DMA(V). The study also reported that women with null genotype of GSTM1 excreted a significantly higher proportion of arsenic as monomethylarsenate than women with the active genotype. The study also found no association between polymorphisms in GSTT1 and arsenic methylation.

There is a report that described severe arsenic-induced neuropathy that developed only in a 5,10-methylenetetrahydrofolate-reductase (MTHFR) deficient member of a family that had been exposed to arsenic (Brouwer et al. 1992). The authors suggest that the MTHFR deficiency in this girl might explain the fact that of all the family members exposed to arsenic, only she developed severe clinical signs of arsenic poisoning. Liver disease does not appear to decrease methylation capacity in humans, at least at low levels of arsenic exposure (Buchet et al. 1982; Geubel et al. 1988).

3.11 METHODS FOR REDUCING TOXIC EFFECTS

This section will describe clinical practice and research concerning methods for reducing toxic effects of exposure to arsenic. However, because some of the treatments discussed may be experimental and unproven, this section should not be used as a guide for treatment of exposures to arsenic. When specific

exposures have occurred, poison control centers and medical toxicologists should be consulted for medical advice. The following texts provide specific information about treatment following exposures to arsenic:

Tintinalli JE, Ruiz E, Krone RL, eds. 1996. Emergency medicine. A comprehensive study. American College of Emergency Physicians. 4th ed. New York, NY: The McGraw-Hill Companies, Inc.

Goldfrank RL, Flomenbaum NE, Lewin NA, et al., eds. 1998. Goldfrank's toxicologic emergencies. 6th ed. Stamford, CT: Appleton and Lange.

Ellenhorn MJ. 1997. Ellenhorn's medical toxicology. Diagnosis and treatment of human poisoning. Baltimore, MD: Williams & Wilkins.

3.11.1 Reducing Peak Absorption Following Exposure

No data were located regarding the reduction of absorption after inhalation exposure to arsenic.

There are a number of methods for reducing absorption of arsenic following oral exposure. In cases of acute high-dose exposure, the removal of arsenic from the gastrointestinal tract may be facilitated by gastric lavage, stomach intubation, induced emesis, or use of cathartics (saline, sorbitol) within a few hours after ingestion (Agency for Toxic Substances and Disease Registry 1990a; Aposhian and Aposhian 1989; Campbell and Alvarez 1989; Driesback 1980; Ellenhorn and Barceloux 1988; EPA 1989e; Haddad and Winchester 1990; Kamijo et al. 1998; Stutz and Janusz 1988). However, the efficacy of several of these methods has been questioned by some authors, and in some cases, the treatments may be contraindicated. For example, vomiting and diarrhea often occur soon after ingesting arsenic, and therefore, use of an emetic or cathartic may not be necessary. Also, emesis should not be induced in obtunded, comatose, or convulsing patients (Campbell and Alvarez 1989; Ellenhorn and Barceloux 1988; EPA 1989e), and saline cathartics should be used with caution in patients with impaired renal function (Campbell and Alvarez 1989). Vantroyen et al. (2004) described a case of a massive arsenic trioxide overdose that was successfully treated by continuous gastric irrigation with sodium bicarbonate, forced diuresis, and administration of BAL and DMSA. Treatments of this sort are unlikely to be required following low-level exposures.

Another possible approach for reducing absorption following oral exposure is to administer substances that bind the arsenic in the gastrointestinal tract. For example, activated charcoal is sometimes used for this purpose (Campbell and Alvarez 1989; EPA 1989e; Stutz and Janusz 1988), although the effectiveness of this treatment is not well established. Because pentavalent arsenic is a phosphate analogue,

administration of phosphate-binding substance such as aluminum hydroxide might possibly be useful, but this has not been investigated. Sulfhydryl compounds might be given to bind trivalent arsenic, but it seems unlikely that these would be effective under the acid conditions in the stomach, and it is not clear that such complexes would have reduced gastrointestinal absorption.

Following dermal or ocular exposure to arsenic, several measures can be taken to minimize absorption. All contaminated clothing should be removed, and contacted skin should be immediately washed with soap and water. Eyes that have come in contact with arsenic should be flushed with copious amounts of clean water (EPA 1989e; Stutz and Janusz 1988).

3.11.2 Reducing Body Burden

Acute arsenic intoxication may require treatment with chelating agents such as dimercaprol (BAL) and D-penicillamine. Although body burden is not necessarily reduced, these chelators bind free arsenic and serve to reduce the body's pool of biologically active arsenic. Chelation therapy is most effective when instituted within a few hours after exposure, and efficacy decreases as time after exposure increases (Agency for Toxic Substances and Disease Registry 1990a; Kamijo et al. 1998; McFall et al. 1998; Peterson and Rumack 1977).

In general, chelating agents should be used with caution, since they may have serious side effects such as pain, fever, hypotension, and nephrotoxicity (Ellenhorn and Barceloux 1988). Some water-soluble and less toxic analogues of BAL such as dimercaptosuccinic acid (DMSA), dimercaptopropyl phthalamadic acid (DMPA), and dimercaptopropane sulfonic acid (DMPS) are currently under investigation and may prove to be promising treatments for arsenic poisoning (Agency for Toxic Substances and Disease Registry 1990a; Aposhian and Aposhian 1989; Aposhian et al. 1997; Guha Mazumder 1996; Kreppel et al. 1995). However, a randomized placebo trial of 2,3-dimercaptosuccinic acid as a therapy for chronic arsenosis due to drinking contaminated water found no significant difference between patients treated with 2,3-dimercaptosuccinic acid and those treated with a placebo (Guha Mazumder et al. 1998a). N-acetylcysteine has been used in animals to chelate arsenic (Haddad and Winchester 1990), and a human case study reported N-acetylcysteine to be successful in treating a case of arsenic poisoning that was not responding well to BAL treatment (Martin et al. 1990). Vantroyen et al. (2004) described a case of a massive arsenic trioxide overdose that was successfully treated by continuous gastric irrigation with sodium bicarbonate, forced diuresis, and administration of BAL and DMSA.

As discussed in Section 3.4.3, once arsenic has been absorbed into the blood stream, it undergoes methylation to yield MMA and DMA. These forms of arsenic are less toxic than inorganic arsenic and are cleared from the body by excretion in the urine. Therefore, if it were possible to enhance arsenic methylation, both body burden and toxicity of arsenic might be reduced. However, experimental evidence in animals and humans suggests that arsenic methylation is not enhanced to any significant degree by supplementation with methylation cofactors (Buchet and Lauwerys 1987; Buchet et al. 1982), presumably because it is enzyme level and not cofactor availability that is rate limiting in arsenic methylation.

3.11.3 Interfering with the Mechanism of Action for Toxic Effects

It is generally thought that trivalent arsenic exerts its toxic effects mainly by complexing with sulfhydryl groups in key enzymes within the body, thereby inhibiting critical functions such as gluconeogenesis and DNA repair (Aposhian and Aposhian 1989; Li and Rossman 1989). Therefore, administration of sulfhydryl-containing compounds soon after exposure could provide alternative target molecules for arsenic, and prevent inhibition of enzyme functions. In fact, many of the chelating agents discussed above (BAL, DMSA, DMPA, DMPS, N-acetylcysteine) contain sulfhydryl groups, and this may account for their efficacy.

The mechanism by which pentavalent arsenic acts is less certain. Since pentavalent arsenic is reduced in the body to the trivalent state, pentavalent arsenic may act in a similar manner as described above for trivalent arsenic. If this is the case, efforts to inhibit the reduction of pentavalent arsenic would decrease its toxicity. However, no methods are currently recognized for blocking this reduction. Pentavalent arsenic may also exert effects by acting as a phosphate analogue. As a phosphate analogue, pentavalent arsenic could potentially affect a number of biological processes, including ATP production, bone formation, and DNA synthesis. However, any effort to interfere in normal phosphate metabolism could produce serious side effects, and no method is known for selectively interfering with arsenate metabolism.

3.12 ADEQUACY OF THE DATABASE

Section 104(I)(5) of CERCLA, as amended, directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of arsenic is available. Where adequate information is not available, ATSDR, in conjunction with the National Toxicology Program (NTP), is required to assure the

initiation of a program of research designed to determine the health effects (and techniques for developing methods to determine such health effects) of arsenic.

The following categories of possible data needs have been identified by a joint team of scientists from ATSDR, NTP, and EPA. They are defined as substance-specific informational needs that if met would reduce the uncertainties of human health assessment. This definition should not be interpreted to mean that all data needs discussed in this section must be filled. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

3.12.1 Existing Information on Health Effects of Arsenic

The existing data on health effects of inhalation, oral, and dermal exposure of humans and animals to inorganic and organic arsenic are summarized in Figures 3-13 and 3-14, respectively. The purpose of this figure is to illustrate the existing information concerning the health effects of arsenic. Each dot in the figure indicates that one or more studies provide information associated with that particular effect. The dot does not necessarily imply anything about the quality of the study or studies, nor should missing information in this figure be interpreted as a "data need". A data need, as defined in ATSDR's *Decision Guide for Identifying Substance-Specific Data Needs Related to Toxicological Profiles* (Agency for Toxic Substances and Disease Registry 1989), is substance-specific information necessary to conduct comprehensive public health assessments. Generally, ATSDR defines a data gap more broadly as any substance-specific information missing from the scientific literature.

As shown in Figure 3-13, there is a substantial database on the toxicity of inorganic arsenicals, both in humans and in animals. The oral route has been most thoroughly investigated, and reports are available on most end points of concern following acute, intermediate, and chronic exposure. The inhalation route has also been studied extensively, mainly in humans, with special emphasis on lung cancer. A number of noncancer end points have also been studied following inhalation exposure, but information on these effects is less extensive. Limited information on the effects of dermal exposure is also available in both humans and animals, focusing mainly on direct irritancy and dermal sensitization reactions. The absence of studies on other effects of inorganic arsenic following dermal exposure is probably not a critical data need, since dermal uptake of inorganic arsenic appears to be sufficiently limited that other routes of exposure (oral or inhalation) would almost always be expected to be of greater concern.

Figure 3-13. Existing Information on Health Effects of Inorganic Arsenic

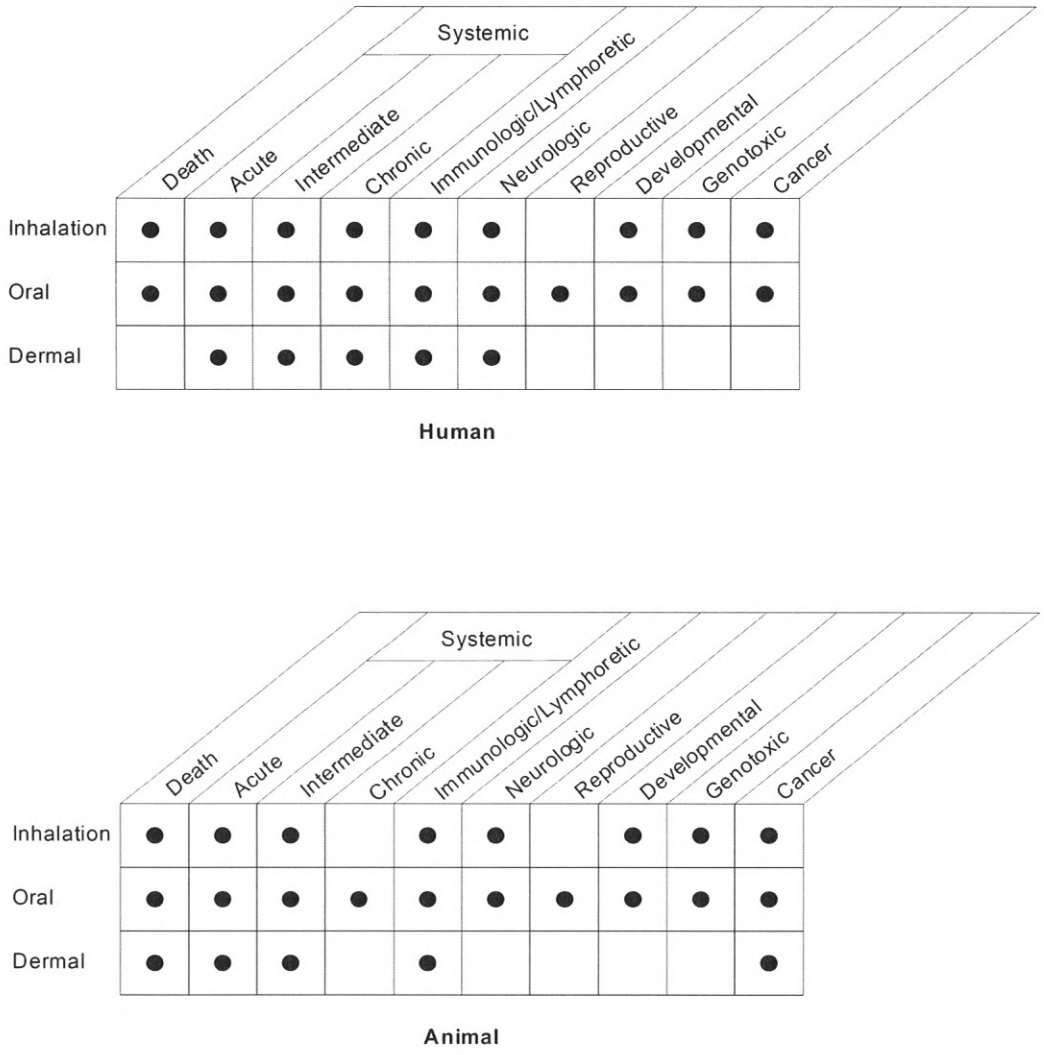
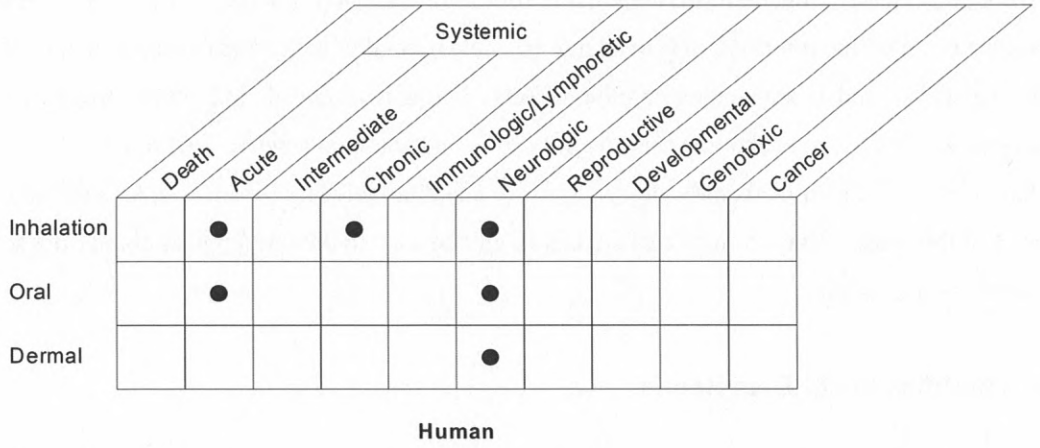
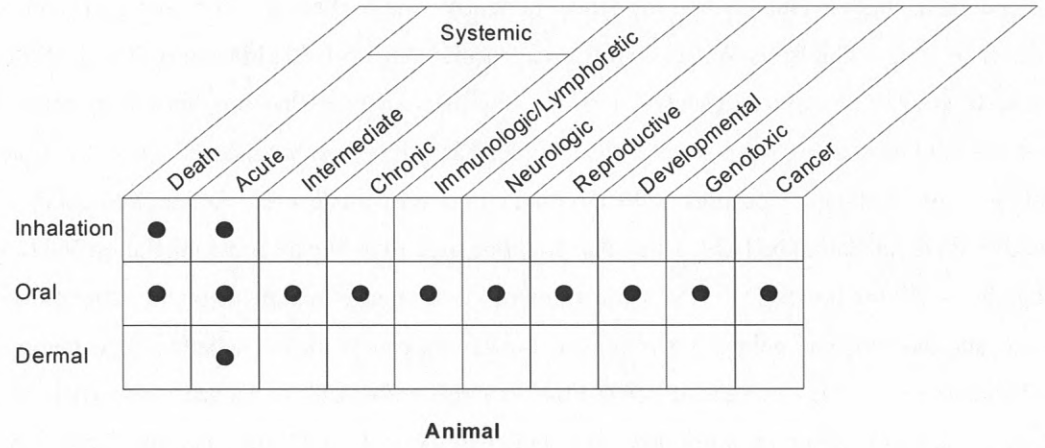


Figure 3-14. Existing Information on Health Effects of Organic Arsenic



Human



Animal

● Existing Studies

As shown in Figure 3-14, very little information is available on the effects of organic arsenic compounds in humans, although there are a number of studies in animals. These studies mainly involve the oral route, since all of these compounds are nonvolatile solids, although a few acute inhalation studies have been performed. Limited information is available on acute dermal lethality and dermal irritancy of some organic arsenicals, but data are lacking on other effects of organic arsenicals following dermal exposure. As discussed previously, in evaluating the adequacy of the database on arsenic, it is important to keep in mind that most studies in animals indicate that they are quantitatively less sensitive to arsenic than humans. For this reason, data from animal studies should be used to draw inferences about effects in humans only with caution.

3.12.2 Identification of Data Needs

Acute-Duration Exposure.

Inorganic Arsenicals. There is only limited information on the effects of acute inhalation exposure to arsenic in humans, but the chief symptoms appear to be irritation of the respiratory and gastrointestinal tracts (Beckett et al. 1986; Bolla-Wilson and Bleecker 1987; Dunlap 1921; Ide and Bullough 1988; Morton and Caron 1989; Pinto and McGill 1953). Quantitative data are lacking, but effects generally appear to be mild even at high-exposure levels. On this basis, it seems that risks of acute effects are probably low for inhalation exposures in the environment or near waste sites. Research to obtain a quantitative acute inhalation NOAEL value that could be used to derive an acute inhalation MRL would, therefore, be useful but not critical. There are numerous case studies in humans on the acute oral toxicity of arsenic, and the main end points (gastrointestinal irritation, pancytopenia, hepatic injury, neuropathy) are well characterized (Armstrong et al. 1984; Fincher and Koerker 1987). An acute oral MRL of 0.005 mg As/kg/day was derived for inorganic arsenic based on a LOAEL for gastrointestinal symptoms and facial edema reported by Mizuta et al. (1956). Additional studies to define an acute oral NOAEL would be useful to reduce uncertainty in the MRL derivation. Acute dermal exposure is unlikely to cause serious systemic injury, but it can lead to contact dermatitis and skin sensitization (Holmqvist 1951; Pinto and McGill 1953). However, available data do not permit a quantitative estimate of the concentration of arsenic on the skin or in air, dust, soil, or water that causes these effects. Further research would be valuable to obtain a quantitative NOAEL for direct dermal effects, since humans may have dermal contact with contaminated soil or water near hazardous waste sites.

Organic Arsenicals. Information on the acute toxicity of organic arsenicals in humans is limited to reports of gastrointestinal irritation in individuals ingesting pesticides containing organic arsenicals (Lee et al. 1995; Shum et al. 1995); these case reports provide limited dosing information. Acute lethality and systemic toxicity data exist for several compounds by inhalation, oral, and dermal exposure of animals. Inhalation data are limited to a lethality study of rats and mice exposed to MMA or DMA that reported respiratory and ocular irritation (Stevens et al. 1979). The oral acute studies consist of lethality studies for MMA (Gur and Nyska 1990; Jaghabir et al. 1988; Kaise et al. 1989), DMA (Kaise et al. 1989), and roxarsone (Kerr et al. 1963; NTP 1989b), systemic toxicity studies (or longer-term studies reporting effects within the first 2 weeks of exposure) for MMA (Irvine et al. 2006), DMA (Ahmad et al. 1999a; Chernoff et al. 1990; Cohen et al. 2001; Crown et al. 1987; Irvine et al. 2006; Kavlock et al. 1985; Rogers et al. 1981; Zomber et al. 1989), or roxarsone (NTP 1989b). For MMA, the available data suggest that the gastrointestinal tract may be the most sensitive target of toxicity; however, the study identifying the lowest LOAEL (Irvine et al. 2006) involved bolus administration and this is not an appropriate exposure route to estimate human risk for gastrointestinal effects following environmental exposure to MMA. The available animal studies for DMA have examined urinary bladder (Cohen et al. 2001) and developmental toxicity (Chernoff et al. 1990, Irvine et al. 2006; Kavlock et al. 1985; Rogers et al. 1981). For DMA, acute-duration studies in rats suggest that the urinary bladder is the most sensitive target of toxicity in rats (Cohen et al. 2001); however, there is evidence from longer-term studies that rats may be more sensitive than humans and other species for bladder effects. Thus, rat data were not considered as the basis of an acute-duration oral MRL for DMA. Other effects observed following acute exposure to DMA include developmental and maternal effects in mice (Kavlock et al. 1985; Rogers et al. 1981) and rabbits (Irvine et al. 2006) and diarrhea and vomiting in dogs receiving a bolus dose of DMA (Zomber et al. 1989). An acute-duration oral MRL was not derived for DMA because it is not known if systemic effects would occur at lower doses than the developmental effects. For roxarsone, the available data suggest that the most sensitive effect following acute oral exposure is neuropathy observed in pigs (Kennedy et al. 1986; Rice et al. 1985). At the only dose tested in this study, tremors, clonic convulsions, and equivocal evidence of myelin degeneration were observed; these were considered serious effects and not suitable for the derivation of an acute-duration oral MRL for roxarsone. Additional studies are needed for MMA, DMA, and roxarsone that examine a variety of end points in several species; studies for roxarsone should also include examination of neurological end points, which would be useful for identifying the critical targets of toxicity and establishing dose-response relationships.

Intermediate-Duration Exposure.

Inorganic Arsenicals. Intermediate-duration inhalation exposure of humans to arsenic appears to result in respiratory tract irritation (occasionally including perforation of the nasal septum) and mild gastrointestinal tract irritation (Ide and Bullough 1988). Quantitative data are too limited (only one study, of one individual) to derive an intermediate-duration inhalation MRL. Further studies to define the NOAEL for intermediate-duration inhalation exposure of humans would be valuable, since humans could be exposed to arsenic-containing airborne dusts near smelters, chemical plants, or waste sites. Effects of intermediate-duration oral exposure are similar to those of acute oral exposure, but may also include development of vascular injury and a characteristic group of skin changes (Franzblau and Lilis 1989; Holland 1904; Wagner et al. 1979). Most studies indicate that these effects occur at doses of about 0.05 mg As/kg/day or higher, but the data do not provide a firm basis for identifying the intermediate-duration NOAEL. For this reason, no intermediate-duration oral MRL has been derived. Further studies to establish the NOAEL would be valuable, since humans could have intermediate-duration oral exposures to arsenic through ingestion of contaminated soil or water near smelters, chemical factories, or waste sites. Since dermal effects appear to be restricted to acute irritancy, intermediate-duration dermal studies are probably not essential.

Organic Arsenicals. No information was located on the intermediate-duration toxicity of organic arsenicals in humans. Several studies have examined the intermediate-duration oral toxicity of MMA; dietary exposure studies in rats and mice (Arnold et al. 2003) identify the gastrointestinal tract as the most sensitive target. Diarrhea and lesions in the cecum, colon, and rectum have been observed. The rat 13-week study (Arnold et al. 2003) was used as the basis of the MRL. Because rats appear to be more sensitive to the toxicity of DMA, rat studies were not considered for MRL derivation. The only non-rat study was a chronic-duration dog study reporting effects during the first 51 weeks of exposure (Zomber et al. 1989); these effects included diarrhea and vomiting. However, because DMA was administered via capsule, this study was not considered adequate for derivation of an MRL. Additional studies are needed for DMA to identify critical targets of toxicity and establish dose-response relationships in non-rat species. The available data for roxarsone suggest that neurotoxicity in pigs is the most sensitive end point. One of the two available neurotoxicity studies in pigs (Edmonds and Baker 1986) did not include sensitive tests of toxicity and was not considered for MRL derivation; the other study identified a serious LOAEL at the only dose tested and thus, was not suitable for MRL derivation. Several comprehensive studies examined the toxicity of roxarsone in rats and mice (NTP 1989b). Renal tubular damage in rats was the most sensitive end point (NTP 1989b); however, the LOAEL for this effect was 9 times higher

than the dose associated with neurotoxicity in pigs. Additional studies are needed to establish a no effect level for neurotoxicity in pigs, which could be used to derive an intermediate duration MRL for roxarsone. Further studies on the intermediate-duration inhalation and dermal toxicity of these compounds would be valuable, especially in humans, since people may be exposed to organic arsenicals during their manufacture or use, or from materials deposited in waste sites.

Chronic-Duration Exposure and Cancer.

Inorganic Arsenicals. The target tissues of chronic-duration exposure of humans to inorganic arsenic are the same as for intermediate-duration exposure for both the oral and inhalation routes. Effects of dermal exposure appear to be restricted to direct irritation of exposed surfaces. Therefore, chronic-duration studies are probably not essential for the dermal route. Quantitative data from one study identify an inhalation exposure level of about 0.1 mg As/m^3 as the LOAEL for skin changes (Perry et al. 1948), but because there are no additional supporting studies and a NOAEL is not clearly established, a chronic-duration inhalation MRL has not been derived. Additional studies in humans to define the chronic inhalation NOAEL for dermal or other effects would be valuable, since humans may be chronically exposed to arsenic dusts in air near smelters, chemical factories, or waste sites. Chronic oral exposure data from studies in humans indicate that the LOAEL for skin lesions and other effects is probably about 0.01–0.02 mg As/kg/day (10–20 µg As/kg/day), and that the NOAEL is probably between 0.0004 and 0.0009 mg As/kg/day (0.4–0.9 µg As/kg/day) (Cebrián et al. 1983; EPA 1981b; Hindmarsh et al. 1977; Tseng 1977; Tseng et al. 1968). The NOAEL of 0.0008 mg As/kg/day from the study by Tseng et al. (1968) is appropriate for derivation of a chronic-duration oral MRL, but an uncertainty factor of 3 was required to account for the fact that the population that constituted the no-effect group were relatively young (possibly decreasing the ability to detect dermal or other effects that increase in prevalence with age). Another issue that needs to be acknowledged, which is common to ecological studies and contributes to uncertainty, is the fact that individual doses were not available and were calculated from group mean arsenic concentrations in well water using estimated water intake parameters. For this reason, further epidemiological studies that do not rely on an ecological-based exposure assessment that would provide additional support for the threshold dose for arsenic in humans would be valuable.

There are numerous studies in humans that support the carcinogenic effects of inorganic arsenic from inhalation exposure (Enterline et al. 1987a, 1987b, 1995; Järup and Pershagen 1991; Järup et al. 1989; Lee-Feldstein 1986; Welch et al. 1982) and oral exposure (Chen et al. 1986, 1988b, 1992; Chiou et al. 1995; Ferreccio et al. 1996; Hsueh et al. 1995; Lander et al. 1975; Liu and Chen 1996; Lüchtrath 1983;

Smith et al. 1992; Tseng 1977; Tseng et al. 1968; Yu et al. 1992; Zaldívar 1974; Zaldívar et al. 1981). Quantitative slope factors have been derived for both routes. There is a noticeable absence, however, of 2-year animal carcinogenicity studies for either the inhalation or oral route of exposure (Chan and Huff 1997). In light of the ongoing controversy over the reasons for the absence of a carcinogenic effect in animals, it seems prudent to firmly establish a negative effect in a 2-year study. The carcinogenic effects of chronic dermal exposure to inorganic arsenicals have not been studied, but dermal exposure is a relatively minor route of exposure, and these studies would not be a top priority.

The mechanism of arsenic carcinogenicity is not known, although the current view is that it functions mainly as a promoter or cocarcinogen. Further studies on the mechanism of arsenic toxicity would be particularly valuable to improve our ability to evaluate human cancer risks from inhalation or oral exposures that might occur near waste sites. Also, mechanistic studies could help in the evaluation of cancer risks from organic derivatives (see below).

Organic Arsenicals. There is very little information on the chronic toxicity of organic arsenicals in humans. One study of workers exposed to arsanilic acid did not identify any adverse effects, but no systematic, clinical, or toxicological examinations of exposed people were performed (Watrous and McCaughey 1945). Chronic toxicity studies are available for rats, mice, and dogs exposed to MMA (Arnold et al. 2003; Waner and Nyska 1988), DMA (Arnold et al. 2006; Zomber et al. 1989), and roxarsone (NTP 1989b; Prier et al. 1963). Chronic exposure to MMA results in diarrhea in rats, mice, and dogs (Arnold et al. 2003; Waner and Nyska 1988) and an increase in progressive nephropathy in rats and mice (Arnold et al. 2003). The increased incidence of progressive nephropathy was used as the basis of the chronic-duration oral MRL for MMA. For DMA, chronic exposure also resulted in an increased incidence of diarrhea and vomiting in dogs (Zomber et al. 1989) and an increased incidence of vacuolization in the urinary bladder and progressive nephropathy in mice (Arnold et al. 2006). The vacuolization in the urinary bladder was used as the basis of a chronic-duration oral MRL for DMA. The available data for chronic-exposure to roxarsone were considered inadequate for derivation of an MRL. The highest doses tested in the rat, mouse, and dog studies (NTP 1989b; Prier et al. 1963) were NOAELs. Intermediate-duration studies identify neurotoxicity in pigs as the most sensitive end point; this has not been adequately examined following chronic exposure and studies are needed.

No information was located on carcinogenic effects of organic arsenicals in humans. The carcinogenic potential of MMA (Arnold et al. 2003), DMA (Arnold et al. 2006), and roxarsone (NTP 1989b) following oral exposure has been investigated in rats and mice. No evidence of carcinogenicity was observed

following oral exposure to MMA (Arnold et al. 2003) and equivocal evidence of carcinogenicity was found in male rats, with no evidence of carcinogenicity in female rats or in male or female mice orally exposed to roxarsone (NTP 1989b). Oral exposure to DMA resulted in an increased incidence of urinary bladder tumors in rats and no evidence of carcinogenicity in mice (Arnold et al. 2006). However, there is concern that the rat is not a good model to assess the carcinogenic potential of DMA in humans due to species differences in the toxicokinetic properties of DMA. No information was located on the carcinogenicity of organic arsenicals following inhalation or dermal exposure. Studies of humans exposed in the workplace would provide valuable information on the carcinogenic potential of organic arsenicals, particularly DMA. Studies on cancer risk following inhalation and dermal exposure to organic arsenicals are would be useful since these are possible routes of exposure for humans.

Genotoxicity.

Inorganic Arsenicals. There are several studies that suggest that inorganic arsenic may cause genotoxicity (mainly chromosomal effects) in exposed humans (Burgdorf et al. 1977; Nordenson et al. 1978), and this is supported by numerous studies in animals (Datta et al. 1986; DeKnudt et al. 1986; Nagymajtényi et al. 1985) and cultured cells (Beckman and Nordenson 1986; Casto et al. 1979; DiPaolo and Casto 1979; Lee et al. 1985; Nakamuro and Sayato 1981; Nishioka 1975; Oberly et al. 1982; Okui and Fujiwara 1986; Sweins 1983; Ulitzur and Barak 1988; Zanzoni and Jung 1980). The mechanism of genotoxicity is not known, but may be due to the ability of arsenite to interfere with DNA repair (Li and Rossman 1989) or to alter apoptosis (Pi et al. 2005) or the ability of arsenate to act as a phosphate analog. Further studies to improve our understanding of the mechanism of genotoxicity would be valuable, since this could aid in the understanding of arsenic-induced cancer risk.

Organic Arsenicals. For organic arsenicals, *in vitro* genotoxicity studies are available for arsenobetaine (Eguchi et al. 1997; Oya-Ohta et al. 1996), MMA (Chun and Killeen 1989a, 1989b, 1989c, 1989d; Eguchi et al. 1997; Oya-Ohta et al. 1996), DMA (Eguchi et al. 1997; Endo et al. 1992; Kato et al. 1994; Kawaguchi et al. 1996; Kitamura et al. 2002; Kuroda et al. 2004; Moore et al. 1997a; Oya-Ohta et al. 1996; Rasmussen and Menzel 1997; Rin et al. 1995; Tezuka et al. 1993; Ueda et al. 1997; Yamanaka et al. 1989b, 1993, 1995, 1997), and roxarsone (Matthews et al. 1993; NTP 1989b; Storer et al. 1996) and *in vivo* studies are available for DMA (Kashiwada et al. 1998; Yamanaka and Okada 1994; Yamanaka et al. 1989a, 1989b, 1993, 2001). The results of these studies suggest that DMA and roxarsone are clastogenic and can cause DNA strand breaks. Additional *in vivo* studies are needed to evaluate the genotoxic potential of MMA and roxarsone.

Reproductive Toxicity.

Inorganic Arsenicals. Several studies have examined reproductive function in populations living in Bangladesh or India exposed to high levels of arsenic in drinking water and found increases in spontaneous abortions/stillbirths or preterm births (Ahmad et al. 2001; von Ehrenstein et al. 2006); another study in U.S. women did not find an increase in adverse reproductive outcomes (Aschengrau et al. 1989). Available animal studies did not find evidence for reproductive effects following inhalation or oral exposure (Holson et al. 1999, 2000), except for a trend toward decreased pups per litter in mice in a 3-generation study (Schroeder and Mitchener 1971) that is consistent with embryolethality observed in developmental studies of inorganic arsenic. Studies on spermatogenesis and reproductive success in arsenic-exposed workers would be valuable in evaluating whether there are significant reproductive risks of arsenic in humans, and this could be further strengthened by studies including histopathological examination of reproductive tissues (which was not done in the existing studies) in animals.

Organic Arsenicals. No information was located on reproductive effects of organic arsenicals in humans and no inhalation or dermal exposure animal studies were located. Intermediate- and chronic-duration oral studies for MMA (Arnold et al. 2003), DMA (Arnold et al. 2006), and roxarsone (NTP 1989b) have not reported histological damage to reproductive tissues. Decreases in pregnancy rate and male fertility index were observed in a two-generation study in rats (Schroeder 1994) and a single generation study in mice (Prukop and Savage 1986) exposed to MMA; the poor reporting in the Prukop and Savage (1986) study limits its usefulness in assessing reproductive toxicity. However, in the two-generation study, the differences between control and exposed rats were not statistically different; the effect was considered biologically significant because effects observed in the exposed rats were outside the range found in historical controls. Another reproductive performance study to confirm these results would be useful. No reproductive effects were observed in a two generation study in rats exposed to DMA (Rubin et al. 1989).

Developmental Toxicity.

Inorganic Arsenicals. There are several epidemiological studies that suggest that inhalation (Ihrig et al. 1998; Nordström et al. 1978a, 1978b, 1979a, 1979b) or oral (Hopenhayn et al. 2003a; Yang et al. 2003) exposure to inorganic arsenic might increase the risk of low birth weight, congenital defects, or abortion in exposed women. These studies do not establish that arsenic was responsible, since all involved exposures to other chemicals or risk factors, but do suggest that additional studies on developmental

parameters in humans exposed to arsenic would be valuable in determining whether this is an effect of concern. Other human studies have not found significant associations between arsenic levels in drinking water and increased neonatal deaths or infant mortality (von Ehrenstein et al. 2006) or the increase in congenital heart defects (Zierler et al. 1988) or neural tube defects (Brender et al. 2006). Studies in animals support the view that oral, inhalation, and parenteral exposure to inorganic arsenic can all increase the incidence of fetotoxicity and teratogenicity, although this appears to occur only at doses that are toxic or even lethal to the dams (Baxley et al. 1981; Beaudoin 1974; Carpenter 1987; Ferm and Carpenter 1968; Ferm et al. 1971; Hanlon and Ferm 1986; Holson et al. 1999, 2000; Hood and Bishop 1972; Hood and Harrison 1982; Hood et al. 1978; Mason et al. 1989; Nagymajtényi et al. 1985; Nemec et al. 1998; Stump et al. 1999; Willhite 1981). There are also some data to suggest that it may increase the risk of transplacental cancer in humans (Smith et al. 2006) and animals (Waalkes et al. 2003). Thus, additional studies in animals may be useful in defining the mechanisms of these developmental effects and in identifying the time of maximum susceptibility of the fetus, but such studies probably will not help identify a safe exposure level for humans.

Organic Arsenicals. No information was located regarding developmental effects in humans after oral or inhalation exposure to organic arsenicals. Animal studies conducted in rats (Chernoff et al. 1990; Irvine et al. 2006; Rogers et al. 1981), mice (Kavlock et al. 1985; Rogers et al. 1981), and rabbits (Irvine et al. 2006) have examined the developmental toxicity of organic arsenicals. Decreases in fetal body weights and delays in ossification were commonly reported at maternally toxic (decreases in body weight gain) doses of DMA (Irvine et al. 2006; Kavlock et al. 1985; Rogers et al. 1981). However, one study found increases in the percentage of fetuses with irregular palatine rugae at DMA doses not associated with maternal toxicity (Rogers et al. 1981). This effect has not been reported in other studies and additional developmental studies are needed to confirm the finding. In view of the apparent differences in susceptibility between animals and humans, it would be valuable to investigate whether there are any measurable effects on development in humans exposed to organic arsenicals in the workplace or the environment.

Immunotoxicity.

Inorganic Arsenicals. No studies were located on immunotoxic effects in humans after oral exposure to inorganic arsenic. One inhalation study in humans (Bencko et al. 1988), an inhalation study in animals (Aranyi et al. 1985), one oral study in animals (Kerkvliet et al. 1980), and one intratracheal instillation study in animals (Sikorski et al. 1989) suggest that arsenic causes little or no functional impairment of the

immune system, but one inhalation study in animals found decreased pulmonary bactericidal activity and increased susceptibility to streptococcal infection in exposed mice (Aranyi et al. 1985). Additional studies (both in humans and animals) would be valuable to investigate this end point further. Dermal exposure of humans to high levels of arsenic dusts may cause dermal sensitization (Holmqvist 1951), but the dose and time dependence of this phenomenon are not known. Studies to determine whether dermal sensitization occurs in people with low level dermal exposures to arsenic in dust or soil, such as might occur for residents near an arsenic-containing waste site, would be valuable in assessing the significance of this effect to nonoccupationally exposed populations.

Organic Arsenicals. No information was located on the effect of organic arsenicals exposure in humans or animals on immune function. Since there are suggestions that inorganic arsenic may cause some changes in the immune system, studies on possible immune effects of the common organic arsenicals might be helpful.

Neurotoxicity.

Inorganic Arsenicals. There is convincing evidence from studies in humans that inorganic arsenic can cause serious neurological effects, both after inhalation (Beckett et al. 1986; Bencko et al. 1977; Blom et al. 1985; Buchancová et al. 1998; Calderón et al. 2001; Danan et al. 1984; Feldman et al. 1979; Gerr et al. 2000; Lagerkvist and Zetterlund 1994; Morton and Caron 1989) and oral exposure (Armstrong et al. 1984; Bartolome et al. 1999; Chakraborti et al. 2003a, 2003b; Civantos et al. 1995; Cullen et al. 1995; Danan et al. 1984; EPA 1977a; Feldman et al. 1979; Fincher and Foy et al. 1992; Franzblau and Lilis 1989; Guha Mazumder et al. 1988; Hindmarsh et al. 1977; Huang et al. 1985; Fincher and Koerker 1987; Levin-Scherz et al. 1987; Lewis et al. 1999; Mizuta et al. 1956; Muzi et al. 2001; Quatrehomme et al. 1992; Silver and Wainman 1952; Szuler et al. 1979; Tsai et al. 2003; Uede and Furukawa 2003; Vantroyen et al. 2004; Wagner et al. 1979). This is based mainly on clinical observations and neurological examinations of exposed persons. Available studies provide a reasonable estimate of LOAEL and NOAEL values by the oral route, but similar data are lacking for the inhalation route. Further studies designed to identify the threshold for neurological effects in humans exposed by the inhalation route would be valuable, since humans may be exposed to arsenic dusts in air from smelters, chemical factories, or waste sites. Adult animals appear to be much less susceptible than humans to the neurological effects of inorganic arsenic, so studies in adult animals would probably not help in estimation of a safe exposure limit. However, in light of recent findings of possible associations between arsenic in drinking water and neurobehavioral alterations in children (Tsai et al. 2003; von Ehrenstein et

al. 2007; Wang et al. 2007; Wasserman et al. 2004, 2007), studies in animals, in which confounding can be eliminated, may be warranted.

Organic Arsenicals. Information on neurological effects of organic arsenicals in humans is limited to an occupational study that did not find increases in the frequency of central or peripheral nervous system complaints (Watrous and McCaughey 1945) and a case report of a women of a women reporting numbness and tingling of the fingertips, toes, and circomoral region who was exposed to organic arsenic in soup (Luong and Nguyen 1999). Neurological effects have also been observed in some animal studies. Decreases spontaneous motility, ataxia, and increased startle response were observed in mice exposed to a single high dose of DMA (Kaise et al. 1989). Degeneration of myelin and axons were observed in several studies involving oral exposure of pigs to roxarsone (Edmonds and Baker 1986; Kennedy et al. 1986; Rice et al. 1985). Hyperexcitability, ataxia, and trembling have also been observed in rats and mice orally exposed to roxarsone (Kerr et al. 1963; NTP 1989b). These findings suggest that more extensive investigations of the neurotoxic potential of roxarsone and other organic arsenicals would be valuable to determine the potential human health risk from these compounds, since humans could be exposed during the manufacture or use of these compounds, or near waste sites where they have been deposited.

Epidemiological and Human Dosimetry Studies. Numerous epidemiologic studies of humans exposed to inorganic arsenic by the oral and inhalation routes constitute the database on arsenic-related cancer and noncancer human health effects. As with virtually all epidemiologic investigations, these studies are limited by possible confounding from factors such as smoking, exposure to other chemicals, and differences in population characteristics (e.g., nutritional state, metabolism, and toxicokinetics) that inhibit extrapolation of study results to a wider population. Moreover, many of these studies lack good dose estimates for study participants. Some studies lack quantitative data altogether. For this reason, improved data on confounding factors and improved methods of human dosimetry would be valuable in any further human epidemiologic studies of arsenic, either in the workplace or in the general environment. Recent work has broadened the qualitative dose-response information beyond the highly exposed Taiwanese population, but additional studies of persons with lower exposure levels would be especially valuable for risk assessments for the U.S. population. From a public health standpoint, well designed studies of common noncancer health outcomes (e.g., cardiovascular disease and diabetes) could be more important than additional studies of cancer. Availability of methods for biomonitoring of exposure are discussed below.

Biomarkers of Exposure and Effect.

Exposure. There are sensitive and specific methods for measuring arsenic in blood, urine, hair, nails, and other tissues, and this is the approach normally employed for measuring arsenic exposure in humans. Usually total arsenic is measured, but methods are available for measuring inorganic arsenic and each of the organic derivatives separately. Urinary levels are generally considered to be the most reliable indication of recent exposures (Enterline et al. 1987a; Milham and Strong 1974; Pinto et al. 1976; Polissar et al. 1990), but if a high urinary level is present, care must be taken to account for the presence of nontoxic forms of arsenic from the diet. Blood levels are sometimes used to evaluate the status of acutely poisoned individuals (Driesback 1980; Heydorn 1970; Hindmarsh and McCurdy 1986; Valentine et al. 1979, 1981), but this approach is not generally useful for biomonitoring of long-term exposure to low levels. Hair and nails provide a valuable indication of exposures that occurred 1–10 months earlier (Agahian et al. 1990; Bencko et al. 1986; Choucair and Ajax 1988; EPA 1977a, 1981b; Milham and Strong 1974; Valentine et al. 1979; Yamauchi et al. 1989), although care must be taken to exclude external contamination of these samples. Cumulative urinary arsenic levels may be used to derive a quantitative estimate of exposure (Enterline et al. 1987a; Pinto et al. 1976), but data on the quantitative relation between exposure and arsenic levels in nails and hair were not located. Efforts to establish an algorithm for estimating past exposure levels from hair or nail levels would be valuable in quantifying average long-term exposure levels in people where repeated urinary monitoring is not feasible.

Effect. The effects of arsenic are mainly nonspecific, but the combined presence of several of the most characteristic clinical signs (e.g., nausea, diarrhea, peripheral neuropathy, anemia, vascular lesions, hyperkeratinization, hyperpigmentation) is usually adequate to suggest arsenic intoxication. Although there are standard clinical methods for detecting and evaluating each of these effects, there are no recognized methods for identifying early (preclinical) effects in exposed persons. Neurophysiological measurements of nerve conduction velocity or amplitude have been investigated (Goebel et al. 1990; Jenkins 1966; Le Quesne and McLeod 1977; Morton and Caron 1989; Murphy et al. 1981), but at present, this approach does not seem to offer much advantage over a standard neurological examination. Changes in urinary excretion levels of several heme-related metabolites appear to be a good indication of preclinical effects of arsenic toxicity in animals (Albores et al. 1989; Sardana et al. 1981; Woods and Fowler 1978; Woods and Southern 1989), but this has not been established in humans and is not specific for arsenic-induced effects. Further efforts to develop these approaches and to identify other more specific biochemical or physiological indicators of arsenic-induced effects would be very valuable in monitoring the health of persons exposed to low levels of arsenic in the environment or near waste sites.

Absorption, Distribution, Metabolism, and Excretion. Available data from toxicokinetic studies in humans reveal that arsenates and arsenites are well absorbed following both oral and inhalation exposure. Data on distribution are limited, but it appears that arsenic is transported to nearly all tissues. Metabolism involves mainly reduction-oxidation reactions that interconvert As(+5) and As(+3) and methylation of As(+3) to yield MMA and DMA. Most arsenic is rapidly excreted in the urine as a mixture of inorganic arsenics, MMA, and DMA, although some may remain bound in tissues (especially skin, hair, and fingernails). These findings are strongly supported by numerous studies in animals. Because methylation represents a detoxification pathway, an area of special interest is the capacity of the human body to methylate inorganic arsenic. Limited data suggest that the methylation system might begin to become saturated at intakes of about 0.2–1 mg As/day (Buchet et al. 1981b; Marcus and Rispin 1988), but this is uncertain. Further studies to define the rate and saturation kinetics of whole-body methylation in humans would be especially helpful in evaluating human health risk from the low levels of arsenic intake that are usually encountered in the environment. Along the same line, further studies to determine the nature and magnitude of individual variations in methylation capacity and how this depends on diet, age, and other factors would be very useful in understanding and predicting which members of a population are likely to be most susceptible.

The toxicokinetics of dermal exposure have not been studied. It is usually considered that dermal uptake of arsenates and arsenites is sufficiently slow that this route is unlikely to be of health concern (except that due to direct irritation), but studies to test the validity of this assumption would be valuable. Also, dermal uptake of organic arsenicals could be of concern, and quantitative data on the rate and extent of this would be helpful in evaluating risks from application of arsenical pesticides or exposures to organic arsenicals in waste sites.

Comparative Toxicokinetics. Available toxicity data indicate that arsenic causes many of the same effects in animals that are observed in humans, but that animals are significantly less sensitive. The basis for this difference in susceptibility is not certain but is probably mainly a result of differences in absorption, distribution, metabolism, or excretion. For example, rats strongly retain arsenic in red blood cells (Lanz et al. 1950), while humans (and most other species) do not. Similarly, marmoset monkeys do not methylate inorganic arsenic (Vahter and Marafante 1985; Vahter et al. 1982), while humans and other animal species do. Because of these clear differences in toxicity and toxicokinetics between species, further comparative toxicokinetic studies that focus on the mechanistic basis for these differences would be very valuable. At a minimum, this would help clarify which laboratory species are the most useful

models for humans and could ultimately lead to development of a PBPK model that would permit reliable extrapolation of observations across species.

Methods for Reducing Toxic Effects. There are a number of general methods for reducing the absorption of arsenic in the gastrointestinal tract and skin, but there are currently no methods for reducing the absorption of arsenic from the lungs. The removal of arsenic from the gastrointestinal tract is usually facilitated by the use of emetics, cathartics, lavages, or activated charcoal (Agency for Toxic Substances and Disease Registry 1990a; Aposhian and Aposhian 1989; Campbell and Alvarez 1989; Driesback 1980; Ellenhorn and Barceloux 1988; EPA 1989e; Haddad and Winchester 1990; Mitra et al. 2004; Stutz and Janusz 1988). Studies that investigate the effects of phosphate-binding chemicals (aluminum hydroxide) and nonabsorbable sulfhydryl compounds on the absorption of pentavalent and trivalent arsenic, respectively, may be useful in developing treatments that are more specific to arsenic intoxication. Once arsenic is in the body, treatment usually involves the use of one or more chelators, such as BAL or penicillamine. However, these agents often exhibit adverse side effects (Agency for Toxic Substances and Disease Registry 1990a; Ellenhorn and Barceloux 1988), and are generally only applied following high-dose acute exposure. Further studies investigating the efficacy of less toxic arsenic chelators, such as DMSA, DMPA, DMPS, and N-acetyl cysteine, may lead to the development of safer treatment methods. Studies on the efficacy of chelators and agents to enhance methylation and elimination in treatment of chronic arsenic exposure would also be helpful, as available treatment methods for chronic arsenic exposure are limited. Trivalent arsenic is generally believed to exert toxic effects by binding to the vicinal sulfhydryl group of key enzymes, thereby interfering with a number of biological processes, such as gluconeogenesis and DNA repair (Li and Rossman 1989; Szinicz and Forth 1988). Since pentavalent arsenic may need to be reduced in the body to the trivalent state before it can exert toxic effects, studies that investigate methods for blocking this conversion may lead to a method for interfering with the mechanism of action for pentavalent arsenic. The insufficient intake of calcium, animal protein, folate, selenium, and fiber may enhance the toxic effects of inorganic arsenic (Mitra et al. 2004), but it is not known if dietary supplementation will prove effective in patients who already show arsenic-induced symptoms.

Children's Susceptibility. Data needs relating to both prenatal and childhood exposures, and developmental effects expressed either prenatally or during childhood, are discussed in detail in the Developmental Toxicity subsection above.

A majority of the data on the effects of exposure of humans to arsenic has focused on adults. Although a few studies of acute poisoning and chronic exposure specifically describe children (Borgoño et al. 1980; Concha et al. 1998a, 1998b, 1999; Foy et al. 1992; Kersjes et al. 1987; Rosenberg 1974; Zaldívar 1974; Zaldívar and Guillier 1977), in general, data are lacking. Specifically, although there is a substantial database on the effect of arsenic on animal development, there are few data describing developmental effects in humans. Additional research in this area, using populations in areas of endemic arsenic exposure, would be useful.

Although there is no reason to suspect that the pharmacokinetics of arsenic differs in children and adults, there are few data available on this topic. Research on absorption, distribution, metabolism, and excretion in children would aid in determining if children are at an increased risk, especially in areas where chronic exposure to an environmental source occurs. With regard to exposure during development, additional research on maternal kinetics, and transfer via breast milk would be useful in obtaining a more complete picture of prenatal and neonatal development, especially with regard to neural development and the possible development of childhood cancer.

Child health data needs relating to exposure are discussed in Section 6.8.1, Identification of Data Needs: Exposures of Children.

3.12.3 Ongoing Studies

A number of researchers are continuing to investigate the toxicity and toxicokinetics of arsenic. Table 3-18 summarizes studies being sponsored by agencies of the U.S. federal government (FEDRIP 2007). Additional research is being sponsored by industry groups and other agencies, and research is also ongoing in a number of foreign countries.

Table 3-18. Ongoing Studies on Health Effects of Arsenic, Federally Funded

Investigator	Affiliation	Title	Sponsor
Ahsan, H	Columbia University, New York, New York	Chemoprevention of arsenic-induced skin cancer	NCI
Ahsan, H	Columbia University, New York, New York	Genetic susceptibility to arsenic-induced skin cancer	NCI
Andrew, A	Darmouth College, Hanover, New Hampshire	Bladder cancer prognostic indicators	NCI
Beckman, K	Children's Hospital and Research Center, Oakland, California	Fetal arsenic-nutrient interaction in adult-onset cancer	NIEHS
Bodwell, J	Darmouth College, Hanover, New Hampshire	Arsenic effects on glucocorticoid receptor action	NIEHS
Calderon, R	EPA, Research Triangle Park, North Carolina	Arsenic-induced skin conditions identified in Southwest United States	HEERL
Christiani, D	Harvard University, Boston, Massachusetts	Arsenic and health in Bangladesh	NIEHS
Dong, Z	University of Minnesota, Minneapolis, Minnesota	Molecular basis of arsenic-induced cell transformation	NCI
Finnell, R	Texas A & M University College Station, Texas	Sensitive genotypes to arsenic as a model environmental toxicant	NIEHS
Frenkel, K	New York University, New York, New York	Metal induced inflammatory factors, oxidative stress, and suppression	NIEHS
Futscher, B	University of Arizona, Tucson, Arizona	Epigenetic remodeling by environmental arsenicals	NCI
Gamble, M	Columbia University, New York, New York	Nutritional influences on arsenic toxicity	NIEHS
Germolec, D	NIH, Research Triangle Park, North Carolina	The role of growth factors and inflammatory mediators in arsenic-induced dermatotoxicity	NIEHS
Guallar, E	Johns Hopkins University, Baltimore, Maryland	Mercury, arsenic, and carotid atherosclerosis	NIEHS
He, K	Northwestern University, Chicago, Illinois	Trace elements and CVD risks factors among young adults	NHLBI
Hei, T	Columbia University, New York, New York	Mechanisms of arsenic carcinogenesis	NIEHS
Huang, C	New York University, New York, New York	Effects of arsenic on PI-3K signaling pathway	NCI
Hudgens, E	EPA, Research Triangle Park, North Carolina	Study of individuals chronically exposed to arsenic in drinking water	HEERL
Hughes, M	EPA, Research Triangle Park, North Carolina	Biomarkers of exposure: a case study with inorganic arsenic	HEERL
Hughes, M	EPA, Research Triangle Park, North Carolina	Tissue dosimetry, metabolism, and excretion of pentavalent arsenic	HEERL
Jing, Y	New York University, New York, New York	Arsenic trioxide and acute myeloid leukemia	NCI

Table 3-18. Ongoing Studies on Health Effects of Arsenic, Federally Funded

Investigator	Affiliation	Title	Sponsor
Jung, M	Georgetown University, Washington, DC	Epigenetic regulation by poly(ADP-ribose) in response to arsenite	NIEHS
Karin, M	University of California San Diego, La Jolla, California	Interaction of heavy metal ions with the human genome	NIEHS
Kelsey, K	Harvard University, Boston, Massachusetts	Arsenic mode of action in cancer—models of epigenetic mechanism	NIEHS
Liu, K	University of New Mexico, Albuquerque, New Mexico	Oxidative mechanisms of arsenic-induced carcinogenesis	NIEHS
Markowski, V	University of Southern Maine, Portland, Maine	Developmental arsenic exposure produces cognitive impairment	NIEHS
Martin, M	Georgetown University, Washington, DC	Arsenic and epigenetic regulation of gene expression	NIEHS
Muscarella, D	Cornell University Ithaca, Ithaca, New York	Arsenite effects on CD40 signaling and B-cell apoptosis	NIEHS
Nichols, R	Dartmouth College, Hanover, New Hampshire	Effect of arsenic on cytochrome P450	NIEHS
Nriagu, J	University of Michigan, Ann Harbor, Michigan	Arsenic exposure and bladder cancer in Michigan	NCI
Rosen, B	Wayne State University, Detroit, Michigan	Mechanisms of arsenical transport	NIGMS
Rosen, B	Wayne State University, Detroit, Michigan	Metal binding domains in metallo-regulatory proteins	NIAID
Rosenblatt, A	University of Miami, Coral Gables, Florida	Environmental arsenic and androgen receptor regulation	NIEHS
Rossman, T	New York University, New York, New York	Investigation and genetic analysis of the human arsenite efflux pump	NIEHS
Schwartz, J	Harvard University, Boston Massachusetts	Epigenetic effects of particles and metals on cardiac health of an aging cohort	NIEHS
Self, W	University of Central Florida, Orlando, Florida	Impact of arsenicals on selenoprotein synthesis	NIEHS
Sens, D	University of North Dakota, Grand Forks, North Dakota	Metallothionein isoform-3 urinary marker bladder cancer	NIEHS
Sheldon, L	Dartmouth College, Hanover, New Hampshire	Arsenic, histone modification, and transcription	NIEHS
Shi, X	University of Kentucky, Lexington, Kentucky	Mechanism of arsenic-induced carcinogenesis	NCI
Smith, A	University of California, Berkeley, California	Arsenic biomarker epidemiology	NIEHS
Spallholz, J	Texas Tech University, Lubbock, Texas	Selenium against arsenic toxicity and skin lesions	NCI
States, C	University of Louisville, Louisville, Kentucky	Arsenic induced miotic arrest associated apoptosis	NIEHS
Styblo, M	University of North Carolina, Chapel Hill, North Carolina	Metabolism and toxicity of arsenic in human liver	NIEHS

Table 3-18. Ongoing Studies on Health Effects of Arsenic, Federally Funded

Investigator	Affiliation	Title	Sponsor
Taylor, P	Division of Cancer Epidemiology and Genetics, NCI, Bethesda, Maryland	Biologic specimen bank for early lung cancer markers in Chinese tin miners	NCI
Taylor, B	University of Louisville, Louisville, Kentucky	Arsenite inhibition of mitotic progression	NIEHS
Vaillancourt, R	University of Arizona, Tucson, Arizona	Modulation of Prostaglandins by Arsenic	NIEHS
Willett, W	Harvard University, Boston, Massachusetts	Prospective studies of diet and cancer in men and women	NCI
Wright, R	Brigham and Women's Hospital, Boston, Massachusetts	Metal mixtures and neurondevelopment	NIEHS
Zhang, D	University of Arizona, Tucson, Arizona	The protective role of Nrf2 in arsenic-induced toxicity and carcinogenicity	NIEHS

EPA = Environmental Protection Agency; NHEERL = National Health and Environmental Effects Research Laboratory; NCI = National Cancer Institute; NHLBI = National Heart, Lung, and Blood Institute; NIEHS = National Institute of Environmental Health Sciences; NIAID= National Institute of Allergy and Infectious Diseases; NIGMS = National Institute of General Medical Sciences; NIH = National Institute of Health

Source: FEDRIP 2007

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4. CHEMICAL AND PHYSICAL INFORMATION

4.1 CHEMICAL IDENTITY

Information regarding the chemical identity of arsenic and some common inorganic and organic arsenic compounds are located in Tables 4-1 and 4-2, respectively.

4.2 PHYSICAL AND CHEMICAL PROPERTIES

Information regarding the physical and chemical properties of arsenic and some common inorganic and organic arsenic compounds is located in Tables 4-3 and 4-4, respectively.

Arsenic appears in Group 15 (V) of the periodic table, below nitrogen and phosphorus. Arsenic is classified chemically as a metalloid, having both properties of a metal and a nonmetal; however, it is frequently referred to as a metal. Elemental arsenic, which is also referred to as metallic arsenic, (As(0)) normally occurs as the α-crystalline metallic form, which is a steel gray and brittle solid. The β-form is a dark gray amorphous solid. Other allotropic forms of arsenic may also exist. In compounds, arsenic typically exists in one of three oxidation states, -3, +3, and +5 (Carapella 1992). Arsenic compounds can be categorized as inorganic, compounds without an arsenic-carbon bond, and organic, compounds with an arsenic-carbon bond.

Table 4-1. Chemical Identity of Arsenic and Selected Inorganic Arsenic Compounds[a]

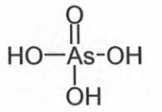
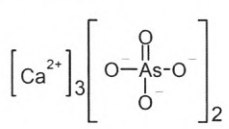
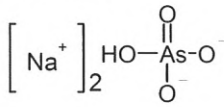
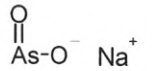
Characteristic	Arsenic	Arsenic acid	Arsenic pentoxide	Arsenic trioxide
Synonym(s)	Arsenic black; colloidal arsenic; gray arsenic, metallic arsenic	Orthoarsenic acid	Arsenic(V) oxide; arsenic acid anhydride; diarsenic pentoxide	Arsenic(III) oxide; arsenious acid; arsenious oxide; white arsenic
Registered trade name(s)	No data	Zotox; Hi-Yield Desiccant H-10; Desiccant L-10; Crab Grass Killer	No data	White Arsenic; Arsenicum Album
Chemical formula	As	H_3AsO_4	As_2O_5	As_2O_3
Chemical structure	As		$[As^{5+}]_2\,[O^{2-}]_5$	$[As^{3+}]_2\,[O^{2-}]_3$
Identification numbers:				
CAS registry	7440-38-2	7778-39-4	1303-28-2	1327-53-3
NIOSH RTECS[b]	CG0525000	CG0700000	CG2275000	CG3325000
EPA hazardous waste	D004	D004, P010	D004, P011	D004, P012
OHM/TADS	No data	No data	No data	No data
DOT/UN/NA/IMDG shipping	UN1558/IMDG 6.1	UN1553 (liquid)/ UN1554 (solid)/ IMDG 6.1 (liquid and solid)	UN1559/IMDG 6.1	UN1561/ IMDG 6.1
HSDB	509	431	429	419
EINECS	231-148-6	231-901-9	215-116-9	215-481-4
NCI	No data	No data	No data	No data

Table 4-1. Chemical Identity of Arsenic and Selected Inorganic Arsenic Compounds[a]

Characteristic	Calcium arsenate	Gallium arsenide	Sodium arsenate	Sodium arsenite
Synonym(s)	Calcium ortho-arsenate; arsenic acid, calcium salt	Gallium mono-arsenide	Disodium arsenate, dibasic; disodium hydrogen arsenate; arsenic acid, disodium salt	Arsenenous acid, sodium salt; sodium meta-arsenite
Registered trade name(s)	Pencal; Security; Turf-Cal; Chip-Cal; SPRA-Cal	No data	No data	Atlas "A"; Penite; Kill-All; Chem-Sen 56; Chem Pels C; Progalumnol Double
Chemical formula	$Ca_3(AsO_4)_2$	GaAs	Na_2HAsO_4	$NaAsO_2$
Chemical structure		Ga:As		
Identification numbers:				
CAS registry	7778-44-1	1303-00-0	7778-43-0	7784-46-5
NIOSH RTECS[b]	CG0830000	LW8800000	CG0875000	CG3675000
EPA hazardous waste	D004	D004	D004	D004
OHM/TADS	No data	No data	No data	7800057
DOT/UN/NA/IMDG shipping	UN1573/IMDG 6.1	UN 2803; Gallium/ IMDG 8.0; Gallium	UN 1685/IMDG 6.1	UN1686 (aqueous solution)/UN2027 (solid)/IMDG 6.1
HSDB	1433	4376	1675	693
EINECS	233-287-8	215-114-8	231-902-4	232-070-5
NCI	No data	No data	No data	No data

[a]All information obtained from HSDB 2007 and CHEMIDplus 2007, except where noted.
[b]RTECS 2007

CAS = Chemical Abstracts Service; DOT/UN/NA/IMDG = Department of Transportation/United Nations/North America/Intergovernmental Maritime Dangerous Goods Code; EINECS = European Inventory of Existing Chemical Substances; EPA = Environmental Protection Agency; HSDB = Hazardous Substances Data Bank; NCI = National Cancer Institute; NIOSH = National Institute for Occupational Safety and Health; OHM/TADS = Oil and Hazardous Materials/Technical Assistance Data System; RTECS = Registry of Toxic Effects of Chemical Substances

Table 4-2. Chemical Identity of Selected Organic Arsenic Compounds[a]

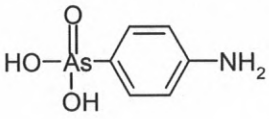
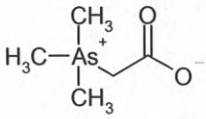
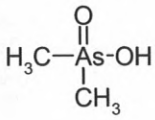
Characteristic	Arsanilic acid	Arsenobetaine	Dimethylarsinic acid
Synonym(s)	(4-Aminophenyl)arsonic acid; antoxylic acid; atoxylic acid, Pro-Gen	Arsonium, (carboxymethyl)-trimethyl-, hydroxide, inner salt	Cacodylic acid; hydroxydimethyl-arsine oxide; DMA; DMAA
Registered trade name(s)	No data	No data	510; Arsan; Phytar 560; Rad-E-Cate 35
Chemical formula	$C_6H_8AsNO_3$	$C_5H_{11}AsO_2$	$C_2H_7AsO_2$
Chemical structure			
Identification numbers:			
CAS registry	98-50-0	64436-13-1	75-60-5
NIOSH RTECS[b]	CF7875000	CH9750000	CH7525000
EPA hazardous waste	D004	No data	U136/D004
OHM/TADS	No data	No data	No data
DOT/UN/NA/IMDG shipping	No data	No data	UN1572/IMDG 6.1
HSDB	432	No data	360
EINECS	202-674-3	No data	200-883-4
NCI	No data	No data	No data

Table 4-2. Chemical Identity of Selected Organic Arsenic Compounds[a]

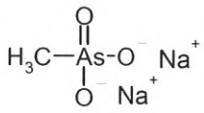
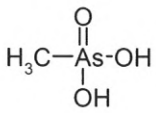
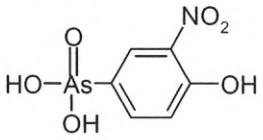
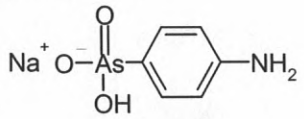
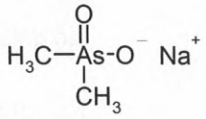
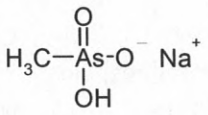
Characteristic	Disodium methane-arsonate	Methanearsonic acid	3-Nitro-4-hydroxy-phenyl-arsonic acid
Synonym(s)	DSMA; disodium monomethane arsonate	Arsonic acid, methyl-; monomethylarsonic acid	Roxarsone; 3-nitro-4-hydroxyphenylarsonic acid; 3-Nitro-10
Registered trade name(s)	Ansar 8100; Arrhenal; Ansar DSMA Liquid; Dinate; Crab-E-Rad; Chipco Crab Kleen; Arsinyl; Sodar; Methar; Drexel DSMA Liquid; Di-Tac; Ansar 184; Weed-E-Rad; Versar DSMA-LQ; Calar-E-Rad; Dal-E-Rad; Jon-Trol; Namate	No data	No data
Chemical formula	$CH_3AsO_3Na_2$	CH_5AsO_3	$C_6H_6AsNO_6$
Chemical structure			
Identification numbers:			
CAS registry	144-21-8	124-58-3	121-19-7
NIOSH RTECS[b]	PA2275000	PA1575000	CY5250000
EPA hazardous waste	D004	D004	D004
OHM/TADS	No data	No data	No data
DOT/UN/NA/IMDG shipping	No data	No data	No data
HSDB	1701	845	4296
EINECS	205-620-7	204-705-6	204-453-7
NCI	No data	No data	C5608

Table 4-2. Chemical Identity of Selected Organic Arsenic Compounds[a]

Characteristic	Sodium arsanilate	Sodium dimethylarsinate	Sodium methanearsonate
Synonym(s)	(4-Aminophenyl)arsonic acid sodium salt; arsanilic acid sodium salt; arsamin; atoxyl; soamin; trypoxyl	Sodium cacodylate; cacodylic acid, sodium salt; sodium dimethylarsonate	Arsonic acid, methyl-, monosodium salt; monosodium acid metharsonate; MSMA
Registered trade name(s)	No data	Ansar 160; Ansar 560; Bolls-Eye; Chemaid; Phytar 560, component of (with 012501); Rad-E-Cate 25.	Ansar 529; Ansar 170; Target MSMA; Phyban H.C.; Deconate; Mesamate; Bueno; Monate Merge 823; Dal-E-Rad; Weed-S-Rad; Arsanote liquid; Silvisar 550.
Chemical formula	$C_6H_7AsNO_3Na$	$C_2H_6AsO_2Na$	CH_4AsO_3Na
Chemical structure			
Identification numbers:			
CAS registry	127-85-5	124-65-2	2163-80-6
NIOSH RTECS[b]	CF9625000	CH7700000	PA2625000
EPA hazardous waste	D004	D004	D004
OHM/TADS	No data	No data	No data
DOT/UN/NA/IMDG shipping	UN2473/IMDG 6.1	UN1688/IMDG 6.1	No data
HSDB	5189	731	754
EINECS	204-869-9	204-708-2	218-495-9
NCI	C61176	No data	C60071

[a]All information obtained from HSDB 2007 and CHEMIDplus 2007, except where noted.
[b]RTECS 2007

CAS = Chemical Abstracts Service; DOT/UN/NA/IMDG = Dept. of Transportation/United Nations/North America/Intergovernmental Maritime Dangerous Goods Code; EINECS = European Inventory of Existing Chemical Substances; EPA = Environmental Protection Agency; HSDB = Hazardous Substances Data Bank; NCI = National Cancer Institute; NIOSH = National Institute for Occupational Safety and Health; OHM/TADS = Oil and Hazardous Materials/Technical Assistance Data System; RTECS = Registry of Toxic Effects of Chemical Substances

Table 4-3. Physical and Chemical Properties of Arsenic and Selected Inorganic Arsenic Compounds[a]

Property	Arsenic	Arsenic acid	Arsenic pentoxide	Arsenic trioxide
Molecular weight	74.9216	141.944	229.840	197.841
Color	Silver-gray or tin-white	White[b]	White	White
Physical state	Solid	Solid[b]	Solid	Solid
Melting point	817 °C (triple point)	35 °C	Decomposes at ~300 °C	313 °C (claudetite) 274 °C (arsenolite)
Boiling point	614 °C sublimes	Loses H_2O at 160 °C [b]	No data	460 °C
Density	5.778 g/cm^3 at 25 °C	~2.2 g/cm^3	4.32 g/cm^3	3.865 g/cm^3 (cubes) 4.15 g/cm^3 (rhombic crystals)
Odor	Odorless	No data	No data	Odorless
Odor threshold:				
Water	No data	No data	No data	No data
Air	No data	No data	No data	No data
Solubility:				
Water	Insoluble	302 g/L at 12.5 °C[b]	2,300 g/L at 20 °C	17 g/L at 16 °C
Organic solvent(s)	No data	Soluble in alcohol, glycerol[b]	Soluble in alcohol	Practically insoluble in alcohol, chloroform, ether; soluble in glycerol
Other	Insoluble in caustic and nonoxidizing acids	No data	Soluble in acid, alkali	Soluble in dilute hydrochloric acid, alkali hydroxide, carbonate solution
Partition coefficients:				
Log K_{ow}	No data	No data	No data	No data
Log K_{oc}	No data	No data	No data	No data
pK_a	No data	pK_{a1}=2.22; pK_{a2}=6.98 pK_{a3}=11.53[c]	No data	No data
Vapor pressure	7.5x10^{-3} mmHg at 280 °C	No data	No data	2.47x10^{-4} mmHg at 25 °C
Autoignition temperature	No data	No data	No data	Not flammable
Flashpoint	No data	No data	No data	No data
Flammability limits in air	No data	No data	No data	No data
Conversion factors	No data	No data	No data	No data
Explosive limits	No data	No data	No data	No data

Table 4-3. Physical and Chemical Properties of Arsenic and Selected Inorganic Arsenic Compounds[a]

Property	Calcium arsenate	Gallium arsenide	Disodium arsenate	Sodium arsenite
Molecular weight	398.072	144.64	185.91	130.92
Color	Colorless	Dark gray	Colorless[d]	White to gray-white
Physical state	Solid	Solid	Solid[d]	Solid
Melting point	Decomposes on heating	1,238 °C	57 °C[d]	No data
Boiling point	No data	No data	No data	No data
Density	3.620 g/cm^3	5.3176 g/cm^3 at 25 °C	1.87 g/cm[d]	1.87 g/cm^3
Odor	Odorless	Garlic odor	Odorless[d]	No data
Odor threshold:				
Water	No data	No data	No data	No data
Air	No data	No data	No data	No data
Solubility:				
Water	0.13 g/L at 25 °C	<1 mg/mL at 20 °C	Soluble 1:3 parts in water[d]	Freely soluble in water
Organic solvents	Insoluble	<1 mg/mg dimethyl sulfoxide, ethanol, methanol, acetone	Slightly soluble in alcohol; soluble in glycerol[d]	Slightly soluble in alcohol
Other	Soluble in dilute acids	Soluble in hydrochloric acid	Slightly soluble in alkaline solution[d]	No data
Partition coefficients:				
Log K_{ow}	No data	No data	No data	No data
Log K_{oc}	No data	No data	No data	No data
pK_a	No data	No data		
Vapor pressure	~0 mmHg at 20 °C	No data	No data	No data
Autoignition temperature	Not combustible	No data	No data	Not combustible
Flashpoint	No data	No data	No data	No data
Flammability limits in air	No data	No data	No data	No data
Conversion factors	No data	No data	No data	No data
Explosive limits	No data	No data	No data	No data

[a]All information from HSDB 2007, except where noted.
[b]Value for arsenic acid hemihydrate
[c]NRC 1999
[d]Value for disodium arsenate heptahydrate

Table 4-4. Physical and Chemical Properties of Selected Organic Arsenic Compounds[a]

Property	Arsenilic acid	Arsenobetaine	Dimethylarsinic acid
Molecular weight	217.06	196.1[b]	138.00
Color	White	No data	Colorless
Physical state	Solid	Solid[b]	Solid
Melting point	232 °C	203–210 °C (decomposes)[b]	195 °C
Boiling point		No data	>200 °C
Density	1.9571 g/cm^3 at 10 °C	No data	No data
Odor	Practically odorless	No data	Odorless
Odor threshold:			
Water	No data	No data	No data
Air	No data	No data	No data
Solubility:			
Water	Slightly soluble in cold water; soluble in hot water	No data	2,000 g/L at 25 °C
Organic solvent(s)	Slightly soluble in alcohol; soluble in amyl alcohol; insoluble in ether, acetone, benzene, chloroform	No data	Soluble in alcohol; insoluble in diethyl ether
Acids	Slightly soluble in acetic acid; soluble in alkaki carbonates; moderately soluble in concentrated mineral acids; insoluble in dilute mineral acids	No data	Soluble in acetic acid
Partition coefficients:			
Log K_{ow}	No data	No data	No data
Log K_{oc}	No data	No data	No data
pK_a	No data	2.2[c]	1.57
Vapor pressure	No data	No data	No data
Henry's law constant	No data	No data	No data
Autoignition temperature	No data	No data	No data
Flashpoint	No data	No data	No data
Flammability	No data	No data	Nonflammable
Conversion factors	No data	No data	No data
Explosive limits	No data	No data	No data

Table 4-4. Physical and Chemical Properties of Selected Organic Arsenic Compounds[a]

Property	Methanearsonic acid	3-Nitro-4-hydroxy-phenylarsonic acid	Sodium arsanilate
Molecular weight	139.97	263.03	239.04
Color	White	Pale yellow	White or creamy white
Physical state	Solid	Solid	Solid
Melting point	160.5 °C	No data	No data
Boiling point	No data	No data	No data
Density	No data	No data	No data
Odor	No data	No data	Odorless
Odor threshold:			
Water	No data	No data	No data
Air	No data	No data	No data
Solubility:			
Water	256 g/L at 20 °C	Slightly soluble in cold water; soluble in about 30 parts boiling water	Soluble 1 part in 3 parts water
Organic solvents	Soluble in ethanol	Soluble in methanol, ethanol, acetone; insoluble in ether, ethyl acetate	Soluble 1 part in 150 parts alcohol; practically insoluble in chloroform, ether
Acids	No data	Soluble in acetic acid, alkalies; sparingly soluble in dilute mineral acids	No data
Partition coefficients:			
Log K_{ow}	No data	No data	No data
Log K_{oc}	No data	No data	No data
pK_a	pK_{a1}=4.1; pK_{a2}=9.02	No data	No data
Vapor pressure at 25 °C	<$7.5x10^{-8}$ mmHg	No data	No data
Henry's law constant	No data	No data	No data
Autoignition temperature	No data	No data	No data
Flashpoint	No data	No data	No data
Flammability	No data	No data	No data
Conversion factors	No data	No data	No data
Explosive limits	No data	No data	No data

Table 4-4. Physical and Chemical Properties of Selected Organic Arsenic Compounds[a]

Property	Disodium methanearsonate	Sodium dimethylarsinate	Sodium methanearsonate
Molecular weight	183.93	159.98	161.95
Color	White	Colorless to light yellow	White
Physical state	Solid	Solid	Solid
Melting point	>355 °C	200 °C	130–140 °C
Boiling point	No data	No data	No data
Density	1.04 g/cm^3	>1 g/cm^3 at 20 °C	1.55 g/mL[d]
Odor	No data	Odorless	Odorless
Odor threshold:			
Water	No data	No data	No data
Air	No data	No data	No data
Solubility:			
Water	432 g/L at 25 °C	200 g/L at 25 °C	580 g/L at 20 °C
Organic solvents	Soluble in methanol; practically insoluble in most organic solvents	No data	Insoluble in most organic solvents
Acids	No data	No data	No data
Partition coefficients:			
Log K_{ow}	<1	No data	-3.10
Log K_{oc}	No data	No data	No data
pK_a	pK_{a1}=4.1; pK_{a2}=8.94	6.29	pK_{a1}=4.1; pK_{a2}=9.02
Vapor pressure at 25 °C	10^{-7} mmHg	No data	$7.8x10^{-8}$ mmHg
Henry's law constant	No data	No data	No data
Autoignition temperature	No data	No data	No data
Flashpoint	No data	No data	No data
Flammability	Nonflammable	No data	Nonflammable
Conversion factors	No data	No data	No data
Explosive limits	No data	No data	No data

[a]All information from HSDB 2007, except where noted.
[b]Cannon et al. 1981 (arsenobetaine as monohydrate)
[c]Teräsahde et al. 1996
[d]Value for Ansar 6.6

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5. PRODUCTION, IMPORT/EXPORT, USE, AND DISPOSAL

5.1 PRODUCTION

Arsenic is presently obtained as a byproduct of the smelting of copper, lead, cobalt, and gold ores. Arsenic trioxide is volatilized during smelting and accumulates in the flue dust, which may contain up to 30% arsenic trioxide. The crude flue dust is further refined by mixing with small amounts of galena or pyrite to prevent the formation of arsensites and roasting to yield arsenic trioxide of 90–95% purity. By successive sublimations, a purity of 99% can be obtained. Elemental arsenic can be prepared by the reduction of arsenic oxide with charcoal. Demand for elemental arsenic is limited and thus, about 95% of arsenic is marketed and consumed in combined form, principally as arsenic trioxide, which is subsequently converted to arsenic acid (Carapella 1992; Hanusch et al. 1985; USGS 2006a).

Since 1985, when the ASARCO smelter in Tacoma, Washington ceased operation, there has been no domestic production of arsenic trioxide or elemental arsenic and consequently, the United States remains entirely dependent on imports (U.S. Bureau of Mines 1988, 1990; USGS 2006a). Prior to its cessation, U.S. production of arsenic trioxide had been 7,300 metric tons in 1983, 6,800 metric tons in 1984, and 2,200 metric tons in 1985 (U.S. Bureau of Mines 1988). In 2005, arsenic trioxide was obtained from the treatment of nonferrous ores or concentrates in 14 countries. In 2005, the world's largest producer of arsenic trioxide was China, followed by Chile and Peru. China is the world leader in the production of commercial-grade arsenic followed by Japan. The United States, with an apparent demand of 8,800 metric tons in 2005, is the world's leading consumer of arsenic, mainly for CCA. This is an increase over 2004 with an apparent demand of 6,800 metric tons, but far less than that of 2003, 21,600 metric tons (USGS 2006a).

Tables 5-1 and 5-2 list facilities in each state that manufacture or process arsenic and arsenic compounds, respectively, as well as the intended use and the range of maximum amounts of arsenic or arsenic compounds that are stored on site. In 2004, there were 58 and 361 reporting facilities that produced, processed, or used arsenic and arsenic compounds, respectively, in the United States. The data listed in Tables 5-1 and 5-2 are derived from the Toxics Release Inventory (TRI04 2006). Only certain types of facilities were required to report. Therefore, this is not an exhaustive list. Current U.S. manufacturers of selected arsenic compounds are given in Table 5-3.

Table 5-1. Facilities that Produce, Process, or Use Arsenic

State[a]	Number of facilities	Minimum amount on site in pounds[b]	Maximum amount on site in pounds[b]	Activities and uses[c]
AK	1	1,000,000	9,999,999	1, 13
AL	18	0	9,999,999	1, 2, 3, 5, 7, 8, 11, 12, 13, 14
AR	4	1,000	999,999	7, 8
AZ	9	0	99,999	1, 3, 4, 5, 8, 12, 13
CA	31	0	9,999,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 11, 12, 13
CO	8	0	999,999	2, 7, 8, 11, 12
FL	10	1,000	999,999	1, 3, 5, 7, 8, 11, 12
GA	16	100	49,999,999	2, 3, 4, 6, 7, 8, 11, 12, 13, 14
HI	1	10,000	99,999	8
IA	4	100	99,999	6, 7, 8
ID	7	0	49,999,999	1, 2, 3, 5, 6, 7, 9, 12, 13
IL	16	0	999,999	1, 3, 4, 5, 6, 7, 8, 12, 14
IN	17	0	999,999	1, 3, 5, 6, 7, 8, 9, 12, 13
KY	9	0	999,999	1, 2, 3, 5, 6, 7, 8, 11
LA	8	0	999,999	1, 2, 3, 7, 8, 12, 13
MA	5	1,000	999,999	3, 7, 8
MD	9	0	999,999	1, 2, 4, 5, 6, 7, 8
MI	10	0	999,999	3, 7, 8, 12, 13
MN	5	100	99,999	1, 7, 8, 13
MO	6	100	999,999	1, 2, 3, 4, 5, 6, 7, 8
MS	9	1,000	49,999,999	2, 3, 4, 7, 8, 9
NC	21	0	49,999,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 12, 13, 14
ND	2	0	99,999	8
NE	1	0	99	8
NJ	9	0	99,999	1, 2, 3, 5, 7, 8, 9
NM	2	10,000	999,999	7, 12
NV	6	1,000	99,999,999	1, 2, 4, 5, 6, 7, 8, 11, 12, 13
NY	4	0	99,999	7, 8, 12
OH	15	0	999,999	1, 2, 3, 4, 5, 8, 9, 12, 13
OK	9	0	99,999	1, 2, 5, 6, 7, 9, 11, 12, 13
OR	6	10,000	999,999	1, 5, 7, 8, 12
PA	24	0	999,999	1, 2, 3, 5, 6, 7, 8, 10, 11, 12, 13
PR	3	1,000	99,999	8, 11
SC	9	0	9,999,999	1, 2, 3, 5, 6, 8, 12
SD	1	10,000,000	49,999,999	1, 7, 11, 13
TN	11	0	999,999	1, 2, 3, 6, 7, 8, 11, 12, 14
TX	29	0	49,999,999	1, 2, 3, 4, 5, 6, 7, 8, 10, 11, 12, 13, 14
VA	8	0	999,999	2, 3, 7, 8, 10

Table 5-1. Facilities that Produce, Process, or Use Arsenic

State[a]	Number of facilities	Minimum amount on site in pounds[b]	Maximum amount on site in pounds[b]	Activities and uses[c]
WA	3	0	99,999	5, 7, 8
WI	9	0	99,999	1, 2, 3, 4, 5, 6, 7, 8, 12
WV	19	100	999,999	1, 2, 3, 5, 7, 8, 10, 11, 12
WY	1	100	999	1, 13

[a]Post office state abbreviations used
[b]Amounts on site reported by facilities in each state
[c]Activities/Uses:

1. Produce
2. Import
3. Onsite use/processing
4. Sale/Distribution
5. Byproduct
6. Impurity
7. Reactant
8. Formulation Component
9. Article Component
10. Repackaging
11. Chemical Processing Aid
12. Manufacturing Aid
13. Ancillary/Other Uses
14. Process Impurity

Source: TRI04 2006 (Data are from 2004)

Table 5-2. Facilities that Produce, Process, or Use Arsenic Compounds

State[a]	Number of facilities	Minimum amount on site in pounds[b]	Maximum amount on site in pounds[b]	Activities and uses[c]
AK	6	1,000	49,999,999	1, 5, 7, 12, 13, 14
AL	37	0	499,999,999	1, 2, 3, 4, 5, 7, 8, 9, 11, 12, 13
AR	20	1,000	99,999,999	1, 2, 3, 7, 8, 9, 11, 12, 13, 14
AZ	29	100	499,999,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14
CA	40	100	99,999,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 11, 12, 13, 14
CO	9	1,000	49,999,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 11, 12
DE	1	10,000	99,999	1, 5, 9
FL	30	0	999,999	1, 3, 4, 5, 7, 8, 9, 11, 12, 13, 14
GA	50	0	49,999,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 11, 12, 13, 14
HI	6	1,000	99,999	7, 8, 11
IA	22	0	9,999,999	1, 3, 4, 5, 6, 7, 8, 9, 11, 12, 13
ID	6	10,000	9,999,999	1, 3, 5, 6, 7, 8, 9, 12, 13
IL	44	0	999,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14
IN	54	0	9,999,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 11, 12, 13, 14
KS	14	0	999,999	1, 3, 4, 5, 6, 7, 8, 12, 13, 14
KY	29	0	999,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14
LA	32	0	499,999,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 11, 12, 13
MA	9	0	999,999	1, 4, 5, 6, 7, 8
MD	19	0	999,999	1, 4, 5, 7, 8, 9, 11, 12, 13
ME	2	1,000	99,999	7
MI	32	0	999,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 11, 12, 13, 14
MN	13	0	999,999	1, 3, 4, 5, 7, 8, 9, 11, 12, 13
MO	32	0	499,999,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 11, 12, 13, 14
MS	28	1,000	49,999,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 11, 12, 13
MT	8	1,000	10,000,000,000	1, 2, 3, 4, 5, 6, 7, 12, 13, 14
NC	65	0	9,999,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14
ND	11	1,000	99,999	1, 5, 8, 9, 11, 12, 13, 14
NE	6	1,000	999,999	1, 2, 3, 4, 5, 6, 8, 9, 12, 13
NH	2	1,000	99,999	8, 11
NJ	35	0	999,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 12, 13
NM	11	1,000	499,999,999	1, 5, 7, 12, 13
NV	31	1,000	10,000,000,000	1, 2, 3, 5, 6, 7, 9, 11, 12, 13, 14
NY	27	0	9,999,999	1, 2, 3, 4, 5, 7, 8, 9, 12, 13
OH	50	0	999,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 11, 12, 13, 14
OK	14	100	9,999,999	1, 2, 3, 4, 5, 6, 8, 12, 13, 14
OR	12	100	99,999	1, 2, 3, 7, 8, 12
PA	53	0	999,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 11, 12, 13, 14
PR	8	1,000	99,999	1, 2, 3, 5, 8, 11
RI	7	100	99,999	7, 8

Table 5-2. Facilities that Produce, Process, or Use Arsenic Compounds

State[a]	Number of facilities	Minimum amount on site in pounds[b]	Maximum amount on site in pounds[b]	Activities and uses[c]
SC	34	0	49,999,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 11, 12, 13, 14
SD	6	1,000	99,999,999	1, 5, 6, 7, 8, 11, 12, 13
TN	29	0	99,999,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12
TX	54	0	499,999,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 11, 12, 13, 14
UT	23	0	499,999,999	1, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13
VA	24	0	499,999,999	1, 2, 3, 4, 5, 7, 8, 9, 11, 12, 13, 14
WA	14	0	999,999	1, 2, 3, 4, 5, 7, 8, 9, 11, 12, 13
WI	13	100	99,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 11
WV	26	0	999,999	1, 2, 3, 4, 5, 6, 7, 8, 9, 12, 13, 14
WY	9	1,000	99,999	1, 3, 4, 5, 7, 8, 9, 12, 13

[a]Post office state abbreviations used
[b]Amounts on site reported by facilities in each state
[c]Activities/Uses:

1. Produce
2. Import
3. Onsite use/processing
4. Sale/Distribution
5. Byproduct
6. Impurity
7. Reactant
8. Formulation Component
9. Article Component
10. Repackaging
11. Chemical Processing Aid
12. Manufacturing Aid
13. Ancillary/Other Uses
14. Process Impurity

Source: TRI04 2006 (Data are from 2004)

Table 5-3. Current U.S. Manufacturers of Selected Arsenic Compounds[a]

Company	Location(s)
Arsenic acid	
Arch Wood Protection, Inc.	Conley, Georgia
Osmose Wood Preserving, Inc.	Millington, Tennessee
Arsanilic acid	
Fleming Laboratories, Inc.	Charlotte, North Carolina
Copper Chromated Arsenic (CCA)	
Arch Wood Protection, Inc.	Conley, Georgia; Kalama, Washington; Smyrna, Georgia[b]; Valparaiso, Indiana
Chemical Specialties, Inc.[b]	Charlotte, North Carolina
Osmose Wood Preserving, Inc.[b]	Buffalo, New York
Calcium acid methanearsonate (CAMA)	
Drexel Chemical Company (formulator)[c]	No information provided
Disodium methanearsonate (DSMA)	
Drexel Chemical Company	Tunica, Mississippi
Monosodium methyl arsonate (MSMA)	
Drexel Chemical Company	Tunica, Mississippi
Gallium arsenide	
Atomergic Chemetals Corporation	Farmingdale, New York

[a]Derived from Stanford Research Institute (SRI 2006), except where otherwise noted. SRI reports production of chemicals produced in commercial quantities (defined as exceeding 5,000 pounds or $10,000 in value annually) by the companies listed.
[b]USGS 2006a
[c]Meister et al. 2006

5.2 IMPORT/EXPORT

Since U.S. production ceased in 1985, all arsenic consumed in the United States is imported. Imports of arsenic (metal and compounds combined) have increased substantially since the mid-1980s, reaching 8,810 metric tons (as arsenic content) in 2005, of which 812 metric tons was as elemental arsenic. In 2005, 11,000 metric tons of arsenic trioxide was imported into the United States. China is the major import source for elemental arsenic from 2001 to 2004, supplying 81%, followed by Japan (15%) and Hong Kong (2%). China is also the major import source in 2001–2004 for arsenic trioxide, supplying 59% to the United States, followed by Morocco (22%), Chile (7%), and Mexico (5%) (USGS 2006a, 2006b).

U.S. exports of elemental arsenic were 220 metric tons in 2004 and are estimated to be 200 metric tons in 2005 (USGS 2006b). In 2005, U.S. import of arsenic was approximately 8.1×10^5 kilograms (810 metric tons) (ITA 2007a, 2007b).

5.3 USE

In 2003, the United States was the world's largest consumer of arsenic, with an apparent demand of 21,600 metric tons. In 2005, the Unites States was still the world's largest consumer of arsenic, mainly for CCA. Production of wood preservatives, primarily CCA, $CrO_3 \cdot CuO \cdot As_2O_5$, accounted for >90% of domestic consumption of arsenic trioxide prior to 2004. In 2005, about 65% of domestic consumption of arsenic trioxide was used for the production of CCA. The remainder was used for the production of agricultural chemicals, including herbicides, and insecticides. The major U.S. producers of CCA in 2005 included Arch Wood Protection, Inc., Smyrna Georgia; Chemical Specialties Inc., Charlotte, North Carolina; and Osmose Wood Preserving, Inc., Buffalo, New York (USGS 2006a). CCA is the most widely used wood preservative in the world. Wood treated with CCA is referred to as 'pressure treated' wood (American Wood Preservers Association 2007; Page and Loar 1993). In 1997, approximately 727.8 million cubic feet (20.6 million cubic meters) of wood products were pressure treated in the United States. CCA is a water-based product that protects several commercially available species of western lumber from decay and insect attack. It is widely used in treating utility poles, building lumber, and wood foundations. CCA comes in three types, A, B, and C, which contain different proportions of chromium, copper, and arsenic oxides. Type C, the most popular type, contains CrO_3, CuO, and As_2O_5 in the proportions 47.5, 18.5, and 34.0%, respectively. The retention levels are 0.25 pounds per cubic feet (pcf) for above ground use such as fencing and decking, 0.40 pcf for lumber used in ground contact such as

fence posts and deck posts, and 0.60 pcf for all weather wood foundations (Chicago Flameproof 2000; Permapost 2000). Piling used for fresh and saltwater contact should contain 0.80 and 2.5 pcf of CCA, respectively. Ammoniacal copper zinc arsenate (ACZA) is another arsenic containing preservative used to treat wood; however, it is not as widely used as CCA–C (Lebow et al. 2000).

In 2003, U.S. manufacturers of arsenical wood preservatives began a voluntary transition from CCA to other wood preservatives in wood products for certain residential uses, such as play structures, picnic tables, decks, fencing, and boardwalks. This phase out was completed on December 31, 2003; wood treated prior to this date could still be used and structures made with CCA-treated wood would not be affected. CCA-treated wood products continue to be used in industrial applications (EPA 2003a).

Elemental arsenic is used as an alloying element in ammunition and solders, as an anti-friction additive to metals used for bearings, and to strengthen lead-acid storage battery grids. In the past, the predominant use of arsenic was in agriculture. The uses of lead arsenate as a growth regulator on citrus, calcium arsenate as an herbicide on turf, sodium arsenite as a fungicide on grapes, and arsenic acid as a desiccant on okra for seed and cotton were voluntarily cancelled in the late 1980s and the early 1990s (EPA 2006). The herbicides, MSMA and DSMA, are registered for weed control on cotton, for turf grass and lawns, and under trees, vines, and shrubs; calcium acid methanearsonate (CAMA) is registered for postemergent weed control on lawns. Cacodylic acid, a defoliant and herbicide, is registered for weed control under nonbearing citrus trees, around buildings and sidewalks, and for lawn renovation (EPA 2006). Approximately 3 million pounds of MSMA or DSMA, and 100,000 pounds of cacodylic acid are applied in the U.S. annually based on EPA's Screening Level Use Analysis data. Data were not available for CAMA. Application to cotton and turf (residential and golf courses) are the major uses of organic arsenical herbicides. Currently, there are approximately 90, 25, 4, and 35 end-use products containing MSMA, DSMA, CAMA, and cacodylic acid, respectively (EPA 2006).

Other organic arsenicals used in agriculture include arsanilic acid, sodium arsanilate, and 3-nitro-4-hydroxyphenylarsonic acid (roxarsone), which are antimicrobials used in animal and poultry feeds (Beerman 1994). While the U.S. Food and Drug Administration (FDA) has authorized the used of these compounds as medicinal feed additives, only one of the arsenical compounds may be used at a time as the sole source of organic arsenic in the feed (EPA 1998k). In 1999–2000, about 70% of the broiler industry added roxarsone to broiler poultry feed; concentrations of roxarsone in feed range from 22.7 to 45.4 g/ton (Garbarino et al. 2003).

From the mid-nineteenth century to the introduction of organic pesticides in the 1940s, inorganic arsenic compounds were the dominant pesticides available to farmers and fruit growers. Calcium arsenate was formerly used to control the boll weevil and cotton worm and was used as an herbicide. Lead arsenate was used on apple and other fruit orchards as well as on potato fields. Sodium arsenite was used to control weeds on railroad right-of-ways, potato fields, and in industrial areas, as well as in baits and to debark trees. Sodium arsenate had some application in ant traps. The use of inorganic arsenic compounds in agriculture has virtually disappeared beginning around the 1960s (Azcue and Nriagu 1994; Meister 1987; Merwin et al. 1994; Sanok et al. 1995). Food uses were voluntarily cancelled in 1993 as was the use of arsenic acid as a defoliant on cotton plants; inorganic arsenic's remaining allowable uses are in ant baits and wood preservatives (EPA 1999h). In 1987, EPA issued a preliminary decision to cancel the registration of most inorganic arsenicals used as nonwood pesticides (Loebenstein 1994) (see Chapter 8). According to the California Department of Pesticide Regulation, arsenic acid, arsenic pentoxide, and arsenic trioxide are registered currently as pesticides in the United States; there are no active registrants listed for calcium arsenate, lead arsenate, or sodium arsenite (NPIRS 2007).

High-purity arsenic (99.9999%) is used by the electronics industry for gallium-arsenide semiconductors for telecommunications, solar cells, and space research (USGS 2006b). Arsenic trioxide and arsenic acid were used as a decolorizer and fining agent in the production of bottle glass and other glassware (Carapella 1992).

Arsenic compounds have a long history of use in medicine. Inorganic arsenic was used as a therapeutic agent through the mid-twentieth century, primarily for the treatment of leukemia, psoriasis, and chronic bronchial asthma; organic arsenic antibiotics were extensively used in the treatment of spirochetal and protozoal disease (NRC 1999). The availability of inorganic arsenicals in Western medicines ended in the 1970s, although they may still be encountered in non-Western traditional medicines. By the 1980s, the only remaining medicinal organic arsenical was melarsoprol for treatment of the meningoencephalitic stage of African trypanosomiasis. There has been renewed interest in arsenic as a therapeutic agent, namely the use of arsenic trioxide in the treatment of acute promyelocytic leukemia (APL) (Gallagher 1998; Kroemer and de Thé 1999; Miller 1998; Wang 2001). In 2000, the FDA approved arsenic trioxide for this use (FDA 2000).

5.4 DISPOSAL

Wastes containing arsenic are considered hazardous wastes, and as such, their treatment, storage, and disposal are regulated by law (see Chapter 8). The main route of disposal of solid wastes containing arsenic is landfilling. EPA has promulgated rules and treatment standards for landfilling liquid arsenical wastes (EPA 1990e). Arsenic-containing electronic components such as relays, switches, and circuit boards are disposed of at hazardous waste sites, and the elemental arsenic is not reclaimed. Process water at wood treatment plants that contained arsenic contained was reused. Gallium-arsenide scrap from the manufacture of semiconductor devices was reprocessed for arsenic recovery. Arsenic was not recovered from arsenical residues and dusts at domestic nonferrous smelters (USGS 2006b).

CCA-treated wood is classified as nonhazardous waste under the Federal Resource Conservation and Recovery Act (RCRA). CCA-treated wood is disposed of with regular municipal trash (i.e., municipal solid waste, not yard waste). It should not be burned in open fires, stoves, residential boilers, or fire places and should not be composted or used as mulch. Treated wood from commercial or industrial applications may only be burned in commercial or industrial incinerators in accordance with state and federal regulations (Adobe Lumber 2002; EPA 2005a).

Arsenic is listed as a toxic substance under Section 313 of the Emergency Planning and Community Right to Know Act (EPCRA) under Title III of the Superfund Amendments and Reauthorization Act (SARA) (EPA 1995c). Disposal of wastes containing arsenic is controlled by a number of federal regulations (see Chapter 8).

6. POTENTIAL FOR HUMAN EXPOSURE

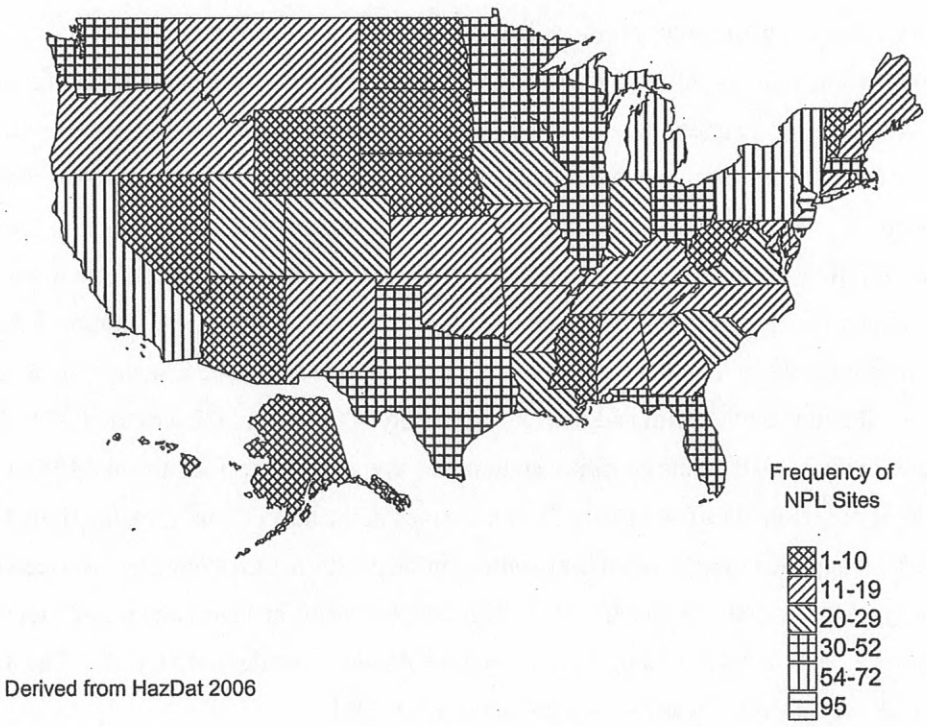
6.1 OVERVIEW

Arsenic has been identified in at least 1,149 of the 1,684 hazardous waste sites that have been proposed for inclusion on the EPA National Priorities List (NPL) (HazDat 2006). However, the number of sites evaluated for arsenic is not known. The frequency of these sites can be seen in Figure 6-1. Of these sites, 1,134 are located within the United States and 11, 2, and 2 are located in the Commonwealth of Puerto Rico, the Virgin Islands, and Guam (not shown).

Arsenic is widely distributed in the Earth's crust, which contains about 3.4 ppm arsenic (Wedepohl 1991). It is mostly found in nature in minerals, such as realgar (As_4S_4), orpiment (As_2S_3), and arsenolite (As_2O_3), and only found in its elemental form to a small extent. There are over 150 arsenic-bearing minerals (Budavari et al. 2001; Carapella 1992). While arsenic is released to the environment from natural sources such as wind-blown soil and volcanoes, releases from anthropogenic sources far exceed those from natural sources. Anthropogenic sources of arsenic include nonferrous metal mining and smelting, pesticide application, coal combustion, wood combustion, and waste incineration. Most anthropogenic releases of arsenic are to land or soil, primarily in the form of pesticides or solid wastes. However, substantial amounts are also released to air and water.

Arsenic found in soil either naturally occurring or from anthropogenic releases forms insoluble complexes with iron, aluminum, and magnesium oxides found in soil surfaces, and in this form, arsenic is relatively immobile. However, under reducing conditions, arsenic can be released from the solid phase, resulting in soluble mobile forms of arsenic, which may potentially leach into groundwater or result in runoff of arsenic into surface waters. In aquatic systems, inorganic arsenic occurs primarily in two oxidation states, As(V) and As(III). Both forms generally co-exist, although As(V) predominates under oxidizing conditions and As(III) predominates under reducing conditions. Arsenic may undergo a variety of reactions in the environment, including oxidation-reduction reactions, ligand exchange, precipitation, and biotransformation (EPA 1979, 1984a; Pongratz 1998; Welch et al. 1988). These reactions are influenced by Eh (the oxidation-reduction potential), pH, metal sulfide and sulfide ion concentrations, iron concentration, temperature, salinity, and distribution and composition of the biota (EPA 1979; Wakao et al. 1988). Much of the arsenic will adsorb to particulate matter and sediment. Arsenic released to air exists mainly in the form of particulate matter. Arsenic released from combustion processes will

Figure 6-1. Frequency of NPL Sites with Arsenic Contamination



Derived from HazDat 2006

generally occur as highly soluble oxides. These particles are dispersed by the wind and returned to the earth in wet or dry deposition. Arsines that are released to the atmosphere as a result of microbial action are oxidized to nonvolatile species that settle back to the ground.

Because arsenic is a natural component of the Earth's crust, low levels of the element are found in all environmental media. Atmospheric levels of arsenic in remote locations (away from human releases) range from 1 to 3 ng/m^3, while concentrations in urban areas may range from 20 to 100 ng/m^3. Concentrations in water are usually <10 µg/L, although higher levels may occur near natural mineral deposits or anthropogenic sources. Natural levels of arsenic in soil usually range from 1 to 40 mg/kg, with a mean of 5 mg/kg, although much higher levels may occur in mining areas, at waste sites, near high geological deposits of arsenic-rich minerals, or from pesticide application. Arsenic is also found in many foods, at concentrations that usually range from 20 to 140 µg/kg. Total arsenic concentrations may be substantially higher in certain seafoods. However, the general consensus in the literature is that about 85–>90% of the arsenic in the edible parts of marine fish and shellfish is organic arsenic (e.g., arsenobetaine, arsenochloline, dimethylarsinic acid) and that approximately 10% is inorganic arsenic (EPA 2003b). Drinking water in the United States generally contains an average of 2 µg/L of arsenic (EPA 1982c), although 12% of water supplies from surface water sources in the north Central region of the United States and 12% of supplies from groundwater sources in the western region have levels exceeding 20 µg/L (Karagas et al. 1998). In January 2001, EPA adopted a new standard that arsenic levels in drinking water were not to exceed 10 µg/L, replacing the previous standard of 50 µg/L. The date for compliance with the new MCL was January 23, 2006 (EPA 2001).

For most people, diet is the largest source of exposure to arsenic. Mean dietary intakes of total arsenic of 50.6 µg/day (range of 1.01–1,081 µg/day) and 58.5 µg/day (range of 0.21–1,276 µg/day) has been reported for females and males (MacIntosh et al. 1997). U.S. dietary intake of inorganic arsenic has been estimated to range from 1 to 20 µg/day, with grains and produce expected to be significant contributors to dietary inorganic arsenic intake (Schoof et al. 1999a, 1999b). The predominant dietary source of arsenic is generally seafood. Inorganic arsenic in seafood sampled in a market basket survey of inorganic arsenic in food ranged from <0.001 to 0.002 µg/g (Schoof et al. 1999a, 1999b). Intake of arsenic from air and soil are usually much smaller than that from food and water (Meacher et al. 2002).

People who produce or use arsenic compounds in occupations such as nonferrous metal smelting, pesticide manufacturing or application, wood preservation, semiconductor manufacturing, or glass production may be exposed to substantially higher levels of arsenic, mainly from dusts or aerosols in air.

Exposure at waste sites may occur by a variety of pathways, including inhalation of dusts in air, ingestion of contaminated soil or water, or through the food chain. The magnitude of the exposures can only be evaluated on a site-by-site basis; however, exposures generally do not exceed background intakes from food and drinking water.

Tables 4-1, 4-2, 4-3, and 4-4 summarize all of the names, abbreviations, and structures of the various arsenic compounds that are discussed in Chapter 6.

6.2 RELEASES TO THE ENVIRONMENT

The Toxics Release Inventory (TRI) data should be used with caution because only certain types of facilities are required to report (EPA 2005k). This is not an exhaustive list. Manufacturing and processing facilities are required to report information to the TRI only if they employ 10 or more full-time employees; if their facility is included in Standard Industrial Classification (SIC) Codes 10 (except 1011, 1081, and 1094), 12 (except 1241), 20–39, 4911 (limited to facilities that combust coal and/or oil for the purpose of generating electricity for distribution in commerce), 4931 (limited to facilities that combust coal and/or oil for the purpose of generating electricity for distribution in commerce), 4939 (limited to facilities that combust coal and/or oil for the purpose of generating electricity for distribution in commerce), 4953 (limited to facilities regulated under RCRA Subtitle C, 42 U.S.C. section 6921 et seq.), 5169, 5171, and 7389 (limited S.C. section 6921 et seq.), 5169, 5171, and 7389 (limited to facilities primarily engaged in solvents recovery services on a contract or fee basis); and if their facility produces, imports, or processes ≥25,000 pounds of any TRI chemical or otherwise uses >10,000 pounds of a TRI chemical in a calendar year (EPA 2005k).

6.2.1 Air

Estimated releases of 4,800 pounds (~2.2 metric tons) of arsenic to the atmosphere from 58 domestic manufacturing and processing facilities in 2004, accounted for about 0.52% of the estimated total environmental releases from facilities required to report to the TRI (TRI04 2006). Estimated releases of 0.13 million pounds (~59 metric tons) of arsenic compounds to the atmosphere from 361 domestic manufacturing and processing facilities in 2004, accounted for about 0.11% of the estimated total environmental releases from facilities required to report to the TRI (TRI04 2006). These releases for arsenic and arsenic compounds are summarized in Table 6-1 and 6-2, respectively.

Table 6-1. Releases to the Environment from Facilities that Produce, Process, or Use Arsenic[a]

		Reported amounts released in pounds per year[b]							
							Total release		
State[c]	RF[d]	Air[e]	Water[f]	UI[g]	Land[h]	Other[i]	On-site[j]	Off-site[k]	On- and off-site
AL	1	51	162	0	110,264	0	110,425	52	110,477
AR	2	0	0	No data	0	0	No data	0	0
AZ	2	10	0	0	20,717	0	20,727	0	20,727
CA	3	13	14	0	5,482	0	13	5,497	5,510
FL	2	4	0	0	0	4,950	4	4,950	4,954
GA	4	8	10	0	1,603	5	13	1,613	1,626
IA	1	0	1	0	0	0	0	1	1
ID	1	39	0	0	361,252	0	361,291	0	361,291
IL	2	250	129	0	14,087	0	379	14,087	14,466
IN	1	5	5	0	13,250	250	5	13,505	13,510
KS	1	0	0	No data	0	0	No data	0	0
KY	1	0	1	0	0	6	1	6	7
MI	2	0	5	0	0	750	5	750	755
MN	1	15	47	0	14,504	0	15	14,551	14,566
MO	1	5	0	0	0	4,040	5	4,040	4,045
MS	2	0	0	0	0	0	0	0	0
NC	4	35	8	0	1	1	43	2	45
NV	1	0	0	0	0	0	0	0	0
NY	4	0	1	0	26,525	1	26,401	126	26,527
OH	2	13	0	0	0	0	13	0	13
OR	1	0	0	0	92,606	0	92,606	0	92,606
PA	5	166	8	0	14,362	26,140	199	40,477	40,676
SC	3	10	10	0	0	1,002	15	1,007	1,022
TN	3	3,988	0	0	0	0	3,988	0	3,988
TX	5	139	376	168,563	12,600	0	181,636	42	181,678

Table 6-1. Releases to the Environment from Facilities that Produce, Process, or Use Arsenic[a]

		Reported amounts released in pounds per year[b]							
							Total release		
State[c]	RF[d]	Air[e]	Water[f]	UI[g]	Land[h]	Other[i]	On-site[j]	Off-site[k]	On- and off-site
WI	2	15	0	0	760	0	15	760	776
WV	1	0	0	0	10,135	0	10,135	0	10,135
Total	58	4,766	778	168,563	698,149	37,145	807,935	101,466	909,401

[a]The TRI data should be used with caution since only certain types of facilities are required to report. This is not an exhaustive list. Data are rounded to nearest whole number.
[b]Data in TRI are maximum amounts released by each facility.
[c]Post office state abbreviations are used.
[d]Number of reporting facilities.
[e]The sum of fugitive and point source releases are included in releases to air by a given facility.
[f]Surface water discharges, waste water treatment-(metals only), and publicly owned treatment works (POTWs) (metal and metal compounds).
[g]Class I wells, Class II-V wells, and underground injection.
[h]Resource Conservation and Recovery Act (RCRA) subtitle C landfills; other on-site landfills, land treatment, surface impoundments, other land disposal, other landfills.
[i]Storage only, solidification/stabilization (metals only), other off-site management, transfers to waste broker for disposal, unknown
[j]The sum of all releases of the chemical to air, land, water, and underground injection wells.
[k]Total amount of chemical transferred off-site, including to POTWs.

RF = reporting facilities; UI = underground injection

Source: TRI04 2006 (Data are from 2004)

Table 6-2. Releases to the Environment from Facilities that Produce, Process, or Use Arsenic Compounds[a]

		Reported amounts released in pounds per year[b]							
							Total release		
State[c]	RF[d]	Air[e]	Water[f]	UI[g]	Land[h]	Other[i]	On-site[j]	Off-site[k]	On- and off-site
AK	1	511	0	1,400,000	1,200,000	0	2,600,511	0	2,600,511
AL	19	4,299	18,127	0	853,469	7,555	875,876	7,574	883,450
AR	12	0	0	0	133	26,435	0	26,568	26,568
AZ	5	5,421	0	0	402,335	422	394,749	13,429	408,178
CA	5	65	14	0	355,660	86,396	160,673	281,461	442,134
CO	1	11	0	0	4,094	0	4,105	0	4,105
CT	1	0	0	0	0	0	No data	0	0
FL	15	3,208	503	0	343,508	4,057	346,310	4,966	351,276
GA	23	8,643	7,823	0	422,124	5,127	437,496	6,221	443,717
HI	1	0	0	0	0	0	No data	0	0
IA	4	1,291	482	0	0	35,324	1,773	35,324	37,097
ID	3	332	20	0	1,056,904	0	1,057,256	0	1,057,256
IL	11	3,960	3,110	0	96,093	21,038	71,819	52,382	124,202
IN	21	13,786	8,282	0	768,297	42,808	632,704	200,470	833,174
KS	4	924	0	0	12,082	1	13,006	1	13,007
KY	18	14,406	8,427	0	616,074	95,285	578,080	156,112	734,192
LA	7	265	23	0	25,426	0	25,563	151	25,714
MA	1	0	0	0	0	500	0	500	500
MD	8	1,870	291	0	34,130	114,115	2,661	147,745	150,406
MI	10	1,123	2,310	68,924	101,857	1,059	77,505	97,769	175,274
MN	2	10	130	0	19,270	0	19,410	0	19,410
MO	6	462	116	0	27,855	936	10,026	19,343	29,369
MS	6	61	121	0	11,676	46	11,228	676	11,904
MT	3	630	0	0	2,138,190	37	2,138,820	37	2,138,857
NC	15	5,626	4,732	0	168,030	2,429	178,388	2,429	180,818
ND	6	6,326	5	0	318,175	0	137,961	186,545	324,506
NE	2	180	0	0	11,000	0	11,180	0	11,180
NJ	2	0	1	0	0	8	0	9	9
NM	2	130	0	0	18,326	0	18,456	0	18,456
NV	10	3,041	30,017	0	98,894,564	0	98,927,328	294	98,927,622
NY	3	67	36	0	27,059	802	27,141	823	27,964
OH	17	8,595	8,352	81,024	741,730	274	668,157	171,818	839,975
OK	4	115	13	0	25,000	4,202	115	29,215	29,330
OR	4	0	5	0	0	4,012	5	4,012	4,017
PA	23	18,963	2,166	0	666,753	69,053	403,582	353,353	756,935
PR	3	0	0	0	0	0	No data	0	0
RI	1	0	8	0	0	1,006	8	1,006	1,014

Table 6-2. Releases to the Environment from Facilities that Produce, Process, or Use Arsenic Compounds[a]

		Reported amounts released in pounds per year[b]							
							Total release		
State[c]	RF[d]	Air[e]	Water[f]	UI[g]	Land[h]	Other[i]	On-site[j]	Off-site[k]	On- and off-site
SC	13	2,178	1,443	0	25,817	22,705	29,438	22,705	52,143
SD	1	0	0	0	0	0	No data	0	0
TN	13	3,379	25,878	0	292,914	17,219	258,643	80,746	339,389
TX	17	4,616	199	33,148	196,385	31,557	226,751	39,155	265,906
UT	5	6,715	4,500	0	6,368,500	3,500	6,379,715	3,500	6,383,215
VA	11	1,911	2,773	0	160,154	8,463	164,789	8,512	173,301
WA	4	0	0	0	0	0	No data	0	0
WI	4	94	21	0	1,313	9,216	223	10,421	10,644
WV	12	2,693	2,417	0	536,628	10,000	441,237	110,501	551,738
WY	2	3,300	0	0	10,800	0	14,100	0	14,100
Total	361	129,205	132,347	1,583,096	116,952,326	625,588	117,346,787	2,075,775	119,422,562

[a]The TRI data should be used with caution since only certain types of facilities are required to report. This is not an exhaustive list. Data are rounded to nearest whole number.
[b]Data in TRI are maximum amounts released by each facility.
[c]Post office state abbreviations are used.
[d]Number of reporting facilities.
[e]The sum of fugitive and point source releases are included in releases to air by a given facility.
[f]Surface water discharges, waste water treatment-(metals only), and publicly owned treatment works (POTWs) (metal and metal compounds).
[g]Class I wells, Class II-V wells, and underground injection.
[h]Resource Conservation and Recovery Act (RCRA) subtitle C landfills; other on-site landfills, land treatment, surface impoundments, other land disposal, other landfills.
[i]Storage only, solidification/stabilization (metals only), other off-site management, transfers to waste broker for disposal, unknown
[j]The sum of all releases of the chemical to air, land, water, and underground injection wells.
[k]Total amount of chemical transferred off-site, including to POTWs.

RF = reporting facilities; UI = underground injection

Source: TRI04 2006 (Data are from 2004)

Arsenic naturally occurs in soil and will be present in the atmosphere as airborne dust. It is also emitted from volcanoes and in areas of dormant volcanism (e.g., fumaroles). Gaseous alkyl arsenic compounds may be released from soil that has been treated with inorganic arsenic compounds as a result of biogenic processes (Schroeder et al. 1987; Tamaki and Frankenberger 1992). Arsenic naturally occurs in sea water and vegetation and is released into the atmosphere in sea salt spray and forest fires. Anthropogenic sources of arsenic include nonferrous metal smelting, coal, oil and wood combustion, and municipal waste incineration. Arsenic naturally occurs in coal and oil and therefore, coal- and oil-fired power plants release arsenic to the atmosphere in their emissions (Pacyna 1987). Arsenic's use in agriculture and industrial processes also contributes to its emissions. One important source of arsenic emissions is cotton ginning in which the cotton seeds are removed from the raw cotton.

The National Air Toxics Assessment reported that total anthropogenic emissions for arsenic compounds in the United States in 1996 were 355 tons/year (EPA 2005b). EPA conducted a modeling study with the Assessment System for Population Exposure Nationwide (ASPEN) in which estimates of emissions of hazardous air pollutants were used to estimate air quality (Rosenbaum et al. 1999). Using 1990 data, the total emissions of arsenic in the conterminous 48 states, excluding road dust or windblown dust from construction or agricultural tilling was estimated to be 3.0 tons/day with 90% of emissions coming from point sources and 5% each from area and mobile sources. U.S. emissions of arsenic to the atmosphere were estimated as 3,300 metric tons per year between 1979 and 1986 (Pacyna et al. 1995). There is evidence that anthropogenic emissions, at least from smelters, are lower than they had been in the early 1980s. It is likely that air releases of arsenic decreased during the 1980s due to regulations on industrial emissions (EPA 1986f), improved control technology for coal-burning facilities, and decreased use of arsenical pesticides.

Nriagu and Pacyna (1988) and Pacyna et al. (1995) estimated worldwide emissions of arsenic to the atmosphere for 1983. Estimates of yearly emissions from anthropogenic sources ranged from 12,000 to 25,600 metric tons with a median value of 18,800 metric tons. Natural sources contributed 1,100–23,500 metric tons annually. Chilvers and Peterson (1987) estimated global natural and anthropogenic arsenic emissions to the atmosphere as 73,500 and 28,100 metric tons per year, respectively. Copper smelting and coal combustion accounted for 65% of anthropogenic emissions. A U.S. Bureau of Mines study on the flow of mineral commodities estimated that global emissions of arsenic from metal smelting, coal burning, and other industrial uses ranged from 24,000 to 124,000 metric tons per year compared to natural releases, mostly from volcanoes, ranging from 2,800 to 8,000 metric tons per year (Loebenstein 1994).

Pirrone and Keeler (1996) compared trends of trace element emissions from major anthropogenic sources in the Great Lakes region with ambient concentrations observed in urban areas of the region. They found that arsenic emissions increased about 2.8% per year from 1982 to 1988 and then decreased steadily by about 1.4% per year to 1993. Coal combustion in electric utilities and in residential, commercial, and industrial facilities was an important source of arsenic in the region, accounting for about 69% of the total emissions. Iron-steel manufacturing accounted for about 13% of the region wide arsenic emissions and nonferrous metals production for 17%.

Arsenic in the particulate phase is the predominant (89–98.6%) form of arsenic in the troposphere (Matschullat 2000). Inorganic species, most commonly trivalent arsenic, is the dominant form of arsenic in the air over emission areas; methylated forms of arsenic are probably of minor significance. Arsenic-containing air samples of smelter or coal-fired power plant origin consist largely of trivalent arsenic in both vapor and particulate form (Pacyna 1987). Oxides are the primary species evolved from fossil fuel and industrial processes. Additionally, arsenic trisulfide has also been reported from coal combustion, organic arsines from oil combustion, and arsenic trichloride from refuse incineration.

Arsenic has been identified in 59 air samples collected from 1,684 current or former NPL hazardous waste sites where it was detected in some environmental media (HazDat 2006).

6.2.2 Water

Estimated releases of 780 pounds (~0.35 metric tons) of arsenic to surface water from 58 domestic manufacturing and processing facilities in 2004, accounted for about 0.09% of the estimated total environmental releases from facilities required to report to the TRI (TRI04 2006). Estimated releases of 1.3x105 pounds (~59 metric tons) of arsenic compounds to surface water from 361 domestic manufacturing and processing facilities in 2004, accounted for about 0.11% of the estimated total environmental releases from facilities required to report to the TRI (TRI04 2006). These releases for arsenic and arsenic compounds are summarized in Tables 6-1 and 6-2, respectively.

Arsenic may be released to water from the natural weathering of soil and rocks, and in areas of vulcanism. Arsenic may also leach from soil and minerals into groundwater. Anthropogenic sources of arsenic releases to water include mining, nonferrous metals, especially copper, smelting, waste water, dumping of sewage sludge, coal burning power plants, manufacturing processes, urban runoff, atmospheric deposition and poultry farms (Garbarino et al. 2003; Nriagu and Pacyna 1988; Pacyna et al. 1995). A contributory

part of mining and coal burning power plants is leaching from abandoned mine tailing and fly ash waste piles. Significant amounts of arsenic are released in liquid effluents from gold-milling operations using cyanide (Environment Canada 1993). Nriagu and Pacyna (1988) and Pacyna et al. (1995) estimated global anthropogenic inputs of arsenic into rivers, lakes, and oceans for 1983; annual estimated inputs ranged from 11,600 to 70,300 metric tons with a median value of 41,800 metric tons. Arsenic was detected in 58% of samples of urban storm water runoff from 8 of 15 cities surveyed in the National Urban Runoff Program at concentrations ranging from 1 to 50.5 µg/L (Cole et al. 1984).

Leaching of arsenic from soil, landfills, or slag deposits is a source of arsenic in groundwater (Francis and White 1987; Wadge and Hutton 1987). The arsenic in soil may be naturally-occurring or a result of the application of arsenic-containing pesticides or sludge. Wood treated with CCA is used in piers, piling and bulkheads and arsenic can leach from the treated wood (Breslin and Adler-Ivanbrook 1998; Brooks 1996; Cooper 1991; Sanders et al. 1994; Weis et al. 1998). Ammoniacal copper zinc arsenate (ACZA) is another arsenic-containing waterborne preservative; however, it is not as widely used as CCA (Lebow et al. 2000).

Arsenic has been identified in 846 groundwater and 414 surface water samples collected from 1,684 NPL hazardous waste sites, where it was detected in some environmental media (HazDat 2006).

6.2.3 Soil

Estimated releases of 0.70 million pounds (~320 metric tons) of arsenic to soils from 58 domestic manufacturing and processing facilities in 2004, accounted for about 77% of the estimated total environmental releases from facilities required to report to the TRI (TRI04 2006). An additional 0.17 million pounds (~77 metric tons), constituting about 19% of the total environmental emissions, were released via underground injection (TRI04 2006). Estimated releases of 117 million pounds (~5.3x104 metric tons) of arsenic compounds to soils from 361 domestic manufacturing and processing facilities in 2004, accounted for about 98% of the estimated total environmental releases from facilities required to report to the TRI (TRI04 2006). An additional 1.6 million pounds (~720 metric tons), constituting about 1.3% of the total environmental emissions, were released via underground injection (TRI04 2006). These releases for arsenic and arsenic compounds are summarized in Tables 6-1 and 6-2, respectively.

The soil receives arsenic from a variety of anthropogenic sources, including ash residue from power plants, smelting operations, mining wastes, and municipal, commercial, and industrial waste. Ash from

power plants is often incorporated into cement and other materials that are used for roads and construction. Arsenic may be released from such material into soil. Nriagu and Pacyna (1988) and Pacyna et al. (1995) estimated global anthropogenic inputs of arsenic into soil for 1983. Excluding mine tailings and smelter slag, annual estimated inputs ranged from 52,000 to 112,000 metric tons with a median value of 82,000 metric tons. Mine tailings and smelter slag were estimated to add an additional 7,200–11,000 and 4,500–9,000 metric tons, respectively. Old abandoned mine tailings undoubtedly contribute still more. Wood treated with CCA used in foundations or posts could potentially release arsenic into the surrounding soil. CCA preservatives have been shown to leach to varying degrees from wood, as well as through soils in both field and laboratory studies (Chirenje et al. 2003a; Hingston et al. 2001; Lebow et al. 2000; Rahman et al. 2004; Stilwell and Graetz 2001; USDA/USDT 2000). Arsenic may also be released on land through the application of pesticides and fertilizer. Senesi et al. (1999) reported the range of arsenic in 32 fertilizers as 2.2–322 ng/g. Roxarsone (3-nitro-4-hydroxyphenyl-arsonic acid), which was used to treat poultry feed in approximately 70% of the broiler poultry operations in 1999–2000, is excreted unchanged in the manure. Poultry litter (manure and bedding) is routinely used as fertilizer to cropland and pasture. In 2000, assuming 70% of the 8.3 billion broiler poultry produced in the United States were fed roxarsone-treated feed, the resulting manure would contain approximately $2.5x10^5$ kg of arsenic (Garbarino et al. 2003). Land application of sewage sludge is another source of arsenic in soil. Arsenic was detected in sewage sludge samples from 23 cities at concentrations of 0.3–53 µg/g (Mumma et al. 1984).

Arsenic has been identified in 758 soil and 515 sediment samples collected from 1,684 NPL hazardous waste sites, where it was detected in some environmental media (HazDat 2006).

6.3 ENVIRONMENTAL FATE

6.3.1 Transport and Partitioning

Arsenic in soil may be transported by wind or in runoff or may leach into the subsurface soil. However, because many arsenic compounds tend to partition to soil or sediment under oxidizing conditions, leaching usually does not transport arsenic to any great depth (EPA 1982c; Moore et al. 1988; Pantsar-Kallio and Manninen 1997; Welch et al. 1988). Arsenic is largely immobile in agricultural soils; therefore, it tends to concentrate and remain in upper soil layers indefinitely. Downward migration has been shown to be greater in a sandy soil than in a clay loam (Sanok et al. 1995). Arsenic from lead arsenate that was used for pest control did not migrate downward below 20 cm in one fruit orchard; in another orchard, 15 years after sludge amendments and deep plowing, essentially all arsenic residues

remained in the upper 40 cm of soil (Merwin et al. 1994). Leaching of arsenic in polluted wetland soil was low; leaching was correlated with the amount of dissolved organic matter in the soil (Kalbitz and Wennrich 1998). The effect of soil characteristics, namely pH, organic matter content, clay content, iron oxide content, aluminum oxide content, and cation exchange capacity (CEC), on the adsorption of various metals, including the metalloid arsenic, to 20 Dutch surface soils was assessed by regression analysis (Janssen et al. 1997). The most influential parameter affecting arsenic adsorption was the iron content of the soil.

Arsenic that is adsorbed to iron and manganese oxides may be released under reducing conditions, which may occur in sediment or flooding conditions (LaForce et al. 1998; McGeehan 1996; Mok and Wai 1994). In addition to reductive dissolution, when nutrient levels are adequate, microbial action can also result in dissolution (LaForce et al. 1998). Interestingly, drying of the previously flooded soil increases arsenic adsorption, possibly due to alterations in iron mineralogy (McGeehan et al. 1998).

Darland and Inskeep (1997) conducted a study to determine the effects of pH and phosphate competition on the transport of arsenate ($H_xAsO_4^{x-3}$) through saturated columns filled with sand containing free iron oxides. At pH 4.5 and 6.5, arsenate transport was strongly retarded, while at pH 8.5, it was rapid. The enhanced transport of arsenate at pH 8 is consistent with the pH dependence of surface complexation reactions describing arsenate sorption by metal oxide minerals that can be categorized as a ligand exchange mechanism. Phosphate was shown to compete effectively with arsenate for adsorption sites on the sand, but the competition was not sufficient to desorb all of the arsenate in batch column experiments, even when the applied phosphate exceeded the column adsorption capacity by a factor of two. The researchers concluded that arsenate desorption kinetics may play an important role in the transport of arsenate through porous media. In a study looking at the effect of competing anions on the adsorption of arsenite and arsenate on ferrihydrite, the effect of phosphate on arsenate adsorption was greater at higher pH than at low pH and the opposite trend was observed for arsenite. While sulfate did not change the affinity of arsenate for ferrihydrite, sulfate reduced the adsorption of arsenite at pHs below 7.0 (Jain and Loeppert 2000).

Smith et al. (1999) investigated the sorption properties of both As(V) and As(III) in 10 Australian soils of widely different chemistry and mineralogy at commonly found arsenic levels. Adsorption of both arsenate and arsenite was rapid (1 hour). The amount of As(V) sorbed varied widely (1.7–62.0 L/kg); soils with lower amounts of oxidic material adsorbed much less arsenic than those with higher amounts of these minerals. Arsenate sorption was highly correlated with the iron oxide content of the soil and this

factor probably accounts for much of the variation in soil adsorptivity. Considerable leaching of arsenic occurred at a separate site where cattle were treated with a dip containing arsenic (cattle dip site) and that contained similar soil properties to that studied by Smith et al. (1999). Arsenite adsorption, which was investigated in four of the Australian soils, was sorbed to a lesser extent than was arsenate. This was attributed to soil minerology and the species of As(V) (arsenate) and As(III) (arsenite) present in solution; at pH 5–7, the dominant As(V) species are $H_2AsO_4^-$ and $HAsO_4^{2-}$ and neutral H_3AsO_3 is the dominant As(III) species. For soils containing low amounts of oxidic minerals, pH had little effect on As(V) sorption, while for oxidic soils, a decrease in sorption was evident as the pH increased. In contrast, As(III) sorption increased with increasing pH (Smith et al. 1999). Jain et al. (1999) reported similar results where arsenite were both found to bind strongly to iron oxides; however, the adsorption of arsenate decreases with increasing pH, while the adsorption of arsenite increases with increasing pH (Jain et al. 1999). As(III), which exists in a neutral form as arsenous acid, H_3AsO_3 (pK_a=9.23, 12.13, 13.4), is less strongly adsorbed on mineral surfaces than the oxyanions of arsenic acid, H_3AsO_4, (pK_a=2.22, 6.98, 11.53) (NRC 1999). Based on its pK_a values, arsenic acid would exist as a mixture of arsenate anions, $H_2AsO_4^-$ and $HAsO_4^{2-}$, under most environmental conditions (pH 5–9).

The practice of liming to remediate contaminated soils and mine tailings has the potential to mobilize arsenic. Experiments performed by Jones et al. (1997) indicate that the increased mobility appears to be consistent with the pH dependence of sorption reactions of arsenic on iron oxide minerals rather than dissolution-precipitation reactions involving arsenic. They recommend that remediation of acidic mine tailings or other arsenic-contaminated soils be carefully evaluated with respect to potential arsenic mobilization, especially at contaminated sites hydraulically connected to surface or groundwaters.

Transport and partitioning of arsenic in water depends upon the chemical form (oxidation state and counter ion) of the arsenic and on interactions with other materials present. Soluble forms move with the water, and may be carried long distances through rivers (EPA 1979). However, arsenic may be adsorbed from water onto sediments or soils, especially clays, iron oxides, aluminum hydroxides, manganese compounds, and organic material (EPA 1979, 1982c; Welch et al. 1988). Under oxidizing and mildly reducing conditions, groundwater arsenic concentrations are usually controlled by adsorption rather than by mineral precipitation. The extent of arsenic adsorption under equilibrium conditions is characterized by the distribution coefficient, K_d, which measures the equilibrium partitioning ratio of adsorbed to dissolved contaminant. The value of K_d depends strongly upon the pH of the water, the arsenic oxidation state, and the temperature. In acidic and neutral waters, As(V) is extensively adsorbed, while As(III) is relatively weakly adsorbed. Trivalent inorganic arsenic exists predominantly as arsenous acid (H_3AsO_3)

at environmental pH and is not strongly adsorbed to suspended solids and sediments in the water column. Pentavalent inorganic arsenic exists predominantly as $H_2AsO_4^-$ and $HAsO_4^{2-}$ in most environmental waters, which has considerably greater adsorption characteristics than arsenous acid. While in acidic and neutral waters, As(V) is more strongly adsorbed relative to As(III), in high-pH waters (pH >9) aquifer K_d values are considerably lower for both oxidation states (Mariner et al. 1996). Sediment-bound arsenic may be released back into the water by chemical or biological interconversions of arsenic species (see Section 6.3.2).

Arsenic enters rivers from where mining operations occurred and is transported downstream, moving from water and sediment into biofilm (attached algae, bacterial, and associated fine detrital material), and then into invertebrates and fish. The source of arsenic in the water column may be resuspended sediment. While arsenic bioaccumulates in animals, it does not appear to biomagnify between tropic levels (Eisler 1994; Farag et al. 1998; Williams et al. 2006).

Most anthropogenic arsenic emitted to the atmosphere arises from high temperature processes (e.g., coal and oil combustion, smelting operations, and refuse incineration) and occurs as fine particles with a mass median diameter of about 1 μm (Coles et al. 1979; Pacyna 1987). These particles are transported by wind and air currents until they are returned to earth by wet or dry deposition. Their residence time in the atmosphere is about 7–9 days, in which time the particles may be transported thousands of kilometers (EPA 1982b; Pacyna 1987). Long-range transport was evident in analyzing deposition of arsenic in countries like Norway; there was no indication that the marine environment contributed significantly to the deposition (Steinnes et al. 1992). Atmospheric fallout can be a significant source of arsenic in coastal and inland waters near industrial areas. Scudlark et al. (1994) determined the average wet depositional flux of arsenic as 49 μg As/m^2/year for two sites in Chesapeake Bay, Maryland from June 1990 to July 1991. They found a high degree of spatial and temporal variability. The elemental fluxes derived predominantly from anthropogenic sources. Golomb et al. (1997) report average total (wet + dry) deposition rates to Massachusetts Bay of 132 μg/m^2/year, of which 21 μg/m^2/year was wet deposition during the period September 15, 1992–September 16, 1993. Hoff et al. (1996) estimated the following arsenic loadings into the Great Lakes for 1994 (lake, wet deposition, dry deposition): Superior, 11,000 kg/year, 3,600 kg/year; Michigan, 5,000 kg/year, 1,800 kg/year; Erie, 5,500 kg/year, 1,800 kg/year; and Ontario, 3,000 kg/year, 580 kg/year. The measured dry deposition fluxes of arsenic at four sampling sites around Lake Michigan ranged approximately from 0.01 to 1.5 μg As/m^2/day; estimated inputs of arsenic into Lake Michigan were reported to be $1.4x10^3$ kg/year (Shahin et al. 2000).

Terrestrial plants may accumulate arsenic by root uptake from the soil or by absorption of airborne arsenic deposited on the leaves, and certain species may accumulate substantial levels (EPA 1982b). Yet, even when grown on highly polluted soil or soil naturally high in arsenic, the arsenic level taken up by the plants is comparatively low (Gebel et al. 1998b; Pitten et al. 1999). Kale, lettuce, carrots, and potatoes were grown in experimental plots surrounding a wood preservation factory in Denmark where waste wood was incinerated to investigate the amount and pathways for arsenic uptake by plants (Larsen et al. 1992). On incineration, the arsenate in the wood preservative was partially converted to arsenite; the arsenic emitted from the stack was primarily particle bound. Elevated levels of inorganic arsenic were found in the test plants and in the soil around the factory. Statistical analyses revealed that the dominating pathway for transport of arsenic from the factory to the leafy vegetables (kale) was by direct atmospheric deposition, while arsenic in the root crops (potatoes and carrots) was a result of both soil uptake and atmospheric deposition. Arsenic accumulation by plants is affected by arsenic speciation. Uptake of four arsenic species (arsenite, arsenate, methylarsonic acid, and dimethylarsinic acid) by turnips grown under soilless culture conditions showed that while uptake increased with increasing arsenic concentration in the nutrient, the organic arsenicals showed higher upward translocation than the inorganic arsenical (Carbonell-Barrachina et al. 1999). The total amount of arsenic taken up by the turnip plants (roots and shoots) followed the trend methylarsenate (MMA)<dimethylarsinic acid (DMA) <arsenite<arsenate. In a similar experiment, conducted with tomato plants, the total amount of arsenic taken up by the tomato plants followed the trend DMA<MMA<arsenate≈arsenite, with arsenic concentrations in the plants increasing with increasing arsenic concentration in the nutrient solution. Arsenic was mainly accumulated in the root system (85%) with smaller amounts translocating to the fruit (1%). However, plants treated with MMA and DMA had higher arsenic concentrations in the shoots and fruit than those treated with arsenite or arsenate (Burlo et al. 1999). Terrestrial plants growing on land bordering arsenic-contaminated waters show relatively little arsenic content, even though the sediments have arsenic concentrations as high as 200 µg/g (Tamaki and Frankenberger 1992). Arsenic concentrations in vegetables grown in uncontaminated soils and contaminated soils containing arsenic, as well as other metals and organic contaminants, were generally <12 µg/kg wet weight. A maximum arsenic concentration of 18 µg/kg wet weight was found in unpeeled carrots grown in soil, which contained a mean arsenic concentration of 27 mg/kg dry weight (Samsøe-Petersen et al. 2002).

In a study by Rahman et al. (2004), CCA-treated lumber was used to construct raised garden beds to determine how far the components of CCA migrated in the soil and the uptake of these components by crops grown in the soil. Arsenic was found to diffuse laterally into the soil from the CCA-treated wood, with the highest concentrations found at 0–2 cm from the treated wood and a steady decline in

concentration with increased distance. The highest average arsenic concentrations found in soil closest (0–2 cm) to the CCA-treated wood were 56 and 46 µg/g in loamy sand and sandy loam soils, respectively. At a distance of 30–35 cm from the CCA-treated wood, arsenic concentrations were approximately 7 µg/g in both soils. All samples were of the top 0–15 cm of soil. Crops grown in both soil types within 0–2 cm of the CCA-treated wood contained higher concentrations of arsenic, 0.186 and 10.894 µg/g for carrots without peal and bean leaves and stems, respectively, than those grown at 1.5 m from the CCA-treated wood, 0.006 and 0.682 µg/g for bean pods and bean leaves and stems, respectively. However, based on FDA guidelines on tolerance limits, these crops would be considered approved for human consumption. Studies by Chirenje et al. (2003a) also showed that elevated arsenic concentrations were found in surface (0–5 cm) soils immediately surrounding, within the first 0.3 m, of utility poles, fences, and decks made with CCA-treated wood. Factors such as the preservative formula, fixation temperature, post treatment handling, and timber dimensions of CCA-treated wood, as well as the pH, salinity, and temperature of the leaching media can affect the leach rates from CCA-treated wood (Hingston et al. 2001). Studies of leaching of the components of CCA- and ACZA-treated wood used to construct a boardwalk in wetland environments reported elevated arsenic levels in soil and sediment below and adjacent to these structures. Generally, these levels decreased with increasing distance from the structure (Lebow et al. 2000). Increased concentrations of arsenic were also observed under CCA-treated bridges. Arsenic levels declined with distance from the bridge and were near background levels at 1.8–3 m from the bridge's perimeter (USDA/USDT 2000).

In a study by Lebow et al. (2003), the use of a water repellent finish on CCA-treated wood significantly reduces the amount of arsenic, as well as copper and chromium, in the run-off water. It was also observed the exposure to UV radiation caused a significant increase in leaching from both finished and unfinished samples of CCA-treated wood. Small amounts of arsenic can be transferred from CCA-treated wood to skin from touching CCA-treated wood surfaces (Hemond and Solo-Gabriele 2004; Kwon et al. 2004; Shalat et al. 2006; Ursitti et al. 2004; Wang et al. 2005).

Breslin and Adler-Ivanbrook (1998) examined the leaching of the copper, chromium, and arsenic from CCA-treated wood in laboratory studies using samples of treated southern yellow pine in solutions simulating estuarine waters. The tank leaching solutions were frequently sampled and replaced to approximate field conditions. Initial 12-hour fluxes ranging from $0.2x10^{-10}$ to $5.2x10^{-10}$ mol/mm^2 d was reported for arsenic. After 90 days, arsenic fluxes decreased to $0.5x10^{-11}$–$3.1x10^{-11}$ mol/mm^2 d. A study by Cooper (1991) demonstrated that the buffer system used in leaching studies of components from CCA-treated wood can significantly change the amount arsenic released from treated wood. Samples of four

species of CCA-treated wood were exposed to four acidic leaching solutions. In the samples exposed to water adjusted to pHs of 3.5, 4.5, and 5.5, losses of arsenic after 13 days were generally <7%. However, when a leaching solution of sodium hydroxide and citric acid buffer (pH 5.5) was used, the percent of arsenic leached ranged from 27.4 to 46.7% (Cooper 1991).

Arsenic bioaccumulation depends on various factors, such as environmental setting (marine, estuarine, freshwater), organism type (fish, invertebrate), trophic status within the aquatic food chain, exposure concentrations, and route of uptake (Williams et al. 2006). Bioaccumulation refers to the net accumulation of a chemical by aquatic organisms as a result of uptake from all environmental sources, such as water, food, and sediment, whereas bioconcentration refers to the uptake of a chemical by an aquatic organism through water (EPA 2003b). Biomagnification in aquatic food chains does not appear to be significant (EPA 1979, 1982b, 1983e, 2003b; Mason et al. 2000; Williams et al. 2006).

Bioconcentration of arsenic occurs in aquatic organisms, primarily in algae and lower invertebrates. Both bottom-feeding and predatory fish can accumulate contaminants found in water. Bottom-feeders are readily exposed to the greater quantities of metals, including the metalloid arsenic, which accumulate in sediments. Predators may bioaccumulate metals from the surrounding water or from feeding on other fish, including bottom-feeders, which can result in the biomagnification of the metals in their tissues. An extensive study of the factors affecting bioaccumulation of arsenic in two streams in western Maryland in 1997–1998 found no evidence of biomagnification since arsenic concentrations in organisms tend to decrease with increasing tropic level (Mason et al. 2000). Arsenic is mainly accumulated in the exoskeleton of invertebrates and in the livers of fish. No differences were found in the arsenic levels in different species of fish, which included herbivorous, insectivorous, and carnivorous species. The major bioaccumulation transfer is between water and algae, at the base of the food chain and this has a strong impact on the concentration in fish. National Contaminant Biomonitoring data produced by the Fish and Wildlife Service were used to test whether differences exist between bottom-feeders and predators in tissue levels of metals and other contaminants. No differences were found for arsenic (Kidwell et al. 1995). The bioconcentration factors (BCFs) of bryophytes, invertebrates, and fish (livers) in Swedish lakes and brooks impacted by smelter emissions were 8,700, 1,900–2,200, and 200–800, respectively (Lithner et al. 1995). EPA (2003b) assessed a large dataset of bioaccumulation data for various fish and invertebrate species. BCF values in this dataset ranged from 0.048 to 1,390.

Williams et al. (2006) reviewed 12 studies of arsenic bioaccumulation in freshwater fish, and proposed that BCF and bioaccumulation factor (BAF) values are not constant across arsenic concentrations in

water. BCF or BAF values from these 12 studies ranged from 0.1 to 3,091. Williams et al. (2006) found that BCF and BAF values appear to be the highest within the range of ambient arsenic concentrations, and decline steeply to relatively low levels as the arsenic concentrations in water increase. Based on this analysis, arsenic concentrations in tissue and BAF values may be a power function of arsenic concentrations in water. EPA (2007b) also reported that for many nonessential metals, including arsenic, accumulation is nonlinear with respect to exposure concentration.

6.3.2 Transformation and Degradation

6.3.2.1 Air

Arsenic is released into the atmosphere primarily as arsenic trioxide or, less frequently, in one of several volatile organic compounds, mainly arsines (EPA 1982b). Trivalent arsenic and methyl arsines in the atmosphere undergo oxidation to the pentavalent state (EPA 1984a), and arsenic in the atmosphere is usually a mixture of the trivalent and pentavalent forms (EPA 1984a; Scudlark and Church 1988). Photolysis is not considered an important fate process for arsenic compounds (EPA 1979).

6.3.2.2 Water

Arsenic in water can undergo a complex series of transformations, including oxidation-reduction reactions, ligand exchange, precipitation, and biotransformation (EPA 1979, 1984a; Sanders et al. 1994; Welch et al. 1988). Rate constants for these various reactions are not readily available, but the factors most strongly influencing fate processes in water include Eh, pH, metal sulfide and sulfide ion concentrations, iron concentrations, temperature, salinity, distribution and composition of the biota, season, and the nature and concentration of natural organic matter (EPA 1979; Farago 1997; Redman et al. 2002; Wakao et al. 1988). Organic arsenical pesticides, such as MSMA, DSMA, and DMA do not degrade by hydrolysis or by aquatic photolysis (EPA 2006). No formation of arsine gas from marine environments has been reported (Tamaki and Frankenberger 1992).

Inorganic species of arsenic are predominant in the aquatic environment. In the pH range of natural waters, the predominant aqueous inorganic As(V) species are the arsenate ions, $H_2AsO_4^-$ and $HAsO_4^{2-}$; the predominant inorganic As(III) species is $As(OH)_3$ (Aurillo et al. 1994; EPA 1982c). As(V) generally dominates in oxidizing environments such as surface water and As(III) dominates under reducing conditions such as may occur in groundwater containing high levels of arsenic. However, the reduction of arsenate to arsenite is slow, so arsenate can be found in reducing environments. Conversely, the oxidation of arsenite in oxidizing environments is moderately slow (half-life, 0.4–7 days in coastal

systems) and therefore, arsenite can be found in oxidizing environments (Mariner et al. 1996; Sanders et al. 1994). The main organic species in fresh water are MMA and DMA; however, these species are usually present at lower concentrations than inorganic arsenic species (Eisler 1994). (The toxicities of MMA and DMA are discussed in Chapter 3.) Aquatic microorganisms may reduce the arsenate to arsenite, as well as methylate arsenate to its mono- or dimethylated forms (Aurillo et al. 1994; Benson 1989; Braman and Foreback 1973; Edmonds and Francesconi 1987; Sanders et al. 1994). Methylated species are also produced by the biogenic reduction of more complex organoarsenic compounds like arsenocholine or arsenobetaine. Water samples from a number of lakes and estuaries, mostly in California, show measurable concentrations of methylated arsenic (equivalent to 1–59% of total arsenic) (Anderson and Bruland 1991). Within the oxic photic zone, arsenate and DMA were the dominant species. A seasonal study of one lake demonstrated that DMA was the dominant form of arsenic in surface waters during late summer and fall. Methylated species declined and arsenate species increased when the lake turned over in late fall. Mono Lake, a highly alkaline body of water, and four rivers did not have measurable concentrations of methylated arsenic. It was hypothesized that the reason why methylated forms were not detected in Mono Lake was that the extremely high inorganic arsenic concentrations in the lake, 230 µM (17 mg/L), could overwhelm the analysis of small amounts of organic forms. Other possibilities are that the high alkalinity or very high phosphate levels in the water, 260 µM (25 mg/L), are not conducive to biogenic methylation (Anderson and Bruland 1991). Both reduction and methylation of As(V) may lead to increased mobilization of arsenic, since As(III), dimethylarsinates, and monomethylarsonates are much less particle-reactive than As(V) (Aurillo et al. 1994). In the estuarial Patuxet River, Maryland, arsenate concentrations peaked during the summer, at 1.0 µg/L in 1988–1989 (Sanders et al. 1994). In contrast, winter to spring levels were around 0.1 µg/L. Arsenite concentrations were irregularly present at low levels during the year. Peaks of DMA occurred at various times, particularly in the winter and late spring and appeared to be linked with algal blooms. The DMA peak declined over several months that was followed by a rise in MMA. The MMA was thought to be occurring as a degradation product of DMA. A similar seasonal pattern of arsenic speciation was observed in Chesapeake Bay. Arsenite methylation took place during the warmer months leading to changes down the main stem of the bay; arsensite production dominated the upper reaches of the bay and methylated species dominated the more saline lower reaches. In coastal waters, reduced and methylated species are present in lower concentrations, around 10–20% of total arsenic (Sanders et al. 1994). In groundwater, arsenic generally exists as the oxyanion of arsenate ($H_xAsO_4^{3-x}$) or arsenite ($H_xAsO_3^{3-x}$), or both; however, the distribution between arsenite and arsenate is not always predictable based on oxidation-reduction potential (Robertson 1989; Welch et al. 1988).

6.3.2.3 Sediment and Soil

In soil, arsenic is found as a complex mixture of mineral phases, such as co-precipitated and sorbed species, as well as dissolved species (Roberts et al. 2007). The degree of arsenic solubility in soil will depend on the amount of arsenic distributed between these different mineral phases. The dissolution of arsenic is also affected by particle size. The distribution between these phases may reflect the arsenic source (e.g., pesticide application, wood treatment, tanning, or mining operations), and may change with weathering and associations with iron and manganese oxides and phosphate minerals in the soil (Roberts et al. 2007; Ruby et al. 1999). Davis et al. (1996) reported that in soil in Anaconda, Montana, a smelting site from 1860 to 1980, contained arsenic that is only in a sparingly soluble form, consisting of primarily arsenic oxides and phosphates.

The arsenic cycle in soils is complex, with many biotic and abiotic processes controlling its overall fate and environmental impact. Arsenic in soil exists in various oxidation states and chemical species, depending upon soil pH and oxidation-reduction potential. Under most environmental conditions, inorganic As(V) will exist as a mixture of arsenate anions, $H_2AsO_4^-$ and $HAsO_4^{2-}$, and inorganic As(III) will exist as H_3AsO_3. The arsenate and arsenite oxyanions have various degrees of protonation depending upon pH (EPA 1982b; McGeehan 1996). As(V) predominates in aerobic soils, and As(III) predominates in slightly reduced soils (e.g., temporarily flooded) or sediments (EPA 1982b; Sanders et al. 1994). As(III) commonly partitions to the aqueous phase in anoxic environments, and would be more mobile. As(V) usually remains bound to minerals, such as ferrihydrite and alumina, limiting its mobility and bioavailability (Rhine et al. 2006).

Arsenite is moderately unstable in the presence of oxygen; however, it can be found under aerobic conditions as well (Sanders et al. 1994). While arsenate is strongly sorbed by soils under aerobic conditions, it is rapidly desorbed as the system becomes anaerobic. Once it is desorbed, arsenate can be reduced to arsenite, which exhibits greater mobility in soils (McGeehan 1996). Transformations between the various oxidation states and species of arsenic occur as a result of biotic or abiotic processes (Bhumbla and Keefer 1994). While degradation of an organic compound is typically considered complete mineralization, in the case of organic arsenic compounds, the element arsenic itself cannot be degraded. However, the organic portion of the molecule can be metabolized (Woolson 1976).

Arsenicals applied to soils may be methylated by microorganisms to arsines, which are lost through volatilization, and organic forms may be mineralized to inorganic forms. Gao and Burau (1997) reported

that the overall percentage of DMA and MMA minerialized after 70 days ranged from 3 to 87% in air-dry soil and a soil near saturation, respectively. The rate of demethylation of DMA increased with soil moisture. Over the same 70-day period, arsenic losses as volatile arsines were much lower than minerialization, ranging from 0.001 to 0.4%. Arsine evolution rates followed the order: DMA>MMA>arsenite=arsenate (Gao and Burau 1997). Woolson and Kearney (1973) reported that ^{14}C-labeled DMA degraded differently in soils under aerobic and anaerobic conditions. Under anaerobic conditions, 61% of the applied DMA was converted to a volatile alkyl arsine after 24 weeks, and lost from the soil system. Under aerobic conditions, 35% was converted to a volatile organo-arsenic compound, possibly dimethyl arsine, and 41% was converted to $^{14}CO_2$ and arsenate after 24 weeks. Similar to microorganisms in soils, Reimer (1989) reported that microorganisms found in natural marine sediments and sediments contaminated with mine-tailings are also capable of methylating arsenic under aerobic and anaerobic conditions. Von Endt et al. (1968) reported that the degradation of ^{14}C-labelled monosodium methanearsonate (MSMA) was found to range from 1.7 to 10% in Dundee silty clay loam soil and Sharkey clay soil after 60 days, respectively. MSMA decomposition to CO_2 was a slow process without a lag period. Sterilized soils were found to produce essentially no $^{14}CO_2$ (0.7%) after 60 days, indicating that soil bacteria contributed to the decomposition of MSMA (Von Endt et al. 1968). Akkari et al. (1986) studied the degradation of MSMA in various soils. At 20% water content, half-lives of 144, 88, and 178 days were reported in Sharkey clay, Taloka silt loam, and Steele-Crevasse sand loam, respectively. The Sharkey soil with the highest clay content was expected to have the greatest adsorptive capacity for both water and MSMA, reducing the amount of MSMA available in the soil solution to microorganisms that degrade the MSMA. The half-lives were 25, 41, and 178 days under anaerobic (flooded) conditions in Sharkey clay, Taloka silt loam, and Steele-Crevasse sand loam, respectively. Under flooded conditions, MSMA degradation occurs by reductive methylation to form arsinite and alkylarsine gas. The authors attributed the longer half-lives for MSMA degradation in the Steele-Crevasse sand loam soil to its low organic matter content, which may have supported fewer microbial populations needed for oxidation demethylation under aerobic conditions. Under flooded conditions, anaerobiosis is expected to be slowest in low organic matter sandy loam soils (Akkari et al. 1986).

Organic arsenical pesticides, such as MSMA, DSMA, and DMA, do not degrade by hydrolysis or by soil photolysis (EPA 2006).

Roxarsone (3-nitro-4-hydroxyphenylarsonic acid) used in poultry feed is found excreted unchanged in poultry litter (bedding and manure). Roxarsone found in poultry litter, which is used to amend agricultural soil, was found to degrade to arsenate in approximately 3–4 weeks upon composting

(Garbarino et al. 2003). In addition, the arsenic in poultry litter was found to be easily mobilized by water; however, its leach rate from amended soils was slow enough that it accumulated in soils (Rutherford et al. 2003).

A sequential fractionation scheme was used to assess the chemical nature, and thus the potential bioavailability, of arsenic at cattle dip sites in Australia where sodium arsenite was used extensively in cattle dips from the turn of the century until the early 1950s (McLaren et al. 1998). Most sites contained substantial amounts, 13% on the average, of arsenic in the two most labile fractions indicating a high potential for bioaccessibility and leaching. The bulk of the arsenic appeared to be associated with amorphous iron and aluminum minerals in soil. Similarly, arsenic in soil and mine waste in the Tamar Valley in England was found to be concentrated in a fraction associated with iron and organic-iron (Kavanagh et al. 1997). Laboratory studies were performed to assess the phase partitioning of trace metals, including the metalloid arsenic, to sediment from the Coeur d'Alene River, a mining area of Idaho, and the release of metals under simulated minor and major flooding events (LaForce et al. 1998). Arsenic was primarily associated with the iron and manganese oxides as seen by its large release when these oxides were reduced. Arsenic levels were comparatively low in the organic fraction and remaining residual fraction and negligible in the extractible fractions.

6.3.2.4 Other Media

Carbonell-Barrachina et al. (2000) found the speciation and solubility of arsenic in sewage sludge suspensions to be affected by pH and Eh. Under oxidizing conditions, the solubility of arsenic was low, with a major portion of the soluble arsenic present as organic arsenic compounds, mainly dimethylarsinic acid (approximately 74% of the total arsenic in solution). Under moderately reducing conditions (0–100 mV), inorganic arsenic accounted for the majority (90%) of the total arsenic in solution, and the solubility of arsenic was increased due to dissolution of iron oxyhydroxides. Under strongly reducing conditions (-250 mV), arsenic solubility was decreased by the formation of insoluble sulfides. The pH of the solution was also found to influence the speciation and solubility of arsenic. At neutral pH, the solubility of arsenic was at its maximum, and decreased under acidic or alkaline conditions. Inorganic arsenic species were the dominant species at pH 5.0; at pH 6.5, the major soluble forms were organic arsenic species. The biomethylation of arsenic was limited at acidic pH, and was at its maximum at near neutral pH (Carbonell-Barrachina et al. 2000).

6.4 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT

Reliable evaluation of the potential for human exposure to arsenic depends in part on the reliability of supporting analytical data from environmental samples and biological specimens. Concentrations of arsenic in unpolluted atmospheres and in pristine surface waters are often so low as to be near the limits of current analytical methods. In reviewing data on arsenic levels monitored or estimated in the environment, it should also be noted that the amount of chemical identified analytically is not necessarily equivalent to the amount that is bioavailable. The analytical methods available for monitoring arsenic in a variety of environmental media are detailed in Chapter 7.

6.4.1 Air

Arsenic in ambient air is usually a mixture of particulate arsenite and arsenate; organic species are of negligible importance except in areas of substantial methylated arsenic pesticide application or biotic activity (EPA 1984a). Mean levels in ambient air in the United States have been reported to range from <1 to 3 ng/m^3 in remote areas and from 20 to 30 ng/m^3 in urban areas (Davidson et al. 1985; EPA 1982c; IARC 1980; NAS 1977a). EPA conducted a modeling study with the Assessment System for Population Exposure Nationwide (ASPEN) in which estimates of emissions of hazardous air pollutants were used to estimate ambient concentrations (Rosenbaum et al. 1999). Using 1990 data to estimate total emissions of arsenic in the conterminous 48 states, excluding road dust or windblown dust from construction or agricultural tilling, the 25th percentile, median, and 75th percentile arsenic concentration were estimated to be 9, 20, and 30 ng/m^3, respectively. Maps illustrating the amount of toxic air pollutant emissions, including arsenic compounds, by county in 1996 for the 48 coterminous states of the United States as well as Puerto Rico and the Virgin Islands are available on the internet at http://www.epa.gov/ttn/atw/-nata/mapemis.html, as of March 2005. Schroeder et al. (1987) listed ranges of arsenic concentrations in air of 0.007–1.9, 1.0–28, and 2–2,320 ng/m^3 in remote, rural, and urban areas, respectively. The average annual arsenic concentration in air at Nahant, Massachusetts, just north of Boston, between September 1992 and September 1993, was 1.2 ng/m^3; 75% of the arsenic was associated with fine (<2.5 μm) particles. The long-term means of the ambient concentrations of arsenic measured in urban areas of the Great Lakes region from 1982 to 1993 ranged from 4.2 to 9.6 ng/m^3 (Pirrone and Keeler 1996). Large cities generally have higher arsenic air concentrations than smaller ones due to emissions from coal-fired power plants (IARC 1980), but maximum 24-hour concentrations generally are <100 ng/m^3 (EPA 1984a). In the spring of 1990, aerosols and cloud water that were sampled by aircraft at an altitude of 1.2–3 km above the Midwestern United States had a mean mixed layer arsenic concentration of 1.6±0.9 ng/m^3 (Burkhard et al. 1994). A mean arsenic concentration of 1.0±0.5 ng/m^3 was reported at

Mayville, New York, a site 400 km to the northwest of the sampling area and directly downwind on most days.

Arsenic was monitored at an application site in the San Joaquin Valley, California and at four sites in nearby communities in 1987 where sodium arsenite was used as a fungicide on tokay grapes (Baker et al. 1996). The maximum arsenic concentration measured 15–20 meters from the edge of the field was 260 ng/m^3. The maximum arsenic concentration at four community sites in the area was 76 ng/m^3. The concentration at an urban background site was 3 ng/m^3 (Baker et al. 1996). Sodium arsenite is no longer registered in California (Baker et al. 1996). The highest historic arsenic levels detected in the atmosphere were near nonferrous metal smelters, with reported concentrations up to 2,500 ng/m^3 (IARC 1980; NAS 1977a; Schroeder et al. 1987).

Arsenic air concentrations measured in several indoor public places (e.g., cafeteria, coffee house, music club, Amtrak train, and several restaurants) with environmental tobacco smoke (ETS) ranged from <0.1 to 1 ng/m^3, with a mean of 0.4±0.3 ng/m^3. Sites that were ETS-free (university office and library) had arsenic concentrations <0.13 ng/m^3 (Landsberger and Wu 1995). The Toxic Exposure Assessment at Columbia/Harvard (TEACH) study measured levels of various toxics in New York City air in 1999. Exposures were assessed in a group of 46 high school students in West Central Harlem. Mean arsenic concentrations in summer home outdoor, home indoor, and personal air of the participants were 0.37, 0.40, and 0.45 ng/m^3, respectively (Kinney et al. 2002). Detected arsenic concentrations in indoor and outdoor air collected as part of the National Human Exposure Assessment Survey (NHEXAS) in Arizona ranged from 3.4 to 22.3 and from 3.5 to 25.7 ng/m^3, respectively, with 71 and 68% below the detection limit (1.8–14.3 ng/m^3) (O'Rourke et al. 1999).

6.4.2 Water

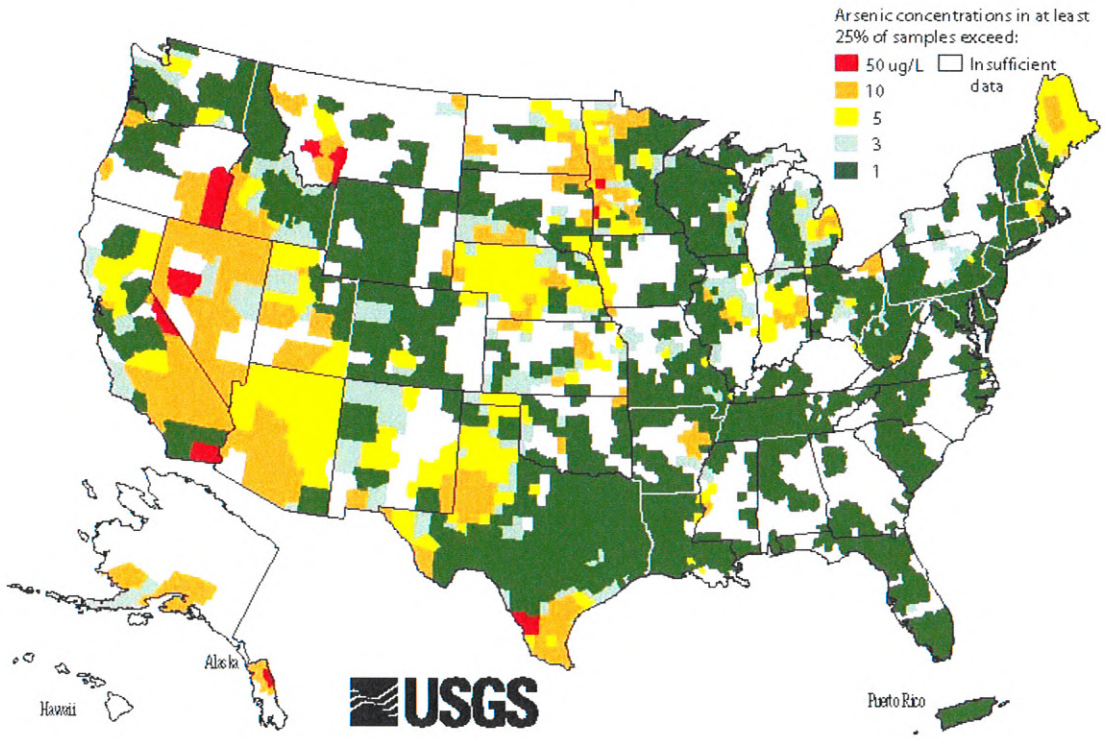
Arsenic is widely distributed in surface water, groundwater, and finished drinking water in the United States. A survey of 293 stations in two nationwide sampling networks on major U.S. rivers found median arsenic levels to be 1 µg/L; the 75th percentile level was 3 µg/L (Smith et al. 1987). Arsenic was detected in 1,298 of 3,452 surface water samples recorded in the STORET database for 2004 at concentrations ranging from 0.138 to 1,700 µg/L in samples where arsenic was detected (EPA 2005c). Two streams in western Maryland that were the focus of a major bioaccumulation study in 1997–1998 had arsenic concentrations of 0.370±0.200 and 0.670±0.460 µg/L (Mason et al. 2000). Surface water will be impacted by runoff from polluted sites. An average arsenic concentration of 5.12 µg/L was reported in

water from Moon Lake, a Mississippi River alluvial floodplain in northwest Mississippi. Intensive cultivation has occurred in this area, including cotton, soybeans, and rice (Cooper and Gillespie 2001). Hard-rock mining activities occurred in the southern part of Colorado and New Mexico north of Taos since the latter part of the 19th century until recently, which have impacted the Rio Grande and its tributaries. A mean arsenic concentration of approximately 0.8 µg/L was reported for the main stem of the Rio Grande sampled in June and September 1994. Arsenic concentrations in the Alamosa River, Colorado were 0.11 and 0.14 µg/L in June and September 1994, respectively, and 1.4 µg/L in Big Arsenic Spring, New Mexico in September 1994 (Taylor et al. 2001). Arsenic concentrations in water from watersheds in Black Hills, South Dakota, an area impacted by gold mining activities ranged from 2.5 to 55 µg/L and from 1.7 to 51 µg/L in unfiltered and filtered samples, respectively; concentrations from reference areas ranged from 1.1 to 3.4 µg/L and from 0.9 to1.9 µg/L in unfiltered and filtered samples, respectively (May et al. 2001). Arsenic concentrations ranged from 0.29 to 34.0 µg/L in water samples from Wakulla River and St. Joseph Bay North, along the Florida Panhandle; arsenic contamination in this area is likely to result from nonpoint source pollution (Philp et al. 2003).

Data on total arsenic in surface water from a number of seas and oceans show levels of <1 µg/L, except in the Antarctic Ocean and Southwest Pacific Oceans where the levels are 1.1 and 1.2 µg/L, respectively. Levels in coastal waters and estuaries are generally somewhat higher, in the range of 1–3 µg/L. However, estuarine water in Salinas, California had arsenic levels of 7.42 µg/L (Francesconi et al. 1994). The dissolved arsenic concentration in water at 40 sites in the Indian River Lagoon System in Florida ranged from 0.35 to 1.6 µg/L with a mean of 0.89±0.34 µg/L (Trocine and Trefry 1996). Thermal waters generally have arsenic levels of 20–3,800 µg/L, although levels as high as 276,000 µg/L have been recorded (Eisler 1994).

Arsenic levels in groundwater average about 1–2 µg/L, except in some western states with volcanic rock and sulfidic mineral deposits high in arsenic, where arsenic levels up to 3,400 µg/L have been observed (IARC 1980; Page 1981; Robertson 1989; Welch et al. 1988). In western mining areas, groundwater arsenic concentrations up to 48,000 µg/L have been reported (Welch et al. 1988). Arsenic concentrations in groundwater samples collected form 73 wells in 10 counties in southeast Michigan in 1997 ranged from 0.5 to 278 µg/L, with an average of 29 µg/L. Most (53–98%) of the arsenic was detected as arsenite (Kim et al. 2002). The U.S. Geological Survey mapped concentrations of arsenic in approximately 31,350 groundwater samples collected between 1973 and 2001; the counties in which at least 25% of wells exceed various levels are shown in Figure 6-2 (USGS 2007a). Most arsenic in natural waters is a

Figure 6-2. Counties in Which at Least 25% of Wells Exceed Different Arsenic Levels



Source: USGS 2007a

mixture of arsenate and arsenite, with arsenate usually predominating (Braman and Foreback 1973; EPA 1982c, 1984a). Methylated forms have also been detected in both surface water and groundwater, at levels ranging from 0.01 to 7.4 µg/L (Braman and Foreback 1973; Hood 1985), with most values below 0.3 µg/L (Hood 1985). In a survey of shallow groundwater quality in the alluvial aquifer beneath a major urban center, Denver, Colorado, arsenic levels in the 30 randomly-chosen wells sampled had median levels of <1 µg/L; the maximum level was 33 µg/L (Bruce and McMahon 1996). Arsenic levels in groundwater sometimes exceeded the EPA maximum contaminant level (MCL), which was 50 µg/L at the time, in the Willamette Valley, Oregon and a nine-county region of southeastern Michigan (USGS 1999b, 1999c).

Arsenic has also been detected in rainwater at average concentrations of 0.2–0.5 µg/L (Welch et al. 1988). This range is consistent with that found in a 1997–1998 study in western Maryland, which was the focus of a major bioaccumulation study (Mason et al. 2000). Arsenic levels in wet deposition in the watershed as well as throughfall into the two streams were 0.345±0.392, 0.400±0.400, and 0.330±0.250 µg/L, respectively. Median arsenic concentrations in 30-day rainwater composite samples collected May-September 1994 from eight arctic catchments in northern Europe at varying distances and wind directions from the emissions of a Russian nickel ore mining, roasting, and smelting industry on the Kola Peninsula ranged from 0.07 to 12.3 µg/L (Reimann et al. 1997). Rain and snow samples were collected during the fall of 1996 and winter of 1997 at eight locations in a semi-circular pattern radiating out (2–15 km) in the direction of the prevailing wind from the Claremont incinerator located in New Hampshire. This incinerator processes 200 tons of solid waste per day. Arsenic concentrations in rainwater and snow ranged from 0.020 to 0.079 µg/L and from 0.80 to 1.28 µg/L, respectively (Feng et al. 2000).

Drinking water is one of the most important sources of arsenic exposure. Surveys of drinking water in the United States have found that >99% of public water supplies have arsenic concentrations below the EPA MCL, which was 50 µg/L at the time (EPA 1984a). In an EPA study of tap water from 3,834 U.S. residences, the average value was 2.4 µg/L (EPA 1982c).

Before the MCL for arsenic in drinking water was lowered from 50 to 10 µg/L, studies were undertaken to ascertain how different standards would affect compliance. One such survey sponsored by the Water Industry Technical Action Fund was the National Arsenic Occurrence Survey (NAOS). NAOS was based on a representational survey of public water systems defined by source type, system size, and geographical location. Additionally, it included a natural occurrence factor, a stratifying variable that could qualitatively describe the likelihood of arsenic occurrence in the supply. To predict finished water

arsenic concentrations, data on the water treatment options, efficiency, and frequency of use were factored in. The results of the NAOS are presented in Table 6-3. The NAOS results are in general agreement with two older and more limited national surveys, EPA's National Inorganics and Radionuclides Survey (NIRS) and the Metropolitan Water District of Southern California Survey (MWDSC). The percentages of water systems that would be out of compliance are estimated to be 1.7, 3.6, 9.3, and 20.7% for arsenic MCLs of 20, 10, 5, and 2 μg/L, respectively. Arsenic concentrations were determined in drinking in EPA Region V (Indiana, Illinois, Michigan, Minnesota, Ohio, and Wisconsin) as part of the NHEXAS; mean arsenic concentration in flushed and standing tap water were both 1.1 μg/L (Thomas et al. 1999). A review by Frost et al. (2003) of existing data from the EPA Arsenic Occurrence and Exposure Database, as well as additional data from state health and environmental departments and water utilities found that 33 counties in 11 states had estimated mean drinking water arsenic concentrations of 10 μg/L or greater. Eleven counties had mean arsenic concentrations of ≥20 μg/L, and two counties had mean arsenic concentrations of ≥50 μg/L (Frost et al. 2003).

The north central region and the western region of the United States have the highest arsenic levels in surface water and groundwater sources, respectively. In a study of drinking water from New Hampshire, arsenic concentrations ranged from <0.01 to 180 μg/L in the 793 households tested. More than 10% of the private wells had arsenic concentrations >10 μg/L, and 2.5% had levels >50 μg/L (Karagas et al. 1998). In New Hampshire, 992 randomly selected household water samples were analyzed for arsenic levels and the results for domestic well users were compared with those for users of municipal water supplies (Peters et al. 1999). The concentrations ranged from <0.0003 to 180 μg/L, with water from domestic wells containing significantly more arsenic than water from municipal supplies; the median concentration of the former was about 0.5 μg/L and the latter was 0.2 μg/L. None of the municipal supplies exceeded an arsenic concentration of 50 μg/L, and 2% of the domestic wells were found to have arsenic concentrations that exceeded 50 μg/L. Approximately 2% of the municipal water users have water with arsenic levels exceeding 10 μg/L compared with 13% of domestic wells. Twenty-five percent of domestic wells and 5% of municipal supplies were found to have arsenic concentrations exceeding 2 μg/L. The highest arsenic levels in New Hampshire are associated with bedrock wells in the south eastern and south central part of the state (Peters et al. 1999). In a study of arsenic in well water supplies in Saskatchewan, Canada, 13% of samples were >20 μg/L and one sample exceeded 100 μg/L (Thompson et al. 1999). It was noted that the samples with high arsenic levels were derived from sites that were in near proximity to each other, indicating the presence of 'hot spots' with similar geological characteristics. As part of an epidemiological study, Engel and Smith (1994) investigated the levels of arsenic in drinking

Table 6-3. Regional Occurrence of Arsenic in U.S. Water Sources and Finished Drinking Water

Geographical region	Arsenic concentration in µg/L			
	<1	1–5	5–20	>20
Occurrence in U.S. surface water sources				
Region 1. New England	50	50	0	0
Region 2. Mid-Atlantic	84	12	4	0
Region 3. South East	93	7	0	0
Region 4. Midwest	24	76	0	0
Region 5. South Central	32	55	13	0
Region 6. North Central	33	22	33	0
Region 7. Western	42	58	0	0
Occurrence in U.S. groundwater sources				
Region 1. New England	71	21	7	0
Region 2. Mid-Atlantic	81	4	11	4
Region 3. South East	82	14	2	0
Region 4. Midwest	40	40	15	5
Region 5. South Central	68	27	15	0
Region 6. North Central	30	40	30	0
Region 7. Western	24	34	28	14
Occurrence in U.S. finished surface water supplies				
Region 1. New England	88	12	0	0
Region 2. Mid-Atlantic	92	8	0	0
Region 3. South East	100	0	0	0
Region 4. Midwest	73	27	0	0
Region 5. South Central	74	19	7	0
Region 6. North Central	44	44	0	12
Region 7. Western	42	58	0	0
Occurrence in U.S. finished groundwater supplies				
Region 1. New England	79	21	0	0
Region 2. Mid-Atlantic	81	4	11	4
Region 3. South East	94	4	2	0
Region 4. Midwest	58	27	12	3
Region 5. South Central	61	27	12	0
Region 6. North Central	40	50	10	0
Region 7. Western	20	40	22	12

Source: National Arsenic Occurrence Survey (Frey and Edwards 1997)

water throughout the United States between 1968 and 1984. They found that 30 counties in 11 states had mean arsenic levels of >5 µg/L, with a range of 5.4–91.5 µg/L; 15 counties had mean levels from 5 to 10 µg/L; 10 counties had mean levels from 10 to 20 µg/L; and 5 counties had levels >20 µg/L. The highest levels were found in Churchill County, Nevada, where 89% of the population was exposed to a mean arsenic concentration of 100 µg/L and 11% to a mean of 27 µg/L. A study by Frost et al. (2003) identified 33 counties from 11 states in which the average arsenic concentration of at least 75% of public wells was >10 µg/L. Arsenic concentrations in drinking water from these counties ranged from 10.3 to 90.0 µg/L in Pinal, Arizona and Churchill, Nevada, respectively (Frost et al. 2003).

Many communities have high levels of arsenic in their drinking water because of contamination or as a result of the geology of the area. In Millard County, Utah, seven towns had median and maximum arsenic levels of 18.1–190.7 and 125–620 µg/L, respectively, in their drinking water (Lewis et al. 1999). The mean arsenic concentration in tap water from homes in Ajo, Arizona, about 2 miles from an open pit copper mine and smelter was 90 µg/L (Morse et al. 1979). The town's water was supplied from five deep wells.

Countries such as Mexico, Bangladesh, India, Chile, Argentina, and Vietnam have highly elevated levels of arsenic in drinking water in some regions (Bagla and Kaiser 1996; Berg et al. 2001; Tondel et al. 1999; WHO 2001; Wyatt et al. 1998a, 1998b). In Bangladesh and West Bengal, the soil naturally contains high levels of arsenic, which leaches into the shallow groundwater that is tapped for drinking water. In West Bengal, India, it is estimated that more than one million Indians are drinking arsenic-laced water and tens of millions more could be at risk in areas that have not been tested for contamination. Analysis of 20,000 tube-well waters revealed that 62% have arsenic at levels above the World Health Organization (WHO) permissible exposure limit (PEL) in drinking water of 10 µg/L, with some as high as 3,700 µg/L (Bagla and Kaiser 1996). Analysis of 10,991 and 58,166 groundwater samples from 42 and 9 arsenic-affected districts in Bangladesh and West Bengal were found to have arsenic levels that were 59 and 34%, respectively, above 50 µg/L (Chowdhury et al. 2000). Berg et al. (2001), studied the arsenic contamination of the Red River alluvial tract in Hanoi, Vietnam and the surrounding rural areas. Arsenic concentrations in groundwater from private small-scale tube-wells averaged 159 µg/L, ranging from 1 to 3,050 µg/L. Arsenic concentrations ranged from 37 to 320 µg/L in raw groundwater pumped from the lower aquifer for the Hanoi water supply (Berg et al. 2001). Several investigators have noticed a correlation between high levels of arsenic and fluoride in drinking water (Wyatt et al. 1998a, 1998b). Arsenic concentrations in drinking water from four villages in Bangladesh ranged from 10 to 2,040 µg/L (Tondel et al. 1999).

6.4.3 Sediment and Soil

Arsenic is widely distributed in the Earth's crust, which contains about 3.4 ppm arsenic (Wedepohl 1991). It is mostly found in nature minerals, such as realgar (As_4S_4), orpiment (As_2S_3), and arsenolite (As_2O_3), and only found in its elemental form to a small extent. There are over 150 arsenic-bearing minerals (Budavari et al. 2001; Carapella 1992). Arsenic concentrations in soils from various countries can range from 0.1 to 50 µg/g and can vary widely among geographic regions. Typical arsenic concentrations for uncontaminated soils range from 1 to 40 µg/g, with the lowest concentrations in sandy soils and soils derived from granites. Higher arsenic concentrations are found in alluvial soils and soils with high organic content (Mandal and Suzuki 2002). Arsenic in soil may originate from the parent materials that form the soil, industrial wastes, or use of arsenical pesticides. Geological processes that may lead to high arsenic concentrations in rock and subsequently the surrounding soil include hydrothermic activity and pegmatite formation (Peters et al. 1999). In the first case, thermal activity results in the dissolution and transport of metals, including the metalloid arsenic, which are precipitated in fractures in rocks. In the second process, cooling magmas may concentrate metals that are injected into rocks, crystallizing as pegmatites. Areas of volcanic activity include large areas of California, Hawaii, Alaska, Iceland, and New Zealand.

The U.S. Geological Survey reports the mean and range of arsenic in soil and other surficial materials as 7.2 and <0.1–97 µg/g, respectively (USGS 1984). The concentrations of arsenic in 445 Florida surface soils ranged from 0.01 to 50.6 µg/g (Chen et al. 1999). The median, arithmetic mean, and geometric mean were 0.35, 1.34±3.77, and 0.42±4.10 µg/g, respectively. Chirenje et al. (2003b) reported a geometric mean arsenic concentrations of 0.40 (0.21–660) and 2.81 (0.32–110) µg/g in surface soil samples (0–20 cm) collected in May–June 2000 from Gainesville and Miami, Florida, respectively. The geometric mean arsenic concentration in 50 California soils was 2.8 µg/g (Chen et al. 1999). In the Florida surface soils, arsenic was highly correlated (α=0.0001) with the soil content of clay, organic carbon, CEC, total iron, and total aluminum. Arsenic tends to be associated with clay fractions and iron and manganese oxyhydroxides. Soils of granitic origin are generally low in arsenic, about 4 µg/g, whereas arsenic in soils derived from sedimentary rocks may be as high as 20–30 µg/g (Yan-Chu 1994). Soils overlying arsenic-rich geologic deposits, such as sulfide ores, may have soil concentrations two orders of magnitude higher (NAS 1977a).

Soils in mining areas or near smelters may contain high levels of arsenic. Arsenic concentrations up to 27,000 µg/g were reported in soils contaminated with mine or smelter wastes (EPA 1982b). Soils at an abandoned mining site in the Tamar Valley in southwest England have arsenic concentrations that may exceed 50,000 µg/g (Erry et al. 1999). The average arsenic levels in the top 2 cm of different soil types in the vicinity of a former copper smelter in Anaconda, Montana, ranged from 121 to 236 µg/g; levels were significantly related to proximity and wind direction to the smelter site (Hwang et al. 1997a). Smelter fallout can contaminate land miles from the source. Soils in mainland southern King County were studied for the presence of arsenic and lead (WSDOE 2005). Soil samples were collected in the fall of 1999 and the spring of 2001 from locations around the ASARCO smelter, which operated in Ruston from the 1890s to 1986. The study area ran roughly from the I-90 corridor south to the King-Pierce county line, from the Puget Sound shore to the Cascade foothills. Almost all of the contamination was found was in the 0–6-inch depths of the cores samples; 62 of the 75 samples were found to have arsenic levels above 20 ppm (WSDOE 2005).

Soil on agricultural lands treated with arsenical pesticides may retain substantial amounts of arsenic. One study reported an arsenic concentration of 22 µg/g in treated soil compared to 2 µg/g for nearby untreated soil (EPA 1982b). Arsenic was measured in soil samples taken from 10 potato fields in Suffolk County on Long Island, New York, where sodium arsenite had been used for vine control and fall weed control for many years. Lead arsenate also may have been used as an insecticide in certain areas. The mean arsenic levels taken at a depth of 0–18 cm from each of the 10 fields ranged from 27.8±5.44 µg/g dry weight (n=10) to 51.0±7.40 µg/g dry weight (n=10). These levels were markedly higher than the level of 2.26±0.33 µg/g (n=10) for untreated control soils (Sanok et al. 1995). A survey was conducted in 1993 to determine the concentrations of arsenic and lead in soil samples from 13 old orchards in New York State. Lead arsenate was used for pest control in fruit orchards for many years, mainly from the 1930s to 1960s, and residues remain in the soil. Concentrations of arsenic ranged from 1.60 to 141 µg/g dry weight (Merwin et al. 1994). Arsenic and lead concentrations were also measured in former orchard soils contaminated by lead arsenate from the Hanford site in Washington State. The mean arsenic concentration in surface (5–10 cm) and subsurface (10–50 cm) soils were 30 (2.9–270) and 74 (32–180) µg/g dry weight, respectively (Yokel and Delistraty 2003). Average arsenic concentration of 5.728, 5.614, and 6.746 µg/g were reported in soils, lake sediments, and wetland sediments, respectively, from Moon Lake, a Mississippi River alluvial floodplain in northwest Mississippi. Intensive cultivation has occurred in this area, including cotton, soybeans, and rice (Cooper and Gillespie 2001). A geometric mean arsenic concentration of 20.6 mg/kg (range 4.6–340 mg/kg) was reported soil collected during the

summer and fall of 2003 from 85 homes in Middleport, New York, where historical pesticide manufacturing was associated with arsenic in the soil (Tsuji et al. 2005).

The Washington State Area-wide Soil Contamination Project provides various data on arsenic contamination in soils across Washington State (Washington State 2006). Arsenic concentrations within areas affected by area-wide soil contamination are highly variable, ranging from natural background levels to >3,000 ppm in smelter areas. Generally, average arsenic concentrations in soil at developed properties are <100 ppm. Areas affected by smelter emissions in King, Pierce, Snohomish, and Stevens Counties have a higher likelihood of arsenic soil contamination than other areas of the State due to historical emissions from metal smelters located in Tacoma, Harbor Island, Everett, Northport, and Trail, British Columbia. Areas where apples and pears were historically grown, such as Chelan, Spokane, Yakima, and Okanogan Counties, also have a higher likelihood of arsenic soil contamination than other areas due to the past use of lead arsenate pesticides. Generally, arsenic contamination in soils from historical smelter emissions and historical use of lead-arsenate pesticides is found in the upper 6–18 inches of soil (Washington State 2006).

The New Jersey Department of Environmental Protection (Historic Pesticide Contamination Task Force 1999) reported on the analysis of soil samples collected from 18 sites for various pesticide residues, including arsenic, from current and former agricultural sites in New Jersey in order to assess contamination from historic pesticide use. Arsenic was detected in all 463 samples, with concentrations ranging from 1.4 to 310 ppm.

Natural concentrations of arsenic in sediments are usually <10 µg/g dry weight, but can vary widely around the world (Mandal and Suzuki 2002). Sediment arsenic concentrations reported for U.S. rivers, lakes, and streams range from about 0.1 to 4,000 µg/g (Eisler 1994; Heit et al. 1984; NAS 1977a; Welch et al. 1988). During August through November 1992 and August 1993, bed sediment in the South Platte River Basin (Colorado, Nebraska, and Wyoming) was sampled and analyzed for 45 elements, including arsenic. The range of arsenic found was 2.8–31 µg/g dry weight and the geometric mean (n=23) was 5.7 µg/g (Heiny and Tate 1997). The arsenic concentration in surface sediment (0–2 cm) at 43 sites in the Indian River Lagoon System in Florida ranged from 0.6 to 15 µg/g dry weight with a mean of 5.0±3.9 µg/g (Trocine and Trefry 1996). Arsenic levels were well correlated with those of aluminum. Correlation with aluminum levels is used to normalize sediment level concentrations to natural levels in Florida estuaries. Surficial sediments collected from 18 locations in 3 major tributaries to Newark Bay, New Jersey, were analyzed for 7 toxic metals, including arsenic (Bonnevie et al. 1994). The highest

concentrations of arsenic were found in the Rahway River adjacent to a chemical plant, 58 µg/g dry weight, and in the Hackensack River adjacent to a coal-fired power plant, 49 µg/g. The average arsenic concentration for all sediments was 17±16 µg/g. Sediments collected from seven sites in Baltimore Harbor, Maryland, at five seasonal periods between June 1987 and June 1988 had a geometric mean maximum of 7.29 µg/g dry weight and a geometric mean minimum of 1.25 µg/g (Miles and Tome 1997). This harbor is one of two sub-tributaries of the Chesapeake Bay where contaminants have been discharged on a large scale.

The upper Clark Fork River basin in western Montana is widely contaminated by metals from past mining, milling, and smelting activities. In a 1991 study, arsenic levels were determined in sediment along the river and in a reservoir 205 km downstream. Total arsenic in sediments from Clark Fork River decreased from 404 µg/g dry weight at the farthest upstream sampling station to 11 µg/g, 201 km downstream. Sediment samples from the Milltown Reservoir had arsenic concentrations ranging from 6 to 56 µg/g (Brumbaugh et al. 1994). Total recoverable arsenic in nonfiltered pore water from the Clark Fork River decreased from 1,740 µg/L at the farthest upstream sampling station to 31 µg/L at the 201 km station (Brumbaugh et al. 1994). The Coeur d'Alene river basin in northern Idaho has been contaminated with heavy metals from mining and smelting operations since 1885 (Farag et al. 1998). A 1994 study determined the metal content of sediment, biofilm, and invertebrates at 13 sites in the basin, 10 with historic mining activity and 3 reference sites. The mean arsenic levels in sediment at the mining sites ranged from 8.3 to 179.0 µg/g dry weight, compared to 2.4–13.1 µg/g dry weight at the reference sites. The mean arsenic levels in biofilm adhering to rock in the water at the mining sites ranged from 7.5 to 155.8 µg/g dry weight, compared to 7.2–27.3 µg/g dry weight at the reference sites. In Whitewood Creek, South Dakota, where as much as 100 million tons of mining and milling waste derived from gold mining activities were discharged between 1876 and 1977, mean and maximum sediment arsenic concentrations were 1,920 and 11,000 µg/g, respectively (USGS 1987). Uncontaminated sediment had mean arsenic levels of 9.2 µg/g. Arsenic concentrations in surface (0–5 cm) sediments from watersheds in Black Hills, South Dakota, an area impacted by gold mining activities, ranged from 23 to 1,951 µg/g dry weight; concentrations from reference areas ranged from 10 to 58 µg/g dry weight (May et al. 2001). Swan Lake, a sub-bay of Galveston Bay in Texas is a highly industrial area that received runoff from a tin smelter in the 1940s and 1950s. Surface sediments at 17 sites where oysters and mussels were collected ranged from 4.53 to 103 µg/g (Park and Presley 1997). A site in the channel leading from the old smelter had arsenic levels of 568 µg/g. Surface sediment was less contaminated than deeper sediment, indicating less arsenic input recently than in the past as a result of the smelter closing.

It has been suggested that the wood preservative most commonly used in dock pilings and bulkheads, CCA, can be toxic to estuarine organisms. Wendt et al. (1996) measured arsenic in surface sediments and oysters from creeks with high densities of docks and from nearby reference creeks with no docks. The average concentrations in the sediments ranged from 14 to 17 µg/g throughout the study area, which is within the range of natural background levels. Weis et al. (1998) sampled sediments along a 10-m transect from CCA-treated wood bulkheads from four Atlantic coast estuaries. Arsenic concentrations were highest in the fine-grained portion of the sediments near the CCA-treated bulkhead (0–1 m); arsenic concentrations were generally at reference levels at distances >1 m from the bulkheads (Weis et al. 1998).

Soils below and around play structures constructed from CCA-treated wood in the City of Toronto, Canada were sampled and analyzed for inorganic arsenic (Ursitti et al. 2004). A mean arsenic concentration of 2.1 µg/g (range 0.5–10 µg/g) was reported in soil samples taken within 1 m of the CCA-treated wood for all play structures. Soil samples that were collected 10 m from the play structures served as a background had arsenic concentration of 2.4 µg/g (range 0.5–13 µg/g). A mean arsenic concentration of 6.2 µg/g (range 0.5–47.5 µg/g) was reported in soil samples taken below CCA-treated wood for all play structures. Of the 217 play structures in the study, 32 had arsenic concentrations under the play structures that exceeded the Canadian federal soil guidelines with arsenic concentrations ranging from 12.4 to 47.5 µg/g. From this study, the authors concluded that arsenic does not migrate laterally, but does accumulate in soil under elevated platforms constructed from CCA-treated wood (Ursitti et al. 2004).

6.4.4 Other Environmental Media

Low levels of arsenic are commonly found in food; the highest levels are found in seafood, meats, and grains. Typical U.S. dietary levels of arsenic in these foods range from 0.02 mg/kg in grains and cereals to 0.14 mg/kg in meat, fish, and poultry (Gartrell et al. 1986). Shellfish and other marine foods contain the highest arsenic concentrations and are the largest dietary source of arsenic (Gunderson 1995a; Jelinek and Corneliussen 1977; Tao and Bolger 1999). Arsenic levels in various fish and shellfish are presented in Table 6-4. In the U.S. Food and Drug Administration (FDA) Total Diet Study, 1991–1997, seafood contained the highest levels of arsenic, followed by rice/rice cereal, mushrooms, and poultry. Concentrations in canned tuna (in oil), fish sticks, haddock (pan-cooked), and boiled shrimp were 0.609–1.470, 0.380–2.792, 0.510–10.430, and 0.290–2.681 mg/kg, respectively (Tao and Bolger 1999). Typically, arsenic levels in foods in the Total Diet Study, 1991–1996 were low, <0.03 mg/kg; only 63 of the 264 foods contained arsenic above this level. Similar results were reported in the Total Diet Study,

Table 6-4. Levels of Arsenic in Fish and Shellfish—Recent Studies

Sample type	Arsenic concentration[a] (µg/g)	Comments	Reference
Yellowtail flounder		Samples collected from Northwest Atlantic 1993	Hellou et al. 1998
Muscle (n=8)	8–37		
Liver (n=6)	7–60		
Gonad (n=6)	1.2–9.4		
Marine organisms		Belgian fish markets in 1991; inorganic arsenic ranged from 0.003 to 0.2 µg/g	Buchet and Lison 1998
Ray (n=8)	16.4		
Cod (n=8)	4.7		
Plaice (n=8)	19.8		
Sole (n=8)	5.1		
Sea-bream (n=8)	2.4		
Mussell (n=8)	3.5		
Bluefin tuna (*Thunnus thynus*) (n=14)	3.2	Virgin Rocks, Grand Banks of Newfoundland, Canada, 1990	Hellou et al. 1992
Fish		National Contaminant Biomonitoring Program, 1984–1985, 112 stations	Kidwell et al. 1995
Bottom feeding (n=2,020)	0.16±0.23 wet weight		
Predatory (n=12)	0.16±0.140 wet weight		
Oysters		South Carolina, private residential docks on tidal creeks, 1994	Wendt et al. 1996
<1 m from docks (n=10)	8.3±1.1		
>10 m from docks (n=10)	7.6±0.9		
Reference (no docks) (n=10	8.4±1.3		
Clams (n=22)	12±1.1	Indian River Lagoon, Florida, 22 sites, 1990	Trocine and Trefry 1996
Marine organisms		Swan Lake, Galveston Bay, Texas, 1993	Park and Presley 1997
Snails	13.3±17.0		
Blue crab	6.61		
Fish	0.82		
Shrimp	1.37±0.64		
Whole crab	5.35±2.51		
Oysters (n=10, pooled)	7.28±1.32		
Mussels (n=7, pooled)	7.75±2.15		
Marine organisms		GPNEP, 1992, Galveston Bay, Texas	Park and Presley 1997
Blue crab	2.31±2.15		
Fish	2.46		
Oysters, two areas		NOAA NS&T Program, 1986–1990	Park and Presley 1997
n=78, pooled	4.50±1.08	Galveston Bay	
n=874, pooled	9.67±7.00	Gulf of Mexico	

Table 6-4. Levels of Arsenic in Fish and Shellfish—Recent Studies

Sample type	Arsenic concentration[a] (µg/g)	Comments	Reference
Marine crustaceans			
Parapenaeus longirostris (pink shrimp) (n=826, 10 pools	34.84±19.21 (12.01–62.60)	Commercial crustaceans from the Mediterranean Sea (Italy)	Storelli and Marcotrigiano 2001
Aristeus antennatus (red shrimp) (n=387, 8 pool)	17.09±3.49 (10.45–20.82)		
Plesionika martia (shrimp) (n=456, 7 pools)	40.82±2.50 (36.37–44.06)		
Nephrops norvegicus (Norway lobster) (n=270, 5 pools)	43.48±14.21 (35.63–69.15)		
Freshwater fish			
Sabalo (*Brycon melanopterus)* (n=3)	0.015–0.101	Fish samples (muscle) were collected in August 1997 from the Candamo River, Peru; a pristine rainforest valley prior to the start of oil-drilling activities	Gutleb et al. 2002
Huazaco (*Hoplias malabaracus)* (n=4)	nd–0.005		
Bagre (*Pimelodus ornatus*) (n=8)	nd–0.201		
Boquichio (*Prochilodus nigricans)* (n=1)	0.063		
Doncello (*Pseudo-platystoma sp.*) (n=1)	0.055		
Freshwater fish			
Bowfin (n=59)	0.32±0.04 wet weight	Savannah River, along and below the Department of Energy's Savannah River Site (SRS); samples analyzed were edible fillets	Burger et al. 2002
Bass (n=47)	0.03±0 wet weight		
Channel catfish (n=50)	0.09±00.02 wet weight		
Chain pickerel (n=19)	0.05±0.01 wet weight		
Yellow perch (n=51)	0.05±0.01 wet weight		
Black crappie (n=52)	0.04±0.01 wet weight		
American eel (n=24)	0.04±0.01 wet weight		
Shellcracker n=52)	0.06±0 wet weight		
Bluegill (n=52)	0.05±0.02 wet weight		
Redbreast (n=43)	0.07±0.01 wet weight		
Spotted sucker (n=35)	0.03±0 wet weight		

Table 6-4. Levels of Arsenic in Fish and Shellfish—Recent Studies

Sample type	Arsenic concentration[a] (µg/g)	Comments	Reference
Horseshoe crabs			
Apodeme (n=74)	7.034±0.65 wet weight	Overall mean in tissues of crabs collected from New Jersey in 2000	Burger et al. 2003
Egg (n=63)	5.924±0.345 wet weight		
Leg (n=74)	14.482±0.685 wet weight		
Apodeme (n=40)	7.513±0.835 wet weight	Overall mean in tissues of crabs collected from Delaware in 2000	
Egg (n=35)	6.766±0.478 wet weight		
Leg (n=40)	18.102±1.489 wet weight		

[a]Concentrations are means±standard deviation, unless otherwise stated. Concentrations are in a dry weight basis, unless otherwise stated.

GM = geometric mean; GPNEP = Galveston Bay National Estuary Program; nd = not detected; NOAA NS&T = National Oceanic and Atmospheric Administration National Status and Trends

1991–1997, where the mean arsenic concentration in all foods was 0.036 mg/kg dry weight and arsenic was not detectable in about 88% of the foods and was detected at trace levels in another 7.8% of foods. The foods with the highest mean arsenic levels were haddock, canned tuna, fish sticks, shrimp, and fish sandwiches, with arsenic concentrations ranging from 5.33 to 0.568 mg/kg dry weight (Capar and Cunningham 2000). Nriagu and Lin (1995) analyzed 26 brands of wild rice sold in the United States and found arsenic levels ranging from 0.006 to 0.142 µg/g dry weight. Arsenic concentrations ranging from 0.05 to 0.4 µg/g are typically reported for rice from North America, Europe, and Taiwan (Meharg and Rahman 2003).

During a comprehensive total diet study extending from 1985 to 1988, foods were collected in six Canadian cities and processed into 112 composite food samples (Dabeka et al. 1993). The mean, median, and range of total arsenic in all samples were 0.0732, 0.0051, and <0.0001–4.840 µg/g, respectively. Food groups containing the highest mean arsenic levels were fish (1.662 µg/g), meat and poultry (0.0243 µg/g), bakery goods and cereals (0.0245 µg/g), and fats and oils (0.0190 µg/g). Of the individual samples, marine fish had the highest arsenic levels, with a mean of 3.048 µg/g for the cooked composites and 2.466 µg/g for the raw samples. Canned fish (1.201 µg/g) and shellfish (2.041 µg/g) also contained high means. Cooked poultry, raw mushrooms, and chocolate bars contained 0.100, 0.084, and 0.105 µg/g, respectively.

National monitoring data from the Food Safety and Inspection Service National Residue Program (NRP) (1994–2000) found that the mean total arsenic concentration in livers of young chickens ranged from 0.33 to 0.43 µg/g, with an overall mean of 0.39 µg/g (Lasky et al. 2004). The mean arsenic concentrations in liver for mature chickens, turkeys, hogs, and all other species over the same time period ranged from 0.10 to 0.16 µg/g. Lasky et al. (2004) used the NRP arsenic data in livers of young chickens to estimate the concentrations of arsenic in muscle tissue, the most commonly consumed part of the chicken. Assuming that 65% of the arsenic in poultry and meat is inorganic, at a mean level of chicken consumption of 60 g/person/day, people may ingest an estimated 1.38–5.24 µg/day of inorganic arsenic from chicken.

A Danish study (Pedersen et al. 1994) reports the arsenic levels in beverages as the mean (range) in µg/L as follows: red wine, 9 (<2–25); white wine, 11 (<2–33); fortified wine, 5 (<2–11); beer, 7 (4–11); soft drinks, 3 (<2–8); miscellaneous juices, 8 (3–13); instant coffee, 4 (0.7–7); and instant cocoa, 5.6 (1.6–12.8).

In a study of dietary arsenic exposure in the Indigenous Peoples of the western Northwest Territories, Canada, fish contained the highest arsenic concentrations in foods consumed by the Dene and Métis populations with the highest concentration, 1.960 µg/g, found in smoked/dried cisco (fish). Other foods derived from land mammals, birds, and plants contained lower arsenic concentrations. A mean arsenic intake of <1.0 µg/kg/day was reported for this population (Berti et al. 1998).

The general consensus in the literature is that about 85–>90% of the arsenic in the edible parts of marine fish and shellfish is organic arsenic (e.g., arsenobetaine, arsenochloline, dimethylarsinic acid) and that approximately 10% is inorganic arsenic (EPA 2003b). However, the inorganic arsenic content in seafood may be highly variable. For example, a study in the Netherlands reported that inorganic arsenic comprised 0.1–41% of the total arsenic in seafood (Vaessen and van Ooik 1989). Buchet et al. (1994) found that, on the average, 3% of the total arsenic in mussels was inorganic in form. Some commercially available seaweeds, especially brown algae varieties, may have high percentages of the total arsenic present as inorganic arsenic (>50%) (Almela et al. 2002; Laparra et al. 2003). Arsenic concentrations ranging from 17 to 88 mg/kg dry weight were found in commercially available seaweeds (van Netten et al. 2000). Other arsenic compounds that may be found in seafood are arsenic-containing ribose derivatives called arsenosugars. Arsenosugars are the common organoarsenicals found in marine algae; they are also found in mussels, oysters, and clams (Le et al. 2004). Less information about the forms of arsenic in freshwater fish is known at this time (EPA 2003b).

Schoof et al. (1999a) reported on the analysis of 40 commodities anticipated to account for 90% of dietary inorganic arsenic intake. In this study, the amount of inorganic arsenic was measured in these foods. Consistent with earlier studies, total arsenic concentrations were highest in the seafood sampled (ranging from 160 ng/g in freshwater fish to 2,360 ng/g in marine fish). In contrast, average inorganic arsenic in seafood ranged from <1 to 2 ng/g. The highest inorganic arsenic concentrations were found in raw rice (74 ng/g), followed by flour (11 ng/g), grape juice (9 ng/g), and cooked spinach (6 ng/g).

Tobacco contains an average arsenic concentration of 1.5 ppm, or about 1.5 µg per cigarette (EPA 1998j). Before arsenical pesticides were banned, tobacco contained up to 52 mg As/kg, whereas after the ban, maximum arsenic levels were reduced to 3 µg/g (Kraus et al. 2000). An international literature survey reports arsenic yields of 0–1.4 µg/cigarette for mainstream (inhaled) cigarette smoke (Smith et al. 1997). The wide range of arsenic yields for flue-cured cigarettes suggests that the field history, soil, and fertilizer conditions under which the tobacco is grown will affect the arsenic concentration (Smith et al. 1997).

Arsenic emission factors of 0.015–0.023 µg/cigarette (mean 0.018±0.003 µg/cigarette) have been measured for sidestream smoke from a burning cigarette (Landsberger and Wu 1995).

A median arsenic concentration of 2.1 µg/g and a deposition rate of 0.008 µg/m^2/day was reported in house dust in homes evaluated as part of the German Environmental Survey in 1990–1992. A mean arsenic concentration of 7.3 µg/g was reported in house dust from 48 residences in Ottawa, Canada (Butte and Heinzow 2002). These arsenic concentrations are expected to be representative of background levels. In general high arsenic concentrations were found in household dust collected from homes in areas with known arsenic contamination. Mean arsenic concentrations of 12.6 (2.6–57) and 10.8 (1.0–49) µg/g were reported in house dust collected from the entryway and child play areas, respectively, from homes in a community in Washington State with a history of lead arsenate use (Wolz et al. 2003). Arsenic was detected in all 135 indoor floor dust samples collected as part of the NHEXAS from Arizona mining communities, ranging from 0.3–50.6 µg/g, (O'Rourke et al. 1999). A geometric mean arsenic concentration of 10.8 µg/g (range 1.0–172 µg/g) was reported in house dust from 96 homes in Middleport, New York, with historical pesticide manufacture, collected during the summer and fall of 2003 (Tsuji et al. 2005).

Arsenic has also been detected in several homeopathic medicines at concentrations up to 650 µg/g (Kerr and Saryan 1986). Some Asian proprietary medicines that are manufactured in China, Hong Kong, and other Asian countries have been reported to contain levels of inorganic arsenic ranging from 25 to 107,000 µg/g (Chan 1994). Fifty medicinally important leafy samples that were analyzed for elemental concentrations contained arsenic at levels ranging from 0.12 to 7.36 µg/g, with a mean of 2.38±1.2 µg/g (Reddy and Reddy 1997). Arsenic concentrations ranged from 0.005 to 3.77 µg/g in 95 dietary supplements purchased from retail stores in the Washington, DC area in 1999 (Dolan et al. 2003). Commercially available samples of Valarian, St. John's Wort, Passion Flower, and Echinacea were purchased in the United States and analyzed for various contaminants; arsenic concentrations were 0.0016–0.0085, 0.0065–0.017.8, 0.0024–0.0124, and 0.0021–0.0102 µg/g, respectively, in these samples (Huggett et al. 2001). Concentrations of heavy metals including the metalloid arsenic were evaluated in 54 samples of Asian remedies that were purchased in stores in Vietnam and Hong Kong that would be easily accessible to travelers, as well as in health food and Asian groceries in Florida, New York, and New Jersey. Four remedies were found to contain daily doses exceeding 0.1 mg. Two of these contained what would have been a potentially significant arsenic dose, with daily doses of 16 and 7.4 mg of arsenic (Garvey et al. 2001).

The possible presence of toxic compounds in waste materials has raised concerns about the fate of these compounds either during the composting process or when the composted product is applied to soils. Three waste compost products generated at the Connecticut Agricultural Experiment Station had arsenic levels of 12.8, 9.8, and 13 µg/g dry weight, respectively (Eitzer et al. 1997). The arsenic levels in municipal solid waste composts from 10 facilities across the United States ranged from 0.9 to 15.6 µg/g dry weight with a mean of 6.7 µg/g (He et al. 1995). These are lower than the EPA 503 regulatory limit for arsenic of 41 µg/g for agricultural use of sewage sludge (EPA 1993b). Concentrations of arsenic in U.S. sewage sludges, which are sometimes spread on soil, were <1 µg/g. Arsenic is a common impurity in minerals used in fertilizers. A comprehensive Italian study found that the arsenic content in a number of mineral and synthetic fertilizers ranged from 2.2 to 322 mg/kg with a sample of triple superphosphate having the highest level (Senesi et al. 1999). Arsenic naturally occurs in coal and crude oil at levels of 0.34–130 and 0.0024–1.63 ppm, respectively, which would account for its presence in flue gas, fly ash, and bottom ash from power plants (Pacyna 1987).

Background arsenic levels in living organisms are usually <1 µg/g wet weight (Eisler 1994). Levels are higher in areas with mining and smelting activity or where arsenical pesticides were used. Eisler (1994) has an extensive listing of arsenic levels in terrestrial and aquatic flora and fauna from literature sources to about 1990. The U.S. Fish and Wildlife Service's National Contaminant Biomonitoring Program have analyzed contaminants in fish at 116 stations (rivers and the Great Lakes) across the United States. The geometric mean concentration of arsenic for the five collection periods starting in 1976 were (period, concentration wet weight basis): 1976–1977, 0.199 µg/g; 1978–1979, 0.129 µg/g; 1980–1981, 0.119 µg/g; 1984, 0.106 µg/g; and 1986, 0.083 µg/g (Schmitt et al. 1999). In 1986, the maximum and 85th percentile arsenic levels were 1.53 and 0.24 µg/g, respectively. The highest concentrations of arsenic for all five collection periods were in bloaters from Lake Michigan at Sheboygan, Wisconsin. Arsenic levels declined by 50% at this site between 1976–1997 and 1984. The major source of arsenic into Lake Michigan was a facility at Marinette, Wisconsin, which manufactured arsenic herbicides. Table 6-4 contains arsenic levels in aquatic organisms from more recent studies. The Coeur d'Alene river basin in northern Idaho has been contaminated with heavy metals from mining and smelting operations since 1885 (Farag et al. 1998). A 1994 study determined the metal content of sediment, biofilm, and invertebrates at 13 sites in the basin, 10 with historic mining activity, and 3 reference sites. The mean arsenic levels in benthic macroinvertebrates at the mining sites ranged from 2.2 to 97.0 µg/g dry weight, compared to 2.1–2.4 µg/g dry weight at the reference sites. A study of aquatic organism in Swan Lake, a highly polluted sub-bay of Galveston Bay, Texas showed that arsenic concentrations were in the order snail>oyster>crab>shrimp>fish (Park and Presley 1997). In contrast to metals like silver, cadmium,

copper, and zinc, arsenic concentrations in oysters and mussels were less than in the sediment from which they were collected. No significant correlation was found between levels of arsenic in clams in the Indian River Lagoon in Florida with those found in sediment or water samples (Trocine and Trefry 1996). Small animals living at mining sites ingest more arsenic in their diet and have higher arsenic levels in their bodies than those living on uncontaminated sites (Erry et al. 1999). Seasonal variations in both arsenic intake and dietary composition may affect the amount of arsenic taken up by the body and transferred to predator animals. Tissue arsenic content of wood mice and bank voles living on both arsenic-contaminated mining sites and uncontaminated sites were greater in autumn than spring. The lower tissue arsenic levels in spring of rodents living on contaminated sites suggest that there is no progressive accumulation of arsenic in overwintering animals.

6.5 GENERAL POPULATION AND OCCUPATIONAL EXPOSURE

Exposure to arsenic may include exposure to the more toxic inorganic forms of arsenic, organic forms of arsenic, or both. While many studies do not indicate the forms of arsenic to which people are exposed, this information may often be inferred from the source of exposure (e.g., fish generally contain arsenic as arsenobetaine). Yost et al. (1998) reported that the estimated daily dietary intake of inorganic arsenic for various age groups ranged from 8.3 to 14 µg/day and from 4.8 to 12.7 µg/day in the United States and Canada, respectively, with 21–40% of the total dietary arsenic occurring in inorganic forms.

Drinking water may also be a significant source of arsenic exposure in areas where arsenic is naturally present in groundwater. While estimates of arsenic intake for typical adults drinking 2 L of water per day average about 5 µg/day (EPA 1982c), intake can be much higher (10–100 µg/day) in geographical areas with high levels of arsenic in soil or groundwater (see Figure 6-2). It is assumed that nearly all arsenic in drinking water is inorganic (EPA 2001).

In the United States, food intake of arsenic has been estimated to range from 2 µg/day in infants to 92 µg/day in 60–65-year-old men (see Table 6-5) (Tao and Bolger 1999). The average intake of inorganic arsenic are estimated to range from 1.34 µg/day in infants to 12.54 µg/day in 60–65-year-old men. Tao and Bolger (1999) assumed that 10% of the total arsenic in seafood was inorganic and that 100% of the arsenic in all other foods was inorganic. The greatest dietary contribution to total arsenic was seafood (76–96%) for all age groups, except infants. For infants, seafood and rice products contributed 42 and 31%, respectively. Adult dietary arsenic intakes reported for other countries range

Table 6-5. Mean Daily Dietary Intake of Arsenic for Selected U.S. Population Groups

Mean daily intake (µg/kg body weight/day)	Date of study		
	1984–1986[a]	1986–1991[b]	1991–1997[c]
Provisional tolerable daily intake (PTDI)[d]	2.1	2.1	2.1
6–11 months	0.82	0.5	0.31
2 years	1.22	0.81	1.80
14–16 years, female	0.54	0.36	0.41
14–16 years, male	0.60	0.39	0.24
25–30 years, female	0.66	0.44	0.44
25–30 years, male	0.76	0.51	0.72
60–65 years, female	0.71	0.46	1.08
60–65 years, male	0.74	0.48	1.14

[a]Gunderson 1995a
[b]Gunderson 1995b
[c]Tao and Bolger 1999
[d]No agreement has been reached on a maximum acceptable intake for total arsenic; the FAO/WHO has assigned a PTDI for inorganic arsenic of 2.1 µg/kg body weight for adults. Data from FDA studies. FDA does not recommend daily intake levels for Arsenic.

from 11.7 to 280 µg/day (Tao and Bolger 1999). Schoof et al. (1999b) estimated that intake of inorganic arsenic in the U.S. diet ranges from 1 to 20 µg/day, with a mean of 3.2 µg/day. In contrast, these estimates of inorganic arsenic intakes are based on measured inorganic arsenic concentrations from a market basket survey.

The FDA conducted earlier Total Diet Studies in 1984–1986 and 1986–1991. For the sampling period of June 1984 to April 1986, the total daily intake of arsenic from foods was 58.1 µg for a 25–30-year-old male with seafood contributing 87% of the total (Gunderson 1995a). For the sampling period from July 1986 to April 1991, the total daily intake of arsenic from foods was lower, 38.6 µg for a 25–30-year-old male. Seafood again was the major source of arsenic, contributing 88% of the total (Gunderson 1995b). Results of the two Total Diet Studies for selected population groups are shown in Table 6-5. The Total Diet Study for the sampling period from September 1991 to December 1996, shows that arsenic, at ≥0.03 µg/g, was found in 55 (21%) of the 261–264 foods/mixed dishes analyzed. The highest concentrations again were found in seafood, followed by rice/rice cereal, mushrooms, and poultry. The estimated total daily intake of arsenic from foods was 56.6 µg for a 25–30-year-old male. Seafood was the major contributor, accounting for 88–96% of the estimated total arsenic intake of adults.

Average daily dietary exposures to arsenic were estimated for approximately 120,000 U.S. adults by combining data on annual diet, as measured by a food frequency questionnaire, with residue data for table-ready foods that were collected for the annual FDA Total Diet Study. Dietary exposures to arsenic were highly variable, with a mean of 50.6 µg/day (range, 1.01–1,081 µg/day) for females and 58.5 µg/day (range, 0.21–1,276 µg/day) for males (MacIntosh et al. 1997). Inorganic arsenic intake in 969 men and women was assessed by a semi-quantitative food frequency questionnaire in combination with a database for total arsenic content in foods and by toenail concentrations of arsenic. The mean estimated average daily consumption of inorganic arsenic was 10.22 µg/day with a range of 0.93–104.89 µg/day. An assumption of 1.5% of the total arsenic in fish and 20% of the total arsenic in shellfish was inorganic arsenic was used in this assessment (MacIntosh et al. 1997).

During a comprehensive total diet study extending from 1985 to 1988, the estimated daily dietary ingestion of total arsenic by the average Canadian was 38.1 µg and varied from 14.9 µg for the 1–4 year-old-age group to 59.2 µg for 20–39-year-old males (Dabeka et al. 1993). Daily intakes of arsenic from food by women in the Shiga Prefecture, Japan, were investigated by the duplicate portion method and by the market basket method. In 1991 and 1992, the daily intakes determined by the duplicate portion

method were 206 and 210 µg, respectively. Those determined by the market basket method were 160 and 280 µg, respectively (Tsuda et al. 1995b).

Arsenic concentrations in human breast milk have been reported to range from 4 to <10 µg/L in pooled human milk samples from Scotland and Finland to 200 µg/L in samples from Antofagasta, Chile, where there is a high natural environmental concentration of arsenic (Broomhall and Kovar 1986). The arsenic concentration in the breast milk of 35 women in Ismir, Turkey, a volcanic area with high thermal activity ranged from 3.24 to 5.41 µg/L, with a median of 4.22 µg/L (Ulman et al. 1998). Sternowsky et al. (2002) analyzed breast milk from 36 women from three different regions in Germany. These regions included the city of Hamburg, a rural area, Soltau, Lower Saxony, and Munster, the potentially contaminated area. Arsenic was not detected (<0.3 µg/L) in 154 of 187 samples, with the highest concentration, 2.8 µg/L, found in a sample from the rural area. The geometric means from the three areas were comparable.

The mean arsenic levels in three groups of cows in the region that grazed on land impacted by lava and thermal activity were 4.71, 4.46, and 4.93 µg/L, compared to 5.25 µg/L for cows kept in sheds and fed commercial pellet feed and municipal water (Ulman et al. 1998). Mean arsenic concentrations in cow's milk ranging from 18.6 to 17.1 µg/L and from 16.7 to 18.0 µg/L were reported for cow's grazing in nonindustrial and an industrial regions, respectively, in Turkey (Erdogan et al. 2004).

A Danish study found that carrots grown in soil containing 30 µg/g of arsenic, which is somewhat above the 20 µg/g limit for total arsenic set by Denmark for growing produce, contained 0.014 µg/g fresh weight of arsenic, all in the form of inorganic As(III) and As(V) (Helgesen and Larsen 1998). An adult consuming 376 grams of vegetables a day (90th percentile) represented solely by carrots would consume 5.3 µg of arsenic a day. The study concluded that the estimated intake of arsenic from produce grown in soil meeting regulatory limits was low compared with other food sources and water.

If vegetables are grown in planters made of wood treated with CCA, arsenic may leach out of the wood and be taken up by the vegetables. In a study by Rahman et al. (2004), arsenic was found to diffuse into the soil from the CCA-treated wood, with the highest concentrations found at 0–2 cm from the CCA-treated wood and a steady decline in concentration with increased distance from the wood. Crops grown within 0–2 cm of the CCA-treated wood contained higher concentrations of arsenic than those grown at 1.5 m from the treated wood. However, the concentrations are below U.S. FDA tolerance limits that have been set for arsenic in select food items. In addition, food grown in this manner is unlikely to constitute a significant part of a person's diet.

In 2003, U.S. manufacturers of arsenical wood preservatives began a voluntary transition from CCA to other wood preservatives in wood products for certain residential uses, such as play structures, picnic tables, decks, fencing, and boardwalks. This phase out was completed on December 31, 2003; wood treated prior to this date could still be used and structures made with CCA-treated wood would not be affected. CCA-treated wood products continue to be used in industrial applications (EPA 2003a). EPA's Consumer Awareness Program (CAP) for CCA is a voluntary program established by the manufacturers of CCA products to inform consumers about the proper handling, use, and disposal of CCA-treated wood. Additional information about this program can be found from EPA (2007a).

The arsenic content in the human body is 3–4 mg and tends to increase with age. Arsenic concentrations in most tissues of the human body are <0.3 to 147 µg/g dry weight, excluding hair, nails, and teeth. Mammals tend to accumulate arsenic in keratin-rich tissues such as hair and nails. The normal concentrations of arsenic range from about 0.08 to 0.25 µg/g in hair, and 0.34 µg/g in nails. The normal concentration of arsenic in urine can range from 5 to 40 µg per day (total) (Mandal and Suzuki 2002). Table 6-6 contains arsenic levels in various human tissues.

A German study investigated the transfer of arsenic from the environment to humans in the northern Palatine region, a former mining area characterized by high soil levels of arsenic (<2–605 µg/g) in residential areas compared to a region in southern lower Saxony with nonelevated levels of arsenic in soil (Gebel et al. 1998a). None of the residents were occupationally exposed to arsenic and the arsenic levels in drinking water were generally below 0.015 mg/L. The mean levels of arsenic in urine and hair were lower in the reference area than in the former mining area (see Table 6-6), although within the mining area, there was a slight increase in arsenic levels in hair and arsenic excreted in urine with increasing arsenic content in soil. Children in the Palatine region did not have higher contents of arsenic in their hair or urine. The most significant factor contributing to elevated levels of arsenic in hair and urine was seafood consumption. In the combined population of people living in mining areas containing high levels of arsenic in soil and other areas, the level of arsenic in urine was positively associated with the extent of seafood consumption. However, the study also showed that seafood consumption does not lead to an extreme increase in excretion of arsenic in the urine. There are apparently other, unidentified factors affecting the urine levels. Only arsenic in urine, not in hair, was significantly correlated with age. The level of arsenic in urine was very slightly, but significantly correlated with the consumption of home-grown produce. Tobacco smoking had no correlation with the arsenic content of either hair or urine (Gebel et al. 1998a).

Table 6-6. Levels of Arsenic in Human Tissue and Urine—Recent Studies

Site population	Sample	Concentration		Units	Reference
		Mean[a]	Range		
Fort Valley, Georgia, Pesticide manufacturing facility (Superfund site)					
40 workers (samples collected at end of work week)	Urine, random	11.6	<1–57	µg/L	Hewitt et al. 1995
	Urine, 24-hour	11.0	<1–54	µg/L	
	Hair	0.78	<0.01–6.3	µg/g	
	Fingernails	0.79	<0.01–6.1	µg/g	
Hermosa, Sonora, Mexico					
Children, ages 7–11, exposed to arsenic in water (mean concentration [mean dose]):	Urine, 24-hour				Wyatt et al. 1998a, 1998b
9 µg/L [0.481 µg/kg/day]		10.26	4.05–19.68	µg/day	
15 µg/L [0.867 µg/kg/day]		10.54	2.82–20.44	µg/day	
30 µg/L [1.92 µg/kg/day]		25.18	5.44–93.28	µg/day	
Glasgow, Scotland					
Adults, normal (n=1,250)	Hair	0.650	0.20–8.17	µg/g	Raie 1996
Adults, postmortem (n=9)	Liver	0.048 [0.024]	0.011–0.152	µg/g	
Infants, postmortem (n=9)	Liver	0.0099 [0.007]	0.0034–0.019	µg/g	
Adults, postmortem (n=8)	Lung	0.044 [0.022]	0.0121–0.125	µg/g	
Infants, postmortem (n=9)	Lung	0.007 [0.0055]	0.0011–0.015	µg/g	
Adults, postmortem (n=9)	Spleen	0.015 [0.008]	0.001–0.063	µg/g	
Infants, postmortem (n=8)	Spleen	0.0049 [0.0045]	0.0011–0.0088	µg/g	
Palatinate Region, Germany (high As)[b]					
Residents (n=199)	Urine, 24-hour	3.96 [3.21]	<0.1–18.32	µg/g	Gebel et al. 1998a
Residents (n=211)	Hair	0.028 [0.016]	<0.005–0.154	µg/g	
Saxony, Germany (low As—reference)[b]					
Residents (n=75)	Urine, 24-hour	7.58 [6.20]	0.29–23.78	µg/g	Gebel et al. 1998a
Residents (n=74)	Hair	0.069 [0.053]	0.013–0.682	µg/g	
Ismir, Turkey, (volcanic area with high thermal activity)					
Nonoccupationally exposed women (n=35)	Breast milk	4.23 [4.26]	3.24–5.41	µg/L	Ulman et al. 1998
Erlangen-Nurenberg Germany 1/92–12/93					
Nonoccupationally exposed people (n=50)	Lung	5.5	<1–13.0	ng/g ww	Kraus et al. 2000
		28.4	<1–73.6	ng/g dw	

Table 6-6. Levels of Arsenic in Human Tissue and Urine—Recent Studies

Site population	Sample	Concentration		Units	Reference
		Mean[a]	Range		
Tarragona (Catalonia, Spain) 1997–1999					
Nonoccupationally exposed people (n=78)	Lung	<0.05		µg/g ww	Garcia et al. 2001
	Bone	<0.05			
	Kidney	<0.05			
	Liver	<0.05			
	Lung	<0.05			
West Bengal, India					
Residents consuming arsenic-contaminated water (n=47)	Fingernail	7.32	2.14–40.25	µg/g	Mandal et al. 2003
	Hair	4.46	0.70–16.17		
Residents consuming nonarsenic-contaminated water (n=15)	Fingernail	0.19	0.11–0.30		
	Hair	0.07	0.03–0.12		
Middleport, NY, USA					
Children <7 years (n=77)	Urine	15.1[c]	2.1–59.6	µg/L	Tsuji et al. 2005
Children <13 years (n=142)	Urine	15.7[c]	2.1–59.9		
Children ≥7 years and adults (n=362)	Urine	15.8[c]	3.9–773		
All participants	Urine	15.7[c]	2.1–773		

[a]Medians, if reported, are in brackets.
[b]The reference group (Saxony) had significantly higher levels of arsenic in urine and hair. However, data from both groups correspond to normal range reference data.
[c]Geometric mean, total arsenic

dw = dry weight; ww = wet weight

A study was performed to look at the arsenic levels, as well as the arsenic species present, in hair and nail samples from individuals in an arsenic-affected area in West Bengal, India. Mean arsenic concentrations in hair and fingernails of the chronically arsenic exposed population were 4.46 and 7.32 µg/g, respectively and were 0.07 and 0.19 µg/g in a control population. Fingernail samples were found to contain mostly inorganic arsenic (>80%) as a mixture of As(III) and As(V), as well as DMA(III) and DMA(V). Hair samples also mostly contained inorganic arsenic (>90%), as well as MMA(V) and DMA(V) (Mandal et al. 2003).

Arsenic in soil in communities surrounding former smelters is a public health concern, especially for infants and children who may consume significant quantities of soil. Since lead arsenate was used in apple and other fruit orchards, often at very high application rates, and this compound would be expected to accumulate and persist in surface soil, there are concerns to human health when these when old orchards are converted into subdivisions or when they are used to grow food crops or forage. However, arsenic in soil may be imbedded in minerals or occur as insoluble compounds such as sulfides and therefore, not be taken up by the body from the gastrointestinal tract. In addition, oxidation of mineral surfaces may result in armoring the primary mineral grain by a secondary reaction product. Arsenic-bearing solids are often encapsulated in insoluble matrices such as silica, further diminishing arsenic availability (Davis et al. 1992).

Sarkar and Datta (2004) examined the bioavailability of arsenic from two soils with different arsenic retention capacities. In this study, Immokalee (Florida) and Orelia (Texas) soils were incubated after spiking with sodium arsenate for 4 months. The Immokalee soil is a sandy spodosol with low Fe/Al, Ca/Mg, and P contents and is likely to have minimal arsenic retention capacity. The Orelia soil is a sandy clay that is expected to have strong arsenic retention capacity. Arsenic speciation and bioavailability were studied immediately after spiking and after 4 months of incubation. Approximately 85% of the total arsenic (soluble and exchangeable fractions) was considered bioavailable and phytoavailable immediately after pesticide application for the Immokalee soil; after 4 months of incubation, this decreased to approximately 46%. Immediately after pesticide application, the amounts of arsenic extracted in the soluble/exchangeable and Fe/Al-bound fractions were similar that of the Immokalee soil. After 4 months, the soluble arsenic decreased to approximately 45% and the Fe/Al-bound arsenic increased to about 40%. Experiments looking at the bioavailability of arsenic from these two soils indicated that the potentially irreversible adsorption of arsenic by the Orelia soil rendered a significant portion of the total arsenic unavailable for absorption by the human gastrointestinal system. Initially after pesticide application,

100% of the arsenic was bioavailable; after 4 months, the bioavailable fraction was found to decrease to 88 and 69% in the Immokalee and Orelia soils, respectively (Sarkar and Datta 2004).

Hamel et al. (1998) used synthetic gastric juice to estimate the bioaccessible fraction of metals in the stomach with varying liquid to solid ratios. They found that the bioaccessibility may vary in different soils and with varying liquid to solid ratios. Bioaccessibility was defined as the amount of metal that is soluble in synthetic gastric juice and therefore, potentially available for uptake across the intestinal lumen, while bioavailability was defined as the amount that was actually taken across the cell membranes. Arsenic bioaccessibility for National Institute of Standards and Technology (NIST) Montana Soil SRM 2710, with a certified arsenic concentration of 626 µg/g, was fairly consistent across the liquid-to-solid ratios and ranged from 41.8±18 to 56±21%. The extractability of a hazardous waste contaminated soil from Jersey City, New Jersey, was different than that observed for the Montana NIST soil. For the Jersey City soil, which had an arsenic concentration of 1,120 µg/g, there was an increase in the bioaccessible arsenic as the liquid-to-solid ratio increased. Bioaccessible arsenic ranged from 4.5±0.8 (at a liquid-to-solid ratio of 100:1) to 25±9% (at a ratio of 5,000:1). Similarly, smelter impacted soils from Anaconda, Montana contain metal-arsenic oxides and phosphates whose bioaccessibility is limited by solubility restraints for residence times typical of the gastrointestinal tract (Davis et al. 1992, 1996).

Inhalation of arsenic from ambient air is usually a minor exposure route for the general population. For example, the dose to a person who breathes 20 m^3/day of air containing 20–30 ng/m^3 (see Section 6.4.1) would be about 0.4–0.6 µg/day. However, smokers may be exposed to arsenic by inhalation of mainstream smoke. Assuming that 20% of the arsenic in cigarettes is present in smoke, an individual smoking two packs of cigarettes per day would inhale about 12 µg of arsenic (EPA 1984a). However, a German study of the arsenic levels in lung tissue of 50 unexposed deceased people (see Table 6-6) found no significant difference in lung arsenic concentrations of smokers versus nonsmokers, nor were there any significant age- or sex-related differences (Kraus et al. 2000). Before arsenical pesticides were banned, tobacco contained up to 52 µg As/g, whereas after the ban, maximum arsenic levels were reduced to 3 µg/g.

Occupational exposure to arsenic may be significant in several industries, mainly nonferrous smelting, arsenic production, wood preservation, glass manufacturing, and arsenical pesticide production and application. Since arsenic compounds are used as a desiccant for cotton, workers involved in harvesting and ginning cotton may be exposed to arsenic. Occupational exposure would be via inhalation and dermal contact. Should any arsenic be retained in the cotton, workers handling the fabric and the general

public would be exposed. The electronics industry is expanding the use of gallium arsenide in the production of electro-optical devices and integrated circuits, and workers in the industry where gallium arsenide is used may be exposed to hazardous substances such as arsenic, arsine, and various acids (Sheehy and Jones 1993). Occupational exposure to arsenic is generally assessed by measuring urinary excretion of arsenic. Past exposure is commonly assessed by arsenic levels in hair. Different types of occupational exposures may result in different uptakes of arsenic because of the bioavailability of the form of arsenic to which workers are exposed. For example, maintenance workers at a Slovak coal-fired power plant exposed to 8-hour TWA arsenic air concentrations of 48.3 $\mu g/m^3$ (range, 0.17–375.2) had urinary total arsenic levels of 16.9 µg As/g creatinine (range, 2.6–50.8), suggesting that bioavailability of arsenic from airborne coal fly ash is about one-third that from in copper smelters and similar settings (Yager et al. 1997). Approximately 90% of the arsenic-containing particulates were ≥3.5 µm. Apostoli et al. (1999) monitored 51 glass workers exposed to arsenic trioxide by measuring dust in the breathing zone. The mean concentration of arsenic in air was 82.9 $\mu g/m^3$ (1.5–312 $\mu g/m^3$); exposure was higher for workers involved in handling the particulate matter. The occupation exposures to principal contaminants, including arsenic, at five coal-fired power plants were evaluated during June–August 2002. Eight air samples were collected per similar exposure group at four of the five facilities; inorganic arsenic concentrations in all samples were below the limit of detection (0.37–0.72 $\mu g/m^3$), as well as being below the OSHA permissible exposure limit (PEL) of 10 $\mu g/m^3$ (Bird et al. 2004).

NIOSH researchers conducted a study of arsenic exposures and control systems for gallium arsenide operations at three microelectronics facilities during 1986–1987 (Sheehy and Jones 1993). Results at one plant showed that in all processes evaluated but one, the average arsenic exposures were at or above the OSHA action level of 5 $\mu g/m^3$, with a maximum exposure of 8.2 $\mu g/m^3$. While cleaning the Liquid Encapsulated Czochralski (LEC) pullers, the average potential arsenic exposure of the cleaning operators was 100 times the OSHA PEL of 10 $\mu g/m^3$. Area arsenic samples collected at the plant in break-rooms and offices, 20–60 feet from the process rooms, had average arsenic concentrations of 1.4 $\mu g/m^3$. At the other two plants, personal exposures to arsenic were well controlled for all processes evaluated.

A study has been conducted to examine the relationship between total arsenic levels in hair of employees in a semiconductor fabrication facility and job responsibility, a surrogate variable for arsenic exposure (de Peyster and Silvers 1995). Airborne arsenic was found in areas where equipment was cleaned but not in administrative areas. The highest airborne arsenic level found in the study, 15 $\mu g/m^3$, was collected from the breathing zone of a maintenance employee who was cleaning a source housing over a period of 2 hours in an area with local exhaust ventilation. A concentration of 2 $\mu g/m^3$ was found during the

remainder of the cleaning period (~53 minutes). Workers in maintenance who were regularly assigned to cleaning equipment, and therefore presumed to have the highest exposure potential, had a mean hair arsenic level of 0.042 µg/g. This was higher than the mean of 0.033 µg/g observed in administrative controls, but the difference was not significant. Maintenance workers who only occasionally cleaned and maintained arsenic-contaminated equipment had a mean hair arsenic level of 0.034 µg/g, which was comparable to the controls. The highest group mean hair arsenic level of 0.044 µg/g, surprisingly, was found in supervisors and engineers who were presumed to have the lowest exposure potential of all workers in the process areas. However, the highest concentrations of hair arsenic in engineers, 0.076 and 0.106 µg/g, were observed in two heavy smokers who smoked 1–2 packs of cigarettes per day. A 2-way analysis of variance indicated that smoking appeared to be a significant contributing factor whereas occupational exposure was not.

Hwang and Chen (2000) evaluated arsenic exposure in 21 maintenance engineers (exposed group) and 10 computer programmers (control group) at 3 semiconductor manufacturing facilities. Samples of air, wipe, and urine, as well as used cleaning cloths and gloves were collected to determine arsenic exposure. Arsenic was undetectable in 46 of the 93 air samples, and most samples were generally below the recommended occupational exposure limit (10 µg/m^3) in work areas during ion implanter maintenance. Arsine was detectable in 22 of the 45 area air samples and in 15 of the 35 personal air samples; however, all concentrations were well below the occupational exposure limit of 50 ppb (160 µg/m^3). Mean arsine concentrations ranged from not detected to 4.0 ppb (15 µg/m^3) in area air samples, and the mean arsine concentration of personal air for maintenance engineers was 4.3 ppb (14 µg/m^3). Arsenic concentrations in wipe samples, used cleaning cloths, and gloves, varied from not detected to 146 µg/cm^2. During ion implanter maintenance, urinary arsenic levels were found to increase (1.0–7.8 µg/g creatinine) in the maintenance engineers, from a mean baseline concentration of 3.6 µg/g creatinine. The average urinary arsenic level for the computer programmers was 3.8 µg/g creatinine (Hwang and Chen 2000). Mean arsenic concentrations in blood of 103 workers in the optoelectronic industry and 67 controls were 8.58 and 7.85 µg/L, respectively (Liao et al. 2004).

Concentrations of various metals, including arsenic, were measured in autopsy tissues (liver, lung, kidney, brain, and bone) collected from 78 nonoccupationally exposed subjects from Tarragona County, Spain between 1997 and 1999. In general, arsenic concentrations were under the analytical detection limit (0.05 µg/g wet weight) in all tissues (Garcia et al. 2001).

CCA preservatives are commonly used for treating timber used in constructions in marine and other humid environments or in contact with the ground. Exposure to CCA compounds may occur through dermal contact and inhalation of dust while working with the treated timber. Nygren et al. (1992) investigated the occupational exposure to airborne dust, chromium, copper, and arsenic in six joinery shops in Sweden where impregnated wood was used for most of their production. The mean airborne concentration of arsenic around various types of joinery machines ranged from 0.54 to 3.1 $\mu g/m^3$. No increased concentrations of arsenic were found in the workers' urine. A study was carried out in Denmark to evaluate arsenic exposure in taxidermists, workers impregnating wood with CCA solutions, fence builders, construction workers, and workers impregnating electric pylons with arsenic solution (Jensen and Olsen 1995). Airborne arsenic exposure was documented in 19 of 27 individuals working with products containing arsenic. The maximum exposure concentration was 17.3 $\mu g/m^3$, found for a single worker who was filling an impregnation container with CCA paste. Median exposures for indoor workers producing garden fences and weekend cottages were 3.7 and 0.9 $\mu g/m^3$, respectively. The maximum urine concentration reported in the study was 294.5 nanomoles arsenic per millimole creatinine (195 µg As/g creatinine) and was from the injector impregnating electric pylons. The median concentration in workers on electric pylons was 80 nanomoles arsenic per millimole creatinine (53 µg As/g creatinine), which was 6 times the concentration in reference individuals. Urine arsenic levels in workers producing garden fences and in taxidermists were 2.9 and 1.8 times the reference level, respectively.

The NIOSH National Occupational Exposure Survey (NOES) conducted in 1981–1983 estimated that about 55,000 workers were potentially exposed to arsenic (NOES 1990). The NOES was based on field surveys of 4,490 facilities that included virtually all workplace environments, except mining and agriculture, where eight or more persons are employed. The principal exposure pathway is probably inhalation of arsenic adsorbed to particulates, but ingestion and possibly dermal exposure may also be common. Since arsenic is no longer produced in the United States (see Section 5.1) and many arsenical pesticide uses have been banned (see Chapter 8), it is likely that the number of workers occupationally exposed to arsenic has decreased markedly in more recent years.

6.6 EXPOSURES OF CHILDREN

This section focuses on exposures from conception to maturity at 18 years in humans. Differences from adults in susceptibility to hazardous substances are discussed in Section 3.7, Children's Susceptibility.

Children are not small adults. A child's exposure may differ from an adult's exposure in many ways. Children drink more fluids, eat more food, breathe more air per kilogram of body weight, and have a larger skin surface in proportion to their body volume. A child's diet often differs from that of adults. The developing human's source of nutrition changes with age: from placental nourishment to breast milk or formula to the diet of older children who eat more of certain types of foods than adults. A child's behavior and lifestyle also influence exposure. Children crawl on the floor, put things in their mouths, sometimes eat inappropriate things (such as dirt or paint chips), and spend more time outdoors. Children also are closer to the ground, and they do not use the judgment of adults to avoid hazards (NRC 1993).

As with adults, most children are exposed to arsenic largely through their diet. Since the greatest dietary intake of arsenic is from fish and seafood, infants and young children for whom a substantial part of their food is milk, would not be exposed to arsenic from dietary sources as much as older children. Even when mothers consumer large amounts of seafood, there does not appear to be any major transfer of arsenobetaine, the major form of arsenic in seafood, from seafood to milk (Grandjean et al. 1995). Arsenic concentrations were very low in human milk sampled from 88 mothers in the Faroe Islands, where the seafood diet includes pilot whale meat and blubber. The total arsenic concentrations ranged from 0.1 to 4.4 µg/kg, with a median of 1.6 µg/kg (Grandjean et al. 1995). The arsenic concentration in the breast milk of 35 women in Ismir, Turkey, a volcanic area with high thermal activity ranged from 3.24 to 5.41 µg/L, with a median of 4.22 µg/L (Ulman et al. 1998). The mean arsenic levels in three groups of cows in the region that grazed on land impacted by lava and thermal activity were 4.71, 4.46, and 4.93 µg/L, compared to 5.25 µg/L for cows kept in sheds and fed commercial pellet feed and municipal water. The arsenic levels in the urine of pregnant women and the cord blood of their infants were 0.625±0.027 and 0.825±0.079 µg/L, respectively. The authors concluded that there was no harmful exposure to arsenic in volcanic areas with high arsenic levels from suckling infants or feeding them local cow's milk, nor was there harm to the newborns from their mother's diet. Sternowsky et al. (2002) analyzed breast milk from 36 women from three different regions in Germany. These regions included the city of Hamburg, a rural area, Soltau, Lower Saxony, and Munster, the potentially contaminated area. Arsenic was not detected (<0.3 µg/L) in 154 of 187 samples, with the highest concentration, 2.8 µg/L, found in a sample from the rural area. The geometric mean arsenic concentrations from the three areas were comparable. Calculated oral intakes of arsenic were between 0.12 and 0.37 µg/day for an infant at 3 months of age and weighing 6 kg.

According to the FDA study of 1986–1991, the mean daily intakes of arsenic are 0.5 and 0.81 µg/kg body weight per day for a 6–11-month-old infant and 2-year-old child, respectively (Gunderson 1995b). This

can be compared to a mean daily intake of 0.51 µg/kg-body weight per day for a 25–30-year-old male (see Table 6-5). A Total Diet Study, from September 1991 to December 1996, estimated that the average inorganic arsenic intake for children of various age/sex groups were (age-sex group, total arsenic intake in µg/day, inorganic arsenic intake in µg/day): 6–11 months, 2.15, 1.35; 2 years, 23.4, 4.41; 6 years, 30.3, 4.64; 10 years, 13.3, 4.21; and 14–16 years (females), 21.8, 5.15; 14–16 years (males), 15.4, 4.51 (Tao and Bolger 1999). The greatest dietary contribution (76–96%) of total arsenic intake for all age groups other than infants was seafood. For infants, 41 and 34% of the estimated total arsenic intakes are from seafood and rice/rice cereals, respectively (Tao and Bolger 1999). Only for toddlers does the intake approach the World Health Organization's (WHO) provisional tolerable daily intake (PTDI) for inorganic arsenic (see Table 6-5). A 1985–1988 Canadian total diet study estimated that 1–4-year-olds ingested 14.9 µg of total arsenic per day compared with 38.1 µg by the average Canadian and 59.2 µg for 20–39-year-old males (Dabeka et al. 1993). Yost et al. (2004) estimated the mean dietary intake for inorganic arsenic for children (1–6 years of age) to be 3.2 µg/day, with a range of 1.6–6.2 µg/day for the 10th and 95th percentiles, respectively. Inorganic arsenic intake was predominantly contributed by grain and grain products, fruits and fruit juices, rice and rice products, and milk (Yost et al. 2004). Total arsenic and arsenobentaine concentrations were measured in 16 baby food samples obtained from manufactures in Spain; total arsenic concentrations ranged from 2.042 to 0.270 µg/g in plaice with vegetables and sole with white sauce, respectively. Arsenobetaine, which is the arsenical commonly found in fish, accounted for essentially 100% of the arsenic present in the samples (Vinas et al. 2003).

Arsenic exposure from drinking water may be elevated especially in groundwater from areas where arsenic occurs naturally in soil such as the western and north central sections of the United States (see Table 6-3 and Figure 6-2).

Arsenic exposure in communities near mining and smelting facilities or where arsenic had formerly been applied to agricultural land are a public health concern, especially for infants and children. Since arsenic remains in the surface soil indefinitely and long past land uses may be forgotten, people may not realize that they are living in areas where high levels of arsenic may occur in soil. Contaminated soils pose a particular hazard to children because of both hand-to-mouth behavior and intentional ingestion of soil (pica) that contains metals and other contaminants (Hamel et al. 1998). In these communities, arsenic may contaminate carpeting or may have been tracked in from outside. Children may be exposed to this arsenic while crawling around or playing on contaminated carpeting. Exposure may also result from dermal contact with the soil, or by inhaling the dust and then swallowing it after mucociliary transport up

out of the lungs. Because much of the arsenic in soil is embedded in or adsorbed to soil particles or insoluble, it may not be in a form accessible for uptake by the body.

Hwang et al. (1997b) studied the arsenic exposure of children in Anaconda, Montana, in the vicinity of a former copper smelter from the summer of 1992 through the summer of 1993. Environmental samples and first morning voided urine samples from 414 children <72 months old were collected. Attention was focused on that fraction of the environmental source that was thought to be of the greatest risk to the child (i.e., arsenic in small particles [<250 μm]) that could most readily adhere to hands and toys and could be inadvertently ingested. Average arsenic levels in different types of soil ranged from 121 to 236 μg/g. Several studies have reported mean soil ingestion values for children ranging from 9 to 1,834 μg /day. Assuming that high arsenic exposure areas have average arsenic levels in soil from 60 to 150 μg/g, the resulting daily arsenic intake from soil could range from 1 to 275 μg/day per child. The geometric mean of speciated urinary arsenic (combined As(III), As(V), MMA and DMA) was 8.6±1.7 μg/L (n=289) in the Hwang study. A nationwide survey on arsenic exposure in the vicinity of smelter sites revealed that children without excess arsenic exposure had average total urinary arsenic levels ranging from 5 to 10 μg/L (Hwang et al. 1997a). Compared to these values, the mean total urinary arsenic values found in the Hwang study were markedly higher, but they were still well below the WHO-recommended maximum excretion level for total arsenic of 100 μg/L as an action level for intervention. The investigators hypothesized that the relatively low urinary arsenic levels found in the study were probably a reflection of the low bioavailability of some forms of arsenic in contaminated soil. Hwang et al. (1997a) stated that arsenic intake through skin contact is insignificant and may be neglected in the assessment of childhood arsenic exposure. They recommend that parents or guardians pay more attention to their children's activity, especially hand-to-mouth behavior, even though the environmental contaminants might be elevated only slightly. Children in the northern Palatine region of German study, a former mining area characterized by high levels of arsenic (<2–605 μg/g) in residential areas did not show higher arsenic levels in their hair or urine than children from a reference area of Germany (Gebel et al. 1998a).

While CCA registrants voluntarily canceled the production of CCA-treated wood for residential use in 2003, there is a potential for exposure to arsenic from existing structures (Zartarian et al. 2006). Based on a review of existing studies, Hemond and Solo-Gabriele (2004) estimated that children with contact with CCA-treated wood may be subjected to doses in the range of tens of micrograms of arsenic per day. The most important route of exposure appeared to be by hand-to-mouth activities after contact with the CCA-treated wood. Kwon et al. (2004) compared the amounts of water-soluble arsenic on hands of children in

contact with CCA-treated wood structures or sand in playgrounds. The mean amount of water-soluble arsenic on children's hands from playgrounds without CCA-treated wood was 0.095 µg (range 0.011–0.41 µg). A mean amount of water-soluble arsenic on children's hands from playgrounds with CCA-treated wood was 0.5 µg (range 0.0078–3.5 µg) (Kwon et al. 2004). Additional data from the study by Kwon et al. (2004) showed that total arsenic collected in hand-washing water (insoluble arsenic on the filter combined with the water-soluble arsenic in the filtrate) was 0.934 and 0.265 µg for the CCA playgrounds and the non-CCA playgrounds, respectively (Wang et al. 2005). Two wood surface swab samples collected from 217 play structures constructed from CCA-treated wood in the City of Toronto, Canada were sampled and analyzed for inorganic arsenic (Ursitti et al. 2004). Dislodgeable arsenic concentrations were found to vary widely from nondetectable (0.08–0.25 µg/100 cm^2) to 521 µg/100 cm^2 (mean = 41.6 µg/100 cm^2), and were found to not be a useful predictor of soil arsenic levels (Ursitti et al. 2004).

Shalat et al. (2006) evaluated postexposure hand rinses and urine for total arsenic for 11 children (13–71 months) in homes in Miami-Dade County, Florida, with and without CCA-treated playgrounds. Seven playgrounds were included in this study, and five of these contained either CCA-treated or partially CCA-treated wood. In addition, samples of wood, soil (5–8 cm from the base of the playground structure), mulch (when present), and synthetic wipes were analyzed for total arsenic. Wood and soil arsenic concentration were <2.0 and <3 mg/kg for the non-CCA-treated playgrounds, respectively. Mean arsenic concentrations of 2,380 mg/kg (range 1,440–3,270 mg/kg) and 19 mg/kg (4.0–42 mg/kg) were reported for wood and soil, respectively, in the playgrounds with CCA-treated wood. An arsenic concentration in mulch at one playground without CCA-treated wood was 0.4 mg/kg, and arsenic concentrations were 0.6 and 69 mg/kg in mulch at two of the playgrounds with CCA-treated wood. The amount of arsenic removed by synthetic wipes from the non-CCA-treated wood was <0.5 µg, while the mean amount of arsenic removed from the CCA-treated wood was 117 µg (range 1.0–313 µg). The amount of arsenic in hand rinses from children who played at the playgrounds with non-CCA-treated wood and at the playgrounds with CCA-treated wood were <0.2 and 0.6 µg (range <0.2–1.9 µg), respectively. The mean urinary total arsenic concentration was 0.0136 µg/L (range 0.0072–0.0231 µg/L) for all children. No association between assess to CCA-treated playgrounds and urinary arsenic levels was found (Shalat et al. 2006).

The potential exposure children may receive from playing in play structures constructed from CCA-treated wood is generally smaller than that they would receive from food and water. For comparison, Yost et al. (2004) estimated the mean dietary intake for inorganic arsenic for children (1–6 years of age)

to be 3.2 µg/day, with a range of 1.6–6.2 µg/day for the 10th and 95th percentiles, respectively. In a Total Diet Study, from September 1991 to December 1996, estimated average total intakes for children aged 6–11 months, 2 years, 6 years, and 10 years were 2.15, 23.4, 30.3, and 13.3 µg/day, respectively. Average inorganic arsenic intakes for the same age groups were estimated as 1.35, 4.41, 4.64, and 4.21 µg/day, respectively, based on data for total arsenic in foods and the assumption that 10% of the total arsenic in seafood was inorganic and that 100% of the arsenic in all other foods was inorganic (Tao and Bolger 1999). Hand washing after play would reduce the potential exposure to children to arsenic after playing on play structures constructed with CCA-treated wood, since most of the arsenic on the children's hands was removed with water (Kwon et al. 2004).

Concentrations of several toxic metals, including the metalloid arsenic, were measured in the placentas of 200 women in two urban cities in Ukraine, Kyiv and Dniprodzerzhinsk. Arsenic was detected in only 5% of the samples with concentrations ranging from <0.156 to 0.378 µg/g. In a study in Bulgaria, placental arsenic concentrations of 7 and 23 µg/g were reported in a control and smelter area, respectively. A placental arsenic concentration of 34 µg/g was reported in a region of Argentina with high concentrations of arsenic in drinking water (Zadorozhnaja et al. 2000).

Parents can inadvertently carry hazardous materials home from work on their clothes, skin, hair, and tools, and in their vehicles (DHHS 1995). Falk et al. (1981b) reported a case of hepatic angiosarcoma in a child that could be associated with arsenic contamination of a parent's clothing, the water supply, and the environment. The father worked in a copper mine and smelter area where his clothing was contaminated with dust containing arsenic. His daughter, who exhibited a high degree of pica, ate soil from the yard, and licked soil off her father's shoes. In a study of arsenic levels in homes in Hawaii, Klemmer et al. (1975) found higher levels in homes of employees of firms that used arsenic for pesticides or wood preservation, compared to homes where residents' work did not involve arsenic. The concentration of arsenic in dust from the homes of workers exposed to arsenic ranged from 5.2 to 1,080 µg/g, compared to concentrations of 1.1–31 µg/g in dust from control homes.

While the harmful effects of many components of tobacco smoke are well known, those due to heavy metals in the smoke have not been sufficiently emphasized. The adverse health effects of these toxic metals on the fetus through maternal smoking are of special concern (Chiba and Masironi 1992). The concentration of arsenic in tobacco is relatively low, usually below detectable limits (<1 µg/g). Although the concentrations of inorganic and organic arsenic in the urine of adults do not appear to be influenced by smoking, a positive association was found between urinary arsenic levels in children and parental

smoking habits. As detailed in a WHO report, the mean arsenic level in the urine of children of nonsmoking parents was 4.2 µg/g creatinine, in children with one smoking parent, it was 5.5 µg/g, and in children with both parents smoking, it was 13 µg/g (Chiba and Masironi 1992). Tsuji et al. (2005) reported geometric mean concentrations of total arsenic of 15.1 and 15.7 µg/L in children <7 and <13 years old, respectively, from households in Middleport, New York, where historical pesticide manufacture was associated with arsenic in soil. Geometric mean concentrations of inorganic arsenic, MMA, and DMA were 0.81, 0.54, and 2.5 µg/L, respectively, in children <7 years old and 0.83, 0.55, and 3.0 µg/L, respectively, in children <13 years old (Tsuji et al. 2005).

The use of Chinese herbal medicines (CHM) appears to be common among Chinese women. Both CHM and Chinese proprietary medicines (CPM) are used for treatment of minor ailments in babies and children. Herbal medicines are available in capsule or tablet form in drug stores, supermarkets, and by mail. The CPM "Sin Lak Pill," "Lu Shen Wan," and other anti-asthma preparations have been found to contain inorganic arsenic levels ranging from 25 to 107,000 µg/g, and cases of acute arsenic poisoning have been found in children and adults using these CPM (Chan 1994). Babies and children are particularly at risk because they may be given higher doses of these preparations per kg of body weight than adults would normally consume. They may also lack the hepatic enzymes responsible for drug biotransformation and detoxification (Chan 1994). Concentrations of heavy metals, including arsenic, were evaluated in 54 samples of Asian remedies that were purchased in stores in Vietnam and Hong Kong that would be easily accessible to travelers, as well as in health food and Asian groceries in Florida, New York, and New Jersey. One remedy that was recommended to treat children's fever would expose a 15 kg child to approximately 5.0 mg of arsenic per day (Garvey et al. 2001). A folk remedy, purchased in California, for the treatment of chicken pox, flu-like symptoms, and nasal congestion, which had been given to two children in Wisconsin, was found to contain 36% arsenic acid. One-half teaspoon of this powder (about 500 mg of arsenic) was dissolved in hot water and taken 2–3 times per day (Werner et al. 2001).

Various metallic pigments and colors in the form of salts or lakes are used in toy production. Therefore, children may be exposed to toxic metals while playing with toys, especially when they lick, suck, or swallow a toy or a piece of a toy. Toys produced in European Union Markets must conform to restrictions concerning the bioavailability of toxic metals, including arsenic. The maximum limit for bioavailability of arsenic from the accessible parts of a toy is set to 0.1 µg/day. This corresponds to an arsenic migration limit of 25 µg/g for all toy material, including modeling clay and paints (Rastogi and Pritzl 1996). A study was carried out to determine whether crayons, water colors, and water-based paints

conform with the migration limits for toxic metals (Rastogi and Pritzl 1996). For the analysis, 94 samples representing 48 products were obtained from China, Taiwan, Japan, the United States, and European countries. Fifty-two samples showed migration of arsenic, ranging from 0.01 to 3.75 µg/g.

6.7 POPULATIONS WITH POTENTIALLY HIGH EXPOSURES

In addition to individuals who are occupationally exposed to arsenic (see Section 6.5), there are several groups within the general population that have potentially high exposures (higher than background levels) to arsenic. These populations include individuals living in proximity to sites where arsenic was produced, used (e.g., as a pesticide), or disposed, and individuals living near one of the 1,684 NPL hazardous waste sites where arsenic has been found at elevated levels in some environmental media (HazDat 2006). It also includes point sources such as smelters, coal-fired power plants, and municipal incinerators. People living in areas of volcanic activity may be exposed to higher levels of arsenic since high levels are more likely to be present in the environment. Other populations at risk of potentially high levels of exposure include those whose water supply contains high levels of arsenic and those consuming large amounts of seafood or seaweed. However, as pointed out previously (see Section 6.4.4), arsenic in fish and shellfish, is largely in the form of the less harmful organic arsenical, arsenobetaine; however, some commercially available seaweeds, especially brown algae varieties, may have high percentages of the total arsenic present as inorganic arsenic (>50%) (Almela et al. 2002; Laparra et al. 2003). While elevated urinary arsenic excretion levels have been associated with the consumption of fish and seafood, in a study of 32 sport fish consumers from Lakes Erie, Huron, and Michigan, only 6 (19%) had detectable urine arsenic concentrations, >4 µg/L, and 5 of these consumed fish from Lake Huron (Anderson et al. 1998). Exposure of high levels of arsenic in drinking water is more apt to be absorbed by the body and be harmful than exposure to arsenic in seafood. For example, a group of 36 people in Zimapán, Mexico who consumed water from an aquifer with 1.0 mg As/L had hair arsenic levels of 2.6–14.1 µg/g (10 µg/g average), compared with 2.4–13.9 µg/g (6.19 µg/g average) for a reference population that consumed bottled water with <0.014 mg/L arsenic (Armienta et al. 1997).

A study was conducted to determine if significant arsenic exposure was occurring at a Superfund site in Fort Valley, Georgia (Hewitt et al. 1995). Random urine, 24-hour urine, hair, and fingernail samples were collected at the end of the workweek from 40 employees at an active pesticide manufacturing facility where arsenical pesticides had been produced for over 50 years prior to the mid-1970s. Measurement of arsenic in the urine is considered to be the best method for monitoring recent exposure in industrial populations. Hair and fingernail analyses may provide an indication of exposures that occurred

up to several months prior to testing, but both can adsorb and strongly retain arsenic from external sources. Since arsenic is rapidly cleared from the blood (half-life of 3–4 hours), blood arsenic levels are not considered suitable for monitoring populations for chronic low-level arsenic exposure. Results of the Hewitt study are summarized in Table 6-6. Urinary arsenic levels for all workers were well within the commonly accepted normal range of <100 μg/L.

As noted above, workers in a number of industries may have high exposures to arsenic, especially if proper safety procedures are not followed. For members of the general population, above-average exposure to arsenic from drinking water is possible in areas of high natural arsenic levels in groundwater or elevated arsenic levels in drinking water due to industrial discharges, pesticide applications, or leaching from hazardous waste facilities. Individuals living in the vicinity of large smelters and other industrial emitters of arsenic may be exposed to above-average arsenic levels both in the air, and as a result of atmospheric deposition, in water and soil and subsequent uptake into crops.

People sawing or drilling arsenic-treated wood without protective masks or burning this wood may be exposed to elevated levels of arsenic in air.

Recreational and subsistence fishers who consume appreciably higher amounts of locally caught fish from contaminated bodies of water may be exposed to higher levels of arsenic associated with dietary intake. Arsenic contamination has triggered the issuance of several human health advisories (EPA 1998g). As of December 1997, arsenic was identified as the causative pollutant in a restricted consumption advisory for the general population for all fish in a 7-mile area including Devil's Swamp Lake and Bayou Baton Rouge in Louisiana. A public health advisory has been issued for consumption of fish and shellfish from the Duwamish River, Seattle, Washington due to arsenic and other chemicals (WSDOE 2005).

6.8 ADEQUACY OF THE DATABASE

Section 104(i)(5) of CERCLA, as amended, directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of arsenic is available. Where adequate information is not available, ATSDR, in conjunction with NTP, is required to assure the initiation of a program of research designed to determine the health effects (and techniques for developing methods to determine such health effects) of arsenic.

The following categories of possible data needs have been identified by a joint team of scientists from ATSDR, NTP, and EPA. They are defined as substance-specific informational needs that if met would reduce the uncertainties of human health assessment. This definition should not be interpreted to mean that all data needs discussed in this section must be filled. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

6.8.1 Identification of Data Needs

Physical and Chemical Properties. The chemical and physical properties of the arsenic species of chief toxicological and environmental concern are sufficiently well characterized to allow estimation of the environmental fates of these compounds. However, more information regarding the K_{ow} and K_{oc} values of the organic arsenicals would help predict the fate of these compounds in the environment.

Production, Import/Export, Use, Release, and Disposal. According to the Emergency Planning and Community Right-to-Know Act of 1986, 42 U.S.C. Section 11023, industries are required to submit substance release and off-site transfer information to the EPA. The TRI, which contains this information for 2004, became available in May of 2006. This database is updated yearly and should provide a list of industrial production facilities and emissions.

While arsenic has not been produced in the United States since 1985, the United States is the largest consumer of arsenic and substantial quantities of arsenic are imported, primarily as arsenic trioxide (USGS 2006a). The agricultural use of inorganic arsenic pesticides have been discontinued in the United States. However, some organic arsenicals still may be used in agriculture. Current production and use data for individual arsenical pesticides and other arsenic compounds would help to estimate human exposure to the various arsenic species. Because arsenical pesticides are so persistent, a more complete picture of past use of these products would enable us to predict what areas may contain high levels of arsenic in soil.

Comprehensive estimates on emissions of arsenic date to the early 1980s (Nriagu and Pacyna 1988). The industrial picture has changed considerably since then and emission controls are being mandated more and more. For example, emission factors for Canadian smelters calculated in 1993 were grossly lower than those estimated in 1983 (Skeaff and Dubreuil 1997). There is a need for accurate and up-to-date measurements of atmospheric arsenic releases from both natural and anthropogenic sources to better assess human exposure to arsenic and guide environmental protection measures.

Environmental Fate. The interconversion of the various arsenic species and transport among the environmental media is complex and not all aspects are well-studied. Additional quantitative data on the rates of oxidation, reduction, and biotransformation reactions of arsenic compounds, and how these depend on environmental conditions would be useful in evaluating and predicting the fate and transport of arsenic at hazardous waste sites and other areas.

Bioavailability from Environmental Media. Toxicokinetic and toxicity studies establish that bioaccessible (e.g., soluble, not strongly adsorbed to soil or embedded in minerals) arsenic is highly absorbed following inhalation and oral exposure (see Sections 3.4.1.2 and 3.4.1.1). Some work has been done on the effect of environmental matrix (soil, food) on accessibility and absorption of arsenic (Davis et al. 1992, 1996; Hamel et al. 1998; Roberts et al. 2002, 2007), but additional data would be valuable. Limited data suggests that dermal absorption of arsenic is very low (see Section 3.4.1.3) (Lowney et al. 2005), further data would be useful to establish whether arsenic uptake occurs from contact with contaminated soil or water, since humans may be exposed by these routes near hazardous waste sites.

Food Chain Bioaccumulation. Bioconcentration factors have been measured for several freshwater and marine species. While some species (mainly marine algae and shellfish) tend to bioconcentrate arsenic (EPA 1980a; Roper et al. 1996), it is not biomagnified through the food chain (Eisler 1994; EPA 1979, 1982b, 1983e, 2003b; Williams et al. 2006).

Carrots growing on land containing somewhat more than the permissible of arsenic in crop land did not contain levels of arsenic that were harmful (Helgesen and Larsen 1998). However, further research on the uptake of arsenic by a variety of plants in a wide range of arsenic polluted sites (e.g., mining area, orchards previously treated with lead arsenate) would be valuable in assessing human exposure near such sites through the consumption of vegetables from home gardens.

Exposure Levels in Environmental Media. Additional reliable monitoring data for the levels of arsenic in contaminated media at hazardous waste sites are needed or need to be made available, so that the information obtained on levels of arsenic in the environment can be used in combination with the known body burden of arsenic to assess the potential risk of adverse health effects in populations living in the vicinity of hazardous waste sites.

Extensive monitoring data are available for total arsenic in all environmental media. Additional monitoring studies, specifically those that include identification of arsenic species, would allow more precise estimation of current exposure levels and possible human health risks.

Exposure Levels in Humans. Arsenic has been detected in human tissues, including blood, urine, hair, nails, and internal organs. Data are available for populations exposed in the workplace and for the general population (de Peyster and Silvers 1995; Jensen and Olsen 1995; Nygren et al. 1992), and some studies have been published on exposures near waste sites (Hwang et al. 1997a; Tsuji et al. 2005). Additional biomonitoring studies of residents near waste sites that contain arsenic would be helpful in evaluating the likely human health risks from these sites.

While some data are available on the speciation of arsenic in food, additional data on the particular species of arsenic, rather than just the total arsenic concentration, present in foods, especially seafood, are needed to better estimate the potential hazards to human health by the consumption of these foods (Ryan et al. 2001).

This information is necessary for assessing the need to conduct health studies on these populations.

Exposures of Children. Contaminated soils pose a particular hazard to children because of pica and hand-to-mouth activities. Some studies have been performed on exposure and body burden (Hwang et al. 1997a), but additional studies, including investigations of unique pathways for exposures of children and the amount of soil a child ingests, would provide valuable data. Small amounts of arsenic were found to be transferred to hands of children playing on play structures constructed from CCA-treated wood (Hemond and Solo-Gabriele 2004; Kwon et al. 2004; Shalat et al. 2006; Ursitti et al. 2004; Wang et al. 2005). Based on a review of existing studies, Hemond and Solo-Gabriele (2004) estimated that children with contact with CCA-treated wood may be subjected to doses in the range of tens of micrograms of arsenic per day and suggested that exposure by this route warrants further study. The PTDI assigned by the Food and Agriculture Organization of the United Nations and the World Health Organization (FAO/WHO) applies to adults. Studies are needed to assess whether children are different in their weight adjusted intake of arsenic. No childhood-specific means for reducing exposure were identified.

Child health data needs relating to susceptibility are discussed in Section 3.12.2, Identification of Data Needs: Children's Susceptibility.

Exposure Registries. No exposure registries for arsenic were located. This substance is not currently one of the compounds for which a sub-registry has been established in the National Exposure Registry. The substance will be considered in the future when chemical selection is made for sub-registries to be established. The information that is amassed in the National Exposure Registry facilitates the epidemiological research needed to assess adverse health outcomes that may be related to exposure to this substance.

6.8.2 Ongoing Studies

The Federal Research in Progress (FEDRIP 2006) database provides additional information obtainable from a few ongoing studies that may fill in some of the data needs identified in Section 6.8.1. These studies are summarized in Table 6-7.

The U.S. Geological Survey, along with other federal and state agencies, industry, and academia, is conducting the National Geochemical Survey (NGS) in order to produce a body of geochemical data for the United States based primarily on stream sediments that have been analyzed using a consistent set of analytical methods. The goal of the NGS is to analyze at least one stream sediment sample in every 289 km^2 area by a single analytical method across the entire United States (USGS 2007b).

EPA is conducting a 4-year (2000–2003) national screening-level study of contaminants in freshwater fish, referred to as the National Fish Tissue Study (EPA 2004c). This study will allow the EPA to develop national estimates of the mean concentrations of 268 chemicals in tissues of fish from lakes and reservoirs of the coterminous United States. EPA analysis of the data from this study was scheduled to begin in January 2005, with the final report scheduled to be released in 2006. Interim raw data have been released each year, and are available from EPA. Fish samples have been analyzed for total inorganic arsenic (As(III) and As(V) combined), arsenic(III), arsenic(V), MMA(V), and DMA(V). Analysis for total arsenic was not performed as part of this study.

The American Water Works Association Research Foundation (AWWARF) supports research on arsenic in drinking water.

Table 6-7. Ongoing Studies on the Environmental Fate and Exposure of Humans to Arsenic

Investigator	Affiliation	Research description	Sponsor
Basta, NT	Ohio State University, School of Natural Resources, Columbus, Ohio	Heavy metal and trace element biogeochemistry in soils; chemical speciation, bioavailability, and toxicity	USDA
Blum, CB	Columbia University Health Sciences, New York, New York	Bioavailability lead and arsenic in soil to humans	NIEHS
Hamilton, JW	Dartmouth College, Hanover, New Hampshire	Toxic metals—biological and environmental implications	NIEHS
Hoppin, J	Not specified	Monitoring of arsenic and other compounds in the blood and urine of a cohort of pregnant women in Norway	NIEHS
Kpomblekou, AK; Ankumah, RO	Tuskegee University, Agriculture and Home Economics, Tuskegee, Alabama	Biochemical processes in soils treated with trace-element-enriched broiler litter; to determine total arsenic and other metal concentrations and the distribution of their chemical forms in soils under long-term broiler litter treatments	USDA
Loeppert, RH	Texas A&M University, Soil and Crop Sciences, College Station, Texas	Inorganic chemical processes influencing soil and water quality	USDA
Peryea, FJ	Wenatchee Tree Fruit Research & Extension Center Washington State University, Pullman, Washington	Quantification of biogeochemical processes in lead arsenate-contaminated orchard soils and development of soil and plant management practices to minimize the toxicity risks that these soils impose on agricultural crops and to human and environmental health	USDA
Miller, DM; DeLaune, P; Miller, WP	University of Arkansas, Crop, Soil and Environmental Sciences, Fayetteville, Arkansas	Arsenic levels in soils of northwest Arkansas	USDA
van Geen, A	Columbia University, Lamont-Doherty Earth Observatory, Palisades, New York	Studies on arsenic in groundwater in Bangladesh	NSF

Table 6-7. Ongoing Studies on the Environmental Fate and Exposure of Humans to Arsenic

Investigator	Affiliation	Research description	Sponsor
Walker, MJ et al.	University of Nevada, Natural Resources and Environmental Sciences, Reno, Nevada	Arsenic in Churchill County, Nevada domestic water supplies	USDA
Zheng, Y	Columbia University Health Sciences, New York, New York	Arsenic mobilization in Bangladesh groundwater	NIEHS

NIEHS = National Institute of Environmental Health Sciences; NSF = National Science Foundation; USDA = U.S. Department of Agriculture

Source: FEDRIP 2006

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7. ANALYTICAL METHODS

The purpose of this chapter is to describe the analytical methods that are available for detecting, measuring, and/or monitoring arsenic, its metabolites, and other biomarkers of exposure and effect to arsenic. The intent is not to provide an exhaustive list of analytical methods. Rather, the intention is to identify well-established methods that are used as the standard methods of analysis. Many of the analytical methods used for environmental samples are the methods approved by federal agencies and organizations such as EPA and the National Institute for Occupational Safety and Health (NIOSH). Other methods presented in this chapter are those that are approved by groups such as the Association of Official Analytical Chemists (AOAC) and the American Public Health Association (APHA). Additionally, analytical methods are included that modify previously used methods to obtain lower detection limits and/or to improve accuracy and precision.

7.1 BIOLOGICAL MATERIALS

Atomic absorption spectrophotometry (AAS) is the most common analytical procedure for measuring arsenic in biological materials (Curatola et al. 1978; Foà et al. 1984; Johnson and Farmer 1989; Mushak et al. 1977; Norin and Vahter 1981; Sotera et al. 1988). In AAS analysis, the sample is heated in a flame or in a graphite furnace until the element atomizes. The ground-state atomic vapor absorbs monochromatic radiation from a source and a photoelectric detector measures the intensity of transmitted radiation (APHA 1989b). Inductively-coupled plasma atomic emission spectrometry (ICP-AES) and ICP-mass spectrometry (ICP-MS) are increasingly common techniques for the analysis of arsenic; both methods can generally provide lower detection limits than absorbance detection methods.

Samples may be prepared for AAS in a variety of ways. Most often, the gaseous hydride procedure is employed (Curatola et al. 1978; Foà et al. 1984; Johnson and Farmer 1989; Norin and Vahter 1981). In this procedure, arsenic in the sample is reduced to arsine (AsH_3), a gas that is then trapped and introduced into the flame. This approach measures total inorganic arsenic, but may not detect all organic forms unless preceded by a digestion step. Digestion or wet-ashing with nitric, sulfuric, and/or perchloric acids degrades the organic arsenic species to inorganic arsenic so that recovery of total arsenic from biological materials can be achieved (Maher 1989; Mushak et al. 1977; Versieck et al. 1983). In microwave assisted digestion, harsh oxidation conditions are used in conjunction with microwave heating (Benramdane et al. 1999b). For accurate results, it is important to check the completeness of the oxidation; however, this is seldom done (WHO 1981).

The arsenic concentration in biological fluids and tissues may also be determined by neutron activation analysis (NAA) (Landsberger and Simsons 1987; Versieck et al. 1983). In this approach, the sample is irradiated with a source of neutrons that converts a portion of the arsenic atoms to radioactive isotopes, which can be quantified after separation from radioisotopes of other chemicals. Neutron activation has limited use because of the limited number of nuclear reactors in the United States providing this service and the need to dispose of radioactive waste. X-ray fluorescence is also capable of measuring arsenic in biological materials (Bloch and Shapiro 1986; Clyne et al. 1989; Nielson and Sanders 1983) and environmental samples (see Section 7.2). This method has the advantage that no sample digestion or separation steps are required. Hydride generation combined with atomic fluorescence spectroscopy (HG-AFS) is a relatively new technique that provides freedom from interference offered by hydride generation with sensitivity better than to 20 parts per trillion and linearity up to 10 ppm (PSA 2000).

Speciation of arsenic (i.e., analysis of organic arsenic compounds or different inorganic species, rather than total arsenic) is usually accomplished by employing separation procedures prior to introduction of the sample material into a detection system. Various types of chromatography or chelation-extraction techniques are most commonly used in combination with AAS, ICP-AES, or ICP-MS detection methods (Dix et al. 1987; Foà et al. 1984; Johnson and Farmer 1989; Mushak et al. 1977; Norin et al. 1987; Thomas and Sniatecki 1995). In one method, high performance liquid chromatography (HPLC) is combined with HG-AFS to quantify As(III), dimethylarsinic acid (DMA), momomethyl arsonic acid (MMA), and As(V) (PSA 2000). Another approach involves selective reduction of arsenate and arsenite (permitting quantification of individual inorganic arsenic species), and selective distillation of methyl arsines to quantify MMA and DMA (Andreae 1977; Braman et al. 1977; Crecelius 1978). Most methods for measuring arsenic in biological samples are unable to measure arsenobetaine with any accuracy because it does not form a hydride and it gives a different response from inorganic arsenic in electrothermal AAS. Ebdon et al. (1999) successfully employed HPLC coupled with ICP-MS to determine arsenic speciation in blood plasma, which was entirely arsenobetaine. Øygard et al. (1999) developed a simple method to determine inorganic arsenic in biological samples. Their method, which involves initially distilling inorganic arsenic from the sample as $AsCl_3$ using HCl, avoids separating and quantifying all of the different arsenic species, which is both costly and time-consuming.

Table 7-1 summarizes a variety of methods for measuring total arsenic and individual arsenic species in biological materials. None of these methods have been standardized by EPA or other federal agencies.

Table 7-1. Analytical Methods for Determining Arsenic in Biological Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Methods for total arsenic:					
Blood	Digestion with nitric acid and hydrogen peroxide; dry ash with magnesium oxide/magnesium nitrate; reduction with sodium borohydride	HGAAS	0.5 µg/L	95–102	Foà et al. 1984
Blood, hair	Wet ash with nitric/perchloric acids; reduction with sodium borohydride	HGAAS	0.1 µg/L[a]	95–105	Valentine et al. 1979
Serum	Irradiation; digestion with nitric/perchloric/sulfuric acids; extraction with toluene	NAA	0.088 ng/mL[a]	94–98	Versieck et al. 1983
Urine	Irradiate epithermally	NAA	40–100 ng/g	93–109	Landsberger and Simsons 1987
Urine	Digestion with nitric and perchloric acid; reduction with tin chloride; generation arsine by addition of zinc; reaction with SDDC	Colorimetric photometry	0.5 µg/sample	90–110	Pinto et al. 1976
Urine	Pretreatment with L-cysteine; reduction with potassium iodide/ascorbic acid	Flow injection HGAAS	0.1 µg/L	95–100	Guo et al. 1997
Urine	Drying sample; irradiation with x-rays	XRF	0.2 µg/L[a]	92–108	Clyne et al. 1989
Hair	Wet ashing with nitric/sulfuric acids and hydrogen peroxide; reduction to arsine with sodium borohydride	HGAAS	0.06 µg/g	93	Curatola et al. 1978
Soft tissue	Digestion with nitric/sulfuric acids; complexation with DDDC in potassium iodide; extraction with chloroform	GFAAS	0.2 ppm	79.8	Mushak et al. 1977
Nails	Wet ashing with nitric/sulfuric acids and hydrogen peroxide; reduction to arsine with sodium borohydride	HGAAS	1.5 µg/g	No data	Agahian et al. 1990
Methods for arsenic speciation:					
Urine	Separation of As^{+3}, As^{+5}, MMA, and DMA on anion/cation exchange resin column; reduction to respective arsines with sodium borohydride	IEC/HGAAS	0.5 µg/L	93–106	Johnson and Farmer 1989
Urine	Reduction of As^{+3}, As^{+5}, MMA, and DMA to arsines with sodium borohydride	HGAAS	0.08 µg/L	97–104	Norin and Vahter 1981

Table 7-1. Analytical Methods for Determining Arsenic in Biological Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Urine	Reduction of As^{+3}, As^{+5}, MMA, and DMA to arsines; collection in cold trap; selective distillation by slow warming	Atomic emission (direct-current plasma)	≤1 ng for all four species	No data	Braman et al. 1977
Urine	Extraction with chloroform/methanol; column separation with chloroform/methanol; elution on cation exchange column with ammonium hydroxide	HGAAS/TLC/HRMS	0.34 mg/sample[a]	No data	Tam et al. 1982
Blood/tissue	Acidification with hydrochloric acid; complexation with TGM; extraction into cyclohexane; separation on capillary column	GLC/ECD	0.1 mg/mL	No data	Dix et al. 1987
Blood plasma	Separation by HPLC	HPLC/ICP-MS	2.5 ng As/mL	~100	Ebdon et al. 1999
Urine	Separation by anion exchange chromatography; detection by direct coupling of column to ICP-MS	IEC/ICP-MS	<0.45 µg/L for all species	No data	Inoue et al. 1994
Marine biota	Extraction with methanol-water; removal of fats by liquid-liquid extraction or solid-phase cartridge	HPLC/ICP-MS	6–25 ng/mL	94.6 (fish muscle CRM)	Sniatecki 1994
Marine biota	Separation by anion exchange coupled with HPLC; on-line microwave oxidation	HPLC/HGAAS	0.3–0.9 ng	95–110 (recovery of spike in fish tissue)	López-Gonzálvez et al. 1994
Biological samples—Inorganic arsenic	Distill inorganic arsenic as $AsCl_3$ using HCl after prereduction of As(V) with KI/HCl	Flow-injection HGAAS	0.045 mg/kg (dry matter)	No data	Øygard et al. 1999

[a]Lowest reported concentration

CRM = certified reference material; DDDC = diethylammonium diethyldithiocarbamate; DMA = dimethylarsinate; ECD = electron capture detector; GFAAS = graphite furnace atomic absorption spectrometry; GLC = gas-liquid chromatography; HGAAS = hydride generation atomic absorption spectrometry; HRMS = high resolution mass spectrometry; ICP-MS = inductively-coupled plasma mass spectrometry; IEC = ion exchange chromatography; HPLC = high-performance liquid chromatography; MMA = monomethylarsonate; NAA = neutron activation analysis; SDDC = silver diethyldithiocarbamate; TGM = thioglycolic acid methylester; TLC = thin layer chromatography; XRF = x-ray fluorescence

Detection limits in blood and urine are about 0.1–1 ppb for most techniques; limits for hair and tissues are usually somewhat higher.

7.2 ENVIRONMENTAL SAMPLES

Arsenic in environmental samples is also measured most often by AAS techniques, with samples prepared by digestion with nitric, sulfuric, and/or perchloric acids (Dabeka and Lacroix 1987; EPA 1983b, 1994a, 1994b; Hershey et al. 1988). Other methods employed include a spectrophotometric technique in which a soluble red complex of arsine and silver diethyldithiocarbamate (SDDC) is formed (APHA 1977; EPA 1983c, 1983d), ICP-AES (EPA 2000c; NIOSH 2003), graphite furnace AAS (EPA 1983b, 1994b; NIOSH 1994b), ICP-MS (EPA 1991, 1994a, 1998j), and x-ray fluorescence (Khan et al. 1989; Nielson and Sanders 1983).

HPLC is currently the most common technique for separation of the species of arsenic found in seafood (Benramdane et al. 1999b; Guerin et al. 1999; Kumaresan and Riyazuddin 2001). An advantage of HPLC over other separation methods (e.g., gas chromatography [GC]) is that the arsenic species do not need to be derivatized prior to separation, avoiding concerns over complete conversion to the derivative for detection.

Since arsenic in air is usually associated with particulate matter, standard methods involve collection of air samples on glass fiber or membrane filters, acid extraction of the filters, arsine generation, and analysis by SDDC spectrophotometry or AAS (APHA 1977; NIOSH 1984).

Methods standardized by the EPA for measuring total arsenic in water and waste water, solid wastes, soil, and sediments include: ICP-MS (EPA 1998j, 1994a, 1991), ICP-AES (EPA 1996d), graphite furnace AAS (EPA 1994b), quartz furnace hydride generation AAS (EPA 1996h), and an electrochemical method using anodic stripping voltammetry (ASV) (EPA 1996e). A modification using cryogenic GC to EPA Method 1632 (HG/AAS) allows the technique to be adopted for the species As(III), As(V), MMA, and DMA to the 0.003 ppb level (EPA 1998l). Similar methods are recommended by APHA for water using AAS/hydride generation (APHA 1989c), AAS/graphite furnace technique (APHA 1989b), ICP (APHA 1989d), or SDDC spectrophotometry (APHA 1989a). The AAS/hydride generation method is generally resistant to matrix and chemical interferences (APHA 1989a). Techniques to compensate for these interferences have been described by EPA (1982b).

Analysis for arsenic in foods is also most frequently accomplished by AAS techniques (Arenas et al. 1988; Dabeka and Lacroix 1987; Hershey et al. 1988; Tam and Lacroix 1982). Hydride generation is the sample preparation method most often employed (Arenas et al. 1988; Hershey et al. 1988), but interferences must be evaluated and minimized.

Speciation of inorganic arsenic in environmental samples is usually accomplished by chromatographic separation, chelation-extraction or elution of As(III), and then reduction of As(V) with subsequent similar treatment (Butler 1988; López-Gonzálvez et al. 1994; Mok et al. 1988; Rabano et al. 1989).

Methods are also available for quantifying organic arsenicals in environmental media, including arsenobetaine in fish (Beauchemin et al. 1988; Cannon et al. 1983) and other organic forms of arsenic in water, soil, and foods using hyphenated methods of separation and detection (HPLC/ICP-MS, HPLC/HGAAS, IC/ICP-MS) (Andreae 1977; Braman et al. 1977; Comber and Howard 1989; Crecelius 1978; Heitkemper et al. 1994; López-Gonzálvez et al. 1994; Odanaka et al. 1983; Teräsahde et al. 1996).

Methods have been developed for extraction of arsenic species from solid seafood samples that included treatment of the sample with mixtures of organic solvents (alcohols or chloroform) and water to extract the arsenic compounds that are soluble in water or polar organic solvents. These extracts can be subsequently analyzed by HPLC. Enzymatic digestion using trypsin has also been used to extract arsenic compounds from seafood samples (Benramdane et al. 1999b). These extraction techniques are used in place of digestion when speciated data are needed.

A summary of selected methods for analysis of total arsenic and individual inorganic and organic arsenic species in environmental samples is presented in Table 7-2.

7.3 ADEQUACY OF THE DATABASE

Section 104(i)(5) of CERCLA, as amended, directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of arsenic is available. Where adequate information is not available, ATSDR, in conjunction with NTP, is required to assure the initiation of a program of research designed to determine the health effects (and techniques for developing methods to determine such health effects) of arsenic.

Table 7-2. Analytical Methods for Determining Arsenic in Environmental Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Methods for total arsenic:					
Air (particulates)	Collection on cellulose ester membrane filter; digestion with nitric acid, sulfuric acid, and perchloric acid	NIOSH Method 7900; HGAAS	0.02 µg/sample	No data	NIOSH 1994a
Air (particulate arsenic and arsenic trioxide vapor)	Collection on Na_2CO_3-impregnated cellulose ester membrane filter and H_2O_2	NIOSH Method 7901; GFAAS	0.06 µg/sample	No data	NIOSH 1994b
Air	Collection on cellulose ester membrane filter; digestion with nitric acid, sulfuric acid, and perchloric acid	NIOSH Method 7300; ICP-AES	0.140 µg/filter	No data	NIOSH 2003
Water/waste water/solid wastes	Acid digestion	EPA Method 6010C; ICP-AES	35 µg/L	86	EPA 2000c
Water/waste water/solid wastes	Digestion with nitric and hydrochloric acids	EPA Method 200.7; ICP-AES	8 µg/L	106	EPA 1994c
Water/soil/ solid waste	Digestion with nitric acid and hydrogen peroxide	EPA Methods 206.2 and 7060A; GFAAS with $Ni(NO_3)_2$ modifier	1 µg/L	85–106	EPA 1983b, 1994b
Water/waste water/solid waste	Digestion with nitric acid	EPA Methods 200.8, 6020 and 6020A ICP-MS	0.4 µg/L	97–114	EPA 1991, 1994a, 1998j
Water/soil/ solid waste	Digestion with nitric/sulfuric acid; reduction to As^{+3} with tin chloride; reduction to arsine with zinc in acid solution	EPA Method 206.3	2 µg/L	85–94	EPA 1983c
Water	Reduction to arsine in acid solution; reaction with SDDC	EPA Method 206.4; SDDC colorimetric spectrophotometry at 510 nm	10 µg/L	100	EPA 1983d
Water	Digestion with 6M HCl; reduction to arsine with sodium borohydride; cold trap and desorption into quartz furnace	EPA Method 1632; HGAAS	2 ng/L	No data	EPA 1998l

Table 7-2. Analytical Methods for Determining Arsenic in Environmental Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Food	Digestion with nitric acid; dry ashing with magnesium oxide; reduction with ascorbic acid; precipitation with APDC in presence of nickel carrier	GFAAS	10 ng	86–107	Dabeka and Lacroix 1987
Food	Digestion with nitric/sulfuric/ perchloric acids; reduction to trivalent arsenic with potassium iodide; reduction to arsine with sodium borohydride	HGAAS	0.1 µg/g	98–110	Hershey et al. 1988
Soil, rock, coal	Preparation of pellet	XRF (backscatter)	4 mg/kg	SRM recoveries: 110±4 in soil; 100±1in rock; 97±18 in coal	Nielson and Sanders 1983
Methods for species of arsenic:					
Air (particulate organo-arsenals)	Collection on PTFE filter	NIOSH Method 5022; ion chromatography/HGAAS	0.2 µg As/sample	No data	NIOSH 1994c
Air (arsine)	Collection on coconut shell charcoal; digestion with nitric acid	NIOSH Method 6001; GFAAS	0.004 µg/sample	No data	NIOSH 1994d
Air particulates (As^{+3} and As^{+5} only)	Collection on PFTE filter in high volume dichotomous virtual impactor; desorption with ethanolic hydrochloric acid; selective reduction of As^{+3} to arsine with zinc in acid and reduction of As^{+5} to arsine with sodium tetrahydrodiborate	HGAAS	1 ng/m^3	95±7 (As^{+3}); 100±8 (As^{+5}) on spiked materials	Rabano et al. 1989
Water	Selective elution of As^{+3} with orthophosphoric acid; elution and conversion of As^{+5} to As^{+3} with sulfur dioxide	IEC/amperometric detector (detects As^{+3} only)	0.9 µg/L	95% of converted As^{+5} recovered	Butler 1988
Water/soil	Selective complexation of As^{+5} with ammonium molybdate; extraction with isoamyl alcohol to separate from As^{+3}	Colorimetric spectrometry at 712 nm	No data	No data	Brown and Button 1979

Table 7-2. Analytical Methods for Determining Arsenic in Environmental Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Water	Selective extraction of As^{+3} with APDC into chloroform; back extraction with nitric acid; reduction of As^{+5} to As^{+3} with thiosulfate and extract	NAA	0.01 ppb	No data	Braman et al. 1977
Food (arsenobetaine in fish)	Extraction of arsenobetaine with methanol/chloroform; digestion with nitric acid/ magnesium nitrate for remainder of As species	HPLC/ICP-MS	0.3 ng as arsenobetaine	101±4 recovery of arsenobetaine	Beauchemin et al. 1988
Water/waste water/soil (inorganic species)	Acidification or digestion with hydrochloric acid	EPA Method 7063; ASV	0.1 µg/L	96–102	EPA 1996e
Water (As(III), As(V), MMA, and DMA)	Cryogenic GC, Digestion with 6M HCl; reduction to arsine with sodium boro-hydride; cold trap and desorption into quartz furnace	EPA Method 1632 appendix; HGAAS	3 ng/L	No data	EPA 1998l
Water	Reduction to arsines; cold trap and selectively warm to separate arsine species	AAS	2 ng/L	91–109	Andreae 1977
Water	Reduction of MMA, DMA and inorganic As (control pH to select As^{+3} or As^{+5}) to arsines with sodium tetra-hydroborate; cold trap and selectively warm to separate arsine species	HGAAS	0.019–0.061 ng	No data	Comber and Howard 1989
Water/soil	Extraction with sodium bicarbonate; reduction of inorganic arsenic, MMA and DMA to hydrides with sodium borohydride; cold trap arsines in n-heptane	HG-HCT/GC-MID	0.2–0.4 µg/L	97–102	Odanaka et al. 1983

AAS = atomic absorption spectrophotometry; APDC = ammonium pyrrolidine dithiocarbamate; ASV = anodic stripping voltammetry; DMA = dimethylarsinate; EPA = Environmental Protection Agency; GC-MID = gas chromatography-multiple ion detection; GFAAS = graphite furnace atomic absorption spectrometry; HGAAS=hydride generation-atomic absorption spectroscopy; HG-HCT = hydride generation-heptane cold trap; HPLC = high performance liquid chromatography; ICP-AES = inductively coupled plasma-atomic emission spectrometry; ICP-MS = inductively coupled plasma-mass spectrometry; IEC = ion exchange chromatography; MMA = monomethylarsonate; NAA = neutron activation analysis; NIOSH = National Institute of Occupational Safety and Health; PTFE = polytetrafluoroethylene; SDDC = silver diethyldithiocarbamate; SRM = standard reference material; XRF = x-ray fluorescence

The following categories of possible data needs have been identified by a joint team of scientists from ATSDR, NTP, and EPA. They are defined as substance-specific informational needs that if met would reduce the uncertainties of human health assessment. This definition should not be interpreted to mean that all data needs discussed in this section must be filled. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

7.3.1 Identification of Data Needs

Methods for Determining Biomarkers of Exposure and Effect. The most common biomarker for arsenic exposure is analysis of total arsenic in urine (Hughes 2006). Existing methods are sufficiently sensitive to measure background levels of arsenic in various tissues and biological fluids for average persons, and to detect increases as a result of above-average exposure (Agahian et al. 1990; Clyne et al. 1989; Curatola et al. 1978; Foà et al. 1984; Gebel et al. 1998b; Landsberger and Simsons 1987; Mushak et al. 1977; Pinto et al. 1976; Valentine et al. 1979; Versieck et al. 1983). The precision and accuracy of these methods are documented. Methods are also available that can distinguish nontoxic forms of arsenic (arsenobetaine) from inorganic and organic derivatives that are of health concern (Braman et al. 1977; Dix et al. 1987; Johnson and Farmer 1989; Norin and Vahter 1981; Tam et al. 1982). Further efforts to improve accuracy, reduce interferences, and detect multiple species using a single analysis would be valuable. Arsenic is believed to act by inhibition of numerous cellular and molecular processes. However, these effects are not specific to arsenic, and most can only be measured in tissue extracts.

Methods for Determining Parent Compounds and Degradation Products in Environmental Media. Arsenic is ubiquitous in the environment. It is found in air, water, soil, sediments, and food in several inorganic and organic forms. Analytical methods exist for the analysis of arsenic species in all of these environmental media, and these methods have the sensitivity to measure background levels and to detect elevated concentrations due to emissions from sources such as smelters, chemical plants, or hazardous waste sites (APHA 1977, 1989c; EPA 1982b, 1983b, 1983c, 1983d, 1991, 1994b, 1994c, 1996f, 1996h, 1998j, 2000c; NIOSH 1994a, 1994b, 2003). However, further research to reduce chemical and matrix interferences may improve the speed and accuracy of the analyses.

Le et al. (2004) pointed out that there is a need for the development of certified reference materials (CRMs) for speciation analysis. A shortcoming of many CRMs is that they are only certified for the total concentration of arsenic, and only limited information is available on the identity and concentrations of specific arsenic species in some CRMs.

Continued improvement of the methods for determination of the particular species of arsenic, rather than just the total arsenic concentration, present in foods, especially seafood, is needed since different arsenic species poses different hazards to individuals consuming these foods.

7.3.2 Ongoing Studies

The information in Table 7-3 was found as a result of a search of the Federal Research in Progress database (FEDRIP 2006).

Table 7-3. Ongoing Studies on Analytical Methods for Arsenic in Environmental and Biological Samples

Investigator	Affiliation	Research description	Sponsor
Styblo, M	University of North Carolina Chapel Hill, Chapel Hill, North Carolina	Optimized hydride generation system for arsenic analysis	Fogarty International Center
Dietze, WT	Tracedetect, Inc., Seattle, Washington	A continuous monitor for arsenic in drinking water	NIEHS
Dasgupta, PK	Texas Tech University, Department of Chemistry, Lubbock, Texas	A green fieldable analyzer for arsenic	NSF

NIEHS = National Institute of Environmental Health Sciences; NSF = National Science Foundation

Source: FEDRIP 2006

8. REGULATIONS AND ADVISORIES

The international and national regulations and guidelines pertaining to arsenic and its metabolites in air, water, and other media are summarized in Table 8-1.

ATSDR has not derived inhalation MRLs or an intermediate-duration oral MRL for inorganic arsenic, or any MRLs for organic arsenic, due to lack of suitable data.

ATSDR has derived an acute-duration oral MRL for inorganic arsenic of 0.005 mg As/kg/day based on a LOAEL of 0.05 mg As/kg/day for gastrointestinal effects and facial edema in Japanese people who ingested arsenic-contaminated soy sauce for 2–3 weeks (Mizuta et al. 1956). An uncertainty factor of 10 (10 for use of a LOAEL and 1 for human variability) was applied.

ATSDR has derived a chronic-duration oral MRL of 0.0003 mg/kg/day for inorganic arsenic based on a NOAEL of 0.0008 mg As/kg/day for dermal effects in a Taiwanese farming population exposed to arsenic in well water (Tseng 1977; Tseng et al. 1968). An uncertainty factor of 3 (for human variability) was applied.

EPA (IRIS 2007) has derived a chronic oral reference dose (RfD) of 0.0003 mg As/kg/day for inorganic arsenic, based on a NOAEL of 0.0008 mg As/kg/day for dermal effects and possible vascular complications in a Taiwanese farming population exposed to arsenic in well water (Tseng 1977; Tseng et al. 1968). An uncertainty factor of 3 (to account for the lack of reproductive data and uncertainty in whether the NOAEL accounts for all sensitive individuals) was applied. No reference concentration (RfC) for chronic inhalation exposures to arsenic was reported. EPA is currently revising the assessment for inorganic arsenic.

The Department of Health and Human Services (DHHS) has determined that inorganic arsenic is known to be a human carcinogen (NTP 2005). The EPA has determined that inorganic arsenic is a human carcinogen and has assigned it the cancer classification, Group A (IRIS 2007). EPA's quantitative estimates of carcinogenic risk from oral exposures include a cancer slope factor of 1.5 mg/kg/day and a drinking water unit risk of $5x10^{-5}$ µg/L. The inhalation unit risk for cancer is 0.0043 µg/m^3 (IRIS 2007).

Table 8-1. Regulations and Guidelines Applicable to Arsenic and Arsenic Compounds

Agency	Description	Information	Reference
INTERNATIONAL			
Guidelines:			
IARC	Carcinogenicity classification for arsenic and arsenic compounds	Group 1[a]	IARC 2004
WHO	Air quality guidelines	$1.5x10^{-3}$ unit risk[b]	WHO 2000
	Drinking water quality guidelines for arsenic	0.01 mg/L[c]	WHO 2004
NATIONAL			
Regulations and Guidelines:			
a. Air			
ACGIH	TLV (TWA) for arsenic and inorganic compounds	0.01 mg/m^3	ACGIH 2004
EPA	Hazardous air pollutant (arsenic and inorganic compounds, including arsine)	Yes	EPA 2004b 42 USC 7412
NIOSH	REL (15-minute ceiling limit) for arsenic and inorganic compounds[d]	0.002 mg/m^3	NIOSH 2005a
	IDLH for arsenic and inorganic compounds[d]	5 mg/m^3	
OSHA	PEL (8-hour TWA) for general industry for arsenic organic compounds	0.5 mg/m^3	OSHA 2005d 29 CFR 1910.1000
	PEL (8-hour TWA) for general industry for arsenic inorganic compounds	10 $\mu g/m^3$	OSHA 2005c 29 CFR 1910.1018
	PEL (8-hour TWA) for construction industry for arsenic organic compounds	0.5 mg/m^3	OSHA 2005b 29 CFR 1926.55
	PEL (8-hour TWA) for shipyard industry for arsenic organic compounds	0.5 mg/m^3	OSHA 2005a 29 CFR 1915.1000
b. Water			
EPA	Designated as hazardous substances in accordance with Section 311(b)(2)(A) of the Clean Water Act	Yes	EPA 2005d 40 CFR 116.4
	Arsenic pentoxide, arsenic trioxide, calcium arsenate, and sodium arsenite		
	Drinking water standards and health advisories for arsenic		EPA 2004a
	DWEL	0.01 mg/L	
	National primary drinking water standards for arsenic		EPA 2002a
	MCLG	Zero	
	MCL	0.01 mg/L[e]	
	Reportable quantities of hazardous substances designated pursuant to Section 311 of the Clean Water Act		EPA 2005e 40 CFR 117.3
	Arsenic pentoxide, arsenic trioxide, calcium arsenate, sodium arsenite	1 pound	

Table 8-1. Regulations and Guidelines Applicable to Arsenic and Arsenic Compounds

Agency	Description	Information	Reference
NATIONAL *(cont.)*			
EPA	Water quality criteria for human health consumption of arsenic:		EPA 2002b
	Water + Organism	0.018 µg/L[f]	
	Organism only	0.14 µg/L[f]	
c. Food			
EPA	Tolerances for residues		
	Dimethylarsinic acid		EPA 2005i 40 CFR 180.311
	Cotton (undelinted seed)	2.8 ppm	
	Methanearsonic acid		EPA 2005j 40 CFR 180.289
	Cotton (undelinted seed)	0.7 ppm	
	Cotton, hulls	0.9 ppm	
	Fruit, citrus	0.35 ppm	
FDA	Bottled drinking water	0.01 mg/L	FDA 2005 21 CFR 165.110
USDA	Nonsynthetic substances prohibited for use in organic crop production	Arsenic	USDA 2004 7 CFR 205.602
d. Other			
ACGIH	Carcinogenicity classification for arsenic and arsenic compounds	A1[g]	ACGIH 2004
	Biological exposure indices for inorganic arsenic plus methylated metabolites in urine at the end of the workweek	35 µg As/L	
EPA	Carcinogenicity classification	Group A[i]	IRIS 2007
	Oral slope factor	1.5 per mg/kg/day	
	Inhalation unit risk	4.3×10^{-3} per µg/m^3	
	RfC	No data	
	RfD	3×10^{-4} mg/kg/day	
	Superfund, emergency planning, and community right-to-know		
	Designated CERCLA hazardous substance		EPA 2005f 40 CFR 302.4
	Reportable quantity		
	Arsenic	Not applicable[j]	
	Arsenic acid, arsenic pentoxide, arsenic trioxide, calcium arsenate, dimethylarsinic acid, and sodium arsenite	1 pound	
	Effective date of toxic chemical release reporting for arsenic	01/01/87	EPA 2005h 40 CFR 372.65

Table 8-1. Regulations and Guidelines Applicable to Arsenic and Arsenic Compounds

Agency	Description	Information	Reference
NATIONAL *(cont.)*			
EPA	Superfund, emergency planning, and community right-to-know		
	Extremely hazardous substances		EPA 2005g 40 CFR 355, Appendix A
	Reportable quantity		
	Arsenic pentoxide, calcium arsenate, and sodium arsenite	1 pound	
	Threshold planning quantities		
	Arsenic pentoxide	100/10,000 pounds	
	Calcium arsenate and sodium arsenite	500/10,000 pounds	
NTP	Carcinogenicity classification	Known human carcinogen	NTP 2005

[a]Group 1: carcinogenic to humans
[b]Cancer risk estimates for lifetime exposure to a concentration of 1 µg/m3.
[c]Provisional guideline value: as there is evidence of a hazard, but the available information on health effects is limited.
[d]NIOSH potential occupational carcinogen
[e]MCL will become effective on 01/23/06.
[f]This criterion is based on carcinogenicity of 10^{-6} risk.
[g]A1: confirmed human carcinogen
[h]A3: confirmed animal carcinogen with unknown relevance to humans
[i]Group A: known human carcinogen
[j]Indicates that no reportable quantity is being assigned to the generic or broad class.

ACGIH = American Conference of Governmental Industrial Hygienists; CERCLA = Comprehensive Environmetnal Response, Compensation, and Liability Act; CFR = Code of Federal Regulations; DWEL = drinking water equivalent level; EPA = Environmental Protection Agency; FDA = Food and Drug Administration; IARC = International Agency for Research on Cancer; IDLH = immediately dangerous to life or health; IRIS = Integrated Risk Information System; MCL = maximum contaminant level; MCLG = maximum contaminant level goal; NAS/NRC = National Academy of Sciences/National Research Council; NIOSH = National Institute for Occupational Safety and Health; NTP = National Toxicology Program; OSHA = Occupational Safety and Health Administration; PEL = permissible exposure limit; REL = recommended exposure limit; RfC = inhalation reference concentration; RfD = oral reference dose; TLV = threshold limit values; TWA = time-weighted average; USC = United States Code; USDA = United States Department of Agriculture; WHO = World Health Organization

EPA is currently revising the assessment for inorganic arsenic. The International Agency for Research on Cancer (IARC) cites sufficient evidence of a relationship between exposure to arsenic and human cancer. IARC classification of arsenic is Group 1 (IARC 2004). The American Conference of Governmental Industrial Hygienists (ACGIH) classifies arsenic (elemental and inorganic compound) as a confirmed human carcinogen, cancer category A1 (ACGIH 2004).

ATSDR has derived an intermediate-duration oral MRL of 0.1 mg MMA/kg/day for MMA based on a $BMDL_{10}$ of 12.38 mg MMA/kg/day for diarrhea observed in rats exposed to MMA in the diet for 13 weeks (Arnold et al. 2003) and an uncertainty factor of 100 (10 for animal to human extrapolation and 10 for human variability).

ATSDR has derived a chronic-duration oral MRL of 0.01 mg MMA/kg/day for MMA based on a $BMDL_{10}$ of 1.09 mg MMA/kg/day for increased incidence of progressive nephropathy in male mice exposed to MMA in the diet for 2 years (Arnold et al. 2003) and an uncertainty factor of 100 (10 for animal to human extrapolation and 10 for human variability).

ATSDR has derived a chronic-duration oral MRL of 0.02 mg DMA/kg/day for DMA based on a $BMDL_{10}$ of 1.80 mg DMA/kg/day for increased vacuolization of the urothelium in the urinary bladder of female mice exposed to DMA in the diet for 2 years (Arnold et al. 2006) and an uncertainty factor of 100 (10 for animal to human extrapolation and 10 for human variability).

EPA has not derived RfD values for organic arsenicals (IRIS 2007).

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10. GLOSSARY

Absorption—The taking up of liquids by solids, or of gases by solids or liquids.

Acute Exposure—Exposure to a chemical for a duration of 14 days or less, as specified in the Toxicological Profiles.

Adsorption—The adhesion in an extremely thin layer of molecules (as of gases, solutes, or liquids) to the surfaces of solid bodies or liquids with which they are in contact.

Adsorption Coefficient (K_{oc})—The ratio of the amount of a chemical adsorbed per unit weight of organic carbon in the soil or sediment to the concentration of the chemical in solution at equilibrium.

Adsorption Ratio (Kd)—The amount of a chemical adsorbed by sediment or soil (i.e., the solid phase) divided by the amount of chemical in the solution phase, which is in equilibrium with the solid phase, at a fixed solid/solution ratio. It is generally expressed in micrograms of chemical sorbed per gram of soil or sediment.

Benchmark Dose (BMD)—Usually defined as the lower confidence limit on the dose that produces a specified magnitude of changes in a specified adverse response. For example, a BMD_{10} would be the dose at the 95% lower confidence limit on a 10% response, and the benchmark response (BMR) would be 10%. The BMD is determined by modeling the dose response curve in the region of the dose response relationship where biologically observable data are feasible.

Benchmark Dose Model—A statistical dose-response model applied to either experimental toxicological or epidemiological data to calculate a BMD.

Bioconcentration Factor (BCF)—The quotient of the concentration of a chemical in aquatic organisms at a specific time or during a discrete time period of exposure divided by the concentration in the surrounding water at the same time or during the same period.

Biomarkers—Broadly defined as indicators signaling events in biologic systems or samples. They have been classified as markers of exposure, markers of effect, and markers of susceptibility.

Cancer Effect Level (CEL)—The lowest dose of chemical in a study, or group of studies, that produces significant increases in the incidence of cancer (or tumors) between the exposed population and its appropriate control.

Carcinogen—A chemical capable of inducing cancer.

Case-Control Study—A type of epidemiological study that examines the relationship between a particular outcome (disease or condition) and a variety of potential causative agents (such as toxic chemicals). In a case-controlled study, a group of people with a specified and well-defined outcome is identified and compared to a similar group of people without outcome.

Case Report—Describes a single individual with a particular disease or exposure. These may suggest some potential topics for scientific research, but are not actual research studies.

Case Series—Describes the experience of a small number of individuals with the same disease or exposure. These may suggest potential topics for scientific research, but are not actual research studies.

Ceiling Value—A concentration of a substance that should not be exceeded, even instantaneously.

Chronic Exposure—Exposure to a chemical for 365 days or more, as specified in the Toxicological Profiles.

Cohort Study—A type of epidemiological study of a specific group or groups of people who have had a common insult (e.g., exposure to an agent suspected of causing disease or a common disease) and are followed forward from exposure to outcome. At least one exposed group is compared to one unexposed group.

Cross-sectional Study—A type of epidemiological study of a group or groups of people that examines the relationship between exposure and outcome to a chemical or to chemicals at one point in time.

Data Needs—Substance-specific informational needs that if met would reduce the uncertainties of human health assessment.

Developmental Toxicity—The occurrence of adverse effects on the developing organism that may result from exposure to a chemical prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the life span of the organism.

Dose-Response Relationship—The quantitative relationship between the amount of exposure to a toxicant and the incidence of the adverse effects.

Embryotoxicity and Fetotoxicity—Any toxic effect on the conceptus as a result of prenatal exposure to a chemical; the distinguishing feature between the two terms is the stage of development during which the insult occurs. The terms, as used here, include malformations and variations, altered growth, and *in utero* death.

Environmental Protection Agency (EPA) Health Advisory—An estimate of acceptable drinking water levels for a chemical substance based on health effects information. A health advisory is not a legally enforceable federal standard, but serves as technical guidance to assist federal, state, and local officials.

Epidemiology—Refers to the investigation of factors that determine the frequency and distribution of disease or other health-related conditions within a defined human population during a specified period.

Genotoxicity—A specific adverse effect on the genome of living cells that, upon the duplication of affected cells, can be expressed as a mutagenic, clastogenic, or carcinogenic event because of specific alteration of the molecular structure of the genome.

Half-life—A measure of rate for the time required to eliminate one half of a quantity of a chemical from the body or environmental media.

Immediately Dangerous to Life or Health (IDLH)—The maximum environmental concentration of a contaminant from which one could escape within 30 minutes without any escape-impairing symptoms or irreversible health effects.

Immunologic Toxicity—The occurrence of adverse effects on the immune system that may result from exposure to environmental agents such as chemicals.

Immunological Effects—Functional changes in the immune response.

Incidence—The ratio of individuals in a population who develop a specified condition to the total number of individuals in that population who could have developed that condition in a specified time period.

Intermediate Exposure—Exposure to a chemical for a duration of 15–364 days, as specified in the Toxicological Profiles.

In Vitro—Isolated from the living organism and artificially maintained, as in a test tube.

In Vivo—Occurring within the living organism.

Lethal Concentration$_{(LO)}$ (LC_{LO})—The lowest concentration of a chemical in air that has been reported to have caused death in humans or animals.

Lethal Concentration$_{(50)}$ (LC_{50})—A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

Lethal Dose$_{(LO)}$ (LD_{Lo})—The lowest dose of a chemical introduced by a route other than inhalation that has been reported to have caused death in humans or animals.

Lethal Dose$_{(50)}$ (LD_{50})—The dose of a chemical that has been calculated to cause death in 50% of a defined experimental animal population.

Lethal Time$_{(50)}$ (LT_{50})—A calculated period of time within which a specific concentration of a chemical is expected to cause death in 50% of a defined experimental animal population.

Lowest-Observed-Adverse-Effect Level (LOAEL)—The lowest exposure level of chemical in a study, or group of studies, that produces statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control.

Lymphoreticular Effects—Represent morphological effects involving lymphatic tissues such as the lymph nodes, spleen, and thymus.

Malformations—Permanent structural changes that may adversely affect survival, development, or function.

Minimal Risk Level (MRL)—An estimate of daily human exposure to a hazardous substance that is likely to be without an appreciable risk of adverse noncancer health effects over a specified route and duration of exposure.

Modifying Factor (MF)—A value (greater than zero) that is applied to the derivation of a Minimal Risk Level (MRL) to reflect additional concerns about the database that are not covered by the uncertainty factors. The default value for a MF is 1.

Morbidity—State of being diseased; morbidity rate is the incidence or prevalence of disease in a specific population.

Mortality—Death; mortality rate is a measure of the number of deaths in a population during a specified interval of time.

Mutagen—A substance that causes mutations. A mutation is a change in the DNA sequence of a cell's DNA. Mutations can lead to birth defects, miscarriages, or cancer.

Necropsy—The gross examination of the organs and tissues of a dead body to determine the cause of death or pathological conditions.

Neurotoxicity—The occurrence of adverse effects on the nervous system following exposure to a chemical.

No-Observed-Adverse-Effect Level (NOAEL)—The dose of a chemical at which there were no statistically or biologically significant increases in frequency or severity of adverse effects seen between the exposed population and its appropriate control. Effects may be produced at this dose, but they are not considered to be adverse.

Octanol-Water Partition Coefficient (K_{ow})—The equilibrium ratio of the concentrations of a chemical in *n*-octanol and water, in dilute solution.

Odds Ratio (OR)—A means of measuring the association between an exposure (such as toxic substances and a disease or condition) that represents the best estimate of relative risk (risk as a ratio of the incidence among subjects exposed to a particular risk factor divided by the incidence among subjects who were not exposed to the risk factor). An OR of greater than 1 is considered to indicate greater risk of disease in the exposed group compared to the unexposed group.

Organophosphate or Organophosphorus Compound—A phosphorus-containing organic compound and especially a pesticide that acts by inhibiting cholinesterase.

Permissible Exposure Limit (PEL)—An Occupational Safety and Health Administration (OSHA) allowable exposure level in workplace air averaged over an 8-hour shift of a 40-hour workweek.

Pesticide—General classification of chemicals specifically developed and produced for use in the control of agricultural and public health pests.

Pharmacokinetics—The dynamic behavior of a material in the body, used to predict the fate (disposition) of an exogenous substance in an organism. Utilizing computational techniques, it provides the means of studying the absorption, distribution, metabolism, and excretion of chemicals by the body.

Pharmacokinetic Model—A set of equations that can be used to describe the time course of a parent chemical or metabolite in an animal system. There are two types of pharmacokinetic models: data-based and physiologically-based. A data-based model divides the animal system into a series of compartments, which, in general, do not represent real, identifiable anatomic regions of the body, whereas the physiologically-based model compartments represent real anatomic regions of the body.

Physiologically Based Pharmacodynamic (PBPD) Model—A type of physiologically based dose-response model that quantitatively describes the relationship between target tissue dose and toxic end points. These models advance the importance of physiologically based models in that they clearly describe the biological effect (response) produced by the system following exposure to an exogenous substance.

Physiologically Based Pharmacokinetic (PBPK) Model—Comprised of a series of compartments representing organs or tissue groups with realistic weights and blood flows. These models require a variety of physiological information: tissue volumes, blood flow rates to tissues, cardiac output, alveolar ventilation rates, and possibly membrane permeabilities. The models also utilize biochemical information, such as air/blood partition coefficients, and metabolic parameters. PBPK models are also called biologically based tissue dosimetry models.

Prevalence—The number of cases of a disease or condition in a population at one point in time.

Prospective Study—A type of cohort study in which the pertinent observations are made on events occurring after the start of the study. A group is followed over time.

q_1*—The upper-bound estimate of the low-dose slope of the dose-response curve as determined by the multistage procedure. The q_1* can be used to calculate an estimate of carcinogenic potency, the incremental excess cancer risk per unit of exposure (usually µg/L for water, mg/kg/day for food, and µg/m^3 for air).

Recommended Exposure Limit (REL)—A National Institute for Occupational Safety and Health (NIOSH) time-weighted average (TWA) concentration for up to a 10-hour workday during a 40-hour workweek.

Reference Concentration (RfC)—An estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious noncancer health effects during a lifetime. The inhalation reference concentration is for continuous inhalation exposures and is appropriately expressed in units of mg/m^3 or ppm.

Reference Dose (RfD)—An estimate (with uncertainty spanning perhaps an order of magnitude) of the daily exposure of the human population to a potential hazard that is likely to be without risk of deleterious effects during a lifetime. The RfD is operationally derived from the no-observed-adverse-effect level (NOAEL, from animal and human studies) by a consistent application of uncertainty factors that reflect various types of data used to estimate RfDs and an additional modifying factor, which is based on a professional judgment of the entire database on the chemical. The RfDs are not applicable to nonthreshold effects such as cancer.

Reportable Quantity (RQ)—The quantity of a hazardous substance that is considered reportable under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA). Reportable quantities are (1) 1 pound or greater or (2) for selected substances, an amount established by regulation either under CERCLA or under Section 311 of the Clean Water Act. Quantities are measured over a 24-hour period.

Reproductive Toxicity—The occurrence of adverse effects on the reproductive system that may result from exposure to a chemical. The toxicity may be directed to the reproductive organs and/or the related endocrine system. The manifestation of such toxicity may be noted as alterations in sexual behavior, fertility, pregnancy outcomes, or modifications in other functions that are dependent on the integrity of this system.

Retrospective Study—A type of cohort study based on a group of persons known to have been exposed at some time in the past. Data are collected from routinely recorded events, up to the time the study is undertaken. Retrospective studies are limited to causal factors that can be ascertained from existing records and/or examining survivors of the cohort.

Risk—The possibility or chance that some adverse effect will result from a given exposure to a chemical.

Risk Factor—An aspect of personal behavior or lifestyle, an environmental exposure, or an inborn or inherited characteristic that is associated with an increased occurrence of disease or other health-related event or condition.

Risk Ratio—The ratio of the risk among persons with specific risk factors compared to the risk among persons without risk factors. A risk ratio greater than 1 indicates greater risk of disease in the exposed group compared to the unexposed group.

Short-Term Exposure Limit (STEL)—The American Conference of Governmental Industrial Hygienists (ACGIH) maximum concentration to which workers can be exposed for up to 15 minutes continually. No more than four excursions are allowed per day, and there must be at least 60 minutes between exposure periods. The daily Threshold Limit Value-Time Weighted Average (TLV-TWA) may not be exceeded.

Standardized Mortality Ratio (SMR)—A ratio of the observed number of deaths and the expected number of deaths in a specific standard population.

Target Organ Toxicity—This term covers a broad range of adverse effects on target organs or physiological systems (e.g., renal, cardiovascular) extending from those arising through a single limited exposure to those assumed over a lifetime of exposure to a chemical.

Teratogen—A chemical that causes structural defects that affect the development of an organism.

Threshold Limit Value (TLV)—An American Conference of Governmental Industrial Hygienists (ACGIH) concentration of a substance to which most workers can be exposed without adverse effect. The TLV may be expressed as a Time Weighted Average (TWA), as a Short-Term Exposure Limit (STEL), or as a ceiling limit (CL).

Time-Weighted Average (TWA)—An allowable exposure concentration averaged over a normal 8-hour workday or 40-hour workweek.

Toxic Dose$_{(50)}$ (TD$_{50}$)—A calculated dose of a chemical, introduced by a route other than inhalation, which is expected to cause a specific toxic effect in 50% of a defined experimental animal population.

Toxicokinetic—The absorption, distribution, and elimination of toxic compounds in the living organism.

Uncertainty Factor (UF)—A factor used in operationally deriving the Minimal Risk Level (MRL) or Reference Dose (RfD) or Reference Concentration (RfC) from experimental data. UFs are intended to account for (1) the variation in sensitivity among the members of the human population, (2) the uncertainty in extrapolating animal data to the case of human, (3) the uncertainty in extrapolating from data obtained in a study that is of less than lifetime exposure, and (4) the uncertainty in using lowest-observed-adverse-effect level (LOAEL) data rather than no-observed-adverse-effect level (NOAEL) data. A default for each individual UF is 10; if complete certainty in data exists, a value of 1 can be used; however, a reduced UF of 3 may be used on a case-by-case basis, 3 being the approximate logarithmic average of 10 and 1.

Xenobiotic—Any chemical that is foreign to the biological system.

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APPENDIX A. ATSDR MINIMAL RISK LEVELS AND WORKSHEETS

The Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) [42 U.S.C. 9601 et seq.], as amended by the Superfund Amendments and Reauthorization Act (SARA) [Pub. L. 99–499], requires that the Agency for Toxic Substances and Disease Registry (ATSDR) develop jointly with the U.S. Environmental Protection Agency (EPA), in order of priority, a list of hazardous substances most commonly found at facilities on the CERCLA National Priorities List (NPL); prepare toxicological profiles for each substance included on the priority list of hazardous substances; and assure the initiation of a research program to fill identified data needs associated with the substances.

The toxicological profiles include an examination, summary, and interpretation of available toxicological information and epidemiologic evaluations of a hazardous substance. During the development of toxicological profiles, Minimal Risk Levels (MRLs) are derived when reliable and sufficient data exist to identify the target organ(s) of effect or the most sensitive health effect(s) for a specific duration for a given route of exposure. An MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. MRLs are based on noncancer health effects only and are not based on a consideration of cancer effects. These substance-specific estimates, which are intended to serve as screening levels, are used by ATSDR health assessors to identify contaminants and potential health effects that may be of concern at hazardous waste sites. It is important to note that MRLs are not intended to define clean-up or action levels.

MRLs are derived for hazardous substances using the no-observed-adverse-effect level/uncertainty factor approach. They are below levels that might cause adverse health effects in the people most sensitive to such chemical-induced effects. MRLs are derived for acute (1–14 days), intermediate (15–364 days), and chronic (365 days and longer) durations and for the oral and inhalation routes of exposure. Currently, MRLs for the dermal route of exposure are not derived because ATSDR has not yet identified a method suitable for this route of exposure. MRLs are generally based on the most sensitive chemical-induced end point considered to be of relevance to humans. Serious health effects (such as irreparable damage to the liver or kidneys, or birth defects) are not used as a basis for establishing MRLs. Exposure to a level above the MRL does not mean that adverse health effects will occur.

MRLs are intended only to serve as a screening tool to help public health professionals decide where to look more closely. They may also be viewed as a mechanism to identify those hazardous waste sites that are not expected to cause adverse health effects. Most MRLs contain a degree of uncertainty because of the lack of precise toxicological information on the people who might be most sensitive (e.g., infants, elderly, nutritionally or immunologically compromised) to the effects of hazardous substances. ATSDR uses a conservative (i.e., protective) approach to address this uncertainty consistent with the public health principle of prevention. Although human data are preferred, MRLs often must be based on animal studies because relevant human studies are lacking. In the absence of evidence to the contrary, ATSDR assumes that humans are more sensitive to the effects of hazardous substance than animals and that certain persons may be particularly sensitive. Thus, the resulting MRL may be as much as 100-fold below levels that have been shown to be nontoxic in laboratory animals.

Proposed MRLs undergo a rigorous review process: Health Effects/MRL Workgroup reviews within the Division of Toxicology and Environmental Medicine, expert panel peer reviews, and agency-wide MRL Workgroup reviews, with participation from other federal agencies and comments from the public. They are subject to change as new information becomes available concomitant with updating the toxicological profiles. Thus, MRLs in the most recent toxicological profiles supersede previously published levels. For additional information regarding MRLs, please contact the Division of Toxicology and Environmental Medicine, Agency for Toxic Substances and Disease Registry, 1600 Clifton Road NE, Mailstop F-32, Atlanta, Georgia 30333.

APPENDIX A

MINIMAL RISK LEVEL (MRL) WORKSHEET

Chemical Name: Inorganic Arsenic
CAS Number: 7440-38-2
Date: August 2007
Profile Status: Post-Public Comment, Final Draft
Route: [ ] Inhalation [X] Oral
Duration: [X] Acute [ ] Intermediate [ ] Chronic
Graph Key: 29
Species: Human

Minimal Risk Level: 0.005 [X] mg/kg/day [ ] ppm

Reference: Mizuta N, Mizuta M, Ito F, et al. 1956. An outbreak of acute arsenic poisoning caused by arsenic-contaminated soy-sauce (shōyu): A clinical report of 220 cases. Bull Yamaguchi Med Sch 4(2-3):131-149.

Experimental design: Mizuta et al. (1956) summarized findings from 220 poisoning cases associated with an episode of arsenic contamination of soy sauce in Japan. The soy sauce was contaminated with approximately 0.1 mg As/mL, probably as calcium arsenate. Arsenic intake in the cases was estimated by the researchers to be 3 mg/day (0.05 mg/kg/day, assuming 55 kg average body weight for this Asian population). Duration of exposure was 2–3 weeks in most cases. Clinical symptoms were recorded. Seventy patients were examined opthalmologically. Laboratory tests were performed on some patients and included hematology, urinalysis, fecal exam, occult blood in gastric and duodenal juice, biochemical examination of blood, liver function tests, electrocardiograph, and liver biopsy.

Effects noted in study and corresponding doses: The primary symptoms were edema of the face, and gastrointestinal and upper respiratory symptoms initially, followed in some patients by skin lesions and neuropathy. Other effects included mild anemia and leukopenia, mild degenerative liver lesions and hepatic dysfunction, abnormal electrocardiogram, and ocular lesions. For derivation of the acute oral MRL, facial edema and gastrointestinal symptoms (nausea, vomiting, diarrhea), which were characteristic of the initial poisoning and then subsided, were considered to be the critical effects.

Dose and end point used for MRL derivation: 0.05 mg As/kg/day

[ ] NOAEL [X] LOAEL

Uncertainty factors used in MRL derivation:

[ ] 1 [ ] 3 [X] 10 (for use of a LOAEL)
[ ] 1 [ ] 3 [ ] 10 (for extrapolation from animals to humans)
[X] 1 [ ] 3 [ ] 10 (for human variability)

Was a conversion factor used from ppm in food or water to a mg/body weight dose? Not applicable.

If an inhalation study in animals, list conversion factors used in determining human equivalent dose: Not applicable.

Was a conversion used from intermittent to continuous exposure? Not applicable.

Other additional studies or pertinent information that lend support to this MRL: The MRL is supported by the case of a man and wife in upstate New York who experienced gastrointestinal symptoms (nausea, diarrhea, abdominal cramps) starting almost immediately after beginning intermittent consumption of arsenic-tainted drinking water at an estimated dose of 0.05 mg As/kg/day (Franzblau and Lilis 1989). Gastrointestinal symptoms have been widely reported in other acute arsenic poisoning reports as well, although in some cases, the doses were higher and effects were severe, and in other cases, dose information was not available. The UF of 1 for intrahuman variability reflects the fact that the database includes persons of various ethnicities and age groups, including infants.

Agency Contact (Chemical Manager): Selene Chou, Ph.D and Carolyn Harper, Ph.D.

MINIMAL RISK LEVEL (MRL) WORKSHEET

Chemical Name: Inorganic Arsenic
CAS Number: 7440-38-2
Date: August 2007
Profile Status: Post-Public Comment, Final Draft
Route: [ ] Inhalation [X] Oral
Duration: [ ] Acute [ ] Intermediate [X] Chronic
Graph Key: 134
Species: Human

Minimal Risk Level: 0.0003 [X] mg/kg/day [ ] ppm

References: Tseng, WP, Chu HM, How SW, et al. 1968. Prevalence of skin cancer in an endemic area of chronic arsenicism in Taiwan. J Natl Cancer Inst 40:453-463.

Tseng, WP. 1977. Effects and dose-response relationships of cancer and Blackfoot disease with arsenic. Environ Health Perspect 19:109-119.

Experimental design: Tseng et al. (1968) and Tseng (1977) investigated the incidence of Blackfoot disease and dermal lesions (hyperkeratosis and hyperpigmentation) in a large number of poor farmers (both male and female) exposed to high levels of arsenic in well water in Taiwan. A control group consisting of 17,000 people was identified. The authors stated that the incidence of dermal lesions increased with dose, but individual doses were not provided. However, incidence data were provided based on stratification of the exposed population into low (<300 µg/L), medium (300–600 µg/L), or high (>600 µg/L) exposure levels. Doses were calculated from group mean arsenic concentrations in well water, assuming the intake parameters described by Abernathy et al. (1989). Accordingly, the control, low-, medium-, and high-exposure levels correspond to doses of 0.0008, 0.014, 0.038, and 0.065 mg As/kg/day, respectively. The NOAEL identified by Tseng (1977) (0.0008 mg As/kg/day) was limited by the fact that the majority of the population was <20 years of age and the incidence of skin lesions increased as a function of age, and because the estimates of water intake and dietary arsenic intake are highly uncertain. Schoof et al. (1998) estimated that dietary intakes of arsenic from rice and yams may have been 15–211 µg/day (mean 61 µg/day), based on arsenic analyses of foods collected in Taiwan in 1993–1995. Use of the 50 µg/day estimate would result in an approximate doubling of the NOAEL (0.0016 mg/kg/day).

Effects noted in study and corresponding doses: A clear dose-response relationship was observed for characteristic skin lesions:

0.0008 mg As/kg/day	= control group (NOAEL)
0.014 mg As/kg/day	= hyperpigmentation and keratosis of the skin (less serious LOAEL)
0.038–0.065 mg As/kg/day	= increased incidence of dermal lesions

Dose and end point used for MRL derivation: 0.0008 mg As/kg/day

[X] NOAEL [ ] LOAEL

Uncertainty factors used in MRL derivation:

[ ] 1 [ ] 3 [ ] 10 (for use of a LOAEL)
[ ] 1 [ ] 3 [ ] 10 (for extrapolation from animals to humans)

[ ] 1 [x] 3 [ ] 10 (for human variability)

Was a conversion factor used from ppm in food or water to a mg/body weight dose? The arithmetic mean concentration of arsenic in well water for the control group (0.009 mg/L) was converted to a NOAEL of 0.0008 mg As/kg/day as described below:

$$\left[\left(\frac{0.009mg}{L}\times\frac{4.5L}{day}\right)+\frac{0.002mg}{day}\right]\div 55kg = 0.0008mgAs/kg/day$$

This NOAEL conversion assumed a water intake of 4.5 L/day and a body weight of 55 kg, and includes an estimation of arsenic intake of 0.002 mg As/kg/day from food. These assumptions are detailed in Abernathy et al. (1989). This approach to deriving a chronic oral MRL is identical to EPA's approach to deriving a chronic oral RfD.

If an inhalation study in animals, list conversion factors used in determining human equivalent dose: Not applicable.

Was a conversion used from intermittent to continuous exposure? Not applicable.

Other additional studies or pertinent information that lend support to this MRL: The MRL is supported by a number of well conducted epidemiological studies that identify reliable NOAELs and LOAELs for dermal effects. EPA (1981b) identified a NOAEL of 0.006–0.007 mg As/kg/day for dermal lesions in several small populations in Utah. Harrington et al. (1978) identified a NOAEL of 0.003 mg As/kg/day for dermal effects in a small population in Alaska. Guha Mazumder et al. (1988) identified a NOAEL of 0.009 mg As/kg/day and a LOAEL of 0.006 mg As/kg/day for pigmentation changes and hyperkeratosis in a small population in India. Haque et al. (2003) identified a LOAEL of 0.0043 mg As/kg/day for hyperpigmentation and hyperkeratosis in a case-control study in India. Cebrían et al. (1983) identified a NOAEL of 0.0004 mg As/kg/day and a LOAEL of 0.022 mg As/kg/day in two regions in Mexico. Borgoño and Greiber (1972) and Zaldívar (1974) identified a LOAEL of 0.02 mg As/kg/day for abnormal skin pigmentation in patients in Chile, and Borgoño et al. (1980) identified a LOAEL of 0.01 mg As/kg/day for the same effect in school children in Chile. Valentine et al. (1985) reported a NOAEL of 0.02 mg As/kg/day for dermal effects in several small populations in California. Collectively, these studies indicate that the threshold dose for hyperpigmentation and hyperkeratosis is approximately 0.002 mg As/kg/day.

Agency Contacts (Chemical Managers): Selene Chou, Ph.D and Carolyn Harper, Ph.D.

MINIMAL RISK LEVEL (MRL) WORKSHEET

Chemical Name:	Monomethylarsonic acid (MMA)
CAS Number:	124-58-3
Date:	August 2007
Profile Status:	Post-Public Comment, Final Draft
Route:	[ ] Inhalation [X] Oral
Duration:	[ ] Acute [X] Intermediate [ ] Chronic
Graph Key:	12
Species:	Rat

Minimal Risk Level: 0.1 [X] mg MMA/kg/day [ ] ppm

References: Arnold LL, Eldan M, van Gemert M, et al. 2003. Chronic studies evaluating the carcinogenicity of monomethylarsonic acid in rats and mice. Toxicology 190:197-219.

Crown S, Nyska A, Waner T. 1990. Methanearsonic acid: Combined chronic feeding and oncogenicity study in the rat. Conducted by Life Science Research Israel Ltd., Ness Ziona Israel. Submitted to EPA Office of Pesticide Programs (MRID 41669001).

Experimental design: Groups of 60 male and 60 female Fischer 344 rats were exposed to 0, 50, 400, or 1,300 ppm MMA in the diet for 104 weeks. Using the average doses for weeks 1–50 reported in an unpublished version of this study (Crown et al. 1990), doses of 0, 3.5, 30.2, and 106.9 mg MMA/kg/day and 0, 4.2, 35.9, and 123.3 mg MMA/kg/day were calculated for males and females, respectively. Body weights, food consumption, and water intake were monitored regularly. Blood was taken at 3, 6, and 12 months for clinical chemistry measurements, and urine samples were collected at the same interval.

Effects noted in study and corresponding doses: Mortality was increased in high-dose males and females during the first 52 weeks of the study. Body weights were decreased in the mid- and high-dose groups of both sexes; however, at 51 weeks, only the body weight for the high-dose males was <10% of the control weight (14.5%). Food and water consumption was increased in the mid- and high-dose groups. Diarrhea was observed in 100% of the high-dose males and females and in 16.7 and 40% of the mid-dose males and females during the first 52 weeks of exposure. Diarrhea first occurred after 3 weeks of exposure to the high dose and 4 weeks of exposure to the mid-dose group; the severity of the diarrhea was dose-related. The gastrointestinal system was the primary target in animals dying early; numerous macroscopic and histological alterations were observed.

Dose and end point used for MRL derivation: Benchmark dose analysis of the dose-response data (Table A-1) for diarrhea in male and female rats exposed to MMA in the diet for 1–52 weeks (incidence data reported in Crown et al. 1990) was conducted. All available dichotomous models in EPA's Benchmark Dose Software (version 1.4.1) were fit to the data. Predicted doses associated with a 10% extra risk were calculated. As assessed by the chi-square goodness-of-fit statistic, all models, with the exception of the quantal linear model for male incidence data and the quantal linear model for female incidence data, provided an adequate fit (X^2 p>0.1) (Table A-2). Comparing across models, a better fit is generally indicated by a lower Akaike's Information Criteria (AIC). As assessed by AIC, the gamma model for the males (Figure A-1) and the 2-degree polynomial multi-stage model for the females (Figure A-2) provide the best fit to the data. The predicted BMD_{10} and $BMDL_{10}$ are 28.25 mg MMA/kg/day and 22.99 mg MMA/kg/day for the male rat incidence data and 16.17 mg MMA/kg/day, and 12.38 mg MMA/kg/day for the female rat incidence data.

Table A-1. Incidences of Diarrhea in Rats Exposed to MMA in the Diet for 1–52 Weeks

Dietary concentration (ppm)	Dose (mg MMA/kg/day)	Incidence
Male rats		
0	0	2/60
50	3.5	0/60
400	30.2	10/60
1,300	106.9	60/60
Female rats		
0	0	0/60
50	4.2	0/60
400	35.9	24/60
1,300	123.3	60/60

Sources: Arnold et al. 2003; Crown et al. 1990

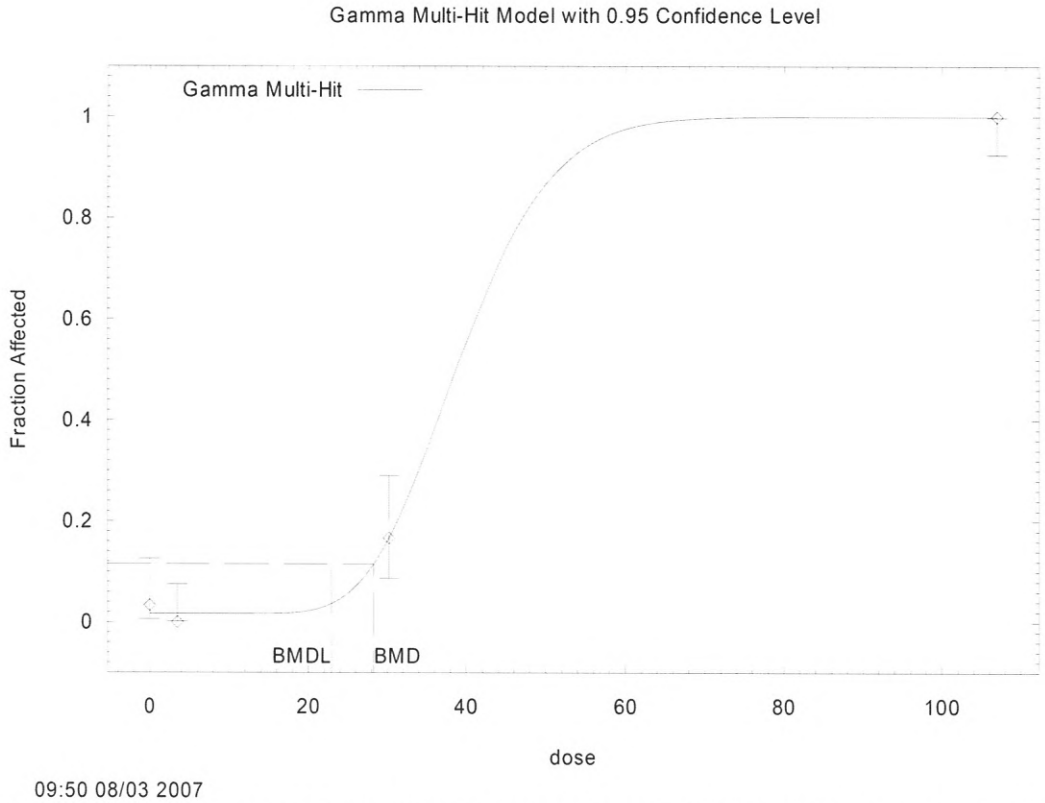
Table A-2. Modeling Predictions for the Incidence of Diarrhea in Rats Exposed to MMA in the Diet for 1–52 Weeks

Model	BMD_{10} (mg MMA/kg/day)	$BMDL_{10}$ (mg MMA/kg/day)	x^2 *p*-value	AIC
Male rats				
Gamma[a]	**28.25**	**22.99**	**0.36**	**78.41**
Logistic	24.60	20.19	0.16	79.59
Log-logistic[b]	29.32	24.73	0.15	80.41
Multi-stage[c]	25.74	19.90	0.35	78.51
Probit	23.11	18.67	0.11	80.02
Log-probit[b]	28.79	24.47	0.15	80.41
Quantal linear	6.317	5.079	0.00	123.06
Weibull[a]	27.99	20.66	0.15	80.41
Female rats				
Gamma[a]	26.81	15.18	1.00	84.76
Logistic	32.85	21.49	1.00	84.76
Log-logistic[b]	31.97	20.16	1.00	84.76
Multi-stage[c]	**16.17**	**12.38**	**0.90**	**83.88**
Probit	29.89	19.11	1.00	84.76
Log-probit[b]	28.95	18.87	1.00	84.76
Quantal linear	5.33	4.33	0.00	106.52
Weibull[a]	27.83	13.58	1.00	84.76

Sources: Arnold et al. 2003; Crown et al. 1990

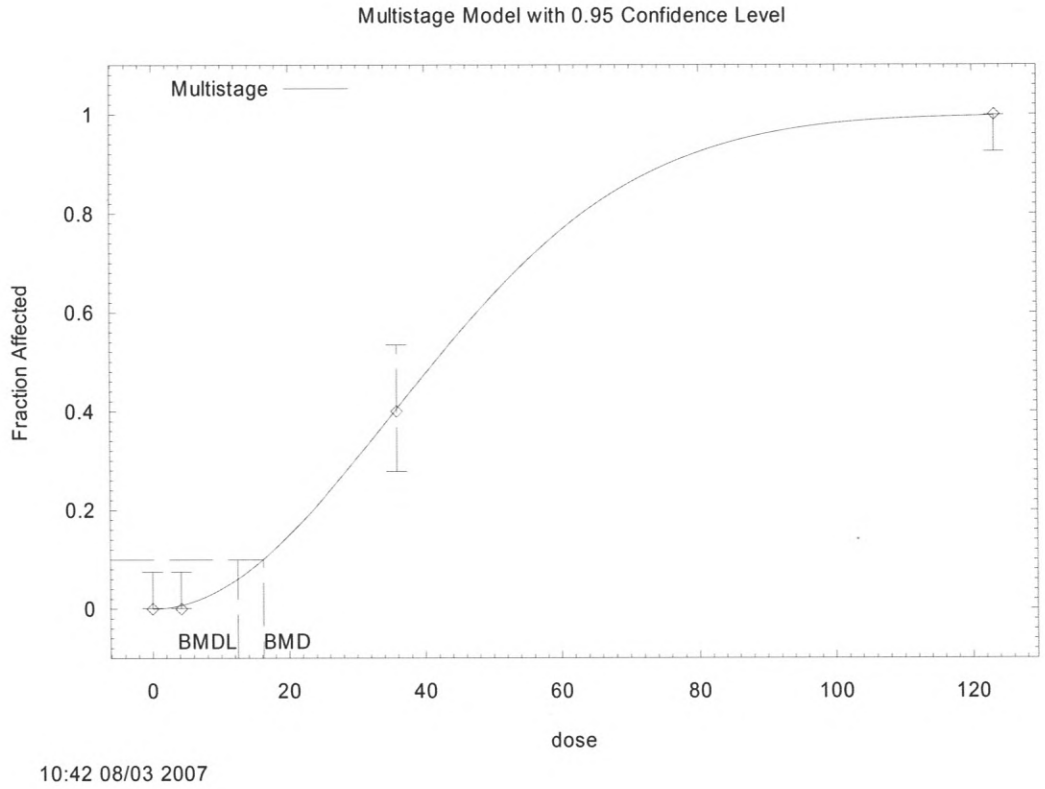
[a]Restrict power ≥1.
[b]Slope restricted to >1.
[c]Restrict betas ≥0; lowest degree polynomial with an adequate fit is reported; degree of polynomial=3.
[d]Restrict betas ≥0; lowest degree polynomial with an adequate fit is reported; degree of polynomial=2.

Figure A-1. Predicted and Observed Incidence of Diarrhea in Male Rats Exposed to MMA in the Diet for 1–52 Weeks*



*BMDs and BMDLs indicated are associated with a 10% extra risk change from the control, and are in units of mg MMA/kg/day.

Figure A-2. Predicted and Observed Incidence of Diarrhea in Female Rats Exposed to MMA in the Diet for 52 Weeks*



*BMDs and BMDLs indicated are associated with a 10% extra risk change from the control, and are in units of mg MMA/kg/day.

The $BMDL_{10}$ of 12.38 mg MMA/kg/day for female rats was selected as the point of departure for deriving the intermediate-duration oral MRL because it was lower than the $BMDL_{10}$ (22.99 mg MMA/kg/day) calculated using the male incidence data.

[ ] NOAEL [ ] LOAEL [X] BMDL

Uncertainty factors used in MRL derivation: 100

[ ] 10 for use of a LOAEL
[X] 10 for extrapolation from animals to humans
[X] 10 for human variability

Was a conversion factor used from ppm in food or water to a mg/body weight dose? Doses calculated using the average of the achieved doses for weeks 1–50 reported in Crown et al. (1990): 0, 3.5, 30.2, and 106.9 mg MMA/kg/day for males and 0, 4.2, 35.9, and 123.3 mg MMA/kg/day for females.

If an inhalation study in animals, list conversion factors used in determining human equivalent dose: Not applicable.

Was a conversion used from intermittent to continuous exposure? Not applicable.

Other additional studies or pertinent information that lend support to this MRL: Increases in the incidence of diarrhea has also been observed in dogs administered via capsule 2 mg MMA/kg/day for 52 weeks (Waner and Nyska 1988); the increased incidence of diarrhea started during weeks 25–28. At 35 mg MMA/kg/day, vomiting was also observed in the dogs. Diarrhea has also been observed in rats and mice exposed to MMA for 2 years (Arnold et al. 2003); the LOAELs are 25.7 and 67.1 mg MMA/kg/day, respectively.

Agency Contacts (Chemical Managers): Selene Chou, Ph.D and Carolyn Harper, Ph.D.

MINIMAL RISK LEVEL (MRL) WORKSHEET

Chemical Name: Monomethylarsonic acid (MMA)
CAS Number: 124-58-3
Date: August 2007
Profile Status: Post-Public Comment, Final Draft
Route: [ ] Inhalation [X] Oral
Duration: [ ] Acute [ ] Intermediate [X] Chronic
Graph Key: 21
Species: Mouse

Minimal Risk Level: 0.01 [X] mg MMA/kg/day [ ] ppm

References: Arnold LL, Eldan M, van Gemert M, et al. 2003. Chronic studies evaluating the carcinogenicity of monomethylarsonic acid in rats and mice. Toxicology 190:197-219.

Gur E, Piraic H, Waner T. 1991. Methanearsonic acid: Combined oncogenicity study in the mouse. Conducted by Life Science Research Israel Ltd., Ness Ziona Israel. Submitted to EPA Office of Pesticide Programs (MRID 42173201).

Experimental design: Groups of 52 male and 52 female $B6C3F_1$ mice were exposed to 0, 10, 50, 200, or 400 ppm of MMA in the diet for 104 weeks. The reported MMA doses were 0, 1.2, 6.0, 24.9, and 67.1 mg MMA/kg/day (males) and 0, 1.4, 7.0, 31.2, and 101 mg MMA/kg/day (females). Body weights, food consumption, and water intake were monitored regularly. Blood was taken at 3, 6, 12, 18, and 24 months for white cell counts. At sacrifice, complete necropsies were performed, including histological examination of at least 13 organs.

Effects noted in study and corresponding doses: No treatment-related increases in mortality were observed. Significant decreases in body weights were observed in males and females exposed to 32.2 or 48.5 mg As/kg/day, respectively; at week 104, the males weighed 17% less than controls and females weighed 23% less. Food consumption was increased in females exposed to 101 mg MMA/kg/day, and water consumption was increased in 67.1 mg MMA/kg/day males and 31.2 and 101 mg MMA/kg/day females. Loose and mucoid feces were noted in mice exposed to 67.1/101 mg MMA/kg/day. No changes were seen in white cell counts of either sex. Small decreases in the weights of heart, spleen, kidney, and liver were seen in some animals, but the decreases were not statistically significant. Squamous metaplasia of the cecum, colon, and rectum was observed at 67.1/101 mg MMA/kg/day. The incidences of metaplasia in the cecum, colon, and rectum were 29/49, 14/49, and 39/49 in males and 38/52, 17/52, and 42/52 in females; metaplasia was not observed in other groups of male or female mice. An increased incidence of progressive glomerulonephropathy (incidence of 25/52, 27/52, 38/52, 39/52, and 46/52 in the 0, 1.2, 6.0, 24.9, and 67.1 mg MMA/kg/day) was observed in males; the incidence was significantly higher (Fisher Exact Test) than controls at $\geq$6.0 mg MMA/kg/day. Significant increases in the incidence of nephrocalcinosis was observed in the males at 24.9 and 67.1 mg MMA/kg/day (Fisher Exact Test) (incidence of 25/52, 30/52, 30/52, 45/522 45/51 and 0/52, 1/52, 1/52, 2/52, and 5/52 in males and females, respectively). The investigators noted that the kidney lesions were consistent with the normal spectrum of spontaneous renal lesions and there was no difference in character or severity of the lesions between groups. A reduction in the incidence of cortical focal hyperplasia in the adrenal gland of male mice exposed to 67.1 mg MMA/kg/day was possibly related to MMA exposure; the toxicological significance of this effect is not known.

Dose and end point used for MRL derivation: Benchmark dose analysis of the dose-response data (Table A-3) for progressive glomerulonephropathy in male mice exposed to MMA in the diet for 2 years

(incidence data reported in Gur et al. 1991) was conducted. All available dichotomous models in EPA's Benchmark Dose Software (version 1.4.1) were fit to the data. Predicted doses associated with a 10% extra risk were calculated. As assessed by the chi-square goodness-of-fit statistic, all models, with the exception of the log-probit model, provided an adequate fit (X^2 p>0.1) (Table A-4). Comparing across models, a better fit is generally indicated by a lower Akaike's Information Criteria (AIC). As assessed by AIC, the log-logistic model (Figure A-3) provided the best fit to the data. The predicted BMD_{10} and $BMDL_{10}$ for the incidence data are 2.09 and 1.09 mg MMA/kg/day.

Table A-3. Incidence of Progressive Glomerulonephropathy in Male Mice Exposed to MMA in the Diet for 2 Years

Dietary Concentration (ppm)	Dose (mg MMA/kg/day)	Incidence
0	0	25/52
10	1.2	27/52
50	6.0	38/52
200	24.9	39/52
400	67.1	46/52

Sources: Arnold et al. 2003; Gur et al. 1991

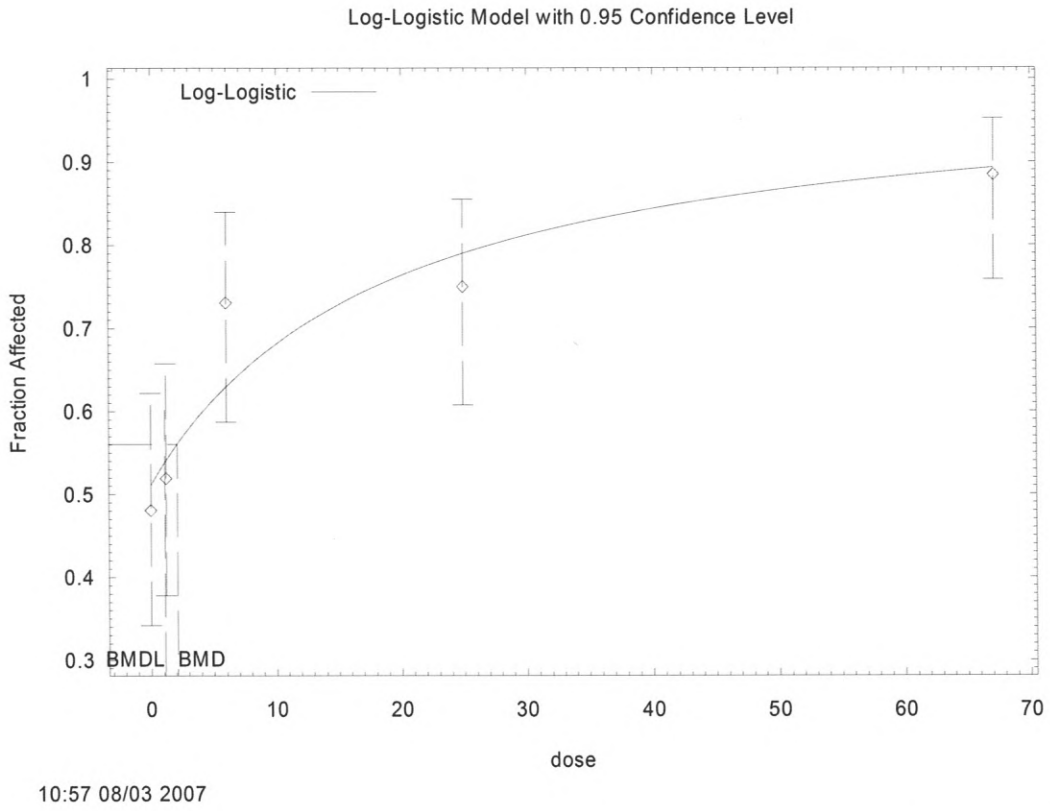
Table A-4. Modeling Predictions for the Incidence of Progressive Glomerulonephropathy in Male Mice Exposed to MMA in the Diet for 2 Years

Model	BMD_{10} (mg MMA/kg/day)	$BMDL_{10}$ (mg MMA/kg/day)	x^2 p-value	AIC
Gamma[a]	4.60	3.15	0.18	309.33
Logistic	6.09	4.45	0.13	310.15
Log-logistic[b]	**2.09**	**1.09**	**0.38**	**307.47**
Multi-stage[c]	4.60	3.15	0.18	309.33
Probit	6.62	5.00	0.11	310.43
Log-probit[b]	8.54	5.50	0.08	311.11
Quantal linear	4.60	3.15	0.18	309.33
Weibull[a]	4.60	3.15	0.18	309.33

Sources: Arnold et al. 2003; Gur et al. 1991

[a]Restrict power ≥1.
[b]Slope restricted to >1.
[c]Restrict betas ≥0; lowest degree polynomial with an adequate fit is reported; degree of polynomial=1.

Figure A-3. Predicted and Observed Incidence of Progressive Glomerulonephropathy in Male Mice Exposed to MMA*



*BMDs and BMDLs indicated are associated with a 10% extra risk change from the control, and are in units of mg MMA/kg/day.

The $BMDL_{10}$ of 1.09 mg MMA/kg/day for male mice was selected as the point of departure for deriving the chronic-duration oral MRL.

[ ] NOAEL [ ] LOAEL [X] BMDL

Uncertainty factors used in MRL derivation: 100

[ ] 10 for use of a LOAEL
[X] 10 for extrapolation from animals to humans
[X] 10 for human variability

Was a conversion factor used from ppm in food or water to a mg/body weight dose? Doses calculated using the average of the achieved doses reported in Gur et al. (1991): 0, 1.2, 6.0, 24.9, and 67.1 mg MMA/kg/day for males and 0, 1.4, 7.0, 31.2, and 101 mg MMA/kg/day for females.

If an inhalation study in animals, list conversion factors used in determining human equivalent dose: Not applicable.

Was a conversion used from intermittent to continuous exposure? Not applicable.

Other additional studies or pertinent information that lend support to this MRL: An exacerbation of chronic progressive nephropathy (an increase in the severity of the nephropathy) has also been observed in rats exposed to ≥33.9 mg MMA/kg/day for 2 years (Arnold et al. 2003).

Agency Contacts (Chemical Managers): Selene Chou, Ph.D and Carolyn Harper, Ph.D.

MINIMAL RISK LEVEL (MRL) WORKSHEET

Chemical Name: Dimethylarsinic acid (DMA)
CAS Number: 75-60-5
Date: August 2007
Profile Status: Post-Public Comment, Final Draft
Route: [ ] Inhalation [X] Oral
Duration: [ ] Acute [ ] Intermediate [X] Chronic
Graph Key: 35
Species: Mouse

Minimal Risk Level: 0.02 [X] mg DMA/kg/day [ ] ppm

References: Arnold LL, Eldan M, Nyska A, et al. 2006. Dimethylarsinic acid: Results of chronic toxicity/oncogenicity studies in F344 rats and B6C3F$_1$ mice. Toxicology 223:82-100.

Gur E, Nyska A, Pirak M, et al. 1989b. Cacodylic acid: Oncogenicity study in the mouse. Conducted by Life Science Research Israel Ltd., Ness Ziona Israel. Submitted to EPA Office of Pesticide Programs (MRID 41914601).

Experimental design: Groups of 56 male and 56 female B6C3F$_1$ mice were exposed to 0, 8, 40, 200, or 500 ppm DMA in the diet for 2 years. The investigators reported the dietary doses were equivalent to approximately 0, 1.3, 7.8, 37, and 94 mg DMA/kg/day. The following parameters were used to assess toxicity: clinical observations, body weight, food consumption, water consumption, differential leukocyte levels measured at 12, 18, and 24 months in mice in the control and 94 mg DMA/kg/day groups, organ weights (brain, kidneys, liver, and testes), and histopathological examination of major tissues and organs.

Effects noted in study and corresponding doses: No deaths were observed. Decreases in body weight gain were observed in the male mice exposed to 94 mg DMA/kg/day; the difference was <10% and was not considered adverse. An increase in water consumption was observed in males exposed to 94 mg DMA/kg/day during weeks 60–96. No treatment-related clinical signs were observed. In the female mice exposed to 94 mg DMA/kg/day, a statistically significant decrease in lymphocytes and increase in monocytes were observed at 24 months. Treatment related nonneoplastic alterations were observed in the urinary bladder and kidneys. In the urinary bladder, increases in the vacuolization of the superficial cells of the urothelium were observed in males exposed to 37 or 94 mg DMA/kg/day (0/44, 1/50, 0/50, 36/45, 48/48) and in females exposed to 7.8, 37, or 94 mg DMA/kg/day (1/45, 1/48, 26/43, 47/47, 43/43); incidence data reported in Gur et al. (1989b). An increased incidence of progressive glomerulonephropathy was observed in males at 37 mg DMA/kg/day (16/44, 22/50, 17/50, 34/45, 30/50) and an increased incidence of nephrocalcinosis was also observed in male mice at 94 mg DMA/kg/day (30/44, 25/50, 27/50, 29/50, 45/50). Neoplastic alterations were limited to an increased incidence of fibrosarcoma of the skin in females exposed to 94 mg DMA/kg/day; the incidence was 3/56, 0/55, 1/56, 1/56, and 6/56 in the 0, 1.3, 7.8, 37, and 94 mg DMA/kg/day groups, respectively; however it was concluded that this lesion was not related to DMA exposure.

Dose and end point used for MRL derivation: Benchmark dose analysis of the dose-response data (Table A-5) for vacuolization of the urothelium in the urinary bladder in female mice exposed to DMA in the diet for 2 years (incidence data reported in Gur et al. 1989b) was conducted. All available dichotomous models in EPA's Benchmark Dose Software (version 1.4.1) were fit to the data. Predicted doses associated with a 10% extra risk were calculated. As assessed by the chi-square goodness-of-fit statistic, all models, with the exception of the quantal linear model, provided an adequate fit (X^2 p>0.1) (Table A-6). Comparing across models, a better fit is generally indicated by a lower AIC. The AIC

values were similar for the logistic, multi-stage, and probit models; of these three models, the multi-stage had the lowest BMD_{10} and was selected for the analysis (see Figure A-4). The predicted BMD_{10} and $BMDL_{10}$ for the incidence data are 2.68 and 1.80 mg DMA/kg/day.

Table A-5. Incidence of Vacuolization of Urotheium in Urinary Bladder of Female Mice Exposed to DMA in the Diet for 2 Years

Dietary concentration (ppm)	Dose (mg DMA/kg/day)	Incidence
0	0	1/45
8	1.3	1/48
40	7.8	26/43
200	37	47/47
500	94	43/43

Sources: Arnold et al. 2006; Gur et al. 1989b

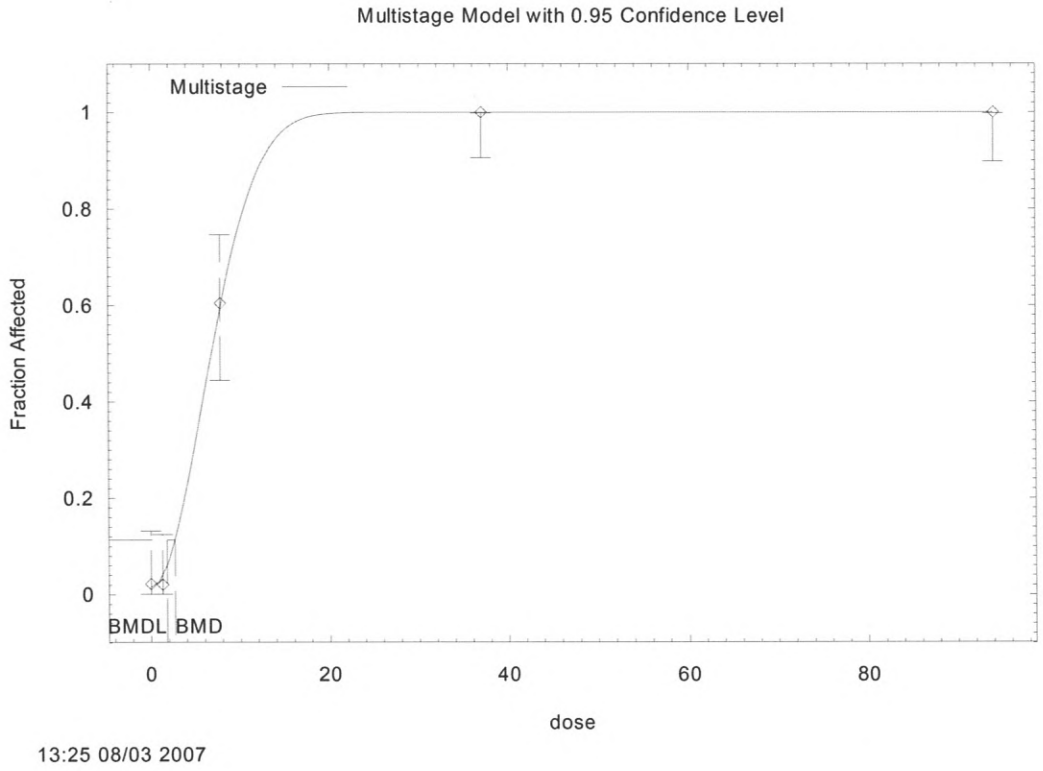
Table A-6. Modeling Predictions for the Incidence of Vacuolization in of Urothelium in Urinary Bladder of Female Mice Exposed to DMA in the Diet for 2 Years

Model	BMD_{10} (mg DMA/kg/day)	$BMDL_{10}$ (mg DMA/kg/day)	x^2 *p*-value	AIC
Gamma[a]	5.01	1.85	1.00	83.03
Logistic	3.66	2.78	0.95	81.37
Log-logistic[b]	6.23	2.34	1.00	83.03
Multi-stage[c]	**2.68**	**1.80**	**0.90**	**81.69**
Probit	3.20	2.46	0.89	81.60
Log-probit[b]	5.03	2.00	1.00	83.03
Quantal linear	0.98	0.76	0.07	91.75
Weibull[a]	4.77	1.88	1.00	83.03

Sources: Arnold et al. 2006; Gur et al. 1989b

[a]Restrict power ≥1.
[b]Slope restricted to >1.
[c]Restrict betas ≥0; lowest degree polynomial with an adequate fit is reported; degree of polynomial=2.

Figure A-4. Predicted and Observed Incidence of Vacuolization of Urothelium in Urinary Bladder of Female Mice*



Source: Arnold et al. 2006

*BMDs and BMDLs indicated are associated with a 10% extra risk change from the control, and are in units of mg DMA/kg/day.

The $BMDL_{10}$ of 1.80 mg DMA/kg/day for female mice was selected as the point of departure for deriving the chronic-duration oral MRL.

[ ] NOAEL [ ] LOAEL [X] BMDL

Uncertainty factors used in MRL derivation: 100

[ ] 10 for use of a LOAEL
[X] 10 for extrapolation from animals to humans
[X] 10 for human variability

Was a conversion factor used from ppm in food or water to a mg/body weight dose? Doses reported in Gur et al. (1989b): 0, 1.3, 7.8, 37, and 94 mg DMA/kg/day.

If an inhalation study in animals, list conversion factors used in determining human equivalent dose: Not applicable.

Was a conversion used from intermittent to continuous exposure? Not applicable.

Other additional studies or pertinent information that lend support to this MRL: One other study has investigated the chronic toxicity of DMA in species other than rats. In this study, administration of 16 mg DMA/kg/day via a capsule for 52 weeks resulted in increases in the incidence of diarrhea; no histological alterations were observed (Zomber et al. 1989).

Agency Contacts (Chemical Managers): Selene Chou, Ph.D and Carolyn Harper, Ph.D.

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APPENDIX B. USER'S GUIDE

Chapter 1

Public Health Statement

This chapter of the profile is a health effects summary written in nontechnical language. Its intended audience is the general public, especially people living in the vicinity of a hazardous waste site or chemical release. If the Public Health Statement were removed from the rest of the document, it would still communicate to the lay public essential information about the chemical.

The major headings in the Public Health Statement are useful to find specific topics of concern. The topics are written in a question and answer format. The answer to each question includes a sentence that will direct the reader to chapters in the profile that will provide more information on the given topic.

Chapter 2

Relevance to Public Health

This chapter provides a health effects summary based on evaluations of existing toxicologic, epidemiologic, and toxicokinetic information. This summary is designed to present interpretive, weight-of-evidence discussions for human health end points by addressing the following questions:

1. What effects are known to occur in humans?

2. What effects observed in animals are likely to be of concern to humans?

3. What exposure conditions are likely to be of concern to humans, especially around hazardous waste sites?

The chapter covers end points in the same order that they appear within the Discussion of Health Effects by Route of Exposure section, by route (inhalation, oral, and dermal) and within route by effect. Human data are presented first, then animal data. Both are organized by duration (acute, intermediate, chronic). *In vitro* data and data from parenteral routes (intramuscular, intravenous, subcutaneous, etc.) are also considered in this chapter.

The carcinogenic potential of the profiled substance is qualitatively evaluated, when appropriate, using existing toxicokinetic, genotoxic, and carcinogenic data. ATSDR does not currently assess cancer potency or perform cancer risk assessments. Minimal Risk Levels (MRLs) for noncancer end points (if derived) and the end points from which they were derived are indicated and discussed.

Limitations to existing scientific literature that prevent a satisfactory evaluation of the relevance to public health are identified in the Chapter 3 Data Needs section.

Interpretation of Minimal Risk Levels

Where sufficient toxicologic information is available, ATSDR has derived MRLs for inhalation and oral routes of entry at each duration of exposure (acute, intermediate, and chronic). These MRLs are not

meant to support regulatory action, but to acquaint health professionals with exposure levels at which adverse health effects are not expected to occur in humans.

MRLs should help physicians and public health officials determine the safety of a community living near a chemical emission, given the concentration of a contaminant in air or the estimated daily dose in water. MRLs are based largely on toxicological studies in animals and on reports of human occupational exposure.

MRL users should be familiar with the toxicologic information on which the number is based. Chapter 2, "Relevance to Public Health," contains basic information known about the substance. Other sections such as Chapter 3 Section 3.9, "Interactions with Other Substances," and Section 3.10, "Populations that are Unusually Susceptible" provide important supplemental information.

MRL users should also understand the MRL derivation methodology. MRLs are derived using a modified version of the risk assessment methodology that the Environmental Protection Agency (EPA) provides (Barnes and Dourson 1988) to determine reference doses (RfDs) for lifetime exposure.

To derive an MRL, ATSDR generally selects the most sensitive end point which, in its best judgement, represents the most sensitive human health effect for a given exposure route and duration. ATSDR cannot make this judgement or derive an MRL unless information (quantitative or qualitative) is available for all potential systemic, neurological, and developmental effects. If this information and reliable quantitative data on the chosen end point are available, ATSDR derives an MRL using the most sensitive species (when information from multiple species is available) with the highest no-observed-adverse-effect level (NOAEL) that does not exceed any adverse effect levels. When a NOAEL is not available, a lowest-observed-adverse-effect level (LOAEL) can be used to derive an MRL, and an uncertainty factor (UF) of 10 must be employed. Additional uncertainty factors of 10 must be used both for human variability to protect sensitive subpopulations (people who are most susceptible to the health effects caused by the substance) and for interspecies variability (extrapolation from animals to humans). In deriving an MRL, these individual uncertainty factors are multiplied together. The product is then divided into the inhalation concentration or oral dosage selected from the study. Uncertainty factors used in developing a substance-specific MRL are provided in the footnotes of the levels of significant exposure (LSE) tables.

Chapter 3

Health Effects

Tables and Figures for Levels of Significant Exposure (LSE)

Tables and figures are used to summarize health effects and illustrate graphically levels of exposure associated with those effects. These levels cover health effects observed at increasing dose concentrations and durations, differences in response by species, MRLs to humans for noncancer end points, and EPA's estimated range associated with an upper- bound individual lifetime cancer risk of 1 in 10,000 to 1 in 10,000,000. Use the LSE tables and figures for a quick review of the health effects and to locate data for a specific exposure scenario. The LSE tables and figures should always be used in conjunction with the text. All entries in these tables and figures represent studies that provide reliable, quantitative estimates of NOAELs, LOAELs, or Cancer Effect Levels (CELs).

The legends presented below demonstrate the application of these tables and figures. Representative examples of LSE Table 3-1 and Figure 3-1 are shown. The numbers in the left column of the legends correspond to the numbers in the example table and figure.

LEGEND

See Sample LSE Table 3-1 (page B-6)

(1) Route of Exposure. One of the first considerations when reviewing the toxicity of a substance using these tables and figures should be the relevant and appropriate route of exposure. Typically when sufficient data exist, three LSE tables and two LSE figures are presented in the document. The three LSE tables present data on the three principal routes of exposure, i.e., inhalation, oral, and dermal (LSE Tables 3-1, 3-2, and 3-3, respectively). LSE figures are limited to the inhalation (LSE Figure 3-1) and oral (LSE Figure 3-2) routes. Not all substances will have data on each route of exposure and will not, therefore, have all five of the tables and figures.

(2) Exposure Period. Three exposure periods—acute (less than 15 days), intermediate (15–364 days), and chronic (365 days or more)—are presented within each relevant route of exposure. In this example, an inhalation study of intermediate exposure duration is reported. For quick reference to health effects occurring from a known length of exposure, locate the applicable exposure period within the LSE table and figure.

(3) Health Effect. The major categories of health effects included in LSE tables and figures are death, systemic, immunological, neurological, developmental, reproductive, and cancer. NOAELs and LOAELs can be reported in the tables and figures for all effects but cancer. Systemic effects are further defined in the "System" column of the LSE table (see key number 18).

(4) Key to Figure. Each key number in the LSE table links study information to one or more data points using the same key number in the corresponding LSE figure. In this example, the study represented by key number 18 has been used to derive a NOAEL and a Less Serious LOAEL (also see the two "18r" data points in sample Figure 3-1).

(5) Species. The test species, whether animal or human, are identified in this column. Chapter 2, "Relevance to Public Health," covers the relevance of animal data to human toxicity and Section 3.4, "Toxicokinetics," contains any available information on comparative toxicokinetics. Although NOAELs and LOAELs are species specific, the levels are extrapolated to equivalent human doses to derive an MRL.

(6) Exposure Frequency/Duration. The duration of the study and the weekly and daily exposure regimens are provided in this column. This permits comparison of NOAELs and LOAELs from different studies. In this case (key number 18), rats were exposed to "Chemical x" via inhalation for 6 hours/day, 5 days/week, for 13 weeks. For a more complete review of the dosing regimen, refer to the appropriate sections of the text or the original reference paper (i.e., Nitschke et al. 1981).

(7) System. This column further defines the systemic effects. These systems include respiratory, cardiovascular, gastrointestinal, hematological, musculoskeletal, hepatic, renal, and dermal/ocular. "Other" refers to any systemic effect (e.g., a decrease in body weight) not covered in these systems. In the example of key number 18, one systemic effect (respiratory) was investigated.

(8) NOAEL. A NOAEL is the highest exposure level at which no harmful effects were seen in the organ system studied. Key number 18 reports a NOAEL of 3 ppm for the respiratory system,

which was used to derive an intermediate exposure, inhalation MRL of 0.005 ppm (see footnote "b").

(9) LOAEL. A LOAEL is the lowest dose used in the study that caused a harmful health effect. LOAELs have been classified into "Less Serious" and "Serious" effects. These distinctions help readers identify the levels of exposure at which adverse health effects first appear and the gradation of effects with increasing dose. A brief description of the specific end point used to quantify the adverse effect accompanies the LOAEL. The respiratory effect reported in key number 18 (hyperplasia) is a Less Serious LOAEL of 10 ppm. MRLs are not derived from Serious LOAELs.

(10) Reference. The complete reference citation is given in Chapter 9 of the profile.

(11) CEL. A CEL is the lowest exposure level associated with the onset of carcinogenesis in experimental or epidemiologic studies. CELs are always considered serious effects. The LSE tables and figures do not contain NOAELs for cancer, but the text may report doses not causing measurable cancer increases.

(12) Footnotes. Explanations of abbreviations or reference notes for data in the LSE tables are found in the footnotes. Footnote "b" indicates that the NOAEL of 3 ppm in key number 18 was used to derive an MRL of 0.005 ppm.

LEGEND

See Sample Figure 3-1 (page B-7)

LSE figures graphically illustrate the data presented in the corresponding LSE tables. Figures help the reader quickly compare health effects according to exposure concentrations for particular exposure periods.

(13) Exposure Period. The same exposure periods appear as in the LSE table. In this example, health effects observed within the acute and intermediate exposure periods are illustrated.

(14) Health Effect. These are the categories of health effects for which reliable quantitative data exists. The same health effects appear in the LSE table.

(15) Levels of Exposure. Concentrations or doses for each health effect in the LSE tables are graphically displayed in the LSE figures. Exposure concentration or dose is measured on the log scale "y" axis. Inhalation exposure is reported in mg/m^3 or ppm and oral exposure is reported in mg/kg/day.

(16) NOAEL. In this example, the open circle designated 18r identifies a NOAEL critical end point in the rat upon which an intermediate inhalation exposure MRL is based. The key number 18 corresponds to the entry in the LSE table. The dashed descending arrow indicates the extrapolation from the exposure level of 3 ppm (see entry 18 in the table) to the MRL of 0.005 ppm (see footnote "b" in the LSE table).

(17) CEL. Key number 38m is one of three studies for which CELs were derived. The diamond symbol refers to a CEL for the test species-mouse. The number 38 corresponds to the entry in the LSE table.

(18) Estimated Upper-Bound Human Cancer Risk Levels. This is the range associated with the upper-bound for lifetime cancer risk of 1 in 10,000 to 1 in 10,000,000. These risk levels are derived from the EPA's Human Health Assessment Group's upper-bound estimates of the slope of the cancer dose response curve at low dose levels (q_1*).

(19) Key to LSE Figure. The Key explains the abbreviations and symbols used in the figure.

SAMPLE

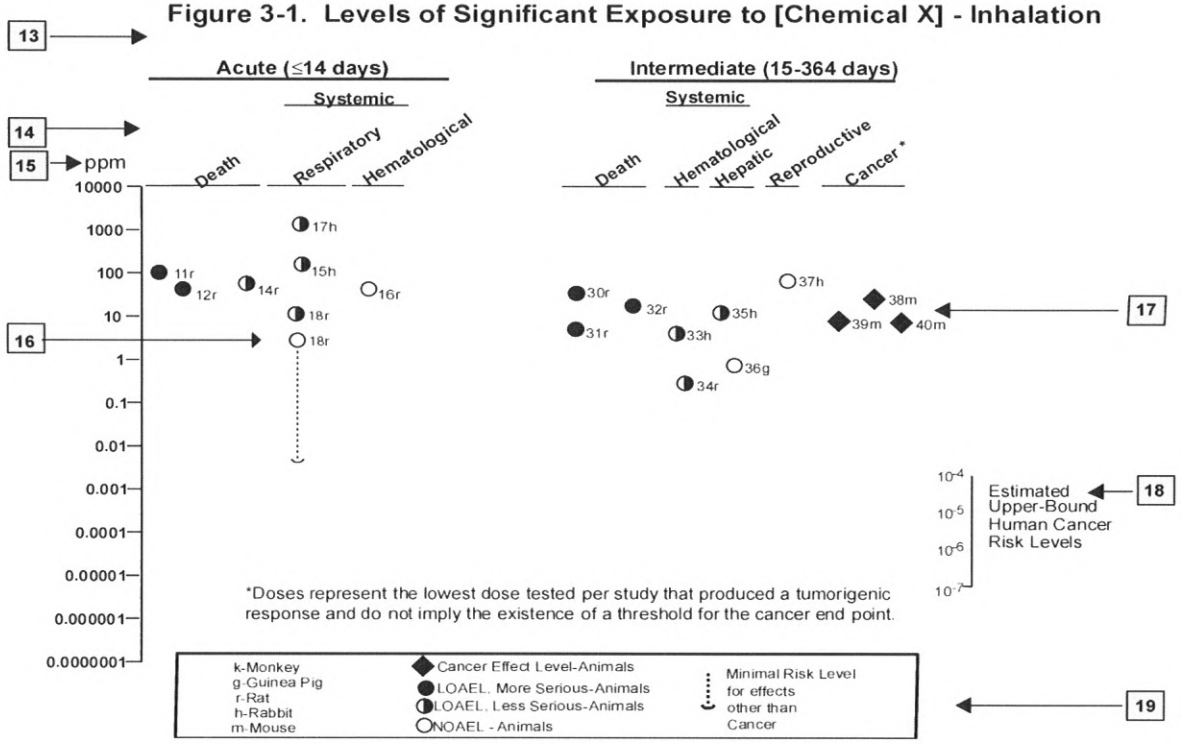
1 → **Table 3-1. Levels of Significant Exposure to [Chemical x] – Inhalation**

	Key to figure[a]	Species	Exposure frequency/ duration	System	NOAEL (ppm)	LOAEL (effect) Less serious (ppm)	Serious (ppm)	Reference
2 →	INTERMEDIATE EXPOSURE							
		5	6	7	8	9		10
3 →	Systemic	↓	↓	↓	↓	↓		↓
4 →	18	Rat	13 wk 5 d/wk 6 hr/d	Resp	3[b]	10 (hyperplasia)		Nitschke et al. 1981
	CHRONIC EXPOSURE							
	Cancer					11 ↓		
	38	Rat	18 mo 5 d/wk 7 hr/d			20	(CEL, multiple organs)	Wong et al. 1982
	39	Rat	89–104 wk 5 d/wk 6 hr/d			10	(CEL, lung tumors, nasal tumors)	NTP 1982
	40	Mouse	79–103 wk 5 d/wk 6 hr/d			10	(CEL, lung tumors, hemangiosarcomas)	NTP 1982

12 → [a] The number corresponds to entries in Figure 3-1.
[b] Used to derive an intermediate inhalation Minimal Risk Level (MRL) of 5×10^{-3} ppm; dose adjusted for intermittent exposure and divided by an uncertainty factor of 100 (10 for extrapolation from animal to humans, 10 for human variability).

SAMPLE

Figure 3-1. Levels of Significant Exposure to [Chemical X] - Inhalation



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APPENDIX C. ACRONYMS, ABBREVIATIONS, AND SYMBOLS

ACGIH	American Conference of Governmental Industrial Hygienists
ACOEM	American College of Occupational and Environmental Medicine
ADI	acceptable daily intake
ADME	absorption, distribution, metabolism, and excretion
AED	atomic emission detection
AFID	alkali flame ionization detector
AFOSH	Air Force Office of Safety and Health
ALT	alanine aminotransferase
AML	acute myeloid leukemia
AOAC	Association of Official Analytical Chemists
AOEC	Association of Occupational and Environmental Clinics
AP	alkaline phosphatase
APHA	American Public Health Association
AST	aspartate aminotransferase
atm	atmosphere
ATSDR	Agency for Toxic Substances and Disease Registry
AWQC	Ambient Water Quality Criteria
BAT	best available technology
BCF	bioconcentration factor
BEI	Biological Exposure Index
BMD	benchmark dose
BMR	benchmark response
BSC	Board of Scientific Counselors
C	centigrade
CAA	Clean Air Act
CAG	Cancer Assessment Group of the U.S. Environmental Protection Agency
CAS	Chemical Abstract Services
CDC	Centers for Disease Control and Prevention
CEL	cancer effect level
CELDS	Computer-Environmental Legislative Data System
CERCLA	Comprehensive Environmental Response, Compensation, and Liability Act
CFR	Code of Federal Regulations
Ci	curie
CI	confidence interval
CL	ceiling limit value
CLP	Contract Laboratory Program
cm	centimeter
CML	chronic myeloid leukemia
CPSC	Consumer Products Safety Commission
CWA	Clean Water Act
DHEW	Department of Health, Education, and Welfare
DHHS	Department of Health and Human Services
DNA	deoxyribonucleic acid
DOD	Department of Defense
DOE	Department of Energy
DOL	Department of Labor
DOT	Department of Transportation

DOT/UN/ NA/IMCO	Department of Transportation/United Nations/ North America/Intergovernmental Maritime Dangerous Goods Code
DWEL	drinking water exposure level
ECD	electron capture detection
ECG/EKG	electrocardiogram
EEG	electroencephalogram
EEGL	Emergency Exposure Guidance Level
EPA	Environmental Protection Agency
F	Fahrenheit
F_1	first-filial generation
FAO	Food and Agricultural Organization of the United Nations
FDA	Food and Drug Administration
FEMA	Federal Emergency Management Agency
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FPD	flame photometric detection
fpm	feet per minute
FR	Federal Register
FSH	follicle stimulating hormone
g	gram
GC	gas chromatography
gd	gestational day
GLC	gas liquid chromatography
GPC	gel permeation chromatography
HPLC	high-performance liquid chromatography
HRGC	high resolution gas chromatography
HSDB	Hazardous Substance Data Bank
IARC	International Agency for Research on Cancer
IDLH	immediately dangerous to life and health
ILO	International Labor Organization
IRIS	Integrated Risk Information System
Kd	adsorption ratio
kg	kilogram
kkg	metric ton
K_{oc}	organic carbon partition coefficient
K_{ow}	octanol-water partition coefficient
L	liter
LC	liquid chromatography
LC_{50}	lethal concentration, 50% kill
LC_{Lo}	lethal concentration, low
LD_{50}	lethal dose, 50% kill
LD_{Lo}	lethal dose, low
LDH	lactic dehydrogenase
LH	luteinizing hormone
LOAEL	lowest-observed-adverse-effect level
LSE	Levels of Significant Exposure
LT_{50}	lethal time, 50% kill
m	meter
MA	*trans,trans*-muconic acid
MAL	maximum allowable level
mCi	millicurie
MCL	maximum contaminant level

MCLG	maximum contaminant level goal
MF	modifying factor
MFO	mixed function oxidase
mg	milligram
mL	milliliter
mm	millimeter
mmHg	millimeters of mercury
mmol	millimole
mppcf	millions of particles per cubic foot
MRL	Minimal Risk Level
MS	mass spectrometry
NAAQS	National Ambient Air Quality Standard
NAS	National Academy of Science
NATICH	National Air Toxics Information Clearinghouse
NATO	North Atlantic Treaty Organization
NCE	normochromatic erythrocytes
NCEH	National Center for Environmental Health
NCI	National Cancer Institute
ND	not detected
NFPA	National Fire Protection Association
ng	nanogram
NHANES	National Health and Nutrition Examination Survey
NIEHS	National Institute of Environmental Health Sciences
NIOSH	National Institute for Occupational Safety and Health
NIOSHTIC	NIOSH's Computerized Information Retrieval System
NLM	National Library of Medicine
nm	nanometer
nmol	nanomole
NOAEL	no-observed-adverse-effect level
NOES	National Occupational Exposure Survey
NOHS	National Occupational Hazard Survey
NPD	nitrogen phosphorus detection
NPDES	National Pollutant Discharge Elimination System
NPL	National Priorities List
NR	not reported
NRC	National Research Council
NS	not specified
NSPS	New Source Performance Standards
NTIS	National Technical Information Service
NTP	National Toxicology Program
ODW	Office of Drinking Water, EPA
OERR	Office of Emergency and Remedial Response, EPA
OHM/TADS	Oil and Hazardous Materials/Technical Assistance Data System
OPP	Office of Pesticide Programs, EPA
OPPT	Office of Pollution Prevention and Toxics, EPA
OPPTS	Office of Prevention, Pesticides and Toxic Substances, EPA
OR	odds ratio
OSHA	Occupational Safety and Health Administration
OSW	Office of Solid Waste, EPA
OTS	Office of Toxic Substances
OW	Office of Water

OWRS	Office of Water Regulations and Standards, EPA
PAH	polycyclic aromatic hydrocarbon
PBPD	physiologically based pharmacodynamic
PBPK	physiologically based pharmacokinetic
PCE	polychromatic erythrocytes
PEL	permissible exposure limit
pg	picogram
PHS	Public Health Service
PID	photo ionization detector
pmol	picomole
PMR	proportionate mortality ratio
ppb	parts per billion
ppm	parts per million
ppt	parts per trillion
PSNS	pretreatment standards for new sources
RBC	red blood cell
REL	recommended exposure level/limit
RfC	reference concentration
RfD	reference dose
RNA	ribonucleic acid
RQ	reportable quantity
RTECS	Registry of Toxic Effects of Chemical Substances
SARA	Superfund Amendments and Reauthorization Act
SCE	sister chromatid exchange
SGOT	serum glutamic oxaloacetic transaminase
SGPT	serum glutamic pyruvic transaminase
SIC	standard industrial classification
SIM	selected ion monitoring
SMCL	secondary maximum contaminant level
SMR	standardized mortality ratio
SNARL	suggested no adverse response level
SPEGL	Short-Term Public Emergency Guidance Level
STEL	short term exposure limit
STORET	Storage and Retrieval
TD_{50}	toxic dose, 50% specific toxic effect
TLV	threshold limit value
TOC	total organic carbon
TPQ	threshold planning quantity
TRI	Toxics Release Inventory
TSCA	Toxic Substances Control Act
TWA	time-weighted average
UF	uncertainty factor
U.S.	United States
USDA	United States Department of Agriculture
USGS	United States Geological Survey
VOC	volatile organic compound
WBC	white blood cell
WHO	World Health Organization

>	greater than
≥	greater than or equal to
=	equal to
<	less than
≤	less than or equal to
%	percent
α	alpha
β	beta
γ	gamma
δ	delta
µm	micrometer
µg	microgram
q_1^*	cancer slope factor
–	negative
+	positive
(+)	weakly positive result
(–)	weakly negative result

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Cancer Statistics

Cancer has a major impact on society in the United States and across the world. Cancer statistics describe what happens in large groups of people and provide a picture in time of the burden of cancer on society.

Statistics tell us things such as how many people are diagnosed with and die from cancer each year, the number of people who are currently living after a cancer diagnosis, the average age at diagnosis, and the numbers of people who are still alive at a given time after diagnosis. They also tell us about differences among groups defined by age, sex, racial/ethnic group, geographic location, and other categories.

Cancer statistics also help us see trends. By looking at cancer rates over time, we can track changes in the risk of developing and dying from specific cancers as well as cancer overall.

For information about chances of surviving cancer and prognosis, see Understanding Cancer Prognosis. NCI also has a collection of statistical summaries for a number of common cancer types.

Although statistical trends are usually not directly applicable to individual patients, they are essential for governments, policy makers, health professionals, and researchers to understand the impact of cancer on the population and to develop strategies to address the challenges that cancer poses to the society at large. Statistical trends are also important for measuring the success of efforts to control and manage cancer.

Statistics at a Glance: The Burden of Cancer in the United States

- In 2024, an estimated 2,001,140 new cases of cancer will be diagnosed in the United States and 611,720 people will die from the disease.
- The most common cancers (listed in descending order according to estimated new cases in 2024) are breast cancer, prostate cancer, lung and bronchus cancer, colon and rectum cancer, melanoma of the skin, bladder cancer, kidney and renal pelvis cancer, non-Hodgkin lymphoma, endometrial cancer, pancreatic cancer, leukemia, thyroid cancer, and liver cancer.

- Prostate, lung, and colorectal cancers account for an estimated 48% of all cancers diagnosed in men in 2024. For women, the three most common cancers are breast, lung, and colorectal, and they will account for an estimated 51% of all new cancer diagnoses in women in 2024.
- The rate of new cases of cancer (cancer incidence) is 440.5 per 100,000 men and women per year (based on 2017–2021 cases).
- The cancer death rate (cancer mortality) is 146.0 per 100,000 men and women per year (based on 2018–2022 deaths).
- The cancer mortality rate is higher among men than women (173.2 per 100,000 men and 126.4 per 100,000 women). When comparing groups based on race/ethnicity and sex, cancer mortality is highest in non-Hispanic Black men (208.3 per 100,000) and lowest in non-Hispanic Asian/Pacific Islander women (82.6 per 100,000).
- As of January 2022, there were an estimated 18.1 million cancer survivors in the United States. The number of cancer survivors is projected to increase to 22.5 million by 2032.
- Approximately 40.5% of men and women will be diagnosed with cancer at some point during their lifetimes (based on 2017–2019 data).
- In 2024, an estimated 14,910 children and adolescents ages 0 to 19 will be diagnosed with cancer and 1,590 will die of the disease.
- Estimated national expenditures for cancer care in the United States in 2020 were $208.9 billion. In future years, costs are likely to increase as the population ages and more people have cancer. Costs are also likely to increase as new, and often more expensive, treatments are adopted as standards of care.

Statistics at a Glance: The Burden of Cancer Worldwide

- Cancer is among the leading causes of death worldwide. In 2022, there were almost 20 million new cases and 9.7 million cancer-related deaths worldwide.
- By 2040, the number of new cancer cases per year is expected to rise to 29.9 million and the number of cancer-related deaths to 15.3 million.
- Generally, cancer rates are highest in countries whose populations have the highest life expectancy, education level, and standard of living. But for some cancer types, such as cervical cancer, the reverse is true, and the incidence rate is highest in countries in which the population ranks low on these measures.

Source: International Agency for Research on Cancer

U.S. Cancer Mortality Trends

The best indicator of progress against cancer is a change in age-adjusted mortality (death) rates, although other measures, such as quality of life, are also important. Incidence is also important, but it is not always straightforward to interpret changes in incidence. A rise in incidence can reflect a real increase in disease occurrence, such as when an increase in exposure to a risk factor causes more cases of cancer. In such a scenario the increased incidence would likely lead to a rise in deaths from the cancer. On the other hand, the incidence of cancer may rise due to a new screening test that detects many cancer cases that would not have caused a problem during someone's life (called overdiagnosis). In this example, the incidence of the cancer would increase, but death rates would not change.

Mortality trends, when compared with incidence trends, can also provide evidence of improved treatments. If death rates drop faster than incidence (or if death rates drop while incidence is rising), this may reflect the availability of better treatments. For example, statistical evidence suggests that improved treatments have likely made a substantial contribution to recent sharp declines in the lung cancer mortality rate.

In the United States, the overall cancer death rate has declined since the early 1990s. Part 1 of the most recent Annual Report to the Nation on the Status of Cancer, released in October 2022, shows that overall cancer death rates decreased by:

- 2.3% per year among men from 2015 to 2019
- 1.9% per year among women from 2015 to 2019
- 1.5% per year among children ages 0–14 from 2015 to 2019

Although death rates for many individual cancer types have also declined, rates for a few cancers have not changed or even increased.

As the overall cancer death rate has declined, the number of cancer survivors has increased. These trends show that progress is being made against the disease, but much work remains. Although rates of smoking, a major cause of cancer, have declined, the rates of other risk factors, such as obesity, have increased in the United States. Also, the U.S. population is aging, and cancer rates increase with age.

The Surveillance, Epidemiology, and End Results (SEER) Program

NCI's Surveillance, Epidemiology, and End Results (SEER) Program collects and publishes cancer incidence and survival data from population-based cancer registries that cover approximately 48% of the U.S. population. The SEER program website has more detailed cancer statistics, including population statistics for common types of cancer, customizable graphs and tables, and interactive tools.

The Annual Report to the Nation on the Status of Cancer provides an annual update of cancer incidence, mortality, and trends in the United States. This report is jointly authored by experts from NCI, the Centers for Disease Control and Prevention, American Cancer Society, and the North American Association of Central Cancer Registries.

Part 1 of the most recent report included a special section about trends in pancreatic cancer. Part 2, released in September 2023, focused on the effect of the COVID-19 pandemic on new cases and deaths from certain cancers. For example, new diagnoses of six major cancer types fell sharply from March to May of 2020, at the start of the pandemic. By July 2020, diagnoses of all of these cancer types except one (prostate cancer) had returned to pre-pandemic levels.

Related Resources

Cancer Stat Fact Sheets

SEER Did You Know? Video Series

Finding Statistics by Race/Ethnicity

State Cancer Profiles

Updated: May 9, 2024

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How Dangerous is Lightning?

Lightning is a major cause of storm related deaths in the U.S. A lightning strike can result in a cardiac arrest (heart stopping) at the time of the injury, although some victims may appear to have a delayed death a few days later if they are resuscitated but have suffered irreversible brain damage.

According to *the NWS Storm Data*, over the last 30 years (1989-2018) the U.S. has averaged 43 *reported* lightning fatalities per year. Only about 10% of people who are struck by lightning are killed, leaving 90% with various degrees of disability. More recently, in the last 10 years (2009-2018), the U.S. has averaged 27 lightning fatalities.

Odds of Becoming a Lightning Victim (based on averages for 2009-2018)				
Estimated U.S. population as of 2019				330,000,000
Average Number of Deaths Reported	27	Estimated number of Injuries	243	270
Odds of being struck in a given year (estimated total deaths + estimated injuries)				1/1,222,000
Odds of being struck in your lifetime (Est. 80 years)				1/15,300
Odds you will be affected by someone struck (10 people for every 1 struck)				1/1,530

United States
Environmental Protection
Agency

Office of Health and
Environmental Assessment
Washington DC 20460

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March 1984
Final Report

Research and Development

EPA

Health Assessment Document for Inorganic Arsenic

Final Report

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Final Report

Health Assessment Document for Inorganic Arsenic

FINAL REPORT

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Research and Development
Office of Health and Environmental Assessment
Environmental Criteria and Assessment Office
Research Triangle Park, NC 27711

TR 2698

NOTICE

This document has been reviewed in accordance with the U.S. Environmental Protection Agency's peer and administrative review policies and approved for presentation and publication. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

PREFACE

The Office of Health and Environmental Assessment, in consultation with other Agency and non-Agency scientists, has prepared this health assessment to serve as a "source document" for Agency-wide use. Specifically, this document was prepared at the request of the Office of Air Quality Planning and Standards.

In the development of this assessment document, the scientific literature has been inventoried, key studies have been evaluated, and summary/conclusions have been prepared such that the toxicity of arsenic is qualitatively and, where possible, quantitatively identified. Observed effect levels and dose-response relationships are discussed where appropriate in order to place adverse health responses in perspective with observed environmental levels.

TR 2700

ABSTRACT

This document summarizes current scientific information regarding the effects of inorganic arsenic on man and the environment. The observed effects, as presented herein, constitute the health basis from which the U.S. Environmental Protection Agency will make determinations regarding regulatory initiatives pursuant to the Clean Air Act. Specifically, this document discusses the following topics--physical and chemical properties of inorganic arsenic; environmental distribution and cycling; inorganic arsenic metabolism; toxicology, including mutagenic and carcinogenic properties; and essentiality--and identifies the factors most germane to assessing quantitative and qualitative human health risks.

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1. INTRODUCTION

This report evaluates health effects associated with arsenic exposure, with particular emphasis placed on health effects thought to be of most concern in regard to exposure to inorganic arsenic of the general U.S. population. Organic arsenic compounds are considered only insofar as certain forms of the element arise via transformation of arsenic in man and other species, or arise by environmental transformation.

This report is organized into chapters which provide a cohesive discussion of all aspects of inorganic arsenic and delineate a logical linking of this information to human health risk. The chapters include: an executive summary (Chapter 2) of the information contained within the text of later chapters; background information on the chemical and environmental aspects of arsenic, including levels of arsenic in media with which U.S. population groups come into contact (Chapter 3); arsenic metabolism, where factors of absorption, biotransformation, tissue distribution, and excretion of inorganic arsenic are discussed with reference to the toxicity of the element (Chapter 4); arsenic toxicology, discussing the various acute, subacute, and chronic health effects of inorganic arsenic in man and animals (Chapter 5); arsenic mutagenesis, discussing the ability of inorganic arsenic to cause gene mutations, chromosomal aberrations, sister chromatid exchanges and inhibition of DNA synthesis (Chapter 6); arsenic carcinogenesis, including discussion of selected dose-effect and dose-response relationships (Chapter 7); arsenic as an essential element, which deals with the current status of inorganic arsenic as a required nutrient in at least some species of animals (Chapter 8); and a human health risk assessment for arsenic, where key information from the preceding chapters is placed in an interpretive and quantitative perspective highlighting those health effects of most concern for U.S. populations (Chapter 9).

This report is not intended to be an exhaustive review of all the arsenic literature, but is focused upon those data thought to be most useful and relevant for human health risk assessment purposes. Particular emphasis is placed on delineation of health effects and risks associated with exposure to airborne arsenic, in view of the most immediate use intended for the present report, i.e., to serve as a basis for decision making regarding the regulation of inorganic arsenic as a hazardous air pollutant under pertinent sections of the Clean Air Act, as amended in 1977. Health effects associated with the ingestion of arsenic or with exposure via other routes are also discussed, providing a basis for possible use for multimedia risk assessment purposes, as well. The background information provided at the outset on sources, emissions, and ambient concentrations of arsenic in various media is presented in order to provide a general perspective against which to view the health effects evaluations contained in later chapters of the document. More detailed exposure assessments, taking into account even more recent, up-to-date emission and ambient concentration data have been prepared separately for use in subsequent EPA regulatory decision making regarding arsenic.

The Agency recognizes that the regulatory decision-making process is a continuous one; therefore, should new information become available in the future that would warrent a reevaluation of the information contained herein, the Agency will undertake such an evaluation as part of its mandate to protect the health of the general U.S. population.

2. SUMMARY AND CONCLUSIONS

As a toxic agent, inorganic arsenic possesses several properties that are not shared with many environmental pollutants. The element exists in various chemical states, e.g., tri- and pentavalent inorganic arsenic and methylated organic arsenic, with each having differing toxicological potential. In man, experimental animals, and other organisms, arsenic undergoes a variety of transformations, the full significance and mechanisms of which are, as yet, not well understood. Furthermore, there appears to be a nutritional requirement for low levels of arsenic in certain experimental animals and this may also be the case for man. All of these factors complicate the analyses of the toxicological effects and the risk for human health associated with environmental exposure to arsenic compounds. The following chapter summarizes these factors as they are presented in depth in the ensuing document text.

2.1 BACKGROUND INFORMATION

2.1.1 Chemical/Physical Aspects of Arsenic

It is the various compounds of arsenic which have been of most importance in the extensive history of the toxicology of the element, the zero-valent metallic form being of minor toxicological interest.

Arsenic is encountered as a component of sulfidic ores of metals such as copper, cobalt and nickel. The smelting of these ores is associated with arsenic release into the environment. Arsenic trioxide, As_2O_3, a toxicologically significant form, is a smelter product arising from air roasting of these sulfidic ores.

Arsenic trioxide, white arsenic, is only sparingly soluble in water and other solvents which do not promote chemical transformation. The compound dissolves in acidic or alkaline aqueous media to yield either the free acid or

salts, with these being soluble in a number of solvents. The oxide readily sublimes (135°C), and this factor is of importance in considering analytical methods for measuring levels of the compound.

The pentavalent arsenic pentoxide, As_2O_5, may be prepared by nitric acid oxidation of the trioxide or the element itself. This form has high solubility in water (63 g/100 g water), forming the strongly oxidizing arsenic acid, H_3AsO_4 ($E^o = 0.56V$).

Stability of the valency forms of arsenic in solution is dependent on the nature of the medium. Oxygenated media and higher pH favor the pentavalent form, while reducing and/or acidic media favor the trivalent state.

The acids of both valency forms of arsenic readily form alkali and alkaline metal salts, with the former being much more soluble than the latter. Organic ester derivatives of arsenic are quite labile to hydrolysis and this chemical behavior has biochemical/toxicological implications in the postulated role of arsenate ion in interfering with phosphorylation reactions.

Arsine (arsenic trihydride, AsH_3) is the most poisonous of the arsenicals, being a strong hemolytic agent, and it can be formed under certain restricted conditions, i.e., reduction of the oxy compounds in the presence of a strong hydrogen source.

Monomethyl and dimethyl arsenic arise by both environmental and <u>in vivo</u> transformation processes.

In high-temperature processes, arsenic is released as a vapor which is then adsorbed or condensed onto small particles. Such adherence to particles of 1-2 μm or less may result in enhanced health risk from the agent since particles in this size range are inhaled and deposited in the deepest part of the respiratory tract.

Arsenic compounds tend to form insoluble complexes with soils and sediments. In the case of soils, the interaction occurs with amorphous aluminum or iron oxides.

2.1.2 The Environmental Cycling of Arsenic

Primary smelting, biocide use and glass manufacturing constitute some of the major inputs of arsenic into the various environmental compartments. Of an estimated total release of approximately 10,000 short tons annually in the U.S., smelter activity accounts for about 50 percent, biocide (pesticide, fungicide, herbicide) use contributes 32 percent, and glass production contributes about 7.0 percent, with the remaining amount being released from various other sources.

The atmosphere is a major conduit for arsenic emitted from anthropogenic sources to the other environmental compartments via wet and dry precipitation processes. Dry and wet fall onto soils may be followed by movement through soils either into groundwater or surface water. Passage of arsenic into surface waters may be followed by transfer to sediments. Such cycling is made complex by chemical and biological transformations which have been reported as occurring in the various environmental compartments.

Trivalent arsenic in the atmosphere or in aerated surface waters can undergo oxidation to the pentavalent state, while pentavalent arsenic in media which are below pH 7.0 and contain oxidizable material can react to form the trivalent form via reduction.

Biological transformations of arsenic have been documented as occurring via both sedimentary bacteria and suspended marine algae. Several different hypotheses have been advanced to explain the biological cycling of arsenic.

Reduction and methylation of inorganic arsenic occur only to a limited extent in soils, one report noting a conversion of only 1-2 percent over a period of months.

With reference to the relative amounts of the annual environmental burden of arsenic, it has been calculated for 1974 that land is the major sink for arsenic, approximately 90 percent, with the atmosphere accounting for 7-8 percent and the smallest quantity appearing in waters.

2.1.3 Levels of Arsenic in Various Media

Available data on levels of arsenic in various media with which man interacts are generally presented as total arsenic, with limited information available for identifying specific chemical forms of arsenic.

2.1.3.1 Levels of Arsenic in Ambient Air--Based on the comprehensive data for U.S. air levels of arsenic obtained by the U.S. EPA's National Air Sampling Network, air levels of arsenic in the U.S. generally do not exceed 0.1 $\mu g/m^3$.

Generally, airborne arsenic is adhered to particulate matter. Although the immediate areas around smelters may contain some arsenic in the vapor form, data are available to indicate rapid adherence to particulate matter when sampling 2-3 km from these emission sites.

The specific chemical form(s) of airborne arsenic is still unclear. Generally, in most urban/suburban areas, arsenic is mainly in the form of a mixture of inorganic arsenic in the tri- and pentavalent states. Only in areas where methylated arsenic is used agriculturally or where biotic transformation can occur has methylated arsenic been found in air samples.

2.1.3.2 Levels of Arsenic in Drinking Water--The National Interim Primary Drinking Water Regulations, promulgated under the Safe Drinking Water Act, set the Maximum Contaminant Level (MCL) for arsenic in U.S. public water supplies at 50 µg/l. In general, arsenic is not found in drinking water at levels exceeding this MCL. Well waters in the western U.S. and Alaska, however, may have much higher levels owing to geochemical enrichment. In Lane County, Oregon, recent analyses report levels up to 2.2 ppm (2.2 mg/liter), while the

highest figure in Alaska was 10 ppm (10 mg/liter), representing both natural and mining residue contributions.

It is reasonable to assume that the chief chemical form of arsenic in most public water supplies would be the pentavalent inorganic form, owing to both aeration and chlorination. Similarly, well waters in Alaska and the western U.S. are reported to mainly contain pentavalent inorganic arsenic.

2.1.3.3 Arsenic in Food--The most recent data base for the arsenic content of foods is the 1975-1976 survey carried out by the U.S. Food and Drug Administration. Shellfish and other marine foods have the highest levels on a food category basis. Overall, the total dietary intake of arsenic in 1975-1976 was approximately 50 μg (elemental arsenic), representing an increase from the preceding years. Whether this increase represents a trend or merely reflects analytical variation in sampling from year to year is still to be determined.

The chemical forms of arsenic in foods are varied and complex. Crustaceans and other marine life store arsenic in complex organoarsenical forms which, based on recent reports, are assimilated by man and generally excreted intact. Toxicologically, these forms are comparatively inert.

2.1.3.4 Arsenic in Soils--Background soil arsenic levels range from less than 1 ppm to over 40 ppm, the latter reflecting agricultural practices as well as air fallout. Soil arsenic is usually bound to clay surfaces, and its mobility is a function of soil pH, phosphate levels, iron and aluminum content, and soil type. The mobile fraction, usually in the pentavalent form, is of concern in terms of movement to plants and water. Little reductive methylation occurs in most soils.

2.1.3.5 Other Sources of Arsenic--Limited data on arsenic content of tobacco suggest that more recent values range from around 1.5 ppm or less, while in the past (1945) values up to 40 ppm were measured. This decrease reflects reduced use of arsenical biocides in tobacco production.

2.2 ARSENIC METABOLISM

2.2.1 Routes of Absorption

Major routes of absorption of arsenic in the general population are inhalation and ingestion. The ingestion of arsenic may be either through the direct intake of food and water or through secondary intake via inhalation and swallowing. Arsenic uptake through the skin appears to be a minor route of exposure. Factors affecting the extent of absorption include chemical forms, particle size, and solubility.

2.2.1.1 Respiratory Absorption--Limited data from human subjects suggest that about 40 percent of most forms of inhaled arsenic is deposited in the lungs, all of which is eventually absorbed, yielding a net absorption of approximately 30 percent or greater of the inhaled amount.

Several studies of smelter workers also confirm that significant absorption of inhaled arsenic occurs, as judged by rapidly rising urine arsenic levels when exposure first occurs. Furthermore, the levels excreted are correlated with workplace air levels.

Animal data also indicate respiratory tract absorption when exposure occurs by inhalation of aerosols or by intratracheal instillation.

2.2.1.2 Gastrointestinal Absorption--Based on a number of reports using human subjects, soluble inorganic arsenic is almost totally absorbed from the gastrointestinal tract. Similar data have been obtained for such experimental animal species as the rat, pig, and monkey.

Less soluble forms of arsenic, such as arsenic trioxide in suspension, lead to considerably lower absorption while insoluble arsenic triselenide passes through the human GI tract with negligible absorption.

2.2.1.3 Transplacental Transfer--Transplacental transfer of arsenic in man appears to occur, based on autopsy data and on one report showing that newborn

cord blood levels approximate those of the mothers. Measurable levels of arsenic in fetal tissue have been determined by the fourth month of gestation, increasing to month seven.

In animals, inorganic arsenic appears to rapidly cross the placental barrier where it is distributed in embryonic tissue.

2.2.2 Biotransformation of Inorganic Arsenic In Vivo

An understanding of inorganic arsenic metabolism in man and other species is complicated by recently revealed biotransformation processes, discovered because of the development of analytical techniques which permit the chemical speciation of arsenic into its various forms. These processes not only relate to pharmacokinetic parameters such as tissue distribution and excretion, but also figure in the toxicology of the element. The two processes of significance for consideration here are the methylation of inorganic arsenic and oxidation-reduction interconversion of inorganic arsenic.

An extensive recent literature documents the *in vivo* methylation of inorganic arsenic to monomethyl and dimethyl arsenic (the latter being the major methylated metabolite) in every mammalian system studied to date, including man.

While the quantitative features of this phenomenon may vary among species, one can generally state that: 1) dimethyl arsenic is the major transformation product in both humans and animals, with the amount of monomethyl arsenic, when formed, being greater in humans; 2) methylation is assumed to be a route of detoxification, the methylated forms being not only much less toxic but also more rapidly excreted; 3) the methylating capacity of a given system can persist over a range of inorganic arsenic exposure but at some point can be overwhelmed; and 4) retrospective assessment of early data on arsenic

metabolism must be reviewed in light of the current knowledge about biomethylation. In man, dimethyl arsenic represents approximately 75 percent of total arsenic excretion, with monomethyl arsenic being excreted in lesser amounts.

The demonstration of interconversion of the two valency forms of inorganic arsenic claimed in earlier literature must be considered in light of the biomethylation phenomenon, and only more recent studies addressing this problem using chemical speciation techniques can be considered reliable. Invariably, the giving of inorganic penta- or trivalent arsenic to experimental animals or human volunteers leads to predominantly methylated forms, with any inorganic arsenic being present in small amounts. These observations and supporting data showing reduction of pentavalent arsenic *in vivo* are consistent with a reductive biomethylation mechanism, including initial reduction of pentavalent to trivalent arsenic prior to methylation. A recent study using speciation methods and human subjects also establishes the *in vivo* reduction of pentavalent to trivalent arsenic in humans.

Even with sophisticated analytical methods permitting chemical speciation in biological media, the lability of arsenic in dosing solution to oxidation-reduction requires careful assessment of the actual form being administered.

2.2.3 Distribution of Arsenic in Man and Animals

Blood is the main vehicle for transport of arsenicals following absorption, and from which arsenic is cleared relatively rapidly to tissues in all species except the rat. In the rat, arsenic-erythrocyte interaction tends to preclude rapid movement to tissues, with a biological half-time of up to 90 days, versus a corresponding time of several days in all other species. Arsenic movement from blood appears to conform to a three-compartment model which must reflect in part the biomethylation of inorganic arsenic noted above.

Exposure of various experimental animals to either tri- or pentavalent inorganic arsenic leads to initial accumulation of the element in liver, kidney, spleen, aorta, and skin. In most species, arsenic clearance from soft tissue is relatively rapid except for the skin, where the high sulfhydryl group content probably promotes tight arsenical binding.

In man, tissue partitioning data are mainly available from autopsy data. Heart, kidney, liver and lung have highest levels on a concentration basis, but skin and excretory/storage organs such as nails and hair have the highest absolute amounts. Brain tissue has levels only slightly below those of other soft tissues.

Recent data on valency and exposure level effects on tissue distribution of arsenic indicate that levels of arsenic in kidney, liver, bile, brain, skeleton, skin, and blood are 2- to 25-fold higher for the trivalent form than for the pentavalent state, and are greatly increased at higher dosing. The difference is held to be due to the relative methylating capacity of either form as well as the level of exposure.

2.2.4 Arsenic Accumulation

The long-held view of arsenic as an element which accumulates in the body was mainly based on the behavior of arsenic in the rat, an anomalous model which does not reflect the case with other species. For other species, including man, long-term accumulation does not generally occur in physiologically active compartments in the body.

In man, the only evidence for tissue accumulation is autopsy data from retired workers with a history of metal smelter exposure in which lung arsenic levels were 8-fold higher than in a control population. This suggests the existence of a very insoluble form of arsenic in smelter ambient air.

2.2.5 Arsenic Excretion

Renal clearance appears to be the major route of excretion of absorbed arsenic in man and animals. Biliary transport of the element leads to enteric reabsorption, with little carriage in feces.

In man, inorganic arsenic is excreted rather rapidly, and in several studies in which continuous exposure resulted in the acquisition of steady state, around 60 percent of a given dose was excreted within one day.

The pattern of renal excretion reflects the *in vivo* biotransformation capacity for inorganic arsenic, one study noting that trivalent arsenic was excreted more slowly than an equivalent dose of the pentavalent form, and higher doses of both forms were cleared relatively more slowly than lower doses.

2.3 ARSENIC TOXICOLOGY

2.3.1 Acute Toxicity

Acute symptoms of arsenic poisoning are similar in both man and experimental animals. With oral exposure, the acute symptoms include severe gastrointestinal damage resulting in vomiting and diarrhea and general vascular collapse leading to shock, coma, and death. Other acute effects are muscular cramps, facial edema, and cardiovascular reactions. Airborne exposure at high levels also results in severe irritation of nasal mucosa, larynx, and bronchi. Sequelae of acute contact with inorganic arsenic include peripheral nervous system disturbances with slow recovery and reversible effects on the hematopoietic system.

Levels of exposure associated with acute arsenic toxicity vary with the valency form of the element, the trivalent state being approximately 4-fold more toxic than pentavalent arsenic. Oral LD_{50} values for trivalent arsenic

vary from 15 to 293 mg/kg b.w. in rats and from 10-150 mg/kg in other test species.

While a number of outbreaks of acute arsenic poisoning have been described, few data exist on actual doses and type of arsenical involved. One report has estimated the human lethal dose for arsenic trioxide to be anywhere from 70 to 180 mg.

2.3.2 Chronic Toxicity

Two categories of chronic arsenic toxicity can be discerned from the available literature: 1) the mutagenicity/carcinogenicity of arsenic; and 2) various non-carcinogenic chronic effects.

2.3.2.1 Mutagenesis of Inorganic Arsenic--Various inorganic compounds of arsenic have been tested for mutagenicity in a variety of test systems ranging in complexity from bacteria to peripheral lymphocytes of exposed human beings. Although many of the data are contradictory, the weight of evidence supports the following conclusions:

1) Arsenic is either inactive or extremely weak for the induction of gene mutations *in vitro*.
2) Arsenic is clastogenic and induces sister chromatid exchanges (SCE) in a variety of cell types, including human cells *in vitro*; trivalent arsenic is approximately an order of magnitude more potent than pentavalent arsenic.
3) Arsenic does not appear to induce chromosome aberrations *in vivo* in experimental animals.
4) Several studies suggest that human beings exposed to arsenic demonstrate higher frequencies of SCE and chromosomal aberrations in peripheral lymphocytes; however, the quality of these studies is generally poor.

5) Arsenic may affect DNA by the inhibition of DNA repair processes or by its occasional substitution for phosphorus in the DNA backbone.

From these conclusions, it can be surmised that arsenic may have the potential to cause chromosomal changes in human beings. Although additional information is needed, it appears that the mutagenic potency of arsenic is weak compared to other known metal mutagens.

2.3.2.2 Carcinogenesis of Inorganic Arsenic--The current status of inorganic arsenic as a human and experimental animal carcinogen has been extensively and critically reviewed by public agencies such as the National Institutes of Occupational Safety and Health, scientific bodies such as the National Academy of Science and the International Agency for Research on Cancer, and in a number of individual assessments.

At present, the collective evidence for an etiological role of inorganic arsenic in human cancers is strongest for cancers of the skin and lung.

In man, chronic oral exposure to arsenic induces a sequence of changes in skin epithelium, proceeding from hyperpigmentation to hyperkeratosis characterized as keratin proliferation of a verrucose nature, and leading in some cases to late onset skin cancers. The skin cancers can be histopathologically characterized as either squamous carcinomas in the keratotic areas or basal cell carcinomas.

Arsenic-associated skin cancers, regardless of type of exposure, differ from those having an ultraviolet light etiology in that they occur on unexposed areas such as the palms and soles and occur as multiple lesions. The latency period for such lesions has been reported to range from 6 to 50 years for skin cancer induced by the administration of arsenical medicinals. The most reliable study of skin cancer associated with arsenic-contaminated drinking water found the minimum human latency period to be 24 years.

Lung cancers associated with occupational exposure to arsenic appear to be mainly of the poorly differentiated and small-cell undifferentiated epidermoid carcinoma type, although well-differentiated epidermoid carcinoma and acinar-type adenocarcinoma have also been noted. The latency period for such lung cancer due to occupational arsenic exposure at smelters has been reported to range from 13 to 50 years.

While other visceral cancers such as hepatic angiosarcomas have also been claimed to be associated with arsenic exposure, the data base for such association is less conclusive than for cancers of the skin and lung.

2.3.2.2.1 Human Epidemiology of Arsenic Carcinogenesis. Cancer- and possible precancerous lesion-producing inorganic arsenic exposures have been demonstrated in both occupational populations, such as copper smelters, pesticide manufacturers and argricultural workers, and in non-occupational populations using arsenical drugs or consuming arsenic-contaminated drinking water and/or food.

Cancer or possible precancerous skin lesions associated with arsenic exposure include lung cancer, skin cancer, peripheral vasculopathy, hyperkeratosis, hyperpigmentation, and depigmentation. Of these, cancers of the lung and skin have received the most attention. Furthermore, epidemiologic reports of cancer or possible precancerous lesions related to arsenic exposures have a wide geographical distribution, with studies reported in the United States, Europe, Asia and South America.

Lung Cancer

An excess mortality in respiratory cancer has been noted among smelter workers and among workers engaged in the production and use of arsenical pesticides. In a number of these studies, the levels of exposure are uncertain and there is simultaneous exposure to agents such as other metals and sulfur dioxide. Furthermore, some of these studies did not take into account the effects of cigarette smoking.

A proportionate mortality study of an English factory which manufactured arsenite as a sheep dip powder found that workers at the facility had a proportion of lung cancer deaths twice that for other workers in the geographic area. Of the total factory group, the chemical workers, who were the most closely associated with the arsenite production, accounted for all of the lung cancer deaths and had a higher proportion of deaths from all cancers than the total factory population. Air exposure information was limited, levels up to 4 mg As/m^3 having been reported only for 1945-1946. The outcome of the earlier English study has been supported by studies of two facilities in the United States. At one facility manufacturing lead-, calcium-, and magnesium arsenate and copper acetoarsenite over the period 1919-1956, the ratio of observed-to-expected lung cancer deaths among workers was evaluated on the basis of exposure level, giving ratios ranging up to 7:1 in the highest exposure category.

The second U.S. facility, in Baltimore, Maryland, has been the subject of two occupational studies. At this operation, production of lead-, calcium-, and sodium arsenate was started in the early 1950s. Air levels of arsenic were not available. In the most recent report--a follow-up of workers employed from 1946 to 1974--statistically significant increases in lung cancer deaths were found in "predominantly arsenical production workers." Information on smoking history was not obtained.

Occupational exposure to arsenic also occurs in smelters. Several reports have centered on workers at a copper smelter in the state of Washington. In the most recent publication concerning cancer deaths at this facility, an increase in overall mortality, a significant increase in cancer deaths, and a highly significant increase in deaths from lung cancer were noted. Although

cigarette smoking data were not available, a clear lung cancer dose response by arsenic exposure was found, suggesting that smoking probably did not confound the lung cancer response believed to be due to arsenic.

Other U.S. studies have been done at smelter sites in Utah and Montana. In the Utah study, smelter workers showed a 3-fold increase in the lung cancer death rate compared to the general population of the state. Exposures to sulfur dioxide and copper, as well as arsenic, were found to be significantly higher for the lung cancer cases. Differences in smoking habits could not explain the excess lung cancer mortality. Smelter workers at the Montana smelter were found to follow a lung cancer dose response by arsenic exposure. Differences in smoking habits could not explain the differences in lung cancer mortality. Little association, if any, was found between sulfur dioxide exposure and lung cancer mortality.

Some of the evidence from the U.S. smelter studies suggests that arsenic may be acting as either a late-stage carcinogen in the multistage theory of carcinogenesis or as a promoter in the carcinogenesis process. Either hypothesis requires further study, however.

Excess lung cancer mortality has also been reported for workers in foreign smelters. Several reports have concerned the smelter facility in Sweden. In this operation, it was found that arsenic exposure was associated with increases in lung cancer deaths, the ratio being 4.6 for a work history of more than 17 years. Sulfur dioxide exposure was not found to be associated with lung cancer, nor could the results be explained by differences in smoking habits. A study of smelter workers in Japan has also reported a positive association between smelter employment and lung cancer. Workers in the highest exposure and longest follow-up category were reported to have a 25-fold increase in lung cancer mortality.

Several studies suggest that populations surrounding arsenic-emitting sources are at a greater risk of lung cancer. One study found that lung cancer in counties with smelters was significantly higher than in counties without smelters. Another study found an association between residence in an area surrounding an arsenic pesticide plant and lung cancer mortality even after controlling for employment at the pesticide plant. Two lung cancer mortality studies of populations in the vicinity of smelters are inconclusive with regard to lung cancer risk in the general population because lung cancer deaths of workers at the smelters were included in the analyses. It should be noted that none of these studies addressed the effects of population migration, however.

Skin Cancer and Precancerous Lesions

All of the occupational studies on arsenic have been mortality studies. Because skin cancer is rarely fatal, the occupational studies, in general, do not report excesses of skin cancer. The English study referred to in the preceding section, however, did note that cancer deaths among those factory workers with skin cancer was 13.6 percent compared to a figure of 1.3 percent in the reference population.

Most of the available information on the association of arsenic with skin cancer has involved non-occupational populations in geographical areas as diverse as Taiwan, Argentina, and northern Europe, and has involved arsenic in drinking water or medicinal preparations.

In Taiwan, exposure started in 1910-1920 with the availability of water from deep wells. In the most comprehensive study of this group, 37 villages with a population of 40,421 were surveyed in 1965 and the prevalence rate of skin cancer was categorized by arsenic exposure and age. The prevalence rate of skin cancer increased with both well water arsenic and age. The greatest

prevalence rate was in the >60-years age group (192.0/1,000 subjects) exposed to well water with an arsenic content of >0.6 ppm. There was a similar ascending gradient for hyperkeratosis, an apparent precondition for the later onset of skin cancer.

In Cordoba, Argentina, arsenical waters have also been reported to be associated with increased rates of skin cancer among the population using this water. In the various reports on this area, it has been noted that over 81 percent of persons with "arsenical-type" skin epitheliomas presenting themselves at a particular dermatology clinic came from areas where high levels of arsenic were known to be present in the water supplies and where arsenicism among individuals was known to occur. Lack of information on the size of the populations in each geographic area limits the conclusions that can be drawn from these studies, however.

In a number of epidemiological surveys conducted in Antofagasta, Chile, the presence of a relatively high level of arsenic, 0.6 ppm, in the public drinking water from 1958 to 1970, was shown to have resulted in a high number of skin lesions including hyperkeratosis which may be a precondition for skin cancer. In one report of cases seen and diagnosed from 1968 to 1971 in Antofagasta, the author reported 457 patients with various cutaneous lesions including leukoderma, melanoderma, hyperkeratosis, and squamous-cell carcinoma; all had high arsenic content in the hair. The number of cases for each diagnosis was not specified.

An investigation of the population having contact with well waters containing elevated levels of arsenic in an area of Oregon did not yield any evidence for skin cancer associated with such exposure, nor did a similar study in Utah. Factors which may have contributed to the difference in results between these studies and the studies in Taiwan, where an association between

skin cancer and arsenic in drinking water was found, include: (1) in addition to arsenic, ergotamine was found in the Taiwan drinking water, (2) the socioeconomic level of the Taiwanese who experienced skin cancer was rather low, which may have had ramifications in terms of diet, personal hygiene and medical care, and (3) racial differences between the Taiwanese and U.S. populations may have had an effect. However, the population sample sizes of the Oregon and Utah studies were too small to detect the risk from skin cancer that would have been predicted, on the basis of arsenic ingestion, from a linear model of the Taiwanese data.

The chronic ingestion of trivalent arsenic present in the medicinal preparation, Fowler's Solution, has been shown to be associated with the typical arsenic dermatopathology, including skin cancer. In one detailed study of patients with a history of Fowler's Solution use, 21 cases of skin cancer and 106 cases of hyperkeratoses were found among 262 subjects. Both the hyperkeratosis and skin cancer prevalence rates were found to increase as the total ingested amounts of the arsenical increased. The minimal latency period for hyperkeratosis was 2.5 years while the minimal latency period for skin cancer was 6 years, with an average of 14 years.

Internal neoplasms associated with arsenic exposure have been reported in subjects exposed to medicinal arsenic as well as in such occupational groups as vintners and smelter workers.

2.3.2.2.2 Experimental studies of arsenic carcinogenesis. Consistent demonstration of arsenic carcinogenicity in test animals, using different chemical forms, routes of exposure, and various experimental species, has not been observed. Part of the difficulty may lie in the selection of an appropriate animal model. The absence of skin cancers in the experimental animals used could be accounted for by their skin being poor models of human skin. Rat

results must be considered suspect because the rat is anomalous in how it metabolizes arsenic.

Recent data indicate that tumorigenicity and possibly carcinogenicity can be demonstrated in animals if the retention of arsenic in the lung is increased. The additional observations that calcium arsenate, as reported from two laboratories, is only slowly cleared from the lung, strongly suggest that this agent may be carcinogenic.

2.3.2.3 Chronic Neurological Effects of Arsenic Exposure--Both peripheral and central nervous system effects have been documented in man and animals exposed to inorganic arsenic.

Peripheral nervous system effects have been noted in workers occupationally exposed to arsenic and in individuals accidentally exposed to food contaminated with arsenic. Some of these effects follow an insidious course, appearing months or years after onset of exposure. Effects are of both the sensory and motor types, sensory deficits manifesting themselves first. The resulting polyneuropathies tend to follow a slow course of recovery over months or years. More subtle neurological effects, such as neuromuscular disturbances and altered nerve conduction velocity, have also been reported by various investigators.

While there are documented cases of central nervous system (CNS) effects in children due to acute or subacute exposure, chronic arsenic intoxication as a factor in such abnormalities as hearing impairment has not been confirmed.

Few useful animal models exist for the central and peripheral nervous system effects seen in humans. One study has reported evidence of CNS functional deficits in rats exposed to arsenic trioxide aerosol, while a second report claims impaired behavioral responses in rats given arsenic trioxide via stomach intubation. Since rats handle arsenic differently than all other species, the significance of these data is not clear.

2.3.2.4 Cardiovascular Effects of Arsenic Exposure--Cardiovascular effects associated with chronic arsenic intake include Blackfoot disease seen in Taiwanese consuming well water having elevated arsenic. This is a peripheral vascular disease leading to gangrene of the extremities. Since ergotamine-like compounds were also present in the waters, the conclusive role for arsenic is not clear. Peripheral vascular changes have been documented among German vintners who were exposed occupationally to arsenic pesticides as well as arsenic in wine.

2.3.2.5 Other Systemic Effects of Arsenic--Non-cancerous respiratory effects of inorganic arsenic are mainly seen with occupational exposure and with arsenic trioxide. In one study of smelter workers, those handling refined arsenic showed nasal septum perforation and rhinopharyngolaryngitis, while workers in roaster, furnace, and convertor areas showed tracheobronchitis and pulmonary insufficiency.

Teratogenic effects of arsenic compounds at relatively high exposure levels have been demonstrated in a number of animal species, including hamsters, rats, and mice. Generally, such effects have been observed after parenteral administration of either arsenite or arsenate. Oral exposures of animals to these same arsenic compounds at lower doses, by contrast, have not been shown to produce any notable effects on reproduction and development. Methylated arsenic, while potentially teratogenic at high doses, is of lower potency than inorganic forms. There is little evidence that inorganic arsenic is a human teratogen.

Hepatic effects have been noted in a number of studies dealing with chronic intake of arsenic. These disturbances present as cirrhosis and portal hypertension. One complicating factor in occupational exposure assessment has been the effect of alcohol consumption.

Chronic exposure to arsenic via well water contaminated by arsenic, medicinals, or the workplace, produces a reversible anemia. Rats, mice, and cats fed either arsenite or arsenate show reduced hemoglobin production via disturbance of the ALA-synthetase and heme-synthetase steps in the heme biosynthetic pathway.

Renal effects seen with arsenite or arsenate exposure in either man or animals have been poorly characterized.

2.3.3 Factors Affecting Arsenic Toxicity

The most widely recognized and studied interactive behavior of arsenic is with selenium, the pair being antagonistic in effect in all animal species studied. Dietary arsenic supplementation is known to protect against selenium toxicity, while selenium protects against either tri- or pentavalent arsenic. Arsenite shows a protective effect for selenite toxicity in cell cultures, but the reverse does not appear to be the case.

Few data exist for interactive relationships between arsenic and other elements. One report notes that cadmium and arsenic given simultaneously by the oral route retarded weight gain in young adult rats to a greater extent than either element given alone.

2.4 ARSENIC AS AN ESSENTIAL ELEMENT

Inorganic arsenic appears to be an essential element in certain animal species--rats, goats, chicks, and minipigs--based on the observation of detrimental effects using diets deficient in the element.

In rats, arsenic-deficient diets in pregnant dams are associated with slow growth, enlarged spleens, erythrocyte dysfunction in post-weaning offspring, and greater perinatal mortality.

In studies using goats and minipigs, diets having less than 50 ppb As produced effects in the adult animals as well as in their offspring. Morta-

lity of adult goats was increased as was the mortality of both kids and piglets. In chicks, arsenic deprivation influenced the effects of dietary arginine, manganese, and zinc, the fluctuations of which variously affected metabolic activity.

Remaining to be independently demonstrated are a physiological role for arsenic, the existence of any specific carrier in the body, or arsenic essentiality in man.

2.5 HUMAN HEALTH RISK ASSESSMENT FOR ARSENIC

This portion of the summary contains the data summarized earlier, presented within a perspective of the possible quantitative risk posed to the general population of the United States by arsenic exposure. Categories of consideration include: (1) levels of arsenic in media relevant to the U.S. population; (2) those effects relevant to the general population; (3) indicators of exposure, specifically "internal dose" measures; (4) dose-effect and dose-response relationships which can be determined from available information; and (5) the identification of groups within the general population who may be at increased risk for the health effects of arsenic.

2.5.1 Exposure Aspects of Arsenic

Arsenic exposure in the general population of the United States occurs via inhalation and ingestion of water and food.

Respiratory intake of arsenic on a daily basis is approximately 0.12 µg, of which 0.03 µg would be absorbed, assuming 30 percent absorption and based on a 1981 national average air value of 0.006 $\mu g/m^3$ of air and a daily ventilation rate of 20 m^3.

Since much of the U.S. drinking water supply is below the 10 µg/liter level, daily consumption of water at a rate of 2 liters would lead to an intake $\leq$ 20 µg.

Based on 1975-76 figures from the Food and Drug Administration, daily arsenic intake from food is approximately 50 μg (elemental arsenic) for adults. If one assumes at least 80 percent absorption of this daily intake, approximately 40 μg is the absorbed amount. It should be noted, however, that arsenic in certain foods is known to be in a chemically complex form that is relatively resistant to metabolism and toxicologically inert; consequently, it is rapidly excreted intact. Therefore, the amount of absorbed food arsenic considered to be toxicologically significant is relatively small compared to total arsenic intake.

Cigarette smoking contributes about 6 μg/pack of cigarettes in mainstream smoke, of which approximately 2.0 μg/pack would be absorbed.

Thus, the aggregate absorbed amount is approximately $\leq$ 60 μg for non-smokers. However, the actual amount of toxicologically significant arsenic taken in daily would probably be closer to 20 μg or less.

2.5.2 Effect/Response Aspects of Arsenic

2.5.2.1 Relevant Health Effects--General population concerns are with effects arising from long-term exposure to moderate levels of arsenic.

One can rank health effects germane to the general population as follows:

1. Respiratory tract cancer.
2. Skin cancer.
3. Non-cancerous skin lesions.
4. Peripheral neuropathological effects.
5. Cardiovascular changes.

Cancer of the respiratory system is clearly associated with exposure to arsenic via inhalation. This association has been especially noted among workers engaged in the production and usage of pesticides and among smelter workers. The latency period for lung cancer due to occupational arsenic exposure has been reported to range from 13 to 50 years.

Cancer of the skin has been found as a dose-dependent effect in a Taiwanese population with lifetime exposure to well water arsenic as well as among people who were treated with large doses of arsenite for skin disorders. Arsenic-associated skin cancers occur on areas of the body generally unexposed to the ultraviolet light of the sun, such as the palms of hands and soles of feet. The latency period for skin cancer has been reported to range from 6 to 50 years for cancers induced via administration of arsenical medicinals. In the Taiwanese drinking water study, the minimum latency period was reported to be about 24 years.

The Carcinogen Assessment Group (CAG) of the U.S. Environmental Protection Agency (EPA) has concluded that there is sufficient evidence that inorganic compounds of arsenic are both lung and skin carcinogens in humans.

Hyperkeratosis and hyperpigmentation, sometimes with precancerous changes, have been a common finding in persons ingesting arsenic. These skin lesions, like the manifest cancer, develop on surfaces usually unexposed to sunlight.

Peripheral nervous system effects range from sensory-motor deficits with higher exposure to changes in electromyography and nerve conduction velocity at long-term, low levels of contact with arsenic.

Vascular effects, such as Blackfoot disease (peripheral vasculopathy) have been noted in a Taiwanese population having life-long arsenic exposure; however, these effects may have been confounded by the presence of ergotamine-like compounds. Peripheral vascular changes have also been found in German vintners exposed occupationally to arsenic pesticides as well as arsenic in wine.

2.5.2.2 Dose-Effect/Dose-Response Relationships--The general question of how to define and employ a dose factor in attempts at quantitative assessments of human health risk for any toxicant is highly dependent upon: 1) the available

information on the body's ability to metabolize the agent, and 2) the assessment of the relative utility of various internal indices of exposure.

The time period over which a given total intake occurs is highly important. For example, intake of one gram of arsenic over a period of years would be quite different pathophysiologically from assimilating this amount at one time, the latter probably having a lethal outcome. This time-dependent behavior is related in part to the relative ability of the body to detoxify inorganic arsenic by methylation as a function of both dose and time.

In cases of acute and sub-acute exposure, indicators of internal exposures, such as blood or urine arsenic levels, are probably appropriate for assessing the intensity of exposure.

With chronic low-level exposure, however, the available data would indicate that the total amount assimilated is probably more important than an indicator concentration without knowledge of the total exposure period. An added problem is the background level of arsenic found in some indicators due to dietary habit. Therefore, in low-level chronic exposures, arsenic levels in blood or urine would only be moderately increased over background levels. Hair arsenic levels cannot be employed as reliable indicators of exposure because no methods exist for distinguishing external contamination levels from those accumulated via absorption and metabolic distribution.

Given the above limitations concerning the use of blood, urinary or hair arsenic concentrations as internal indices of cumulative, long-term low-level arsenic exposure, the dose-effect/dose-response relationships summarized below are done so mainly in terms of external arsenic exposure levels via either inhalation or ingestion.

From available data, the Carcinogen Assessment Group (CAG) has estimated carcinogenic unit risks for both air and water exposures to arsenic. The

quantitative aspect of carcinogen risk assessment is included here because it may be of use in setting regulatory priorities, evaluating the adequacy of technology-based controls, and other aspects of the regulatory decision-making process. However, the imprecision of presently available technology for estimating cancer risks to humans at low levels of exposure should be recognized. At best, the linear extrapolation model used (see Section 7.3) provides a rough but plausible estimate of the upper limit of risk--that is, with this model it is not likely that the true risk would be much more than the estimated risk, but it could be considerably lower. The risk estimates presented below should not be regarded, therefore, as accurate representations of true cancer risks even when the exposures involved are accurately defined. The estimates presented may, however, be factored into regulatory decisions to the extent that the concept of upper-risk limits is found to be useful.

The air estimates were based on data obtained in five separate studies involving three independently exposed worker populations. Linear and quadratic response models in both the absolute and relative form were fitted to the worker data. It was found that for the models that fit the data at the $p = 0.01$ or better level, the corresponding unit risk estimates ranged from 1.05×10^{-4} to 1.36×10^{-2}. However, linear models were found to fit better than quadratic models and absolute models fit better than relative models. The CAG also felt that exposure to trivalent arsenic was more representative of low environmental exposure than pentavalent arsenic. Restricting their unit risk estimates to those obtained from linear absolute models where exposure was to trivalent arsenic gave a range of 1.25×10^{-3} to 7.6×10^{-3}. A weighted average of the five estimates in this range gave a composite estimate of 4.29×10^{-3}.

The unit risk estimates for water were based on an extensive drinking water study which was conducted in a rural area of Taiwan. An association between arsenic in well water and skin cancer was observed in the study population. Using the male population, who appeared to be more susceptible, the CAG estimated that the unit risk associated with drinking water contaminated with 1 μg/ℓ of arsenic was 4.3×10^{-4}.

To compare the air and water unit risks, the CAG converted the exposure units in both cases to mg/kg/day absorbed doses, which resulted in unit risk estimates of 50.1 and 15.0, respectively.

The potency of arsenic compared to other carcinogens was evaluated by noting that an arsenic potency of $2.25 \times 10^{+3}$ $(\text{mMol/kg/day})^{-1}$ lies in the first quartile of the 52 suspect carcinogens that have been evaluated by the CAG.

The U.S. EPA is presently examining information from studies on both patient and general populations which have been exposed to arsenic via medicinals or drinking water, respectively, in order to determine whether quantitative dose-response relationships can be established for non-cancerous skin lesions.

While the qualitative evidence for peripheral neurological effects and cardiovascular changes in arsenic-exposed populations is well established, the data are insufficient for determining quantitative dose-response relationships at the present time.

2.5.3 Populations at Special Risk to Health Effects of Arsenic

From a Japanese study, which reported on the poisoning of children exposed to arsenic in infant milk formula, young children may be considered at risk for acute exposure to arsenic. From the clinical reports published at the time of the mass poisoning, as well as those from follow-up studies, a

number of signs of central nervous system involvement were noted at both the time of the episode and much later, with the follow-up studies showing behavioral problems, abnormal brain wave patterns, marked cognitive deficits, and severe hearing loss.

Because children consume more water per unit body weight than do adults, the daily intake of arsenic via drinking water per kilogram body weight would be greater in children. This might have implications regarding chronic exposure effects in children. However, it should be noted that serious health effects due to chronic exposure of arsenic in drinking water have not been found at a greater frequency in children than adults.

Individuals residing in the vicinity of certain arsenic-emitting sources, e.g., certain types of smelters, may be at risk for increased arsenic intake because of both direct exposure to arsenic in air and indirect exposure via arsenic secondarily deposited from air onto soil or other human exposure media. The relative contribution from such indirect exposures to increased risk would be difficult to define, however.

A less defined group at risk would be cigarette smokers due to some arsenic in tobacco, but it is not clear just what the quantitative increase in risk would be.

3. BACKGROUND INFORMATION

3.1 CHEMICAL/PHYSICOCHEMICAL ASPECTS

Compounds of arsenic in various chemical forms have most prominently figured in the extensive history of the toxicology of the element. The physical properties for several of these compounds are presented in Table 3-1. In contrast, the element in the metallic, zero-valent form is of minor toxicological interest.

Geochemically, arsenic is encountered as a component of sulfidic ores, occurring as the arsenides and diarsenides of metals such as nickel, cobalt, and copper, and is present in rocks and soils at trace levels. Smelting of commercially important metal ores, therefore, often has associated with it the release into the environment of significant quantities of certain arsenic compounds. For example, arsenic trioxide, As_2O_3, a major form of the element in terms of its toxicological history, is a smelter product arising from air roasting of metallic arsenides or arsenic-containing sulfides.

Arsenic trioxide, white arsenic, is only slightly soluble in water and other solvents which do not promote chemical transformation. Its solubility in solvents which mimic physiological media may not necessarily be the same as for simple solvents, e.g., gastric juice versus water. Arsenic trioxide sublimes, the process becoming pronounced at 135°C. This property appears to have been overlooked through the years in considering analytical methods for measuring levels of the compound. Dissolution of the trioxide in aqueous media leads to formation of arsenous acid, H_3AsO_3, while alkaline treatment leads to formation of the arsenite ion, $AsO(OH)^-_2$, with both the acid and the salt being freely soluble in a number of solvents.

TABLE 3-1. PHYSICAL PROPERTIES OF ARSENIC AND ARSENIC COMPOUNDS

Chemical name	Atomic/ molecular weight	Melting point (°C)	Boiling point (°C)	Density (g/cm^3)	Crystal system	CAS Number
Arsanilic acid	217.07	232	---	1.9571^{20}	monoclinic needles from water or ethanol	98-50-0
Arsenic	74.92	817 (28 atm) (triple-point)	613 (sublimes)	5.727^{14}	hexagonal, rhombic	7440-38-2
Arsenic pentoxide	229.84	315 (dec.)	---	4.32	amorphous	1303-28-2
Arsenic sulphide	246.04	300	707	3.43	yellow or red monoclinic needles (change from yellow to red at ~170°C)	1303-33-9
Arsenic trioxide[a]	197.84	312.3	465	3.738	amorphous or vitreous	1327-53-3
Arsine	77.95	-113.5	-55 (dec. 230)	2.695 (gas)[b] 1.689^{849} (liq.)	colourless gas	7784-42-1
Calcium arsenate	398.08	---	---	3.62	amorphic powder	7778-44-1
Dimethylarsinic acid	138.00	200	---	---	prism	75-60-5
Lead arsenate	347.12	720 (dec.)	---	5.79	monoclinic leaves	7784-40-9
Methanearsonic acid, disodium salt	183.9	132-139	---	---	crystalline	144-21-8
Methanearsonic acid, monosodium salt	161.9	115-119	---	---	crystalline	2163-80-6
Potassium arsenate	180.04	288	---	2.867	tetrahedral	7784-41-0
Potassium arsenite	254.8	---	---	---	powder	13464-35-2
Sodium arsenate dodecahydrate	423.93	86.6	---	1.752-1.804	trigonal or hexagonal prism	7631-89-2
Sodium arsenite	129.91	---	---	1.87	powder	7784-46-5
Sodium cacodylate	159.98		200	---	crystalline	124-65-2

[a]Vapour pressure 0.653 (200°C)

[b]Specific gravity (air = 1)

Source: Adapted from International Agency for Research on Cancer (1980).

Arsenic pentoxide, As_2O_5, may be readily prepared by nitric acid oxidation of elemental arsenic or the trioxide. Compared to the trioxide, the pentoxide has considerable solubility in water (63.0 g/100 g water), presumably dissolving to form the relatively strong arsenic acid, H_3AsO_4. In acid media, arsenic acid has oxidizing potential (E^o=0.56V).

The relative stability of solutions of arsenic or arsenous acids to oxidation-reduction is of considerable importance in terms of valency-dependent arsenic toxicity. In oxygenated media, one would expect the pentavalent form to dominate, while reducing media would favor the trivalent state.

Arsenous and arsenic acids both form mono-, di- and tri-metal salts, the alkali-metal salts such as potassium and sodium arsenite being freely soluble in water and the alkaline salts such as calcium or magnesium arsenite being slightly soluble.

While tri-organic esters of the tri- and pentavalent arsenic acids are known, they are labile to hydrolysis and one would expect the mono- and di-organic derivatives to be even more so. This behavior has implications in the postulated role of arsenate ions in interfering with phosphorylation reactions.

Arsine (arsenic trihydride, AsH_3) is a strong hemolytic toxicant and probably the most poisonous of the arsenicals. Although generally a minor factor in the environmental chemistry of arsenicals, it can form under certain restricted conditions, i.e., via reduction in the presence of an active hydrogen-generating source.

Monomethyl and dimethyl arsenic, in the form of methylarsonous and methyl arsonic, dimethylarsinous and dimethylarsinic (cacodylic) acids, occur both in the environment and are formed via <u>in vivo</u> transformation in many mammalian

species, including man. Such organic arsenic compounds are also of commercial significance. For instance, both methylarsonic and dimethylarsinic acids, usually in the form of the mono- or dialkali salts, are employed as herbicides which, when released into the environment, may undergo reduction to the corresponding labile arsine compounds, CH_3AsH_2 (methylarsine) and $(CH_3)_2$ AsH (dimethylarsine) (Arsenic. NAS, 1977). Like trivalent inorganic arsenic, methylarsonous acid can interact with thiol groups (as can cacodylic acid) to form the CH_3-As(-S-)$_2$ and $(CH_3)_2$-As-S groups, respectively. The physical forms of arsenic in the environment depend on its mode of emission and subsequent interactions with other materials.

Arsenic, along with other trace metals, can be mobilized in association with airborne particles derived from high-temperature sources such as fossil-fueled power plants, metallurgical smelters and blast furnaces.

Arsenic compounds form insoluble complexes with soils and sediments. With soils, the interaction involves clay surfaces containing amorphous aluminum or iron oxides (Woolson, 1976).

3.2 ENVIRONMENTAL CYCLING OF ARSENIC

Inorganic arsenic is released into the environment from a number of anthropogenic sources which include primary copper, zinc and lead smelters, glass manufacturers (specifically those that add arsenic to the raw materials) and arsenic chemical manufacturers. Figure 3-1 presents a generalized scheme for the geochemical cycling of arsenic through various compartments of the environment. The atmosphere is a major conduit for arsenic emitted from anthropogenic sources to the balance of the cycle via wet and dry precipitation processes. The rate of movement of arsenic from the atmosphere is not known at present.

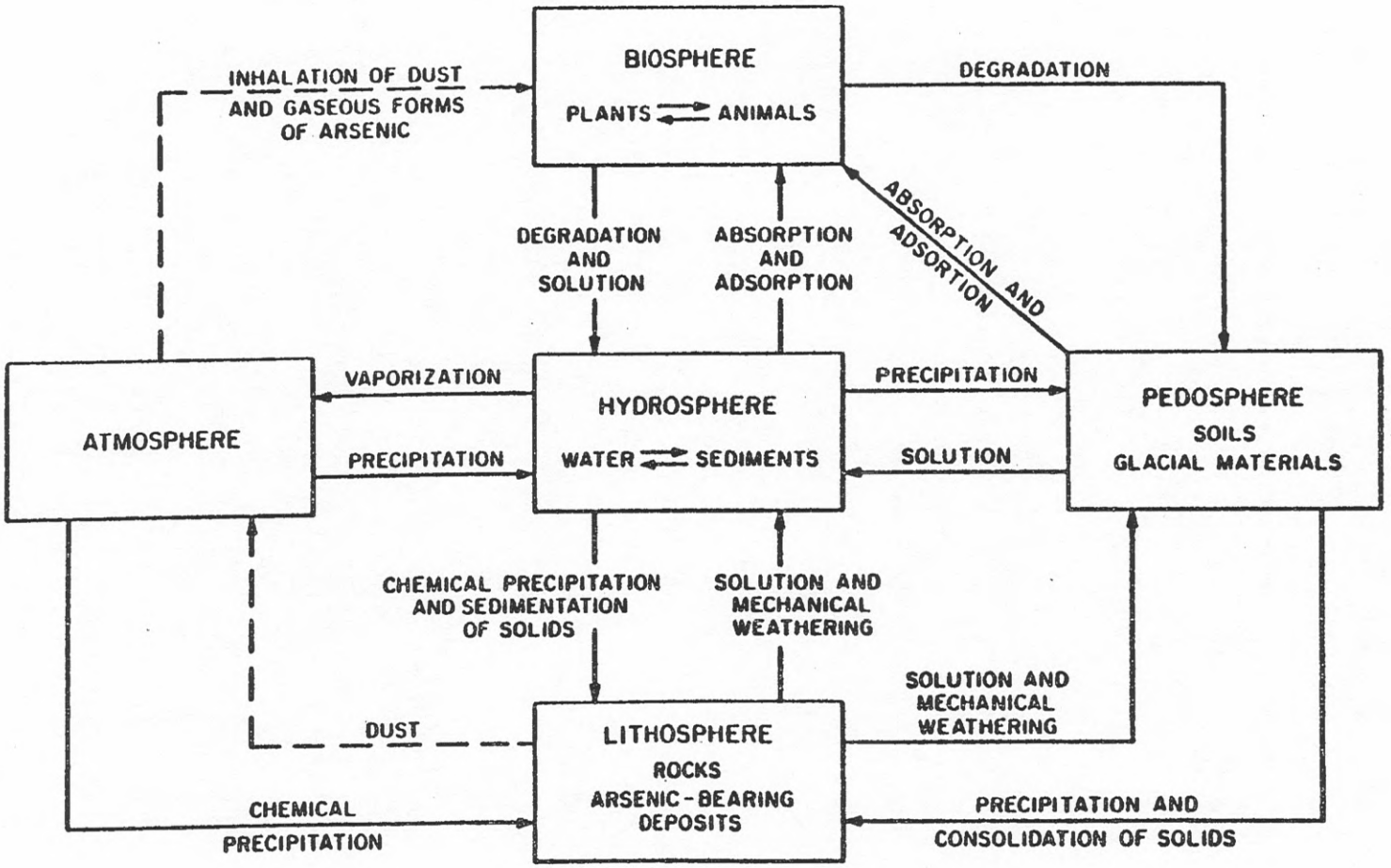

Figure 3-1. The generalized geochemical cycle for arsenic.

Source: Union Carbide (1977).

Dry and wet fall onto soils may be followed by movement through soils either into ground water or surface water. Passage of arsenic into surface waters may then be followed by further transfer to sediments.

Complicating an understanding of the environmental cycling of arsenic is the existence of chemical and biochemical transformations which occur within the cycle.

Trivalent arsenic in the atmosphere can undergo oxidation to the pentavalent state. Such conversion can also occur in aerated surface waters. On the other hand, pentavalent arsenic in an aqueous medium which is somewhat acidic is an oxidant, and, in the presence of oxidizable material, it will react to form trivalent arsenic (NAS, 1977).

One hypothesis of the biological cycling of arsenic is presented in a generalized scheme set forth in Figure 3-2. In this scheme, Wood (1974) proposes that sedimentary bacteria reduce arsenate to arsenite, which in turn may be altered to form methyl- and dimethyloxy arsenicals. Further action of bacteria and molds transforms these intermediates to di-and tri-methyl arsine. These volatile products pass into the hydrosphere and then into the atmosphere, where oxidative transformation to dimethyl-arsinic acid and, further, to inorganic arsenic occurs.

More recent reports by Andreae and co-workers (Andreae and Klumpp, 1979; Andreae, 1979; 1980; 1983) dispute this hypothesis with respect to marine environments. In analyses performed by Andreae and other workers, no volatile organoarsenic compounds were found to be formed in seawater, negating the hypothesis suggesting that reductive biomethylation resulting in volatile compounds serves as a contributing source to the atmospheric cycling of arsenic.

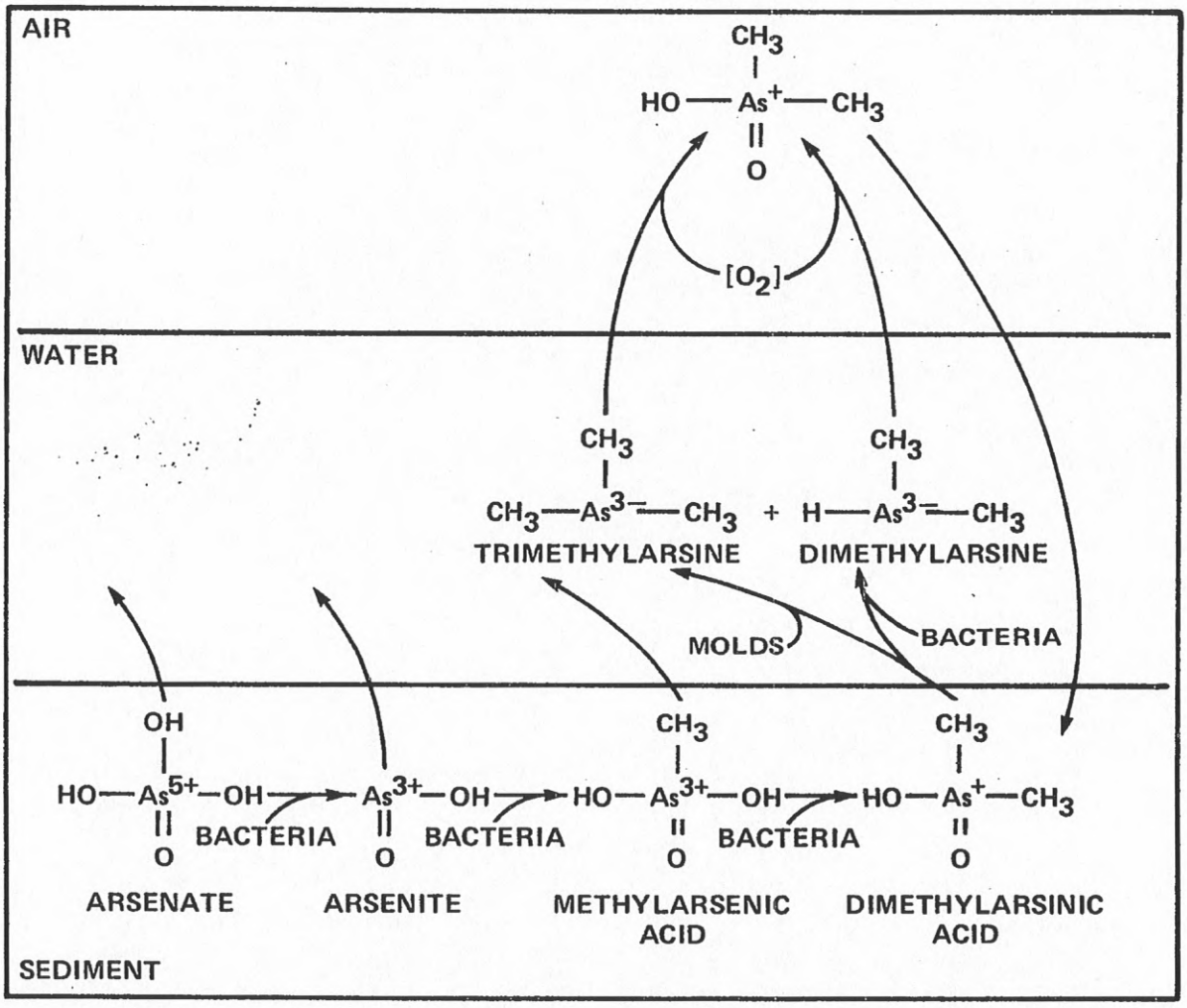

Figure 3-2. The proposed biological cycle for arsenic.

Source: Wood (1974)

While the authors did note the occurrence of biomethylation, the observed products were non-volatile, water-soluble methylated oxoacids of low toxicity. Further, the site of biotransformation was reported to be planktonic algae residing in the photic zone, rather than sedimentary bacteria. Similarly, the authors noted that methylated species were not found in a number of rain samples collected along the Pacific coast between 1976-1978. Such species would be expected if significant ocean-to-atmosphere transfer by biomethylation reactions was occurring. Andreae suggested that a global mass balance could be constructed for the atmospheric arsenic cycle which derived its major input from anthropogenic, rather than biogenic, sources.

Reduction and methylation of inorganic arsenic occur only to a limited extent in soils, 1-2 percent over a period of months having been reported in one study (Woolson, 1976).

In terms of the relative amounts of arsenic partitioned among the various environmental compartments, Suta (1980) has calculated that land is the major sink for arsenic, accounting for approximately 90 percent of the dissipation for the year 1974. The atmosphere accounts for 7-8 percent dissipation with the least quantity appearing in waterborne effluents.

3.3 LEVELS OF ARSENIC IN VARIOUS MEDIA

As was noted in the previous section, geochemical and biological cycling mechanisms contribute to arsenic burden in various media. Such burdening of a given medium is augmented from specific sources, e.g., agro chemicals containing arsenic applied to agricultural lands.

Available information on the arsenic content of media with which man interacts is generally in the form of total amounts of the element, with limited data available for assessing specific chemical forms. Since the toxicity of arsenicals varies with chemical form, any supporting data for determining chemical states will be discussed in this report, however fragmentary.

3.3.1 Levels of Arsenic in Ambient Air

The most comprehensive data for ambient air levels of arsenic in the U.S. are those of the National Air Sampling Network conducted by the U.S. EPA. Measurements from this network are summarized in Table 3-2. All values were determined from nuclear activation analysis of individual 24-hour high volume particulate samples. As shown in Table 3-2, the number of observations available is considerably different from year to year. This is due to changes in the participation of state and local agencies operating the individual sites and, for the year 1981, only about half the samples collected have been analyzed and reported into the network data base at this time. Thus, direct comparison of the summary statistics from year to year may be of limited utility.

A closer examination of the NASN data by site indicates that in areas not influenced by copper smelters, maximum 24-hour concentrations do not exceed 0.1 $\mu g/m^3$. There are only two exceptions of approximately 600 site/years represented in the table where there were observations above 0.1 $\mu g/m^3$--Omaha, Nebraska, and Charleston, West Virginia. The site in Charleston ceased operation after 1978; therefore, it is difficult to interpret the single value above 0.1 $\mu g/m^3$. Repeated observations above 0.1 $\mu g/m^3$ have occurred at the site in Omaha, Nebraska.

Using the NASN data base, U.S. annual arithmetic mean arsenic concentrations are plotted in Figure 3-3. The plot suggests considerable variability over the five-year period with no clear direction of trend. Perhaps the most striking feature in the data is the relatively low annual arsenic level observed in 1980. A partial explanation for this observation may be the strike which idled most of the nation's copper smelters from June through September of 1980 (Eldred et al., 1983).

TABLE 3-2. CUMULATIVE FREQUENCY DISTRIBUTION OF NASN INDIVIDUAL 24-HOUR AMBIENT AIR ARSENIC LEVELS

Year	Minimum Detection Limit	Number of Observations	Percentile[a]				Arithmetic	
			30	50	70	99	Mean	(SD)
1977	.004	5385	0	0	.004	.048	.0049	.0165
1978	.006	1679	.006	.006	.008	.075	.0109	.0253
1979	.005	1263	.005	.005	.005	.077	.0091	.0192
1980	.007	2934	0	0	0	.037	.0026	.0113
1981	.007	688	0	0	0	.058	.0059	.0275

[a]Percentile values indicate the percentage of stations below the given air level. Values in $\mu g/m^3$.

Source: National Arsenic Data Base, OAQPS/OANR, U.S. Environmental Protection Agency (Akland, 1983).

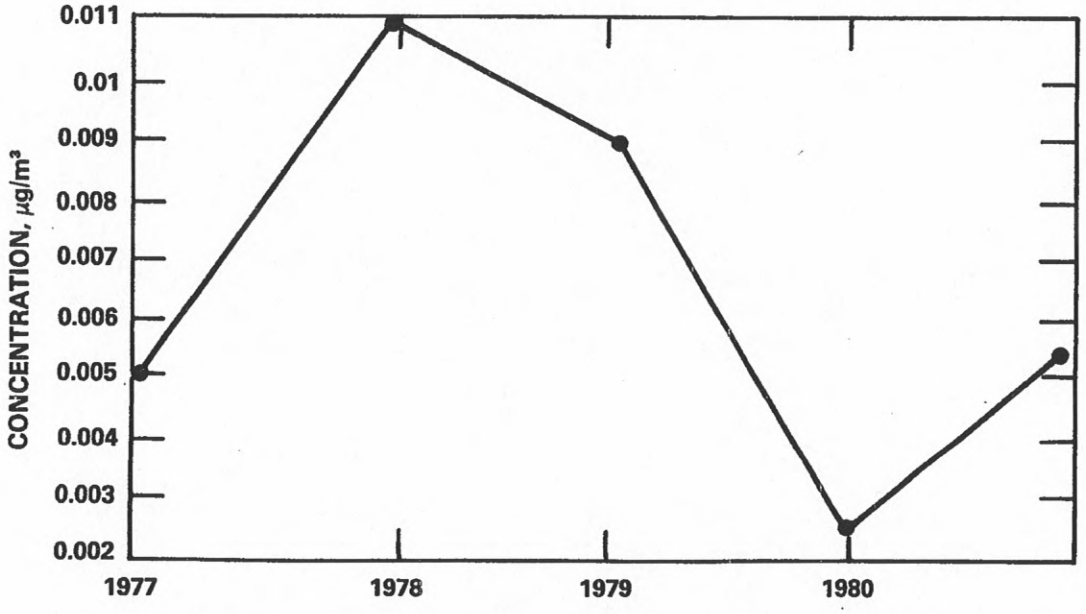

Figure 3-3. NASN annual average arsenic concentrations.

Source: National Atmospheric Data Base, OAQPS/OANR, U.S. Environmental Protection Agency (Akland, 1983).

The locations of these primary copper smelters in the U.S. are listed in Table 3-3. Examination of the NASN data by individual sites shows that the highest arsenic levels are consistently recorded in areas of Arizona, Montana, Tennessee, Texas, and Washington, which are impacted by the copper smelting industry. Thus, the closure of many of these plants for a substantial period in 1980 may have had the effect of depressing the nationwide average concentration of arsenic in ambient air for that year. Unfortunately, the possible effect of the 1980 copper smelter strike cannot explain the low arsenic levels observed in that year nationwide. Even urban areas in the Northeast, which would not be affected, exhibited lowered concentrations and the possibility that the analytical methodology may have systematically affected results cannot be ruled out.

Several factors of importance in assessing these data concern the partitioning of arsenic between particulate-bound fractions and vapor material as well as the lability of arsenic on air sampling filters. Non-particulate arsenic would chiefly be a problem in the immediate area of smelter emissions, adhesion to particulates increasing with residence time and distance from the emission source. Thompson (1976) has noted that all of the arsenic in the air in regions of smelters is adhered to particulates when sampled 2-3 kilometers from the operation. Lao et al. (1974) have cautioned about the hazard of arsenic loss, chiefly as the trioxide, from samplers at levels of 1.0 microgram or less. Walsh et al. (1977a), however, could not remobilize particulate arsenic once trapped in samplers. Whatever the hazard, the NASN values are internally consistent, remote areas having the lowest values and regions of smelter operations having the highest levels.

An important consideration in assessing the significance of air exposure of arsenic to health risk is the chemical form or forms of arsenic in the

TABLE 3-3. PRIMARY COPPER SMELTERS IN THE UNITED STATES

	Location	Company
1.	Anaconda, Montana	Anaconda Company
2.	Tacoma, Washington	Asarco, Inc.
3.	Garfield, Utah	Kennecott Copper Corp.
4.	El Paso, Texas	Asarco, Inc.
5.	McGill, Nevada	Kennecott Copper Corp.
6.	Hidalgo, New Mexico	Phelps Dodge Corp.
7.	Hurley, New Mexico	Kennecott Copper Corp.
8.	Hayden, Arizona	Kennecott Copper Corp.
9.	Hayden, Arizona	Asarco, Inc.
10.	Miami, Arizona	Inspiration Consolidated Copper Corp.
11.	Morenci, Arizona	Phelps Dodge Corp.
12.	Ajo, Arizona	Phelps Dodge Corp.
13.	Douglas, Arizona	Phelps Dodge Corp.
14.	San Manuel, Arizona	Magma Copper Company
15.	Copper Hill, Tennessee	Cities Services Company
16.	White Pine, Michigan	Copper Range Company

Source: National Arsenic Data Base, OAQPS/OANR, U.S. Environmental Protection Agency (Akland, 1983).

ambient air of the United States. Work by Johnson and Braman (1975), as well as that of Attrep and Anirudhan (1977), indicates that methylated arsenic, possibly in significant amounts, has been found in air samples, but its presence can likely be ascribed to either biotic activity or the use of methylated arsenics as herbicides. This is not in total agreement with Andreae (1983), who suggests that methylated atmospheric arsenic is due predominantly to anthropogenic sources, based upon his studies of marine environments. Methylated forms become a minor factor in suburban and urban areas.

It is not clear from the available data what forms of inorganic arsenic are in most air samples: trivalent, pentavalent or mixtures of these two oxidation forms. Crecelius (1974) found that rain water samples for an urban area of the western U.S. contained only about one-third (35 percent) trivalent arsenic. In a study conducted at various sites along the Pacific coast, Andreae (1980) observed wide variations in the ratio of arsenite to arsenate in rain. He attributed this variability to emissions of predominantly pentavalent arsenic from the sea surface and trivalent arsenic from industrial emissions (particularly those from a copper smelter in the Northwest), and by redox reactions during the residence of arsenic in atmospheric particulates and hydrometeors. Caution should be exercised, however, in interpreting any extrapolations from washout samples to original air composition, given the lability of inorganic arsenic to oxidize or reduce depending on aeration, acidity of the rain sample, and presence of oxidizable matter.

In summary, then, one can assume that methylated arsenic is of minor concern in suburban and urban/industrial air samples, and that the major inorganic portion is a variable mixture of the trivalent and pentavalent forms.

3.3.2 Levels of Arsenic in Drinking Water

The National Interim Primary Drinking Water Regulations, promulgated under the Safe Drinking Water Act, set the Maximum Contaminant Level (MCL) for arsenic in U.S. public water supplies at 50 µg/l (40 CFR Part 141). EPA is currently reviewing the arsenic MCL as part of its program to promulgate National Revised Primary Drinking Water Regulations (EPA, 1983).

In general, arsenic is not found in drinking water at levels exceeding the MCL. The Community Water Supply Survey conducted in 1969 found only 2 of the 969 supplies examined (0.2 percent) with levels exceeding 50 µg/l (McCabe et al., 1970). More recently, the Rural Water Survey conducted in 1978 reported that 0.8 percent of rural households exceeded the 50 µg/l level. Small rural communities showed a much higher population (6.6 percent) of households exceeding 50 µg/l than large rural communities (0.0 percent) and other rural areas (0.4 percent). The proportion of households exceeding 50 µg/l was greatest in the West (2.1 percent) and North Central (1.8 percent); none were found to exceed 50 µg/l in the Northeast or South (Francis et al., 1982). Compliance monitoring of public water supplies as required by the current drinking water regulations has revealed that approximately 100 of the nation's 60,000 public water supplies (0.2 percent) have levels exceeding the current MCL (Wentworth, 1983).

Notable exceptions to the generally favorable picture for U.S. population exposure to drinking water arsenic are isolated well water sources associated with geochemical enrichment by arsenic found mainly in the western U.S. and Alaska (Arsenic. NAS, 1977; Whanger et al., 1977; Harrington et al., 1978; Southwick et al., 1981). Whanger et al. (1977) have noted that well water arsenic levels in Lane County, Oregon, have ranged up to 2.2 ppm (one well) with levels generally increasing with well depth. Harrington et al. (1978) also noted that an area of Fairbanks, Alaska, had well water levels

ranging as high as 10 ppm, representing geochemical input as well as contamination by residues from prior gold-mining activity. Southwick et al. (1981) reported levels ranging from 0.18-0.27 ppm in desert communities in Utah.

As with arsenic in air, it is important to take into account available information regarding the chemical forms of arsenic in the potable water supplies. It is reasonable to assume that the chief form of arsenic in most municipal water supplies, particularly surface reservoirs, would be pentavalent arsenic due to aeration and chlorination. Similarly, the major forms of arsenic in well waters relatively enriched in arsenic have been analyzed and also appear to be predominantly in the pentavalent inorganic state (Whanger et al., 1977; Harrington et al., 1978; Southwick et al., 1981). The chemical character of arsenic-rich well water in the U.S. versus other regions of the world will be taken up elsewhere.

3.3.3 Arsenic in Food

Perhaps the most useful body of data for assessment of the contribution of food arsenic to the total exposure picture in the U.S. is the recent survey carried out from August 1975 to July 1976 by the U.S. Food and Drug Administration (Johnson et al., 1981a,b). In Table 3-4 are summarized the average arsenic levels in various adult food classes for the period noted above; values are expressed analytically as arsenic trioxide. Corresponding average arsenic levels in food classes of 6-month-old infants and 2-year-old toddlers are summarized in Table 3-5.

In comparing the mean levels in comparable food categories, it appears that for children and adults, meat, fish, and poultry constitute the greatest dietary source of arsenic. Within this category, shellfish and other marine foods contain the highest levels of arsenic (Jelenik and Corneliussen, 1977). For infants, grain and cereal products constitute the only known source of arsenic intake from the categories measured.

TABLE 3-4. LEVELS OF ARSENIC (As_2O_3) BY FOOD CLASS IN ADULT FOOD COMPOSITES FROM 20 U.S. CITIES (AUGUST, 1975 - JULY, 1976)

Food Class Composite	No. of Positive Composites	As, ppm Mean (Range)
Dairy products	1	0.004(0.08)[a]
Meat, fish and poultry	17	0.19(0.03-0.46)
Grain and cereal products	8	0.02(0.03-0.10)
Potatoes	ND[b]	----
Leafy vegetables	ND	----
Legume vegetables	1	0.004(0.07)
Root vegetables	1	0.004(0.07)
Garden fruits	1	0.005(0.10)
Fruits	ND	----
Oils, fats and shortening	1	0.002(0.04)
Sugar and adjuncts	ND	----
Beverages (including drinking water)	1	0.008(0.15)

[a]Mean values are based on 20 composites for every food class.

[b]ND = not detected

Source: Adapted from Johnson et al. (1981a).

TABLE 3-5. LEVELS OF ARSENIC (As_2O_3) BY FOOD CLASS IN INFANT AND TODDLER FOOD COMPOSITES FROM 10 U.S. CITIES (AUGUST, 1975 - JULY, 1976)

Food Class Composite	No. of Positive Composites	As, ppm Mean (Range)	
		Infant	Toddler
Water	ND[a]	----	----
Whole milk, fresh	ND	----	----
Other dairy and substitutions	ND	----	----
Meat, fish and poultry	ND(I) 7(T)	----	0.092 (0.06-0.29)[b]
Grain and cereal products	3(I) 2(T)	0.018(0.04-0.09)	0.008(0.03-0.05)
Potatoes	ND	----	----
Vegetables	ND	----	----
Fruits and fruit juices	ND	----	----
Oils and fats	ND(I) 1(T)	----	0.003(0.03)
Sugar and adjuncts	ND(I) 1(T)	----	0.004(0.04)
Beverages	ND	----	----

[a]ND = not detected

[b]Mean values are based on 10 composites for every food class.

Source: Adapted from Johnson et al. (1981a).

Johnson et al. (1981a) have calculated that the total adult daily intake of arsenic (as As_2O_3) for August 1975 to July 1976 was approximately 65 µg. (Corresponding elemental content can be obtained by multiplying by 0.75. Thus, the intake of elemental arsenic would be 50 µg.) This represents an increase over the 1974 value of 21 µg reported by Jelenik and Corneliussen (1977). Differences in the two years can primarily be accounted for by increases in the arsenic content of meat, fish, and poultry; grains and cereal products; beverages; and dairy products. Johnson et al. (1981a) did not discuss whether the apparent increase in arsenic levels in certain categories represented a trend or merely reflected analytical variation from year to year. It should be noted, however, that arsenic mean levels in all food categories generally declined over the years 1967-1974. Therefore, data collected over the past few years (1977-present) but, as yet, unanalyzed, should be closely examined in order to determine whether the increases seen in 1975-1976 have actually constituted the beginning of a new trend.

In no other medium is the issue of chemical forms of arsenic more complex and simultaneously more important than in food, given the fact that the diet is a major, if not the main, source of arsenic for most of the U.S. population. As will be pointed out in a later section, arsenic in crustaceans and other marine life is present in the form of various chemically complex organoarsenicals, which appear to be not only resistant to metabolism but are rapidly excreted intact. Comparatively speaking, then, these forms are regarded as being toxicologically inert.

3.3.4 Arsenic in Soils

Soil arsenic levels are mainly of concern in this section to the extent that arsenic mobility and transformation in this medium allow for passage of the element to ground water, air and the food chain (via plant uptake). This

area has been reviewed in some detail (Arsenic. NAS, 1977; Woolson, 1977; Walsh et al., 1977b).

Background levels of arsenic in soils range from less than 1 ppm to above 40 ppm, and the relative enrichment of this background level with agricultural practices is secondary to fallout from air in the regions of industrial activity and can be of the order of 100 times. In Table 3-6 are listed some comparative values for uncontaminated soils versus soils contaminated by the repeated use of defoliants and insecticides containing arsenic (Walsh and Keeney, 1975).

Arsenic in soils is usually bound to clay surfaces containing amorphous aluminum or iron oxides, the degree of immobilization (adsorption) being a function of soil type, soil pH, phosphate levels, levels of iron or aluminum as well as residence in soil. Soil-adsorbed arsenic is rather inert to transformation or movement and it is the soluble fraction which is of interest, usually in the pentavalent form. Pentavalent arsenic arises from both soil aeration and degradation of methylated arsenic herbicides. Little reductive methylation of arsenic occurs in typical soils compared to sediments, Woolson (1976) observing that only 1-2 percent conversion of arsenate occurred over a period of months.

Transfer of soil arsenic to plants entails the soluble, labile fraction of arsenic and the site of uptake is the root system where highest levels are found. Edible portions of most food plant classes are low. This is also the case for terrestrial flora, but marine plant life such as algae accumulates considerable levels of arsenic (Irgolic et al., 1977).

3.3.5 Other Sources of Arsenic

Small and McCants (1962) found an average of 1.5 ppm arsenic in tobacco residues taken from U.S. tobacco grown in soils having average arsenic levels

TABLE 3-6. A COMPARISON OF ARSENIC LEVELS IN ARSENIC-TREATED AND UNCONTAMINATED SOILS IN NORTH AMERICA

Sampling site	Total As content, ppm: uncontaminated soil	Total As content, ppm: treated soil[a]	Crop
Colorado	1.3 - 2.3	13 - 69	Orchard
Florida	8	18 - 28	Potato
Idaho	0 - 10	138-204	Orchard
Indiana	2 - 4	56 - 250	Orchard
Maine	9	10 - 40	Blueberry
Maryland	19 - 41	21 - 238	Orchard
New Jersey	10.0	92 - 270	Orchard
New York	3 - 12	90 - 625	Orchard
North Carolina	4	1 - 5	Tobacco
Nova Scotia	0 - 7.9	10 - 124	Orchard
Ontario	1.1 - 8.6	10 - 121	Orchard
Oregon	2.9 - 14.0	17 - 439	Orchard
	3 - 32	4 - 103	Orchard
Washington	6 - 13	106 - 830	Orchard
	8 - 80	106 - 2553	Orchard
	4 - 13	48	Orchard
Wisconsin	2.2	6 - 26	Potato

[a]These are results from soils that had been repeatedly treated with an As pesticide or defoliant. Soils treated experimentally are not included.

Source: Walsh and Keeney (1975).

of 3 ppm. Of the total arsenic content of cigarette tobacco, 10-15 percent is in mainstream smoke (Thomas and Collier, 1945) in an unidentified form. In the past, levels of up to 40 ppm arsenic were detected in U.S. cigarettes (Holland and Acevedo, 1966) owing to arsenical use as pesticides. Lower current levels probably reflect curtailed use of arsenic as a pesticide in tobacco growing.

While current levels of arsenic may be lower in tobacco than had been the case, past exposure of cigarette smokers remains a health factor in considering respiratory cancer risk, given the long clinical induction period (decades) for this health effect (see Chapter 7).

4. ARSENIC METABOLISM

4.1 ROUTES OF ARSENIC ABSORPTION

The significance of various routes of arsenical intake for man and various other animal species is dependent upon the physical and chemical form of the arsenical, the mode of exposure, and the animal species under study. The major routes that are of significance to general public health are inhalation and ingestion, either via direct intake of food and water or secondary intake via the inhalation of arsenic in a form and size where it is eventually swallowed. Inhalation is probably of more significance in occupational settings, while oral intake is the major exposure route for the population at large.

Percutaneous absorption of arsenic, while poorly studied, appears to be a relatively minor route of exposure except under certain occupational exposure conditions.

4.1.1 Respiratory Absorption

Some quantitative and qualitative information about the respiratory deposition and absorption of arsenic by human subjects has been reported. Holland and co-workers (1959) used a group of hospital patients (lung cancer) to assess the deposition and absorption of inhaled arsenic using arsenite-containing cigarettes labeled with arsenic-74 as well as arsenite-containing aerosols. Deposition amounted to approximately 40 percent and more than three-fourths (75 to 85 percent) of the deposited arsenic was absorbed from the lungs within 4 days. While it may be argued that the health status of these subjects may have influenced the extent of absorption, it is nevertheless reasonable to infer that relatively rapid and extensive absorption of arsenic from the human lung likely occurs.

A study of a group of workers (Pinto et al., 1976) exposed to airborne arsenic in a copper smelter in 5-day test periods demonstrated average urinary arsenic excretion values ranging from 38 to 539 µg/liter to be associated with averages of air levels of arsenic ranging from 3 to 295 $\mu g/m^3$ (overall 53 µg As/m^3). Urinary arsenic was correlated with workplace air exposure (0.53, $p < 0.01$). Either direct pulmonary absorption or swallowing of larger particulate matter was evident as seen from elevations of urinary arsenic within 24 hours.

In a later study of copper smelter workers in which urinary excretion of arsenic was determined as total levels and chemically variant forms, Smith et al. (1977) studied control subjects and individuals from low, medium, and high arsenic exposure groups. In that study, the variations in concentrations of all arsenic forms isolated in urine--trivalent, pentavalent, methyl, and dimethylarsenic--were directly correlated with levels of airborne exposure (the relevant issue of arsenic biotransformation in vivo being discussed elsewhere in this chapter). An important feature of the Smith et al. (1977) report was the observation of a difference in the tightness of the correlation between excretion and exposure as a function of particle size. Both smaller, clearly respirable (<5 µm) and larger, less respirable (>5 µm) arsenic particles correlated well with excretion levels, but the less respirable arsenic-excretion relationship was seen to be much stronger than that for the finer mode particles. According to the authors, this is due to the swallowing of the large particle fraction and significant absorption from the GI tract.

Some animal data have also been reported on arsenic absorption via the respiratory tract. Bencko and Symon (1970) observed that hairless mice breathing a solid aerosol of fly ash containing 180 µg As/m^3 for several weeks had

increases in tissue arsenic values. Since the particle size was determined to be only less than 10 μm, part of this intake may have occurred via the GI tract. Increases in tissue arsenic in two exposure groups also occurred when rats were exposed to arsenic trioxide (condensation aerosols: 1.0, 3.7, and 46 $\mu g/m^3$) for 90 days (Rozenshtein, 1970).

Relatively rapid absorption of pentavalent arsenic (arsenate solution) was noted by Dutkiewicz (1977) when rats were exposed intratracheally (arsenate solution labeled with arsenic-74; 0.1 and 4.0 mg/kg). Arsenic tissue distribution dynamics were similar for intratracheal and companion intravenous exposure studies, indicating that the rate of intratracheal arsenic uptake more closely resembles that from parenteral administration than do oral or percutaneous exposures.

The pulmonary retention of arsenic compounds with different solubilities has recently been studied by two research groups.

Inamasu et al. (1982) gave 61 male Wistar rats single intratracheal instillations of arsenic trioxide or calcium arsenate suspended in phosphate buffer (pH 6.9). Controls (19) were given instillations of the phosphate buffer solution. The total dose of arsenic administered to each animal was about 2 mg in 0.2 ml suspensions.

Four to five of the arsenic-exposed animals were killed at intervals from 15 minutes to 168 hours after instillation. The average amounts of arsenic recovered in lungs of rats at 15 minutes after the instillation of calcium arsenate and arsenic trioxide were 1146 μg and 620 μg, respectively. After 24 hours, almost all of the deposited arsenic trioxide had disappeared from the lungs, whereas only about 50 percent of the calcium arsenate had been cleared as shown in Figure 4-1.

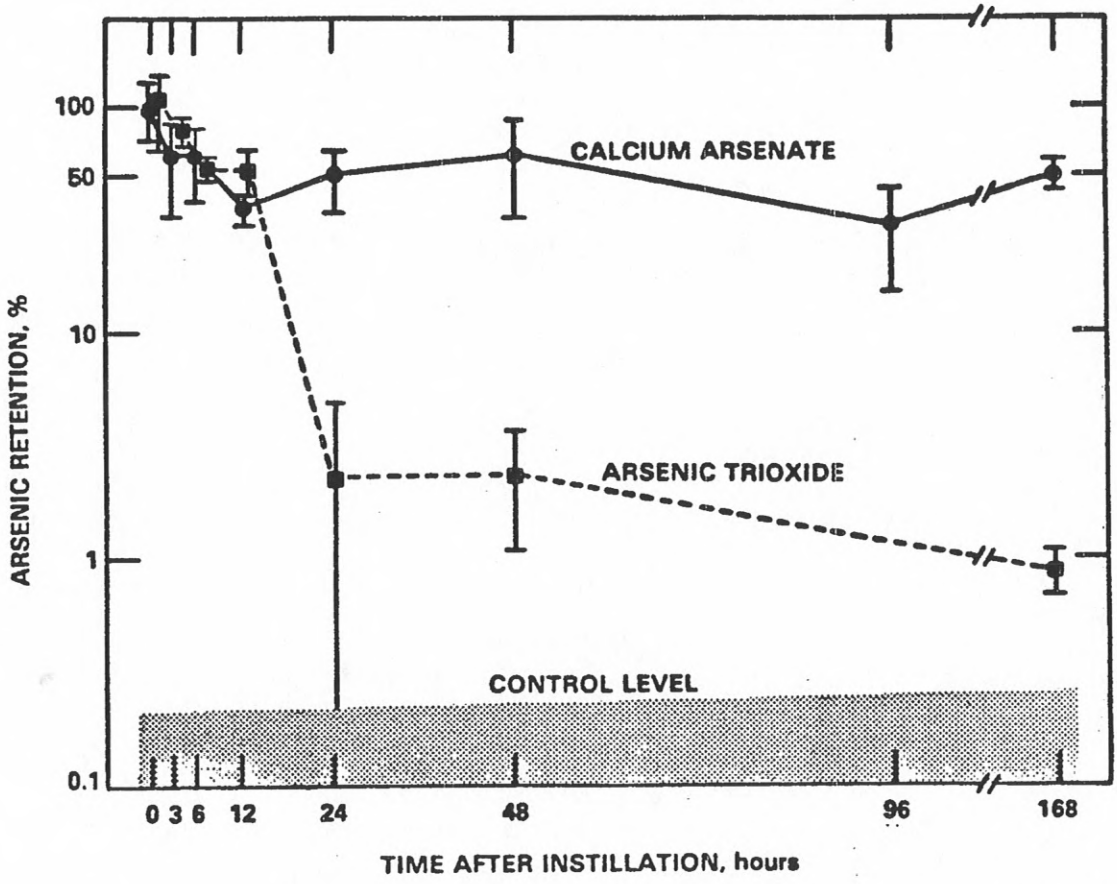

Figure 4-1. Arsenic retention in rat lungs following intratracheal instillation of a single dose. Percentage values are based on the average amount of arsenic present in rat lungs at 15 minutes after instillation of arsenic trioxide (- ■ -) or calcium arsenate (—●—). Vertical bars: means ± S.D.

Source: Inamasu et al. (1982).

Of the small remaining amount of arsenic trioxide, most gradually disappeared over the next several days, declining to a level of 5.6 µg at 168 hours after instillation, a level slightly higher than that seen in the controls (1.3 µg). In contrast, calcium arsenate remained at about the same level 168 hours after instillation as was observed after 24 hours (768 µg), clearly demonstrating a much higher level of retention compared to arsenic trioxide.

In the study by Pershagen et al. (1982), male Syrian golden hamsters were given four weekly intratracheal instillations of suspensions of arsenic trioxide, arsenic trisulfide and calcium arsenate in doses of 0.3, 0.5 and 0.5 mg arsenic, respectively. The suspensions were made in 0.9 percent NaCl, and sulfuric acid was added accordingly to equalize the acidity of the three different suspensions. Twenty animals were assigned to each treatment group. Five animals in each group were killed immediately after the first instillation. Two to five animals were then killed one week after two or four instillations and two weeks after four instillations.

The mortality was highest among the animals exposed to arsenic trioxide. In this group, 9 of the remaining 11 animals not sacrificed for tissue analysis had died by the week following the third instillation. In contrast, at the second instillation, two animals died in the group receiving arsenic trisulfide but no further deaths occurred in this group. A total of three animals receiving calcium arsenate died during the first week following the fourth instillation. Aside from those animals specifically sacrificed for tissue analysis, no other deaths occurred in this group either.

In the lungs, the amounts of arsenic were 386, 755 and 866 mg/kg wet weight immediately following instillation of arsenic trioxide, arsenic sulfide and calcium arsenate, respectively. One week after the second instillation

the amounts were 0.81, 9.2 and 579 mg/kg, respectively. In Figure 4-2 it can be seen that after the fourth instillation the differences between arsenate-exposed animals and the other groups were even more pronounced. Examination of the lungs revealed severe lung damage only among animals exposed to calcium arsenate. In all groups, areas with epithelial hyperplasia and metaplasia were seen.

Although different species and different time intervals were used in the above studies, the results were very consistent, i.e. arsenic trioxide was rapidly cleared from the lungs, whereas calcium arsenate was very slowly eliminated. The differences appear to be related to the relative solubility of the compounds, calcium arsenate having the lowest solubility. The doses in these two experiments were of the same magnitude, but the lung damage reported by Pershagen et al. among the arsenate-exposed animals might have influenced the clearance mechanisms. In addition, the possibility of higher acidity in the suspensions used by Pershagen et al. may also have had an influence.

The large differences in retention of arsenic compounds demonstrated in these two studies are of great interest in relation to the association between airborne arsenic and lung cancer. These differences in retention might explain the relatively high concentration of arsenic found in deceased smelter workers whose last exposure to arsenic occurred many years prior to death (Brune et al., 1980) (see Section 4.4). These workers were thought to be exposed to arsenic trioxide, but it may be that the retained fraction noted in the lungs was another arsenic compound of less solubility.

4.1.2 Gastrointestinal Absorption

In both man and experimental animals, factors which govern the absorption of arsenic from the gastrointestinal tract include the chemical form of the element, its physical characteristics, and dosing level. It can be stated

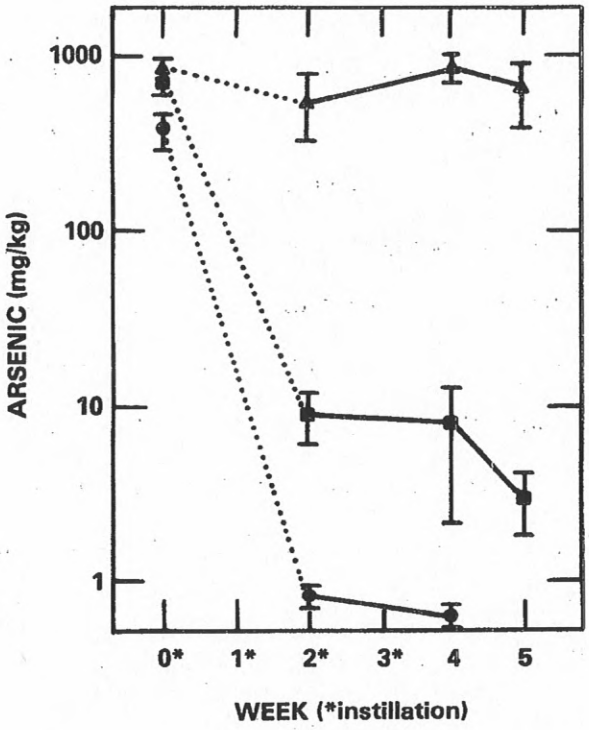

Figure 4-2. Lung concentrations of arsenic in hamsters given weekly intratracheal instillations of arsenic trioxide (●), arsenic trisulfide (■), or calcium arsenate (▲) (bars indicate ±1 S.D.). Animals at Week 0 were killed immediately following the first instillation; other animals were killed either 1 or 2 weeks after an instillation.

Source: Pershagen et al. (1982).

that soluble arsenicals will be generally more extensively absorbed than the insoluble forms. On the other hand, one should be cautious in extending correlations of simple water solubility to the chemical milieu existing in the GI tracts of various species.

Taken collectively, the reports of Coulson et al. (1935), Ray-Bettley and O'Shea (1975), Crecelius (1977), Mappes (1977), and Buchet et al. (1981a,b) demonstrate that very substantial absorption of soluble inorganic trivalent arsenic from the GI tract into the bloodstream typically occurs. Greater than 95 percent of inorganic arsenic taken orally by man appears to be absorbed, with less than 5 percent of the administered amount appearing in feces (Coulson et al., 1935; Ray-Bettley and O'Shea, 1975).

Consistent with the above observations, Mappes (1977) observed that daily oral intake of an aqueous solution of around 0.8 mg trivalent arsenic resulted in a daily urinary excretion of 69 to 72 percent of the daily dose in one subject. Also, Crecelius (1977) reported that ingestion of 50 µg trivalent and 13 µg pentavalent inorganic arsenic in a wine sample led to the appearance of 80 percent of all the ingested arsenic in urine within 61 hours. Crecelius (1977), however, reported that ingestion of well water mainly containing identified pentavalent inorganic arsenic led to urinary clearance of half the intake within approximately 3 days.

More recently, Buchet et al. (1981b) found that daily arsenic excretion via urine in human volunteers exposed to the dose range 125-1000 µg/day amounted to 60 percent of the dose. Steady state was achieved within 5 days after arsenic dosing began.

In contrast to the relatively high absorptive rate for soluble inorganic arsenic, Mappes (1977) reported that insoluble arsenic triselenide (As_2Se_3), when taken orally, passes through the GI tract with negligible absorption.

Arsenic intake via the diet of non-occupationally exposed populations requires that one consider the issue of bioavailability. Arsenic in foodstuffs is probably incorporated into the matrix of these commodities in a variety of ways.

The "shrimp" arsenic present in crustaceans and other fish appears to represent a complex organic form of the element which has prompted considerable recent study (LeBlanc and Jackson, 1973; Westöö and Rydälv, 1972; Munro, 1976; Edmonds et al., 1977; Penrose et al., 1977; Crecelius, 1977; Edmonds and Francesconi, 1977). In brief, the results of such studies indicate that the arsenic present in shellfish and other marine foods appears to be extensively absorbed and rapidly excreted intact as a complex organoarsenical by man and animals, and, as such, does not appear to pose a particular health threat to man.

Studies of the oral intake and absorption of arsenicals in experimental animals have also been conducted and generally confirm the findings derived from the above human studies. More specifically, soluble inorganic arsenic, delivered as either trivalent or pentavalent solutions, is almost completely absorbed from the GI tract of rats (Coulson et al., 1935), with 88 percent absorption being observed for arsenic trioxide solution (Urakabo et al., 1975; Dutkiewicz, 1977) and 70 to 90 percent for arsenate solution. Similar observations have been made for pigs (Munro et al., 1974), with 90 percent of arsenic trioxide solution being absorbed, and monkeys (Charbonneau et al., 1978a), with 98 percent of arsenic trioxide being absorbed. Also, Charbonneau et al. (1978b) fed arsenic-containing fish (Atlantic grey sole) to adult female monkeys as a homogenate (1 mg fish arsenic/kg body weight) and noted that about 90 percent of the intake was absorbed, of which about 75 percent appeared in urine after 14 days. In a related study, swine and adolescent

monkeys were seen to absorb approximately 70 and 50 percent, respectively. On the other hand, arsenic trioxide in suspension given orally to rabbits and rats was reported to result in only about 40 and 30 percent absorption, respectively (Ariyoshi and Ikeda, 1974).

4.1.3 Transplacental Passage

Potential fetal exposure to toxic elements via the mother is a matter of major importance given the potential sensitivity of *in utero* development to deleterious impacts of exogenous toxic agents.

In an arsenic-detection study of maternal-newborn blood groups, Kagey et al. (1977) reported that cord blood levels approximated those of mothers in 101 subject sets. Tissue analysis (Kadowaki, 1960) of fetus arsenic in a presumably healthy Japanese population indicated measurable element levels by at least month four of gestation which increased to month seven. Of importance in this study was the observation that brain levels, as well as those of bone, liver, and skin, were the highest of all tissue tested.

Complicating the issue is the chemical nature of the tissue arsenic assayed in either of the two studies noted above, inasmuch as precise chemical speciation was not attempted. Also, the Japanese study presumably did not select material in a manner such that dietary histories could be discerned. Thus, questions can be raised regarding implications of these data for fetotoxicity.

Transplacental transfer of arsenic has also been demonstrated in experimental animals. Transplacental transfer of arsenate administered parenterally in hamsters has been demonstrated by Ferm's laboratory (Ferm, 1977; Hanlon and Ferm, 1977). The movement was rapid, with embryonic tissues showing levels close to those in maternal blood 24 hours after dosing. Trivalent arsenic exposure results in transplacental passage in pregnant rats. Arsenic was detected in newborn rats when the dams received arsenic trioxide in their diets.

4.2 BIOTRANSFORMATION PROCESSES IN VIVO

An understanding of the metabolism of inorganic arsenic by man and a number of other species is substantially complicated by a series of newly-revealed biotransformations, including methylation of inorganic arsenic. It is thus appropriate to discuss *in vivo* transformation processes at this point, since many of the data dealing with blood transport, tissue distribution and subsequent excretion are much better understood in light of these findings.

A major factor in the determination of transformation processes for arsenic in man and other animals was the evolution of appropriate analytical methods within the decade which permit chemical speciation of chemically variant forms of arsenic with reference to both oxidation-state lability and inorganic versus organo-substituted arsenic.

These procedures involve different analytical approaches and include selective reduction of various arsenic forms to the hydride, and subsequent analysis by colorimetry (Lakso et al., 1979), emission spectrometry (Braman and Foreback, 1973; Crecelius, 1977), atomic absorption spectrometry (Edmonds and Francesconi, 1977; Buchet et al., 1980), and gas-liquid chromatography (Andreae, 1977; Talmi and Bostick, 1975). Alternatively, inorganic arsenic (III) or (V) and methylated forms can be directly measured by ion-exchange chromatographic techniques (Tam et al., 1978; Henry and Thorpe, 1980).

There are a number of points germane to consideration of *in vivo* transformations of arsenic: 1) biomethylation of inorganic arsenic; 2) oxidation-reduction of inorganic arsenic *in vivo*; 3) the relative chemical stability of inorganic arsenic to oxidation-reduction as it affects experimental dosing and chemical speciation in biological media.

4.2.1 Biomethylation of Inorganic Arsenic in Humans and Experimental Animals

An extensive literature has recently appeared documenting the *in vivo* methylation of inorganic arsenic to monomethyl and dimethyl arsenic (the latter

being the major methylated metabolite) in every mammalian system studied to date, including man.

While the quantitative features of this phenomenon may vary among species, one can generally state that: 1) dimethyl arsenic is the major transformation product in both humans and animals, with higher amounts of monomethyl arsenic, when formed, found in humans; 2) methylation is assumed to be a route of detoxification of the more toxic inorganic forms; 3) dimethyl arsenic appears to be a terminal metabolite, formed relatively rapidly and rapidly excreted; 4) while the in vivo methylating capacity of a given system may persist over a range of inorganic arsenic exposure, at some point the body burden of the unmethylated fraction is enough to induce toxic effects, evidenced by the extensive literature dealing with inorganic arsenic toxicity; 5) retrospective assessment of earlier data dealing with arsenic metabolism, including distribution and excretion, must be viewed in light of current knowledge about biomethylation in different species; and 6) biomethylation appears to be a reductive process involving step-wise arsenic reduction and methyl transfer steps.

4.2.1.1 Human Studies--Using a method that permits the determination of tri- and pentavalent inorganic arsenic as well as mono- and dimethylarsenic acids via selective reduction, volatilization, and helium-arc emission detection, Braman and Foreback (1973) analyzed the urinary excretion of arsenic in four human subjects. About 66 percent of the total urine arsenic concentration (22.5 ppb) was present as dimethylarsinic acid and 17 percent as pentavalent inorganic arsenic. Trivalent inorganic arsenic and methylarsonic acid were present in equal amount, approximately eight percent each.

Crecelius (1977) reported the urinary excretion of form-variable arsenic when a human subject ingested arsenic-rich wine (50 µg trivalent and 13 µg pentavalent). About 80 percent of the arsenic ingested with the wine was

excreted within 61 hours. Of the total excreted, 63 percent was in the form of dimethylarsenic acid, 18 percent was monomethyl arsenic acid, and approximately 9 percent each was in the two inorganic forms.

Consumption of well water containing 200 µg of arsenate by a subject in the same study showed urinary trivalent arsenic at near background levels with an elevation in pentavalent form as well as significant excretion of dimethylarsenic. Of the total amount ingested, about 50 percent was recovered in urine by 3 days. Arsenic as contained in canned crab tissue was also studied in this experiment. It has been established that arsenic is present in marine foods in an organic form which is excreted intact.

The study of Smith et al. (1977), using basically the same speciation/analysis techniques noted in the previous study and involving urinary profiles for a group of copper smelter workers, also confirmed transformation processes in vivo. In controls, as well as in three study groups that varied as to intensity of airborne trivalent arsenic oxide exposure, dimethyl arsenic was the dominant species in urine, followed by methyl arsenic, trivalent arsenic and pentavalent arsenic, in descending order.

In another smelter worker study, Buchet et al. (1980) assessed the distribution of arsenic and metabolites in urine samples in different groups according to the degree of inorganic arsenic exposure. Total urinary arsenic in exposure groups ranged from 74 to 934 µg/liter, of which 75 percent represented methylated forms (mono- and dimethyl), with dimethyl arsenic predominating. Control subjects showed a somewhat higher level of methylated arsenic in urine, approximately 90 percent, suggesting some dependency of the extent of methylation on the level of exposure.

A number of recent studies have described in more detail the biomethylation of inorganic arsenic using human volunteers.

Buchet et al. (1981a) followed the urinary excretion of inorganic and methylated arsenic in 3-5 volunteers ingesting single amounts of arsenic at a dose of 500 µg, in the form of either arsenite, monomethyl or dimethyl arsenic. After 96 hours, 46 percent of the dose in subjects given arsenite (trivalent arsenic) was excreted, 25 percent in the inorganic form and 75 percent as methylated metabolites. Of the latter, one-third was monomethyl arsenic and two-thirds was the dimethylated form. Dimethyl arsenic was excreted intact, 75 percent of the ingested amount appearing in urine by 96 hours. With monomethyl arsenic, excretion reached 80 percent by 96 hours, with around 13 percent of the urine level representing conversion to the dimethyl form.

In a follow-up report, these workers (Buchet et al., 1981b) monitored the urinary excretion of various arsenical forms in 4 human subjects undergoing repeated ingestion (5 days) of trivalent inorganic arsenic as a meta arsenite salt at 4 levels--125, 250, 500 or 1000 µg As. By 14 days, the percent of methylated forms of total forms ranged from 74-93 percent over the intake range. From this study, it would appear that the methylating capacity of the human subject was unaffected up to the 500-µg As level, at which point some decrease in methylated arsenic as a percentage of total was observed.

Yamauchi and Yamamura (1979) reported their results with 3 volunteer subjects who ingested an arsenic-rich extract (prepared from a particular kind of seaweed) containing 2.88 ppm total arsenic. Of the total amount, 86 percent was pentavalent inorganic arsenic, 7 percent was trivalent inorganic arsenic and 7 percent was dimethyl arsenic. These volunteers ingested the preparation as a single dose at a level of 10 µg/kg body weight, for total amounts of 650, 680, and 760 µg in the three subjects. By 48 hours, urine levels of total arsenic amounted to 36 percent of the dose. Of the excreted amount, dimethyl and monomethyl arsenic accounted for 47.4 and 25.3 percent, respectively.

4.2.1.2 Animal Studies--To date, biomethylation processes involving inorganic arsenic and experimental animals have been documented in dogs (Lakso and Peoples, 1975; Charbonneau et al., 1978a; Tam et al., 1979a), mice (Vahter, 1981), rabbits (Marafante et al., 1980; Bertolero et al., 1981), the bovine (Lakso and Peoples, 1975), and the rat (Odanaka et al., 1978). While the level of methylated forms of arsenic in most experimental species resembles that in man, approximately 80 percent, there is a greater amount of the dimethyl and a lesser amount of monomethyl arsenic.

Vahter (1981) has shown: (1) that the degree of biomethylation is dose-dependent, at least in mice, falling off in relative percentage with increasing level of dosing; (2) that this dependency probably accounts for the observation of dose-dependent retention in mice; and (3) methylation occurs to a greater extent with trivalent arsenic than with the pentavalent form, although retention, relative to total dose, is greater with the trivalent form.

Recently, Vahter et al. (1982) have reported that the Marmoset monkey, alone among all mammalian experimental species studied thus far, does not methylate inorganic arsenic.

4.2.2 In Vivo Oxidation/Reduction of Inorganic Arsenic In Mammalian Systems

From all available evidence, the biochemical mechanism of *in vivo* methylation of inorganic arsenic appears to be a reductive process, and sequential arsenic reduction and transmethylation steps in the pathway have been documented in microbial systems (Challenger, 1978; McBride et al., 1978). In mammalian systems, recent studies support a similar reduction/methylation sequence as observed in microflora.

Oxidation of trivalent inorganic arsenic to the pentavalent state has been claimed in dogs (Ginsberg, 1965), rats (Winkler, 1962), mice (Bencko et al., 1976), and humans (Mealey et al., 1959). An important factor in considering these studies critically is the fact that none of the reports considered

the presence of methylated arsenic, which may well have affected the analytical techniques employed and the analytical data obtained. Secondly, except for the Bencko et al. (1976) study, it is not clear that careful attention was paid to the oxidation state composition of dosing media or the effect of sample handling on oxidation state stability. In the Mealey et al. (1959) report, the analytical method involved acidification of urine with hydrochloric acid and extraction of the presumed "trivalent" arsenic into benzene, leaving the presumed "pentavalent" form in the aqueous phase. Since Mushak et al. (1977) have shown that methylarsonic and dimethylarsinic (cacodylic) acid behave like the pentavalent inorganic form in this extraction procedure, it is probable that the "arsenate" fraction was mainly methylated arsenic.

In the study of Crecelius (1977), where chemical speciation techniques were employed, it does not appear that ingestion of a sample containing mainly arsenite (trivalent form) is associated with excretion of pentavalent inorganic arsenic as the chief inorganic form. After 61 hours, 80 percent of the ingested amount appeared in urine, with the two inorganic forms each constituting minor fractions, mono- and dimethyl arsenic being the main forms.

Evidence for the in vivo reduction of pentavalent to trivalent inorganic arsenic has been claimed in several early reports. Lanz et al. (1950) reported some reductive conversion (10-15 percent) of arsenate to arsenite in rats, using as a method the precipitation from urine of arsenate as a mixed salt and analysis of the supernatant for arsenic (III). The accuracy of this method for partitioning trace arsenic levels is questionable. Furthermore, at the time of this study, the presence of methylated arsenic was not known. Therefore, it is not possible to accept the authors' conclusions since unprecipitated arsenic could also have consisted of methylated forms.

Ginsberg (1965) reported that 14 percent of urinary and 6 percent of plasma arsenic in dogs receiving intravenous infusion of arsenate was in the

form of trivalent arsenic. In this study, trivalent was presumably separated from pentavalent arsenic by chelation-extraction using ethyl xanthate. Based on current knowledge that methylated arsenic was present, it is difficult to accept the data without knowledge of the behavior of mono- and dimethyl arsenic in this analytical method.

In the recent report of Tam et al. (1979b) using dogs dosed with arsenate, a small amount of trivalent inorganic arsenic was detected in urine, using ion-exchange and thin-layer chromatographic techniques. These authors did not independently determine the extent of artifactive interconversion between the two forms using these techniques.

In a recent study by Vahter (1981), in which mice and rats were administered ^{74}As-labeled trivalent or pentavalent arsenic, the author reported that increases in retention with dose were less pronounced for the pentavalent form than for the trivalent form due to the fact that elimination of pentavalent arsenic seemed to be less dependent on methylation. Nevertheless, increases in retention with pentavalent arsenic were observed. Vahter discussed the possibility that the observed dose-related increase in retention after exposure to pentavalent arsenic may have been partly due to *in vivo* reduction of the pentavalent to trivalent form. Noting the work of McBride et al. (1978), whose studies indicated that certain microorganisms required reduction of pentavalent arsenic to trivalent before methylation could proceed, Vahter suggested that a similar mechanism might have been functioning in both the mice and rats. Evidence to support this hypothesis was presented in the author's observation that trivalent arsenic seemed more readily methylated than pentavalent.

Two recent studies, carefully designed for the specific purpose of addressing the oxidation/reduction issue for inorganic arsenic *in vivo*, have demonstrated that pentavalent arsenic (arsenate) undergoes reduction *in vivo* to

the trivalent state in the rat (Rowland and Davies, 1982) as well as in mice and rabbits (Vahter and Envall, 1983). In both of these investigations, the issue of artifactual interconversion of these two valence states was carefully addressed.

In the rat (Rowland and Davies, 1982), administration of moderate doses of pentavalent arsenic led to rapid reduction to the trivalent form. In mice and rabbits, the rate of conversion was somewhat slower than in the rat, but still occurred at a significant rate. Trivalent arsenic was measured in arsenate-dosed mice plasma by 1 hour post-dosing.

In a summary report, Peoples (1983) reported, without experimental detail, that the feeding of sawdust containing chromated copper arsenate did not result in measurable urinary levels of trivalent arsenic. Since these animals were exposed to copper as well as chromium (VI), in addition to arsenate, it is difficult to differentiate any influence these agents may have had on the results. Peoples (1983) also noted that renal perfusion of dogs with a very dilute solution of arsenate did not lead to renal reduction of pentavalent to trivalent arsenic. In the absence of experimental details, it is not possible to determine what steps were taken to avoid artifactual conversion of trivalent back to pentavalent arsenic, if the lower valence form was indeed formed.

Studies by Lerman and Clarkson (1983) of penta- and trivalent arsenic in the rat are fully consistent with a reductive methylation process. Using in vivo and in vitro techniques, the authors showed that the isolated rat liver hepatocyte readily methylates trivalent arsenic, while virtually no conversion occurs with the pentavalent form, although it is known that pentavalent arsenic is also extensively methylated in vivo. These data suggest that arsenate must first be converted to arsenite elsewhere in the organism.

Two recent studies using human subjects and identical chemical speciation techniques for arsenic appear to offer conflicting data regarding pentavalent arsenic reduction.

Crecelius (1977) noted that ingestion, by a single subject, of a sample of well water tested as having 200 µg As only in the pentavalent form resulted in a urinary level of trivalent arsenic which was virtually the same as background concentration before taking the arsenic sample. Although urine was collected for approximately 3 days, a significant amount of the total dose was unaccounted for, making it difficult to draw any conclusions from the study.

Yamauchi and Yamamura (1979) fed a preparation of seaweed containing 86 percent pentavalent arsenic and 7 percent each of trivalent inorganic and dimethyl arsenic to 3 human subjects as one dose at a total dosing of 650, 680, and 760 µg total arsenic. By 48 hours, based on their method which was the Braman et al. (1977) procedure, 36 percent of the original dose appeared in urine, with 75 percent present as methylated forms and about 17 percent present as trivalent arsenic (6.3 percent of the total amount ingested). The authors calculated that the amount of trivalent inorganic arsenic was greater than could be ascribed to the small amount ingested originally and they stated that the fraction represented in vivo reduction of pentavalent arsenic. Since the mean intake was approximately 700 µg, the 7 percent present as trivalent inorganic arsenic amounted to 49 µg, of which 36 percent or 18 µg would have been expected to appear in urine in some form. Using 75 percent methylation, only approximately 4-5 µg would have been present as the trivalent form, when in fact a mean value of 43.4 was found (range: 36-51 µg). Since the Braman et al. (1977) method is a reasonably accurate speciating technique and there is little evidence that samples were handled in a way to promote artifactive formation of trivalent arsenic after excretion, the data cannot be readily questioned on this basis.

4.2.3 Chemical Stability of Trivalent and Pentavalent Inorganic Arsenic to Oxidation-Reduction

In aerated water, trivalent inorganic arsenic will undergo extensive oxidation to the pentavalent form, particularly when present at low levels (Feldman, 1979).

The pH of aqueous solutions appears to be the major factor in the relative stability of either valency form. Buchet et al. (1980) found that trivalent arsenic in solutions at pH of 7.0 or 9.6 were oxidized to the extent of 70-90 percent within one week, compared to 25 percent conversion at pH 4.8.

Vahter and Norin (1980) also noted rapid oxidation of As (III) in aqueous solution at room temperature, while storage at 4°C showed little conversion.

Pentavalent inorganic arsenic, on the other hand, is stable at neutral or alkaline pH but undergoes reduction with decreasing pH (Durrant and Durrant, 1966).

In studies directed to *in vivo* transformations of inorganic arsenic, urine levels are commonly used and some data exist regarding valency stability of arsenic in urine.

Buchet et al. (1980) found that trivalent inorganic arsenic in urine at pH 7.0 or less was relatively stable, with only 10 percent oxidation occurring by 7 days. At pH 9.5, 50 percent of oxidation occurred within one day.

4.3 DISTRIBUTION OF ARSENIC IN MAN AND ANIMALS

Blood is the main vehicle for transport of arsenicals from absorption sites to the tissues, with the hemokinetic character of arsenic being dependent on the animal species studied.

It is readily apparent from the literature that the rat constitutes an anomalous model for studies of the fate of inorganic arsenicals *in vivo* and this includes the clearance behavior of rat blood-borne arsenic (Hunter et al., 1942; Ducoff et al., 1948; Lanz et al., 1950; Ariyoshi and Ikeda, 1974;

Klaassen, 1974; Tsutsumi and Kato, 1975; Dutkiewicz, 1977). In the case of the rat, arsenic in blood is only slowly cleared following exposure, with about 80 percent of the total blood arsenic content localized in the erythrocyte. The half-times of blood clearance for inorganic arsenic in the rat (trivalent or pentavalent) is on the order of 60 to 90 days (Lanz et al., 1950; Ariyoshi and Ikeda, 1974).

Arsenic in the blood of other species--man (Ducoff et al., 1948; Mealey et al., 1959; Tam et al., 1979b), mice (Lanz et al., 1950; Crema, 1955), rabbit (Hunter et al., 1942; Ducoff, 1948; Klaassen, 1974), dog (Lanz et al., 1950; Hunter et al., 1942), and primates (Hunter et al., 1942; Klaassen, 1974)--whether given as the pentavalent form or as the trivalent form, is rapidly cleared. Normal blood arsenic values for individuals in the U.S. and Europe are in the range of 1-5 μg total arsenic/liter whole blood (Bergstromn and Wester, 1969; Damsgaard et al., 1973; Kagey et al., 1977; and Valentine et al., 1979). According to Kagey et al. (1977), cigarette smokers showed mean blood arsenic levels approximately 50 percent higher than nonsmokers. It is reasonable to assume that human background blood levels reflect mainly dietary arsenic, much of which would likely be in various organo-arsenical forms that are extensively absorbed and rapidly cleared.

Clearance of arsenic in dog and man was found to fit a three-compartment model by Charbonneau et al. (1978a) and Tam et al. (1979b) with half-times of 1, 5, and 35 hours, respectively. When contrasted with the work of Tam et al. (1978), which reported the time-dependent *in vivo* methylation of arsenic and excretion in dogs, the various components presumably relate to initial excretion of inorganic arsenic, followed by clearance of dimethyl arsenic.

The tissue partitioning of arsenic in man has been studied using both autopsy and dosing data. Kadowaki (1960) found (measurements in ppm, wet

weight) that nails (0.89), hair (0.18), bone (0.07-0.12), teeth (0.08) and skin (0.06) generally housed the highest absolute amounts of arsenic, while heart, kidney, liver and lung contained somewhat lower levels (0.04-0.05). Brain tissue (0.03) had an arsenic level only slightly lower than other soft tissues. Liebscher and Smith (1968), analyzing tissue samples (ppm dry weight) from non-exposed sources in Scotland, observed lung to have the highest levels (0.09), with liver and kidney levels (0.03) not materially different from other soft tissue. Like the Kadowaki study, hair (0.46), nails (0.28) and skin (0.08) had the highest absolute values; however, bone and teeth (0.05) did not contain levels appreciably different from some other tissues (pectoral muscles, 0.06; ovary, 0.05; and pancreas, 0.05).

In addition to the autopsy studies by Kadowaki (1960) and Liebscher and Smith (1968), Larsen et al. (1979) have recently reported on a detailed study of the topographical distribution of arsenic in normal human brain tissue. Arsenic is distributed throughout all brain regions, with white matter showing higher levels than gray matter.

In looking at tissue distribution of arsenic in experimental animals, exposure of various species to either tri -or pentavalent arsenic leads to the initial accumulation of the element in liver, kidney, lung, spleen, aorta, and skin (Hunter et al., 1942; Ducoff et al., 1948; Lanz et al., 1950; Peoples, 1964; Ariyoshi and Ikeda, 1974; Cikrt and Bencko, 1974; Klaassen, 1974; Tsutsumi and Kato, 1975; Urakabo et al., 1975; Dutkiewicz, 1977; Sabbioni et al., 1979; Marafante et al., 1980). With the exception of the rat, a species in which metabolism of arsenic is only a very limited model for study of this element (vide supra), clearance from soft tissue is rather rapid except for the skin, where the high sulfhydryl group content may promote tight trivalent arsenical binding. As also seen with human tissue, arsenic is apparently lodged in

brain of experimental animals exposed to arsenic, with slow clearance reported (Crema, 1955).

Recently, Vahter and Norin (1980) compared the dependency of dose and valency form of inorganic arsenic on tissue compartmentalization of arsenic in mice. Unlike most of the earlier reports, these workers used chemical speciation techniques (ion-exchange chromatography) to verify that their dosing media contained purely tri- or pentavalent arsenic. Using single oral dosing at 0.4 or 4.0 mg/kg levels and radioisotopic tri- or pentavalent arsenic, levels of arsenic in kidney, liver, bile, brain, skeleton, skin and blood were always greater (2-10 fold) in terms of percent total dose for the trivalent form than for the pentavalent form, and most pronounced at the higher dose. These workers ascribe much of this difference to relative methylating efficiency as a function of exposure level and valence form.

In a similar study using Golden Hamsters exposed to injected tri- or pentavalent radioisotopic arsenic, with care taken to assure valence purity, Ckirt et al. (1980) found that levels of arsenic in liver, kidneys, gut wall and bile were always greater, 2 to 25-fold, with trivalent arsenic exposure.

4.4 ARSENIC ACCUMULATION

The long-held view of arsenic as an element that accumulates in the body was mainly based on the behavior of arsenic in the rat, an animal model which in retrospect was the least helpful in understanding the fate of the toxicant *in vivo* for other mammalian species and man.

Based on current arsenic elimination data for all mammalian species studied other than the rat (*vide supra*), one concludes that marked long-term accumulation of arsenic generally does not occur in physiologically vital components of the body. This is in contrast to, say, long-term lead accumulation in bone or cadmium accumulation in renal cortex. Autopsy tissue data for

human subjects of different ages are not conclusive regarding possible long-term tissue accumulation. Kadowaki (1960) did observe higher mean levels of arsenic in skin and kidney samples of subjects approximately 50 years of age versus infant values, but dietary histories of the subjects were not available to allow for differentiation of increases in arsenic levels due to current versus past exposures for the older subjects. Deposition in hair is really excretory in nature, not accumulative.

Brune et al. (1980) have reported that lung tissue from retired smelter workers from the Rönnskär smelter in Sweden, on autopsy, had median values for arsenic which were about 8 times higher than that for a control group. Kidney and liver values, however, were not significantly different between smelter worker groups and controls. Arsenic accumulation in the lung of smelter workers even after several years of retirement and removal from workplace exposure (interval of 2-19 years) suggests that a very insoluble form of arsenic exists in smelter ambient air and is inhaled by these workers.

Lindh et al. (1980) measured the arsenic in autopsy femur samples of 7 occupationally exposed workers. The time between retirement and death ranged from 0-21 years. A control sampling from 5 autopsy cases was included. Using both neutron activation analysis and proton-induced X-ray emission (PIXIE) techniques, no clear evidence of significant arsenic accumulation in bone was seen. The scatter of levels was wide in the worker group, 0.006-0.21 ppm, with a median of 0.014 ppm, versus a range of 0.005-0.007 ppm in the control samples.

4.5 ARSENIC EXCRETION IN MAN AND ANIMALS

Renal clearance appears to be the major route of excretion of absorbed arsenic in man and animals, biliary transport of the element leading to enteric reabsorption with little carriage in feces.

Recent data for normal or background levels of arsenic in urine of human subjects in the U.S. reveal values of less than 20 µg/liter (20 ppb). If seafood has been consumed, such values can rise considerably to levels of 1,000 µg/liter or higher (Westöö and Rydälv, 1972; Pinto, 1976).

In a study designed to assess the utility of urine arsenic measurement in occupational exposure settings, Mappes (1977) reported excretion data for both single and multiple daily dosing for a human subject ingesting an arsenite solution. By 3 hours, renal excretion was maximal, with about one-quarter of the single dose appearing in the urine by day 1 post-exposure. With successive arsenite ingestion (0.8 mg As), daily urinary clearance after 5 days was about two-thirds of daily intake.

Buchet et al. (1981b), in their study of human subjects ingesting arsenite in amounts ranging from 125-1000 µg/day for 5 days, calculated a steady state occurring within 5 days. With steady state, 60 percent of daily intake is excreted daily. This figure is in good agreement with that of Mappes (1977) cited above.

Crecelius (1977) noted that following ingestion of arsenic in wine [50 µg As (III), 13 µg As (V)], approximately 80 percent of the dose was excreted within 61 hours. Oral ingestion of arsenic (V) in well water (200 µg), however, led to about 50 percent urinary excretion by 3 days post-ingestion. Mealey et al. (1959) measured urine arsenic in patients given trivalent arsenic by intravenous administration, with approximately 60 percent of the dose amount appearing in the urine within 24 hours. Hunter et al. (1942) noted that a group of human subjects given arsenic via parenteral administration exhibited considerable variance in the urinary clearance of arsenic, ranging from 30 to 80 percent after 4 to 5 days.

As might be predicted from the <u>in vivo</u> behavior of arsenicals in the rat, urinary excretion of arsenic in this species is very slow (due to erythrocyte

retention) on the order of two to five percent of the arsenic intake by several days post-dosing (Coulson et al., 1935; Ariyoshi and Ikeda, 1974). Urakabo et al. (1975) calculated a half-time of 84 days for arsenic in the rat.

Slow clearance of arsenic from the rat gave rise to the widely-held assumption for many years that arsenic was one of the elements that accumulated in the body. Other species excrete arsenic rapidly. Mice, rabbits, swine, dogs, and monkeys clear the majority of injected trivalent arsenic within 24 hours, with excretion usually being $\geq$70 percent within that time period (Ducoff et al., 1948; Crema, 1955; Munro et al., 1974; Lakso and Peoples, 1975; Tam et al., 1978; Charbonneau et al., 1978a). Other studies also indicate rapid urinary clearance of arsenic given in the pentavalent form to species other than the rat (DuPont et al., 1942; Ginsberg and Lotspeich, 1963; Peoples, 1964; Lakso and Peoples, 1975).

Several studies have compared the relative rates of elimination of radiolabeled (^{74}As) trivalent and pentavalent inorganic arsenic (Vahter and Norin, 1980; Vahter, 1981) where precautions were taken to assure the purity of the respective dosing solutions as to valency state. Whole-body retention of trivalent inorganic arsenic in mice was 2-3 times greater than that of arsenate while retention times for both forms were dose-dependent, increasing with increasing exposure. In these studies, the animals received single oral doses of either form at levels of 0.04 to 4.0 mg As/kg. Differences in elimination rates appeared to relate to the relative degree of methylation of inorganic arsenic to the rapidly excreted methylated forms, chiefly dimethyl arsenic. Furthermore, differences in excretion rates were dose-dependent. At 0.04 mg As/kg, there was no difference between tri- and pentavalent arsenic elimination (Vahter, 1981).

Biliary transport of arsenic has been reported for a number of species. Bile-excreted arsenic is reabsorbed. Cikrt and Bencko (1974) noted that the

rat had a higher biliary excretion rate for the trivalent than for the pentavalent form (approximately 10:1). Klaassen (1974) noted that the biliary excretion rate was much greater for the rat than for either the rabbit or the dog.

Cikrt et al. (1980) monitored biliary exretion in the Golden Hamster using penta- or trivalent inorganic arsenic. Significant differences in biliary excretion rates and cumulative excretion were seen between the two forms, being much greater for the trivalent form. However, fecal and urine arsenic content were greater with pentavalent arsenic administration. Biliary transport data for man are not available.

Deposition of arsenic in such organs as hair and nails can be considered an excretory mechanism for arsenic. Although hair analysis has had a long history in the chemical and forensic arsenic literature, for reasons of both analytical convenience and the possibility of establishing an exposure history from sectional analysis, many questions remain unanswered. The relationship between arsenic deposition in hair and various exposure parameters has not been well defined on a quantitative basis, nor are the physiological mechanisms well understood. The chemical nature of hair arsenic is also largely unknown.

5. ARSENIC TOXICOLOGY

The acute and chronic toxicity of arsenic will largely depend on the chemical form and physical state of the compound involved. Inorganic trivalent arsenic is generally regarded as being more acutely toxic than inorganic pentavalent arsenic, which in turn is more toxic than methylated forms of arsenic (NAS, 1977; Pershagen and Vahter, 1979; WHO, 1981). The previously noted (Chapter 3) "fish arsenic" is regarded as nontoxic. It is thus necessary to always specify, if possible, arsenic compounds when discussing effects and constructing dose-effect and dose-response relationships. In addition, factors like particle size and solubility must be taken into account. Trivalent compounds with low solubility, e.g., arsenic sulfide, will have low oral toxicity but may be retained in the lung (Pershagen et al., 1982).

The following chapter discusses the non-mutagenic/non-carcinogenic effects of exposure to inorganic arsenic. Because of the large volume of information available regarding the mutagenic and carcinogenic effects of inorganic arsenic, these topics have been discussed in the following chapters.

5.1 ACUTE TOXICITY OF ARSENIC IN MAN AND ANIMALS

In animal experiments the oral LD_{50} has been found to vary from 15 to 293 mg/kg body weight in rats and from 10-150 mg/kg in other animals (Dieke and Richter, 1946; Harrison et al., 1958). The lower values refer to experiments with soluble arsenic compounds. Franke and Moxon (1936) found that the LD_{75} 48 hours after i.p. administration was 4-5 mg As/kg body weight for sodium arsenite and 14-18 mg/kg for sodium arsenate.

Acute effects seen in animals after oral exposure are similar to effects seen in human beings and include gastroenteritis, diarrhea and cardiovascular effects (Nelson et al., 1971; Selby et al., 1977).

A large number of acute arsenic poisonings are described in the literature, but few data exist on actual doses and type of compound. Vallee et al. (1960) estimated the lethal dose to be on the order of 70 to 180 mg for arsenic trioxide. Acute symptoms are due to severe gastrointestinal damage, resulting in vomiting and diarrhea and general vascular injury which may lead to shock, coma or even death. Other acute symptoms are muscular cramps, facial edema, and cardiovascular reactions (Holland, 1904; Done and Peart, 1971).

Acute symptoms have also been seen after airborne exposure to high concentrations of arsenic trioxide, causing severe irritation of nasal mucosa, larynx, and bronchi (Holmqvist, 1951; Pinto and McGill, 1953).

Reversible effects on the hematopoietic and cardiovascular systems and peripheral nervous disturbances with slow recovery have also been noted (Ohta, 1970; Heyman et al., 1956; Jenkins, 1966; Nagamatsu and Igata, 1975: O'Shaughnessy and Kraft, 1976; Hamamoto, 1955; Chhuttani et al., 1967; LeQuesne and McLeod, 1977).

Over the years, a number of large-scale poisonings have occurred due to contamination of beer (Kelynack et al., 1900), soy sauce (Mizuta et al., 1956), dried infant milk (Tokanehara et al., 1956), and well water (Yoshikawa et al., 1960). These episodes mainly caused subacute and chronic symptoms and will be discussed in the following sections.

5.2 CHRONIC TOXICITY OF ARSENIC IN MAN AND ANIMALS

5.2.1 Neurotoxic Effects

Arsenic neurotoxicity, including both peripheral and central nervous system injury, has long been recognized as being associated with acute, subacute, and chronic exposures to relatively high levels of inorganic arsenic. These have been well characterized as to their major pathophysiological features, clinical course, sequelae and associated histopathology.

Reynolds (1901) provided one of the earliest detailed descriptions of arsenic-induced neurotoxic effects in his report on the clinical assessment of more than 500 patients who had consumed arsenic-contaminated beer.

Neurological involvement started with sensory changes, e.g., paresthesias, hyperesthesias, and neuralgias, accompanied by considerable muscle tenderness. Varying degrees of motor weakness, progressing from distal to proximal muscle groups, also occurred and culminated at times in paralysis of affected muscle groups or extremities. Certain indications of central nervous system (CNS) damage, e.g., loss of memory and general mental confusion, were also observed but were discounted by Reynolds (1901) as being less likely due to arsenic than chronic alcoholism or concurrent excessive selenium intake.

Peripheral nervous system (PNS) effects similar to those described by Reynolds (1901) have since been observed in numerous other cases of acute, subacute, and chronic arsenic exposures (Silver and Wainman, 1952; Mizuta et al., 1956; Heyman et al., 1956; Jenkins, 1966; Hara et al., 1968; Chhuttani et al., 1967; Ishinishi et al., 1973; Nakamura et al., 1973; Nagamatsu and Igata, 1975; O'Shaughnessy and Kraft, 1976; Frank, 1976; Garb and Hine, 1977; LeQuesne and McLeod, 1977) and are now recognized as classic clinical symptoms of arsenic poisoning. Such symptoms include peripheral sensory effects characterized by the appearance of numbness, tingling, or "pins and needles" sensations in the hands and feet, as well as decreases in touch, pain, and temperature sensations in a symmetrical distribution. These symptoms are often variously accompanied by burning sensations, sharp or shooting pains, and marked muscle tenderness in the extremities. Peripheral neuritis symptoms originate distally and, over the course of a few weeks, often progressively become more widespread in both lower and upper extremities, usually appearing first in the feet and later in the hands.

Collectively, the above components of the classical clinical syndrome associated with excessive arsenic exposure are highly indicative of progressive peripheral polyneuropathy, involving both sensory and motor nerves, and most intensively affecting long-axon neurons. In addition, biopsy and autopsy studies have provided histopathological evidence verifying peripheral nerve damage, especially Wallerian degeneration of long-axon myelinated nerve fibers in cases of human arsenic exposure where frank neurological signs and symptoms were manifested (Heyman et al., 1956; Jenkins, 1966; Chhuttani et al., 1967; Ohta, 1970; LeQuesne and McLeod, 1977).

The pattern of development of peripheral neuropathic effects is closely associated with the type of exposure. Acute exposure to a single high dose of arsenic can produce a fairly rapid onset of both motor dysfunctions and paresthesias. In one report, the onset was within 10 days (LeQuesne and McLeod, 1977) after exposure. Slow, incomplete recovery is usually seen in these cases.

Under more chronic occupational exposure conditions to lower levels of arsenic compounds, the development of neuropathy symptoms can be more gradual and insidious, and not only bilateral, but unilateral polyneuropathies without motor paralysis have been reported (Ishinishi et al., 1973; Nakamura et al., 1973). Again, the time course for recovery from the neuropathies, once induced, tends to be slow and on the order of years. Gradual onsets of peripheral neuropathies and slow recoveries have also been reported with subacute or chronic exposures to arsenic via ingestion of contaminated soy sauce (Mizuta et al., 1956) or anti-asthmatic herbal preparations containing arsenic trioxide or arsenic sulfide (Tay and Seah, 1975).

It is difficult to determine the levels of arsenic associated with the induction of peripheral neuropathies. For subacute or chronic poisoning situations, information has been provided in only a few studies by which

effective exposure parameters can be estimated. Mizuta et al. (1956), for example, reported that peripheral neuropathies occurred in 20 percent of 220 patients of all age groups poisoned by ingestion of arsenic-contaminated soy sauce, with approximately 3 mg arsenic (likely as calcium arsenate) estimated to be ingested daily for 2-3 weeks, resulting in total effective doses up to approximately 60 mg. Also, Tay and Seah (1975) reported polyneuropathies in approximately 50 percent of 74 patients poisoned by daily ingestion of 3.3 or 10.3 mg/day of arsenic trioxide or arsenic sulfide in anti-asthmatic medicinal pills.

More subtle peripheral neurotoxic effects arising from chronic exposure to lower levels of arsenic in occupational or non-occupational groups are more difficult to establish, particularly as indexed by abnormal electromyographic or nerve conduction velocity findings. In one such study, Landau et al. (1977) reported relationships between length and intensity of occupational arsenic exposure (mainly to arsenic trioxide via inhalation) of smelter workers and alterations in peripheral nerve functioning. The manner in which the data were reported, however, precludes precise characterization of dose-effect/dose-response relationships.

In their study of arsenic in the drinking water of residents from Millard County, Utah, Southwick et al. (1981) conducted neurological examinations on all study participants 47 years of age and younger (see Section 7.1.2.2 for discussion of the total study population). Neurological examination revealed that conduction velocities for nerves studied (ulnar motor, median motor, ulnar sensory, median sensory, peroneal, sural) did not vary significantly with respect to age or community. In those individuals that exhibited below-normal conduction velocities, a slightly greater proportion was seen in exposed participants--12 percent of 67 controls versus 16 percent of 83 exposed. The

sural nerve seemed most often to be affected even after adjusting by a correction factor of 1.8 m/s/degree in individuals who had nerve temperatures below 30° C. (Velocities below 37 m/s at 30° C or above were considered abnormal). Slowing of sural nerve conduction was reported equally in exposed and control participants. Nerve conduction velocities regressed against annual arsenic dose and the log of the dose showed no significant associations.

Similar difficulties have been encountered in attempts to characterize dose-effect/dose-response relationships for arsenic-induced peripheral nerve functional deficits (as demonstrated by electromyographic recording techniques) in studies of two other populations chronically exposed to arsenic: (1) a population of Yellowknife Canadian Indians exposed via occupational contact with arsenic in a gold mining and smelting facility, or, in the case of the families of such workers, via arsenic emissions from the facility into the ambient environment (Canadian Public Health Assoc., 1978); and (2) a Nova Scotia population exposed, via geological arsenic contamination of wells, to levels >0.05 ppm arsenic in drinking water (Hindmarsh et al., 1977).

Several of the clinical reports discussed above not only document peripheral nerve damage but also contain descriptions of arsenic-induced central nervous system (CNS) disturbances or encephalopathy effects ranging in severity from memory losses and general mental confusion to convulsions, stupor, coma and even death (Heyman et al., 1956; Jenkins, 1966: Frank, 1976; Nagamatsu and Igata, 1975; O'Shaughnessy and Kraft, 1976; Garb and Hine, 1977). The onset and courses of such CNS effects have not been well defined, but they appear to closely parallel the development of peripheral neuropathy effects. Cases of prolonged encephalopathy indexed by electroencephalogram (EEG) recordings of abnormal brain wave patterns up to a year after cessation of exposure have been reported (Freeman and Couch, 1978; Bental et al., 1961). Such effects

appear to be a much less constant feature of arsenic-induced neurotoxic effects in adults than are peripheral neuropathies.

Certain studies suggest, in contrast, that children may be more susceptible to arsenic-induced CNS damage. For example, severe CNS deficits have been observed in children exposed for several months as babies to arsenic-contaminated powdered milk formulas in Morinaga, Japan (Hamamoto, 1955; Okamura et al., 1956; Yamashita et al., 1972; Masahiki and Hideyasu, 1973; Japanese Pediatric Society, 1973). Follow-up studies on the children exposed to arsenic as infants have revealed: (1) increased incidence of severe hearing loss (>30 dB) in 18 percent of 415 children examined compared to less than 1 percent incidence of hearing loss in corresponding age-group children; (2) increased incidence of abnormal electroencephalographic (EEG) brain wave patterns in 14 percent of the exposed children, more than double the expected rate for comparable normal pediatric populations; and (3) observations of increased incidences of persisting mental retardation, epilepsy, and other indications of severe brain damage.

In another study (Bencko and Syman, 1977), hearing losses in children were reported to be associated with arsenic exposure derived from emissions from a nearby coal-fired power plant combusting high-arsenic-content coal. Both air and bone conduction hearing losses were observed, suggesting inner ear damage. Failure to find analogous hearing losses in children exposed to atmospheric arsenic emitted from a copper smelter in the United States (Milham, 1977) has raised questions regarding arsenic-induced damage to the inner ear in children.

Very few animal toxicology studies have focused on investigation of neurotoxic effects of arsenic on the CNS. Rozenshtein (1970), for example, reported evidence of CNS functional deficits, as indexed by altered conditioned reflexes, as well as histopathologic evidence of CNS structural damage,

e.g,. pericellular edema and neuronal cytolysis in the brain, in rats exposed for three months to an arsenic trioxide aerosol resulting in an arsenic concentration of 46 $\mu g/m^3$. Similar but less severe effects were also obtained with exposure of other rats to a 3.7 $\mu g\ As/m^3$ aerosol. CNS deficits, indexed by impaired avoidance conditioning in the absence of demonstrable histopathologic changes in brain tissue, were also reported (Osato, 1977) for suckling rats administered 2 or 10 mg arsenic trioxide via stomach intubation over a 40-day period.

5.2.2 Cardiovascular Effects

A specific cardiovascular effect is "Blackfoot" disease, a peripheral vascular disease leading to gangrene of the toes, feet, legs and fingers. This disease has been reported in an area of Taiwan, where exposure to inorganic arsenic via drinking water is known to occur. In their skin cancer study of the Taiwanese population (see Section 7.1.2.2 for complete discussion of the total study population), Tseng and co-workers (1968, 1977) also investigated the occurrence of Blackfoot disease. The total prevalence of Blackfoot disease was lower than the prevalence of skin cancer, but higher in the younger age groups (Table 5-1). The overall prevalence rate for Blackfoot disease was 0.9-1.2 percent for males and 0.7 percent for females after age 39.

A group of 1108 patients with Blackfoot disease from the endemic area was identified during 1958 to 1975 (Tseng, 1977). There were 669 males and 439 females. Patients were included in the series if they had: 1) objective signs of ischemia, and 2) subjective symptoms of ischemia. Follow-up was attempted using a variety of methods to trace the subjects. At the end of follow-up, 528 patients had died, a fatality rate of 47.7 percent.

A history of typical ischemic symptoms such as numbness was used to estimate the date of onset of Blackfoot disease. Duration of intake of arsenic

TABLE 5-1. PREVALENCE OF BLACKFOOT DISEASE (per 1000) BY AGE AND ARSENIC EXPOSURE (ppm)

Arsenic content of drinking water (ppm)	Age 20-39	40-59	>60
<0.3	4.5	10.5	20.3
0.3 - 0.6	13.2	32.0	32.2
>0.6	14.2	46.9	61.4

Source: Adapted from Tseng, 1977.

water at the time of onset represents the period of time between first use of such intake and the time of onset of the disease. Duration of intake of arsenical water represents the duration of time during which the patient started drinking artesian well water up to the time of survey or up to the time of change of source of drinking water. For native patients, the duration is estimated to be equivalent to their ages, but for patients who came from areas without artesian wells the duration was counted as starting from the year of arrival.

A classification system of percentage of permanent disability was created and each patient was assigned to the appropriate category.

It was determined (determination not specified) that all patients with Blackfoot disease had consumed artesian well water before the onset of disease, and none of the residents of the endemic area who had consumed surface water or water from shallow wells developed Blackfoot disease.

In some parts of the arsenic endemic area, a new source of drinking water was provided in 1956. The incidence of Blackfoot disease was therefore examined in year of onset periods (1955 and before, 1956-1965, and 1966-1975). There were no cases of Blackfoot disease among area residents who were born after

the tap water supply was instituted in 1956. Furthermore, as the duration of intake of arsenical water increased (across all 3 exposure levels) the incidence of Blackfoot disease increased. In addition, the degree of permanent disability of patients was significantly correlated with duration of intake of arsenical water at time of onset of the disease.

There are also data indicating that other substances may be involved in the etiology of Blackfoot disease. Lu et al. (1977, 1978) found fluorescent compounds in water samples from an area with endemic Blackfoot disease. Of the compounds discovered, tentative identifications of D-lysergic acid and/or ergometrine, ergotamine and calciferol have been made (Irgolic, 1982). These substances may have been at least contributing factors to this disease, since some of them, or similar compounds, are known vasoactive agents.

Vascular changes were also noted among persons living in Antofagasta, Chile (see Section 7.1.2.2 for discussion of study groups). Raynauds syndrome and acrocyanosis were reported to occur in 30 and 27 percent, respectively, in a group of 100 persons studied by Borgono and Greiber (1972).

Raynauds syndrome has also been reported to occur among German vintners. Butzengeiger (1940) studied 180 persons and found that 22.8 percent had evidence of vascular disorders of the extremities. Butzengeiger (1949) studied 192 vinegrowers and found that 28.7 percent had ECG changes. There was, however, no control group.

In epidemiological studies of smelters (see Section 7.1.2.1 for complete discussion of studies), peripheral vascular disease has generally not been found. However, mortality studies indicate that there might be some cardiovascular effects, although study results have been conflicting. Thus, Axelson et al. (1978) found a higher mortality in cardiovascular disease, but analysis of the data indicate that if such an effect occurred it probably needed higher

exposure levels than those causing lung cancer. A study by Ott et al. (1974) indicated, on the other hand, that the arsenic-exposed workers had less mortality than expected.

In studies on workers at the Anaconda Copper Smelter in Montana, both Lee and Fraumeni (1969) and Lee-Feldstein (1983) reported that cardiovascular mortality was significantly elevated in the workers--SMR=118 and SMR=129, respectively ($p < 0.01$)--but not related to duration of arsenic exposure. In a study cohort of these same workers, Higgins et al. (1982) reported that cardiovascular mortality increased with increasing ceiling arsenic exposure among smokers, but not among nonsmokers--at 500-4999 ug/m^3, SMR=165 for smokers ($p < 0.01$), SMR=100 for nonsmokers; at >5000 ug/m^3, SMR=182 for smokers ($p < 0.01$), SMR=166 for nonsmokers. In contrast, Lubin et al. (1981) did not find an excess in cardiovascular disease mortality (SMR=108) in their study cohort of workers from the same smelter. The cohorts in all four of these studies were slightly different.

The conflicting findings of these reports suggest that the relationship between arsenic exposure and cardiovascular disease is quite complex and in need of additional research.

5.2.3 Teratogenesis and Developmental Effects

5.2.3.1 Animal Studies--In a recent review of the toxicological effects of prenatal exposure to arsenic, Hood (1983) discussed the number of variables that influence effects on offspring of maternal arsenic exposure during pregnancy. Included in the variables are the forms of arsenic administered, species and individual differences in susceptibility, dose level and exposure route, peak level attained in the conceptus, maternal metabolism and excretion, and timing of exposure during gestation; the length of the list being indicative of the complex nature of arsenic toxicity induced during prenatal exposure.

Teratogenic effects of arsenic compounds, at least at relatively high exposure levels, have been demonstrated in a number of animal species. Studies by Ridgeway and Karnofsky (1952), for example, demonstrated no gross abnormalities in chick embryos following injection of sodium arsenate into embryonate eggs at 0.20 mg As/egg on day 4 of gestation. Retardation in body weight gain and feather growth, as well as certain other abnormalities, were, however, observed in chickens hatched from arsenic-treated eggs.

Later experimental studies on mammalian species have demonstrated teratogenic effects of arsenic in hamsters, rats and mice.

Ferm and Carpenter (1968) produced malformations in 15-day hamster fetuses via intravenous (I.V.) injections of sodium arsenate into pregnant dams on day 8 of gestation at dose levels of 15, 17.5 or 20 mg/kg body weight. The variety of malformations obtained with prenatal arsenic exposure of hamsters--including exencephaly, encephaloceles, skeletal defects and genitourinary system defects and the effects of other related experimental manipulations, e.g., protective effects of co-treatment with selenium--were reviewed in a later report by Ferm (1977).

Willhite (1981) injected arsenate (20 mg/kg) or arsenite (2-10 mg/kg) into pregnant golden hamsters at day 8 of gestation and observed axial skeletal disorders in offspring--cranioschisis aperta with exencephaly and cranioschisis occulta--while 10 hours after dosing, embryos showed a delay in neural fold elevation and neural tube closure with arsenate exposure.

Teratogenic and embryotoxic effects of prenatal arsenic exposure of mice have also been reported (Hood and Bishop, 1972; Hood and Pike, 1972; Hood et al., 1977). Increased fetal resorption, decreased fetal weights and various malformations (such as exencephaly, micrognathia, agnathia, exophthalmos, anophthalmia, hydroencephaly, cleft lip, ectrodactyly, micromelia, fused vertebrae and forked ribs) were observed following single intraperitoneal (I.P.)

injections of sodium arsenate (45 mg As/kg body weight) in Swiss-Webster mice (the single injection occurring on one day between days 6 and 12 of gestation) (Hood and Bishop, 1972). Co-treatment with 2,3-dimercaptopropanol (BAL) reduced arsenic-associated malformations (Hood and Pike, 1972; Hood et al., 1977).

Many similar embryotoxic and fetal teratogenic effects, along with other effects (renal and gonadal agenesis), have also been observed following I.P. injections of sodium arsenate in pregnant rats (Beaudoin, 1974; Burk and Beaudoin, 1977), again at relatively high dose levels (e.g., 30 mg/kg body weight).

Compared to pentavalent arsenic, trivalent arsenic as the arsenite salt appears to be proportionally more embryotoxic. For example, the fetotoxic effects seen by Baxley et al. (1981) in mice exposed to 40-45 mg/kg As as arsenite were comparable to effects observed by Hood et al. (1978), in which a much higher level of arsenate (120 mg/kg As) was administered.

The above studies are suggestive of significant effects on reproduction and development of mammalian species being induced by prenatal arsenic exposure. However, only very minimal effects, or none at all on fetal development, have been observed in studies on chronic oral exposure of pregnant rat or mice dams to relatively low levels of arsenic via drinking water (Schroeder and Mitchener, 1971). Nadeyenko et al. (1978) reported that intubation of rats with arsenic solution at a dose level of 0.0025 mg/kg for a period of 7 months, including pregnancy, produced no significant embryotoxic effects and only very infrequent slight expansion of ventricles of the cerebrum, renal pelvises and urinary bladder. Also, Hood et al. (1977) reported that very high single oral doses of arsenate solutions (120 mg/kg) to pregnant mice were necessary to cause prenatal fetal toxicity, while multiple doses of 60 mg/kg on 3 days had little effect. This report suggests that the higher doses required with oral versus

parenteral exposure relate to the more rapid methylation to less toxic forms of oral arsenic owing to its initial passage through the liver, where methylation may occur. Similar results were obtained with mice in a later study (Hood et al., 1978).

Given the presence of biomethylation in mammalian species exposed to arsenic, the question arises as to whether fetotoxicity resides only in the untransformed inorganic arsenic or is due to some of the metabolites formed in vivo. Hood et al. (1982a) have demonstrated that methylated metabolites cross the placental barrier in mice given arsenite and that these methylated forms are actually the major form of arsenic in fetuses by 12 hours post-dosing.

Recently, three groups of investigators have reported their results on the comparative teratogenicity of methylated arsenicals, administered as such, to different species.

Willhite (1981) found no teratogenic response when pregnant golden hamsters were given methylated arsenic at single doses up to a level of 100 mg As/kg. Rogers et al. (1981) administered dimethylarsenic to pregnant CD rats and CD-1 mice on days 7-16 of gestation via oral gavage. Dosing was from 7.5 to 60 mg/kg/day for rats and 200 to 600 mg/kg/day for mice. Fetal and maternal toxicity was observed in both species. A teratogenic response in mice was confined to cleft palate in the 400- and 600-mg regimens. In the rat, there was a dose-dependent incidence of irregular palatine rugae.

Hood et al. (1982b) exposed pregnant golden hamsters to either dimethyl- or monomethyl arsenic at dosages of either 900 or 1000 mg/kg of the former agent and 500 mg/kg of the latter. The levels of dimethylarsenic administered were seen to be acutely toxic to dams and were associated with significant resorption rates and malformations in survivors. In the case of the monomethyl arsenic, the overall teratogenic potency was observed to be lower.

Harrison et al. (1980) exposed CD-1 mice to monomethyl arsenic by injection (1500 mg/kg salt, i.p.) on one of gestation days 8, 9, or 10. Treatment at days 9 and 10 of gestation resulted in increased resorption and mortality rates of 37 and 43 percent, respectively, while the day 8 group showed no such effects. Skeletal malformations were also seen at the 9 and 10 gestation day exposures. While details for dimethylarsenic were not provided, it was noted that such treatment also resulted in fetotoxicity and teratogenicity, with exencephaly the primary gross malformation observed.

The available data, in summary, indicate that while the methylated arsenicals are less teratogenic and fetotoxic on an equivalent dose basis, the nature of the effects is comparable. There also appears to be a species sensitivity difference for arsenical teratogenicity and fetotoxicity, the rat being more sensitive than mice or golden hamsters.

Animal studies on the effects of early postnatal administration of arsenic compounds on growth and development have generally failed to yield any significant positive results at sublethal arsenic dose levels. Tamura (1978), for example, reported no effects on the growth and development of postnatal rats fed arsenic trioxide in their diet from the 7th to 21st day following birth at a dose level of 1.5 mg/kg/day, in comparison to a 50 percent mortality rate at a 15.0 mg/kg body weight dose. Similarly, Ferslew and Edds (1979) observed no significant effects on growth or development of young swine fed arsanilic acid at 0.01 percent concentration for 31 days commencing at 3 weeks of age, despite observations of significant alterations by organo-arsenic of white blood cell counts, serum alkaline phosphatase activity, and other blood chemistry parameters and significant increases of arsenic in various soft tissues and urine. In another study (Heywood and Sortwell, 1979), both 3.75 and 7.5 mg/kg/day doses of an arsenic compound fed to adolescent or infant rhesus monkeys resulted in mortality in most of the exposed animals, but no notable

effects in growth or development of animals surviving the dosing period. Unfortunately, the lack of experimental data in the above studies on the effects of exposure across a range of dose levels, besides the ones employed, greatly limits their utility in terms of determining possible dose-effect or dose-response relationships between postnatal arsenic exposure and induced effects on growth and development.

It should be noted that, whereas some of the above animal studies provide highly suggestive evidence for arsenic effects on reproduction and development, at least at high exposure levels, one cannot confidently extrapolate the results to estimate the probability of occurrence of similar or analogous effects in man. Still, some suggestions of possible arsenic effects on human reproduction and development have been derived from certain epidemiology studies discussed below.

5.2.3.2 Human Studies--Available data are mainly from studies in Sweden on male and female smelter workers. These studies were not designed specifically to study effects of arsenic but rather to study the effects, in general, of the smelter work. While data from these studies suggest a low-level effect of smelter pollutants on neighboring (proximate) populations, the diverse agents involved preclude making conclusive statements about the specific effects of arsenic.

Congenital malformations were found to occur at about the same rate, 3.0 percent among women employed at the Rönnskär smelter, as among women living in six areas belonging to the hospital serving the Rönnskär area (Nordström et al., 1978c). However, mean birthweights were lower among offspring to female Rönnskär workers (Nordström et al., 1978a, 1978b).

The number of spontaneous abortions was also increased among women working in this smelter; the highest rate (17 percent) was found among women

employed during pregnancy or who had been employed prior to pregnancy and lived close to the smelter. Women working in close connection with smelting processes had a rate of 28 percent of spontaneous abortion compared with other female employees. When both parents were employed, the abortion rate was 19.4 percent compared to 13.5 percent when the father was not employed.

Studies on spontaneous abortion among women living in the vicinity of the smelter were also conducted (Nordström et al., 1978d). In four areas, the rate varied between 7.6 and 11.0 percent. The highest rate occurred in the area closest to the smelter, but many women employed at the smelter live in that area.

5.2.4 Hematological Effects

The hematopoietic system in man has been shown to be affected by arsenic exposure in cases of acute, subacute or chronic intake, taking the form of anemia, leukopenia, granulocytopenia and eosinophilia. Such effects appear to be reversible, the system recovering in a matter of weeks after exposure ends.

Hamamoto (1955), in his report of infant poisoning by arsenic-contaminated milk in Japan, described marked anemia and leukopenia with lymphocytosis in most of a group of 59 infant patients. Erythropoiesis was disturbed in bone marrow of 19 children studied. Within a month, the hematology appeared to show normal values. Similarly, Mizuta et al. (1956) found blood disturbances, including anemia with leukopenia and lymphocytosis, in subjects surveyed for ingestion of soy sauce contaminated with arsenic.

Two recent studies dealing with acute and subacute arsenic poisoning (Feussner et al., 1979; Lerman et al., 1980) have demonstrated arsenic-induced megaloblastic anemia. Feussner et al. (1979) demonstrated that arsenic was present in bone marrow by using electron-probe microanalysis.

Chronic exposure to arsenic occasions hematological effects which resemble those seen with subacute exposure. Terada (1960), in his survey of patients exposed to arsenic in well water contaminated by industrial activity in Niigata, Japan, saw anemia as a common feature, with the anemia being either normochromic (50 percent) or hyperchromic (30 percent). In their study on individuals living in communities in Utah where arsenic was present in drinking water, Southwick et al. (1981) also reported the presence of anemia in certain individuals; however, anemia was not significantly more prevalent in exposed populations. Anemia has been reported in subjects exposed to arsenic occupationally or in medicinals (Kyle and Pease, 1965; Westhoff et al., 1975).

In animals, decreased hemoglobin production has been seen in rats fed both arsenate (Mahaffey and Fowler, 1977) and arsenite (Byron et al., 1967) and in cats given either form orally (Massmann and Opitz, 1954). The study of Woods and Fowler (1977), in which arsenate was given orally to rats and mice at 20, 40 or 85 ppm in drinking water, showed that the sites of disturbance of the heme biosynthetic pathway by arsenate mainly involved depression of ALA-synthetase and heme-synthetase activity, with elevation in the urinary levels of chiefly uroporphyrin and also coproporphyrin. The increase in uroporphyrin appears to be specific to arsenic.

5.2.5 Hepatic Effects

In the reports of Hamamoto (1955) and Mizuta et al. (1956), dealing with arsenic contamination in infant milk and soy sauce, respectively, swollen livers appeared to be a common clinical feature. Of the children exposed to milk arsenic, all subjects presented with this feature (61/61). In the autopsies of fatal outcome cases, hemorrhagic necrosis and fatty degeneration of the liver were seen. In the survivors, liver function tests were not very revealing, being within normal limits in most cases. In both of the above episodes, liver size returned to normal after exposure ceased.

Over the years, chronic intake of arsenic has been reported to be associated with hepatic damage in the form of portal hypertension, malignant liver disease and cirrhosis. In the Manchester beer poisoning episode, Reynolds (1901) noted widespread liver disease in drinkers of such beer, with the extent of the disease being related to the amount of arsenic in the beverage.

The incidence of hepatic cirrhosis among German vintners has been reviewed by Luchtrath (1972), who noted that the frequency of liver cirrhosis decreased with the banning of arsenical pesticides. The use of arsenic as an anti-syphilitic is also known to be associated with hepatic cirrhosis (Baldridge, 1934).

Non-cirrhotic portal hypertension has been infrequently noted in the literature (Morris et al., 1974; Szuler et al., 1979). Szuler described one case report of presinusoidal portal hypertension in a patient taking an arsenic antiasthmatic for 55 years. Cirrhosis was absent and liver function was not disturbed.

In the smelter study by Axelson et al. (1978) there was a tendency towards an increased mortality in liver cirrhosis among arsenic-exposed workers.

5.2.6 Renal Effects

Functional and/or biochemical impairment of the human renal system is mainly seen in acute poisoning by arsine, AsH_3 (Uldall et al., 1970; Fowler, 1977). Oligouria and anuria progressing to renal failure are common acute responses. Persistent renal sequelae in subjects surviving the acute stage of arsine poisoning include chronic renal insufficiency and hypertension. Histologically, the injury is mainly tubular and interstitial.

Acute or chronic renal effects associated with arsenate or arsenite exposure are less well characterized. Gerhardt et al. (1978) have recently described a case of acute arsenic poisoning from contaminated illicit liquor.

Acute renal bilateral cortical necrosis was diagnosed in the patient who survived the acute stage to eventually develop reduced renal size and cortical calcification.

In the clinical survey of Hamamoto (1955) of Japanese infants poisoned with arsenic-contaminated milk, possible renal injury was diagnosed by the presence of hematuria, leukocyturia and glycosuria (23.7 percent, 42.3 percent and 13.5 percent, respectively). Reversibility of these indices was apparent, with only three percent of the patients still showing pathological changes after one month. Terada (1960) also noted proteinuria in cases of arsenic poisoning in Niigata, Japan, arising from ground water contamination from an arsenic plant.

5.2.7 Respiratory Effects Other Than Cancer

Nasal septum perforation is a rapid tissue response in workers encountering high airborne arsenic levels (NAS, 1977; Hine et al., 1977; Lundgren, 1954).

In the detailed smelter worker study of Lundgren (1954), 1,276 subjects in a worksite with levels up to 7 mg As/m^3 showed two types of respiratory disturbances relating to the nature of the processing and presumably the form of the arsenic. Refined arsenic handling was associated with septal perforation and rhinopharyngolaryngitis, while workers in the roaster, furnace, and connector areas showed tracheobronchitis and signs of pulmonary insufficiency. In the latter group, exposure was mixed, including both arsenic and sulfur dioxide. A recent report has suggested, furthermore, that workplace arsenic may also be present as the sulfide (Smith et al., 1976).

Chilean children exposed to arsenic in drinking water (Borgono et al., 1977) showed a chronic cough and bronchitic history.

5.2.8 Immunosuppressant Effects

The role of inorganic arsenic as an immunosuppressant in man is mainly inferred from indirect data accumulated over the years (Arsenic. NAS, 1977).

First, the therapeutic utility of arsenicals, such as arsenite-based Fowler's solution in the treatment of steroid-responding disorders and as a lymphocytostatic agent, suggests action as an immunosuppressant.

Secondly, certain manifestations indicative of likely immune system disorders have been observed with arsenic exposure, (e.g., the occurrence of herpes simplex and chronic pulmonary infections) and suggest a role of arsenic as an immunosuppressant (Arsenic. NAS, 1977). Histories of chronic cough and bronchitis in Chilean children exposed to arsenic in drinking water (Borgono et al., 1977) would tend to support such a role.

5.3 FACTORS AFFECTING ARSENIC TOXICITY

The most widely recognized and studied arsenic interactive behavior is with selenium, and much of the early data has been reviewed by Levander (1977).

The known antagonistic relationship of arsenic and selenium in a number of animal species was first described by Moxon and co-workers (Moxon and Dubois, 1939; Dubois et al., 1940), who also demonstrated the utility of dietary arsenic supplementation in protecting livestock from the toxic levels of selenium in certain fodders. Both penta- and trivalent arsenic are equally effective in protecting against selenium toxicity, and do so regardless of the chemical form by which selenium exposure occurs.

An understanding of the <u>in vivo</u> mechanisms by which arsenic imparts a protective effect on selenium toxicity has only recently been gained.

The ability of arsenic to retard the formation of volatile selenium in the form of dimethyl selenide (Kanstra and Bonhorst, 1953) apparently involves inhibition of microsomal methyl transferase, an enzyme sensitive to arsenite (Ganther and Hsieh, 1974). An overall protective effect still exists, however, since arsenic promotes the biliary excretion of selenium (Levander and Baumann, 1966; Ganther and Baumann, 1962). According to Levander (1977), enhanced biliary

clearance of selenium in the presence of arsenic probably involves an excretory conjugate of both, since selenium likewise enhances the biliary excretion of arsenic.

Rössner et al. (1977) showed a protective effect for arsenite against the cytotoxicity of selenite, using suspension cultures of mouse fibroblasts exposed to these agents at 10^{-5} to 10^{-11} M. Interestingly, selenite, in turn, had only a low protective effect against arsenite cytotoxicity.

Few data exist for interactive relationships between arsenic and other elements. In one of the few pertinent studies bearing on this issue, the effects of concomitant oral exposure to cadmium, lead and arsenic versus single-agent exposure effects have been reported by Mahaffey and Fowler (1977). Cadmium and arsenic together retarded weight gain in young adult rats to a greater extent than either element alone.

6. ARSENIC MUTAGENICITY

Various inorganic compounds of arsenic have been tested for mutagenicity in a variety of test systems ranging in complexity from bacteria to peripheral lymphocytes of exposed human beings. Information on these tests has been reviewed herein and elsewhere (Flessel, 1978; NAS, 1977; Leonard and Lauwerys, 1980; WHO, 1981). The following chapter is divided into five major sections discussing studies indicative of mutagenic damage, as well as interactions of arsenic with other mutagens and possible mechanisms of mutagenic action.

6.1 GENE MUTATION STUDIES

6.1.1 Prokaryotic Test Systems (Bacteria)

Arsenic does not appear to induce gene mutations in bacteria (Table 6-1). Sodium arsenite ($NaAsO_2$) was tested for its ability to induce reverse mutations in E. coli (Nishioka, 1975). Three bacterial strains auxotrophic for tryptophan were tested for growth in the absence of tryptophan after arsenic treatment. Nishioka reported that arsenic induced mutations in wild type cells and in cells deficient in excision repair ($uvrA^-$) but not in cells deficient in recombinational repair ($recA^-$). This suggested that the rec function is necessary for arsenic-induced mutagenesis in E. coli.

The observations by Nishioka were not reproducible in subsequent studies by Rossman et al. (1980). In these latter studies, the authors examined sodium arsenite-induced mutagenesis in five strains of E. coli, all auxotrophic for tryptophan and carrying different mutations for DNA repair capacities. In addition, Rossman et al. used three protocols for quantifying the presence of mutant cells: the spot test, the plate test and the fluctuation test. Arsenite did not increase the mutation frequency in any E. coli strain using any of the

TABLE 6-1. SUMMARY OF MUTAGENICITY OF ARSENIC: GENE MUTATIONS

Reference	Test system	Chemical Information	Results	Comments
Nishioka, 1975	Reverse mutation in *E. coli* Strains: WP2 (trp^-) WP2 uvrA ($uvrA^-$, trp^-) CM571 ($recA^-$, trp^-)	$NaAsO_2$ 8.0×10^{-4} M in WP2 1.6×10^{-4} M in WP2 uvrA 1.6×10^{-4} M in CM571 Source: Nakarai Chemical LTD (reagent grade) Solvent: H_2O	$NaAsO_2$ positive for mutations in WP2 and WP2 uvrA but not in CM571. Increases were approximately 10x background.	1. Doses of arsenite were selected to kill 60-70% of cells. 2. Lack of mutagenesis in CM571 suggests that a rec function is required for mutagenesis in *E. coli*. 3. Rossman et al. (1981) were unable to reproduce these mutation studies. They claimed (a) that the induced mutation frequencies observed by Nishioka were within the normal range of background, (b) that they observed a 31-fold difference in cytotoxicity studies compared to Nishioka, and (c) that Nishioka used an incorrect method for determining mutation frequency.

TABLE 6-1. (continued)

Reference	Test system	Chemical Information	Results	Comments
Rossman et al., 1980	Induction of reverse mutations in E. coli at the trp locus. Assays: Spot test, Plate test, Fluctuation test Strains: WP2 (trp^-); $WP2_S$ (trp^-, uvrA-); WP6 (trp^-, $polA1^-$); WP10 (trp^-, $recA1^-$); $WP44_S$-NF (trp^-, $uvrA^-$, tif-1/sti^-). tif-1 mutation confers a thermally inducible SOS repair system resulting in normal mutation at 30°C and a 20-fold increase in mutation at 42°C.	$NaAsO_2$: 50 µl of 0.1 M in spot tests with $WP44_S$-NF (30°C), WP2, WP6, and WP10. $NaAsO_2$: 10 µl of 0.01 M in spot test $WP44_S$-NF, 10 µl of 0.1 M in spot test $WP44_S$-NF. $NaAsO_2$: 25 mM in plate tests WP2. $NaAsO_2$: 0.4, 1, 2, mM in fluctuation test WP2.	Arsenic did not increase the mutation frequency in any of the assays. Arsenic showed a dose-dependent decrease in mutations in $WP44_S$-NF at 42°C.	1. Results indicate that arsenic may inhibit SOS repair.
Lofroth and Ames, 1978 (abstract only)	Salmonella microsome assay	Arsenite and arsenate	Negative	1. No data available since information comes from an abstract.

TABLE 6-1. (continued)

Reference	Test system	Chemical Information	Results	Comments
Singh, 1983	Gene conversion at the trp locus and reverse mutation at the ilv locus in S. cerevisiae. Strain D7 = $\frac{a\ ade\ 2\text{-}40\ \ trp\text{-}5\text{-}12\ \ ilv\ 1\text{-}92}{\alpha\ ade\ 2\text{-}119\ \ trp\ 5\text{-}27\ \ ilv\ 1\text{-}92}$	$NaAsO_2$ (0.1 M added to well, volume not indicated) Solvent: H_2O	Negative for conversion. Weak positive for mutation.	1. Study lacking sufficient experimental details.
Amacher and Paillet, 1980	Forward gene mutation at the thymidine kinase (TK) locus in mouse L5178Y cells.	Na_2HAsO_4 Doses tested: (0.83×10^{-4}, 1.1×10^{-4}, 1.47×10^{-4}, 1.96×10^{-4}, 2.26×10^{-4} M) Source: Fisher Solvent: Normal saline	Negative	1. Exposed 3 hrs at 37°C. 2. Survival ranged from 66% at the low dose to 35% at the high dose. 3. Other metals such as cadmium, nickel, and trans-platinum were positive.
Rossman et al., 1980	Induction of forward mutations in Chinese hamster cells in vitro at HGPRT locus and the sodium-potassium ATPase locus.	$NaAsO_2$ (0.5×10^{-6} M, 2 days) ouabain resistance (5.0×10^{-6} M, 1 hour) ouabain resistance (20×10^{-6} M, 1.5 hours) thioguanine resistance (100×10^{-6} M, 25 min) thioguanine resistance	No increased mutation	1. UVC and MNNG used as positive controls. 2. Doses of arsenite used varied from slightly inhibitory to cell growth to fairly toxic.

TABLE 6-1. (continued)

Reference	Test system	Chemical Information	Results	Comments
Oberly et al., 1982	Forward gene mutation at the thymidine kinase (TK) locus in mouse L5178Y cells.	$NaAsO_2$ (3.8×10^{-6}, 7.7×10^{-6}, 11.5×10^{-6}, 15.4×10^{-6}, 19.2×10^{-6} M) Na_2HAsO_4 (7.5×10^{-5}, 9.7×10^{-5}, 11.8×10^{-5}, 14.0×10^{-5} M) Source: Mallinckrodt	$NaAsO_2$ was negative in the presence of Aroclor-induced rat S-9 mix; $NaAsO_2$ was positive for the three highest doses tested in the absence of S-9 mix; Na_2HAsO_4 was negative in the absence of an Aroclor-induced rat S-9 mix; Na_2HAsO_4 was positive at the three highest doses tested in the presence of an S-9 mix.	1. Chemical exposure was for 4 hours. 2. Only positive data were shown; negative results were only mentioned in the text. 3. The spontaneous mutation rate varied a great deal between experiments; between 2.5 and 17.9 mutants per 10^5 survivors. Most of the arsenic-induced mutant frequencies were between or just slightly above this spontaneous range. 4. The increases in mutant frequencies occurred at very low survival levels for both compounds; the highest doses caused 97% lethality. 5. At survivals above 10% none of the mutant frequencies exceeded the limits of the control mutant frequency range.

test protocols. Indeed, arsenic showed a dose-dependent suppression of mutations in strain $WP44_S$-NF. This strain carries a mutation (tif-1) which confers a thermally inducible SOS repair system (error-prone repair) resulting in normal spontaneous mutation at 30°C and a 20-fold increase in mutation at 42°C. The presence of sodium arsenite in the medium was sufficient to suppress this temperature-induced increase in the mutation frequency by one-half. This observation suggests that arsenic may inhibit SOS repair, a pathway which is highly important in bacterial mutagenesis. Such a repair pathway has not been detected in mammalian cells.

Rossman et al. (1980) offered explanations for the discrepancies between their results and those of Nishioka. First, they pointed out that the arsenic-induced mutation frequencies reported by Nishioka were all within the normal range of background. Second, they observed a 31-fold difference in cytotoxicity in the same bacterial strains. Third, they noted that Nishioka used an incorrect method for determining mutation frequency, basing his calculations on the initial size of the cell inoculum instead of on the final size of the plated population.

Arsenite and arsenate have also been found to be negative in the Ames Salmonella microsome assay (Lofroth and Ames, 1978). Although this work is reported only in abstract form, it may be assumed the assay was performed properly as Ames is a cited author.

Consideration of the above results alone, however, should not be taken as proof that inorganic arsenic is non-mutagenic. Bacterial systems are generally insensitive for the detection of metal mutagens because of the large amount of magnesium salts, citrate and phosphate in the minimal medium which prevent the entry of metal mutagens into bacterial cells (McCann et al., 1975).

6.1.2 Eukaryotic Microorganisms (Yeast, Fungi)

Sodium arsenite was tested for its activity in inducing reverse mutation and mitotic gene conversion in the yeast Saccharomyces cerevisiae (Singh, 1983). The diploid strain used in this study (D7) is auxotrophic for tryptophan, isoleucine, and valine, and measures gene conversion at the trp locus and reverse mutation at the ilv locus. Arsenite was inactive for gene conversion and weakly positive for mutation. This study was generally lacking in details and raw data were not shown.

6.1.3 Mammalian Cells In Vitro

Sodium arsenate was tested for the induction of forward mutations at the thymidine kinase locus in mouse L5178Y cells (Amacher and Paillet, 1980). Doses of arsenate were selected such that between 66 percent to 35 percent of cells survived a three-hour treatment. Arsenate was found not to increase the spontaneous mutation rate in these cells, while other known or suspected mutagenic metals (cadmium, nickel, and trans-platinum) were positive.

Using the same system, Oberly et al. (1982) tested sodium arsenate and sodium arsenite in the presence and in the absence of an Aroclor-induced rat S-9 mix. Sodium arsenite gave positive results at the three highest doses when tested in the absence of S-9 mix. In the presence of S-9 mix, the results were reported to be negative, although no data were presented. Sodium arsenate gave positive results at the three highest doses tested in the presence of S-9 mix. Again, without presenting data, the outcome in the absence of metabolic activation was reported to be negative. The authors concluded that these two arsenic compounds were weak mutagens. There are, however, several problems with this interpretation. First, the spontaneous mutation rate varied a great deal in these studies: between 2.5 and 17.9 mutants per 10^5 survivors. Most of the arsenic-induced mutant frequencies fell between or just slightly above

this spontaneous range. Second, the increases in mutant frequencies occurred at very low survival levels for both compounds; the highest doses used caused 97 percent lethality. Thus, at survivals exceeding 10 percent none of the mutant frequencies exceeded the limits of the range of control mutant frequencies. Taking these observations into consideration, the authors' conclusions do not seem well supported.

Sodium arsenite was also tested for the induction of forward mutations at two loci in V79 cells (Chinese hamster lung fibroblasts) (Rossman et al., 1980). The two genes studied were hypoxanthine guanine phosphoribosyl transferase (HGPRT) and membrane-bound sodium potassium ATPase. Mutations in these two enzymes were enumerated through the observation of cell clones resistant to thioguanine or ouabain, respectively. Both the concentration of the chemical as well as the incubation times were varied; there was, however, no increase in the mutation frequency at either locus. The positive controls, UVC (ultraviolet light 254 mm) and methylnitronitrosoguanidine (MNNG) were effective in elevating the mutant frequency.

6.2 CHROMOSOMAL ABERRATION STUDIES

6.2.1 Chromosomal Aberrations In Vitro

A large number of studies indicate that both trivalent and pentavalent arsenic compounds are capable of breaking chromosomes in vitro (Table 6-2). One of the earliest reports on the clastogenic potential of arsenic was from a study performed with mitogenically stimulated human peripheral lymphocytes (Petres and Hundeiker, 1968). Although the test compound was reported to be Na_2HAsO_3, it is assumed the authors meant Na_2HAsO_4. Positive results were reported, although no actual raw data were presented.

Paton and Allison (1972) tested both sodium arsenite and sodium arsenate for the induction of chromosomal aberrations in human diploid fibroblasts and

TABLE 6-2. SUMMARY OF MUTAGENICITY OF ARSENIC: CHROMOSOME ABERRATIONS

Reference	Test System	Chemical Information	Results	Comments
Petres and Hundeiker, 1968 (paper in German, English summary)	Chromosome aberrations induced in human peripheral lymphocytes exposed in vitro.	Na_2HAsO_3 0.5×10^{-6} and 10^{-6} g/ml of medium (assume Na_2HAsO_4 is meant) 1.6×10^{-6} M and 3.2×10^{-6} M	Positive at both doses.	1. No raw data were presented in this paper.
Paton and Allison, 1972	Chromosomal aberrations in human fibroblasts and human peripheral lymphocyte (HPL) cultures exposed in vitro.	$NaAsO_2$ (2.9×10^{-9} to 1.8×10^{-8} M) HPL. Na_2HAsO_4 (5.8×10^{-8} M) HPL. $NaAsO_2$ (2.9×10^{-9} to 5.8×10^{-8} M) fibroblasts. Source: British Drug House Chemical LTD. Solvent: H_2O	Positive for $NaAsO_2$ in HPL. Positive for $NaAsO_2$ in fibroblasts. Negative for Na_2HAsO_4 in HPL.	1. Incubation with chemical was for 48 hrs and 24 hrs for HPL and fibroblasts, respectively. 2. "Subtoxic" doses were used.
Larramendy et al., 1981	Induction of chromosomal aberrations in Syrian hamster embryo (SHE) cells and human peripheral lymphocytes (HPL) in vitro.	$NaAsO_2$ (7.7×10^{-6} M) in HPL and SHE. Na_2HAsO_4 (3.2×10^{-5} M) in HPL and SHE. Source: Chemical Services Inc. "100% pure" Solvent: Cell culture medium	Highly significant increase in the aberration frequency with both compounds in HPL and SHE.	1. Arsenite was about an order of magnitude more genotoxic than arsenate. 2. Both compounds induced mainly chromatid type aberrations. 3. Doses tested were generally non-cytotoxic. 4. Exposure to arsenic was for 24 and 48 hrs. in SHE and HPL, respectively.

TABLE 6-2. (continued)

Reference	Test System	Chemical Information	Results	Comments
Nakamuro and Sayato, 1981.	Chromosomal aberrations in cultured human peripheral lymphocytes (HPL) and fibroblasts.	As_2O_3 (3×10^{-7}, 12×10^{-7}, 36×10^{-7}M). $AsCl_3$ (6×10^{-7}, 24×10^{-7}, 72×10^{-7}M). $NaAsO_2$ (6×10^{-7}, 24×10^{-7}, 72×10^{-7}M). Na_2HAsO_4 (24×10^{-7}, 72×10^{-7}, 240×10^{-7}M). H_3AsO_4 (6×10^{-7}, 24×10^{-7}, 72×10^{-7}M). As_2O_5 (3×10^{-7}, 12×10^{-7}, 36×10^{-7}M). Source: Wako Pure Chemical Co. Solvent: H_2O	1. All arsenic compounds were clastogenic, all gave linear dose-response functions in lymphocytes. $NaAsO_2$ and H_3AsO_4 were positive with linear dose-response functions in fibroblasts. 2. Trivalent compounds were more potent than pentavalent compounds. The observed order for decreasing potency was: As_2O_3 > $AsCl_3$; Na AsO_2 >> Na_2HAsO_4 > H_3AsO_4; As_2O_5.	1. Treatment of lymphocytes was for the last 24 hours of culture. 2. Fibroblasts were exposed for 48 hrs. 3. All compounds induced more chromatid-type aberrations.

TABLE 6-2. (continued)

Reference	Test System	Chemical Information	Results	Comments
Nordenson et al., 1981	Chromosomal aberrations in peripheral lymphocytes of 3 normal volunteers - *in vitro* exposure.	$NaAsO_2$ (77×10^{-8}, 150×10^{-8}, 230×10^{-8}, 310×10^{-8} M). Na_2HAsO_4 (77×10^{-8}, 150×10^{-8}, 230×10^{-8}, 310×10^{-8} M). Source: Merck Solvent: Normal saline	$NaAsO_2$ caused a dose-related increase in gaps and chromatid breaks. Na_2HAsO_4 was negative.	1. Arsenic added 24 hours after initiation of culture, harvested at 72 hours. 2. Only scored gaps, chromatid and chromosome breaks. 3. Also examined G_0 effects: 24 hr. exposure without PHA, remove arsenic, add PHA, harvest after 48 hours; examined "$NaAsO_4$" - do not know what compound was really tested. 4. Reason for negative result with arsenate is that a sufficiently high dose was not tested. Should have increased concentration by an order of magnitude.

TABLE 6-2. (continued)

Reference	Test System	Chemical Information	Results	Comments
Wan et al., 1982	Induction of chromosome aberrations in vitro in CHO cells and human peripheral lymphocytes (HPL).	$NaAsO_2$ (10^{-6}, 5×10^{-6}, 10^{-5} M) CHO; (0.5×10^{-6}, 10^{-6}, 5×10^{-6} M) HPL Na_2HAsO_4 (5×10^{-5}, 8×10^{-5}, 10^{-4} M) CHO. Purity: Analytical grade Source: Fisher Scientific Co. Solvent: H_2O	Dose-related increase for both compounds in CHO. $NaAsO_2$ gave dose-related increase in HPL.	1. Trivalent was 5 to 10 x more potent than pentavalent. 2. All doses tested were inhibitory to CHO cell growth. 3. Arsenic present for entire culture period (22 hrs.) in CHO cells, and final 48 hrs of culture in HPL.
Poma et al., 1981b	Induction of chromosomal aberrations in mouse bone marrow and spermatogonia in vivo.	As_2O_3, single I.P. injection (4, 8 and 12 mg As/kg). Solvent: H_2O	Negative in bone marrow. Negative in spermatogonia.	1. Mouse strain: Swiss Albino 2. Sex: male. 3. Age: 12 weeks 4. Number of animals per dose group: 4-8. 5. Cells per animal: 100. 6. Sacrifice times: 12, 24, 36, 48 hrs post injection.

mitogenically stimulated human peripheral lymphocytes. Sodium arsenite gave positive results in both cell types while sodium arsenate was tested only in lymphocytes and was reported to be negative. Since arsenate (which most investigators find to be considerably less potent than arsenite) was tested at a lower concentration, the negative result is not surprising.

In a more recent study, the effects of sodium arsenite and sodium arsenate on chromosomal aberration frequencies were examined in cultured human peripheral lymphocytes and in Syrian hamster embryo cells (Larramendy et al., 1981). Both compounds gave highly significant increases in chromosomal aberrations in both cell types. Arsenite was more potent by approximately an order of magnitude, and both compounds induced mainly chromatid-type aberrations.

Nakamuro and Sayato (1981) tested six arsenic compounds for the induction of chromosomal aberrations in cultured human peripheral lymphocytes and in human skin fibroblasts. All arsenic compounds tested were clastogenic and all gave linear dose-response functions in lymphocytes. Trivalent compounds were more potent than pentavalent compounds. The observed order for decreasing potency was As_2O_3 > $AsCl_3$; $NaAsO_2$ >> Na_2HAsO_4 > H_3AsO_4; As_2O_5 (Figure 6-1). $NaAsO_2$ and H_3AsO_4 were positive, showing linear dose-response functions in fibroblasts. All compounds induced predominantly chromatid-type aberrations.

In another study, the effects of sodium arsenite and sodium arsenate on the induction of chromosomal aberrations in human peripheral lymphocytes exposed in vitro were examined using two protocols (Nordenson et al., 1981). In the first protocol, cells were mitogenically stimulated with PHA, arsenic was added after 24 hours and cells were harvested after 72 hours (48-hour arsenic exposure). Using this method, sodium arsenite was found to increase the frequency of chromatid breaks and gaps in a dose-dependent fashion. Sodium arsenate was reported to be negative, but these investigators employed

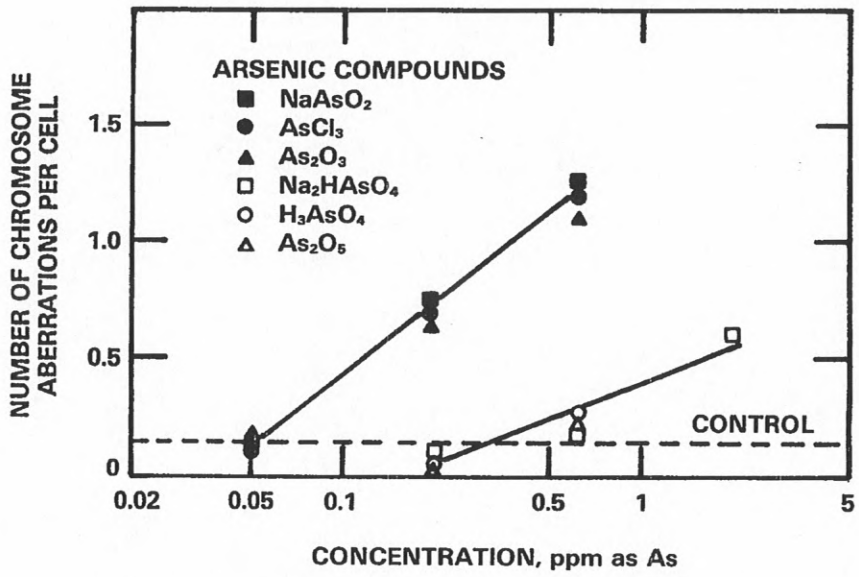

Figure 6-1. The induction of chromosome aberrations in cultured human peripheral lymphocytes by six arsenic compounds.

Source: Nakamuro and Sayato (1981).

the same concentrations of arsenate as were tested for arsenite. It is possible that higher doses of arsenate would also have yielded positive results. In the second protocol, G_0 (unstimulated) lymphocytes were exposed to arsenic for 24 hours, and the cells were washed, stimulated with PHA and harvested after 48 additional hours. Using this protocol the authors reported that "$NaAsO_4$" was negative. One may assume that the authors meant $NaAsO_2$, since having observed a lack of activity for arsenate in the first protocol, it would seem unwarranted to test it in the second. If the test compound was indeed arsenite, these observations suggest that arsenic has its effect through some influence on DNA synthesis and not by directly damaging DNA.

In the most recent study on in vitro clastogenic effects of arsenic compounds, sodium arsenite and sodium arsenate were tested in CHO cells and human peripheral lymphocytes (Wan et al., 1982). Both compounds showed dose-dependent increases in aberrations in CHO cells; arsenite was also positive in lymphocytes. Again, trivalent arsenic was 5 to 10 times more potent than pentavalent arsenic.

6.2.2 Chromosomal Aberrations In Vivo

There is only one report in the literature (excluding abstracts) in which the clastogenic effects of arsenic were tested in a mammalian species in vivo (Poma et al., 1981b). These authors examined chromosomal aberration frequencies in mouse bone marrow cells and spermatogonia after administration of As_2O_3 (4, 8 and 12 mg of arsenic/kg). This trivalent form of arsenic was previously shown to be the most potent form in vitro (Nakamuro and Sayato, 1981). Four to 8 animals were included in each dose group; animals were killed at 12, 24, 36 and 48 hours after exposure and 100 metaphase cells per animal were scored. This represents an acceptable protocol, and the study appears to have been properly performed. There was no significant increase in aberrations in either

bone marrow or spermatogonia following arsenic treatment. An important question in this study is whether sufficiently high doses were tested. The LD_{50} for arsenic trioxide in rats is 104 mg As/kg; thus, the highest dose used in this mouse study is only 13 percent of the rat LD_{50}. One can crudely compare the doses of arsenic trioxide which were effective in vitro to those used in this study by simply equating the test animal to an equivalent volume of water. Such a comparison indicates the mice were "1.6×10^{-4} M" effective for arsenic while the same compound was effective for inducing aberrations in vitro at approximately 0.7 to 7.0×10^{-4} M arsenic. Clearly this represents a very crude comparison since intact animals can bind, compartmentalize and excrete a toxicant while cells in culture cannot. Thus, it is not clear whether higher doses should have been tested in this study.

6.2.3 Chromosomal Aberrations and SCE in Cells of Arsenic-Exposed Human Beings

The majority of studies indicate that people exposed to arsenic due to occupation or pharmaceutical treatment display increased levels of chromosomal aberrations and SCE in peripheral lymphocytes (Table 6-3). It should be noted that most of the studies which have examined aberrations and SCE are poor in quality due either to errors in experimental protocol, misclassification of aberrations, poor choice in controls and/or not performing studies in a blind fashion.

Beckman et al. (1977) examined the frequency of chromosomal aberrations in peripheral lymphocytes of nine smelter workers who were exposed to arsenic. The levels and the forms of arsenic to which the workers were exposed were not indicated. A statistically significant increase in aberrations was found in the exposed population. There are several problems with this study. First, the authors use an incorrect definition of gaps. They state: "Gaps are commonly defined as achromatic regions exceeding the width of a chromosome." This, in

TABLE 6-3. SUMMARY OF MUTAGENICITY OF ARSENIC: CHROMOSOMAL ABERRATIONS AND SCE IN CELLS OF EXPOSED HUMANS

Reference	Test System	Chemical Information	Results	Comments
Beckman et al., 1977	Chromosomal aberrations in lymphocytes of 9 smelter workers exposed to arsenic.	Arsenic from smelter	Positive, six-fold increase in percent aberrant cells; eight-fold increase in aberrations per cell.	1. Authors used an incorrect definition of gaps. 2. Cells cultured too long (72 hours). 3. Cells scored per individual were unknown. 4. Number of control individuals and cells per control individual were not specified. 5. Some workers were also exposed to lead and selenium.
Nordenson et al., 1978	Chromosomal aberrations in lymphocytes of 33 smelter workers.	Arsenic from smelter	Positive	1. Divided workers into high exposure (18 individuals), medium exposure (11), low exposure (4) and new employees (6). 2. The controls were an unspecified number of apparently historical controls. 3. No dose effect. 4. Wrong definition of gaps. 5. Cell culture time too long. 6. Large difference between controls and new employees.

TABLE 6-3. (continued)

Reference	Test System	Chemical Information	Results	Comments
Burgdorf et al., 1977	Compared SCE and chromosomal aberrations in lymphocytes of 6 patients treated with arsenic, with results from 44 control individuals.	All treated with Fowler's solution (1% $KAsO_2$ in H_2O), for time periods between 4 and 27 years. Five of these individuals had not been treated for at least 24 years.	No difference in frequencies of chromosomal aberrations. SCE frequencies were increased more than 2-fold in arsenic-treated patients.	1. Cultured cells for 72 hours - too long for examination of aberrations. 2. No indication that study was scored blind. 3. Patients exposed to other agents (e.g. 4000 rad x-irradiation, 5000 rad x-irradiation, fluoroscopy twice weekly while receiving arsenic, 4 had asthma).
Petres et al., 1977	Chromosome aberrations in lymphocytes of 31 individuals exposed to arsenic.	Arsenic exposure related to treatment for psoriasis or associated with vine-growing.	Positive, nine-fold increase in aberrations among arsenic-exposed individuals.	1. 31 exposed individuals, 31 controls. 2. Cell culture time too long (72 hours). 3. Scored both gaps and achromatic lesions - same aberration. 4. Scored secondary constrictions - not generally considered an aberration. 5. No indication of the number of cells per person scored. 6. Saw a 5-fold increase in aneuploidy among arsenic-exposed individuals, always hypodiploidy, which suggests an artifact.

TABLE 6-3. (continued)

Reference	Test System	Chemical Information	Results	Comments
Nordenson et al., 1979	Chromosome aberrations and SCE in peripheral lymphocytes of 8 psoriatic patients treated with arsenic.	Total arsenic dose per individual varied from a low of 300 mg up to 1200 mg. Most had not been treated for 15 years.	Psoriatic patients treated with arsenic showed significantly higher (three-fold) levels of aberrations compared to control psoriatics. Psoriatic patients treated with arsenic had the same levels of SCE as controls.	1. Slides were scored blind. 2. Investigators controlled for age and sex but not for ethanol use, smoking, drug use, or infection. 3. The increases in aberrations were not dose-related. 4. Cultured cells for 72 hours: too long for aberrations. 5. Scored too few cells for SCE in control patients; provided total number of cells scored, but number of cells per individual was unknown.

TABLE 6-3. (continued)

Reference	Test System	Chemical Information	Results	Comments
Wen et al., 1981	SCE in peripheral lymphocytes of 13 Blackfoot disease patients (arsenic-exposed) and 13 controls.	Exposure to arsenic from well water; years of use ranged from 15 to 58. Most had not consumed contaminated water for 12 years.	Arsenic-exposed individuals showed small but statistically higher SCE level. Ranges for arsenic-exposed (9.1 to 17.5 SCE/cell) and controls (7.8 to 12.0 SCE/cell) showed considerable overlap.	1. Patients exposed to a large number of other drugs, including pantopan, scopolamine, promethazine hydrochloride, meperidine, ketamine hydrochloride, Pyrabital, Valium, ampicillin, Kanamycin, Sedes, diphenhydramine hydrochloride, Kolantyl, Complamin, Venostatin, Ulcerin, metoclopramide, Sulpyrin, chloramphenicol, reserpine, Bartropine, dextromethorphan, furosemide, and Hustazol. 2. All patients had undergone leg or foot amputation.

fact, is a definition for a break. A gap is commonly defined as an achromatic lesion not exceeding the width of a chromatid arm. Second, the total number of cells examined are given but the cells per individual worker, cells per individual control, and total number of control individuals are not listed. Third, these investigators cultured the lymphocytes for 72 hours, a duration 24 hours longer than optimum, since most chromosome aberrations are cytotoxic, and cells with such lesions generally do not survive more than a single cell cycle. After 72 hours of culture, the majority of cells have divided three times, eliminating many damaged cells. Clearly, however, this type of error tends to underestimate the frequency of aberrations. Finally, workers were also exposed to other potentially clastogenic agents such as lead and selenium.

A report one year later by the same group (Nordenson et al., 1978) extended this study to a total of 33 smelter workers. In this study individuals were grouped into high exposure (18 people), medium exposure (11), low exposure (4) and new employees (6). The groupings were based on the nature of the job; quantitative measurements of exposure were not performed. The workers were reported to have a higher level of chromosome aberrations than did the controls. However, the controls were of an unspecified number and, apparently, historical, the definition of gaps was incorrect, cells were cultured for 72 hours, and large differences were found between historical controls and new employees. Due to these problems, the positive findings reported are questionable.

Burgdorf et al. (1977) compared SCE and chromosomal aberration frequencies in lymphocytes of six patients treated with arsenic (for asthma, psoriasis or anxiety) to results from 44 control individuals. All patients had been treated with Fowler's solution (1% $KAsO_2$ in water) for time periods varying between 4 and 27 years. Five of these individuals had not been treated for at least 24 years. The authors found no difference in frequencies of chromosomal aberrations, but reported a more than 2-fold higher SCE frequency in arsenic-treated

patients. Each of the patients had an SCE level which was significantly higher than the mean level for controls. Problems with this study included a 72-hour culture period for aberrations, no indication that slides were scored "blind," and the fact that patients were exposed to other agents (4000 rad x-irradiation, 5000 rad x-irradiation, fluoroscopy twice weekly concomitant to arsenic exposure).

In a similar study, Petres et al. (1977) compared chromosome aberrations in lymphocytes of 31 arsenic-exposed people to 31 controls. Arsenic exposure resulted from treatment for psoriasis or was associated with vine-growing. The levels and forms of arsenic exposure were not indicated. A statistically significant increase in aberrations was found in the exposed group. These authors also reported a five-fold increase in aneuploidy among arsenic-exposed individuals. Problems in this study include: (1) a 72-hour cell culture period; (2) no indication of the number of cells per person scored; (3) scoring both gaps and achromatic lesions, identical endpoints; (4) scoring secondary constrictions, which are generally not considered to be aberrations; and (5) all aneuploid cells were hypodiploid, which suggests an artifact.

Nordenson et al. (1979) compared chromosome aberrations and SCE in peripheral lymphocytes of 8 arsenic-treated psoriatic patients to 8 untreated psoriatic controls. Total arsenic dose per individual varied from a low of 300 mg up to 1200 mg. Most had not been treated for 15 years. Psoriatic patients treated with arsenic showed significantly higher levels of aberrations compared to controls, but showed similar frequencies of SCE. The increase in aberrations was not related to the total arsenic dose. Although these authors controlled for age and sex, there was no apparent control for smoking, drug use or ethanol consumption. An average of 15 cells per individual were scored for SCE; generally, 20 cells per individual is considered the acceptable minimum. As in the other studies, the cells were cultured for 72 hours.

Frequencies of SCE were compared in 13 patients exposed to arsenic in drinking water to SCE frequencies in 13 control individuals (Wen et al., 1981). All patients displayed symptoms of Blackfoot disease, a peripheral vascular disease resulting from chronic arsenic intoxication. Patients had used contaminated water for 15 to 58 years; most had switched to uncontaminated tap water 12 years before this study. Arsenic-exposed individuals showed a small but statistically higher SCE level. Ranges for arsenic-exposed (9.1 to 17.5 SCE/cell) and controls (7.8 to 12.0 SCE/cell) showed considerable overlap. Sources of error in this study are large since the arsenic-exposed group had also been exposed to over 20 different pharmaceuticals.

6.3 OTHER STUDIES INDICATIVE OF MUTAGENIC DAMAGE

6.3.1 Preferential Killing of Repair-Deficient Bacterial Strains

Arsenic compounds have generally been found to preferentially kill bacteria that carry particular mutations in DNA repair pathways (Table 6-4). Both sodium arsenite and sodium arsenate gave positive results in the B. subtilus "rec assay" (Nishioka, 1975). In this assay, test chemicals are spotted onto filter discs and the discs are placed at the centers of a bacterial lawn composed of rec^+ cells (H17) or rec^- cells (M45, deficient in recombinational DNA repair). The size of the zone of growth inhibition is measured for both strains, with a differential response (more killing of M45) indicative of a DNA-damaging agent. Sodium arsenite was reported to give a moderately positive response while sodium arsenate was reported to give a weakly positive response.

The results for sodium arsenate were reproduced in the B. subtilus rec assay and positive responses for four other arsenic compounds (As_2O_5, As_2O_3, $AsCl_3$, $3AsO_5$) have been reported (Kanematsu et al., 1980). These authors indicated that all arsenic compounds gave "strongly positive" responses (greater than 6 mm growth difference).

TABLE 6-4. MUTAGENICITY OF ARSENIC: ASSAYS INDICATIVE OF DNA DAMAGE OR REPAIR

Reference	Test System	Chemical Information	Results	Comments
Nishioka, 1975	Rec assay in B. subtilus. Strains: H_{17} (rec^+, arg^-, trp^-) M45 (rec^-, arg^-, trp^-	$NaAsO_2$ (0.05 M) Na_2HAsO_4 (0.05 M) 0.05 ml aliquot spotted onto filter disc. Source: Nakarai Chemical LTD. Solvent: H_2O	$NaAsO_2$ moderate positive response in rec assay. Na_2HAsO_4 weak positive response in rec assay.	
Kanematsu et al., 1980	Implication of DNA damage through the measurement of growth of normal (rec+) and recombination-repair-deficient (rec^-) B. subtilis, "rec assay." Strains: H_{17} (rec^+, agr^-, trp^-) M45 (rec^-, arg^-, try^-).	As_2O_5 (0.05 M) As_2O_3 (0.05 M) $AsCl_3$(0.03 ml) $3AsO_5$ (0.05 M) Na_2HAsO_4 (0.1 M) 0.05-ml portions of aqueous solutions at the indicated concentration are applied to the paper disc. Source: Marvichi Chemical LTD. Solvent: H_2O	All arsenic compounds gave strong positive responses. (Greater than 6-mm difference in growth).	1. Plates kept at 4°C for 24 hrs. prior to incubation at 37°C. This "cold incubation" increases the sensitivity of the assay 20 to 50 times.

TABLE 6-4. (continued)

Reference	Test System	Chemical Information	Results	Comments
McCarroll et al., 1981	E. coli micro-suspension assay. Measures preferential killing of repair-deficient strains. Strains WP2 (wild type) WP2 UVRA ($uvrA^-$) CM611 ($lexA^-$, $uvrA^-$) WP67 ($polA^-$, ($uvrA^-$) WP100 ($recA^-$, $uvrA^-$) WP3110 (thy^-) P3478 ($polA^-$, thy^-)	Na_2HAsO_4 500, 250, 125, 62.5, 31.3, 15.6, 7.8, 3.9, 1.9, 0.98, 0.5, 0.2 (µg/well). $NaAsO_2$ Same	Na_2HAsO_4 was positive at 130 µg/well in strain WP100. $NaAsO_2$ was positive at 63 µg/well in strain CM 611. Results in all other strains were negative.	1. The total volume per well is not clearly stated, thus the molarity of the arsenic solutions can not be calculated 2. Strain WP100 is deficient in excision repair and in postreplicational repair (both SOS error-prone and recombinational). 3. Strain CM611 is deficient in excision repair and in post-replicational error-prone (SOS) repair.
Nordenson et al., 1981	SCE in peripheral lymphocyes, in vitro exposure.	Source: Merck Solvent: Normal saline $NaAsO_2$ (390×10^{-8} M)	Positive SCE response (1.5-fold increase).	1. Added arsenic to cultures 24 hours after initiation of culture, harvested at 72 hours.

TABLE 6-4. (continued)

Reference	Test System	Chemical Information	Results	Comments
Larramendy et al., 1981	Induction of SCE in Syrian hamster embryo (SHE) cells and human peripheral lymphocytes (HPL) in vitro.	$NaAsO_2$ (7.7×10^{-7}, 1.9×10^{-6} M) in HPL. Na_2HAsO_4 (1.6×10^{-5}, 3.2×10^{-5} M) in HPL. $NaAsO_2$ (3.8×10^{-7}, 3.8×10^{-6}, 7.7×10^{-6} M) SHE. Na_2HAsO_4 (3.2×10^{-6}, 8×10^{-6}, 1.6×10^{-5}, 3.2×10^{-5} M) SHE. Source: Chemical Services Inc. "100% pure" Solvent: Cell culture medium	Dose-related increases in SCE with both compounds in both HPL and SHE (two-fold increases).	1. Arsenite was about an order of magnitude more genotoxic than arsenate. 2. Doses tested were generally non-cytotoxic. 3. Both compounds were less efficient in inducing SCE in human whole blood cultures than in purified lymphocyte cultures. 4. Exposure to arsenic was for 24 and 48 hrs. in SHE and HPL, respectively.
Andersen, 1983	Sister chromatid exchange in cultured human lymphocytes (3 donors); and in P388D cells (continuous line of macrophage cells derived from DBA/2 mouse).	$NaAsO_2$ (10^{-6}, 10^{-7}, 10^{-8} M) P388D cells. Na_2HAsO_4 (10^{-5}, 10^{-6}, 10^{-7} M) P388D cells. $NaAsO_2$ (10^{-6} M) human lymphocytes. Solvent: H_2O	Both compounds negative in P388D cells. $NaAsO_2$ positive in lymphocytes from all three donors.	1. Chemical exposure was 48 hrs. in P388D cells. 2. Chemical exposure 24, 48, and 72 hrs. in lymphocytes. 3. Results in lymphocytes variable between donors, ranging from 30% to 117% increases in SCE frequencies for the three individuals.

TABLE 6-4. (continued)

Reference	Test System	Chemical Information	Results	Comments
Crossen, 1983	Sister chromatid exchange in cultured peripheral lymphocytes from 4 normal human volunteers.	Na_2HAsO_4 (1.34×10^{-5}, 2.68×10^{-5} M) $NaAsO_2$ (7.69×10^{-7}, 1.54×10^{-6} M) Source: BDH Chemicals Solvent: H_2O	Na_2HAsO_4 - 1 donor increased SCE, 2 donors unchanged SCE, 1 donor decreased SCE. $NaAsO_2$ - 2 donors increased SCE, 2 donors unchanged. Both compounds negative when cells treated during G_o and <u>not</u> present during replication.	1. Results suggest that arsenic does not damage DNA but may interfere with DNA replication. 2. Even positive responses were generally not dose-related. 3. Large variation in baseline SCE levels between individuals. 4. Both compounds present during final 48 hrs of culture.

TABLE 6-4. (continued)

Reference	Test System	Chemical Information	Results	Comments
Ohno et al., 1982	SCE induction in DON Chinese hamster cells in vitro.	$NaAsO_2$ (7.7×10^{-6} M) As_2O_5 (1.4×10^{-5} M) Na_2HAsO_4 (5.4×10^{-6} M)	All compounds gave a significant increase in the SCE frequency (1.5-fold, 1.6-fold and 1.5-fold, respectively).	1. Chemical exposure was for 28 hrs. 2. Doses tested caused a 50% inhibition in cell growth.
Wan et al., 1982	Induction of SCE in CHO cells in vitro.	$NaAsO_2$ (10^{-6}, 10^{-5} M) Purity: analytical grade. Source: Fisher Scientific Co. Solvent: H_2O	Dose-related increase in SCE (2.4-fold increase).	1. Arsenic present for entire culture period (24 hrs).

TABLE 6-4. (continued)

Reference	Test System	Chemical Information	Results	Comments
Tkeshelashvili et al., 1980	Fidelity of DNA synthesis components: 1. E. coli DNA polymerase. 2. Artificial DNA template poly-[d(A-T)]. 3. Radiolabeled nucleotide triphosphates	Na_2HAsO_4 (0.1, 0.5, 1.0., 5.0 mM) As_2O_5 (0.1, 0.5, 2.5, 10.0 mM) Source: Either ICN Corp. or J.T. Baker Purity: 99.9%	Neither arsenic compound affected the "natural" error rate.	1. Other metals such as chromium increase the error rate in this system. 2. This is a very artificial system, i.e., the polymerase is a bacterial-repair enzyme, the DNA is an artificial template containing only two nucleotide bases and the system is carried out entirely in vitro.
Fornace and Little, 1979	Induction of DNA-protein crosslinking and single-strand DNA breaks in mouse C3H/10T 1/2 cells (alkaline elution).	$NaAsO_2$ (1 mM) Solvent: Cell culture medium	No crosslinks detected. Positive for single-strand breaks (equivalent to 120 rad of X-ray)	1. Cells were treated for 1 hour; only 2.2% of cells survived this treatment.

Sodium arsenate and sodium arsenite were also found positive in the E. coli microsuspension test (McCarroll et al., 1981). In this assay, a variety of E. coli strains carrying mutations for DNA repair are incubated in multiwell microplates with a serially-diluted test compound. The highest dose at which growth is evident is compared in wild type and DNA repair-deficient strains. Again, a differential sensitivity to growth inhibition is indicative of DNA damage. Sodium arsenate was found to preferentially inhibit the growth of strain WP100 ($recA^-$, $uvrA^-$) compared to wild type cells. This strain is deficient in excision as well as recombinational repair. Sodium arsenite was positive in strains WP100 and CM611 ($lexA^-$, $uvrA^-$). This latter strain is deficient in excision repair and is not inducible for post-replicational error-prone (SOS) repair. Negative results were seen in strains which are only deficient in excision repair, implying that arsenic-induced damage is not repaired by this pathway or that arsenic has no effect on enzymes which repair spontaneous damage through excision repair.

6.3.2 DNA Damage in Mammalian Cells In Vitro

Fornace and Little (1979) examined the effects of sodium arsenite on the induction of DNA-protein crosslinks and single-strand DNA breaks in mouse C3H/10T 1/2 cells using alkaline elution (Table 6-4). This technique measures the rate at which radiolabeled DNA passes through a polyvinyl chloride filter having a defined pore size. Treatment of cells for one hour did not induce DNA-protein crosslinks but did cause a significant increase in single-strand breaks. The level of breakage observed was equivalent to treating the cells with 120 rad of x-ray. It should be noted that the treatment protocol was highly toxic with only 2.2 percent of cells surviving the treatment.

6.3.3 Fidelity of DNA Synthesis

Some metals, such as chromium, are thought to be mutagenic by interfering with a DNA polymerase-editing function. As a result they increase the rate at

which "errors" are made in DNA replication. Loeb and co-workers have designed an *in vitro* system that measures the rate at which particular nucleotides are inappropriately incorporated into DNA (Sirover and Loeb, 1976; Tkeshelashvili et al., 1980) (Table 6-4). In this system, the DNA template is a repeating sequence of adenine and thymidine (poly[d(A - T]) which is incubated with *E. coli* DNA polymerase I, and ^{32}P-labelled dTTP and ^{3}H-dGTP. By monitoring the ratio of the two isotopes in acid precipitable material one can quantify the frequency with which an error in incorporation is made. Neither sodium arsenate nor arsenic pentoxide (As_2O_5) affected the "natural" error rate. Chromium was shown to be positive in this assay. It should be cautioned that this is a very artificial system, i.e., the polymerase is a bacterial-repair enzyme, the DNA is an artificial template containing only two nucleotide bases, and the system is carried out entirely *in vitro*.

6.3.4. Induction of Sister Chromatid Exchanges (SCE) In Vitro

Arsenic compounds have been extensively tested for the induction of SCE in a variety of cell types *in vitro*. Almost without exception the results are positive (Table 6-4). Significant increases in SCE frequencies were shown in human peripheral lymphocytes treated with sodium arsenite (Nordenson et al, 1981; Larramendy et al., 1981; Anderson, 1983; Crossen, 1983) and sodium arsenate (Larramendy et al., 1981; Crossen, 1983). The studies by Crossen, however, suggested that individuals may vary significantly in their susceptibility to arsenic-induced SCE. Crossen noted that arsenite increased the SCE frequency in cells from two donors but had no effect in cells from two other donors. Arsenate increased the SCE frequency in one donor, had no effect in two other donors and slightly decreased the SCE frequency in a fourth donor. Crossen also used a protocol in which cells were exposed to arsenic in G_0 (unstimulated), washed and then cultured for SCE analysis. The results were

similar to those seen for chromosomal aberrations (Nordenson et al., 1981), i.e., neither arsenite nor arsenate increased SCE levels when treatment occurred during a nonreplicative phase. Again, these results indicate that arsenic must be present during DNA synthesis (SCE occur during S phase) to have an effect.

Arsenic has also been tested for SCE induction in Chinese hamster lines *in vitro*. Wan et al. (1982) reported a dose-related increase in SCE in CHO cells exposed to sodium arsenite, while Ohno et al. (1982) reported significant increases in the SCE frequency in DON cells exposed to single doses of sodium arsenite, sodium arsenate, and arsenic pentoxide.

6.4 INTERACTIONS OF ARSENIC WITH OTHER MUTAGENS

6.4.1. Bacterial Studies

The effects of sodium arsenite (1 mM) on the frequencies of UVC-induced mutations were measured in *E. coli* strain WWP_2 (trp^-, $uvrA^-$), a strain deficient in excision repair (Rossman et al., 1977). Arsenite was found to reduce the number of UVC-induced mutations by 30 to 40 percent. This observation suggests that arsenic may interfere with SOS (error prone) DNA repair, and may, therefore, be a bacterial antimutagen (Table 6-5).

In a later study, Rossman (1981) further examined the effect of sodium arsenate and sodium arsenite on frequencies of UVC-induced mutations. In *E. coli* WP2, which is proficient in all repair pathways, arsenite increased UVC mutagenesis at doses up to 0.25 mM and then decreased the mutation frequency at higher doses. The increase in mutation was seen only in excision repair-proficient strains. These observations suggest that arsenic interferes with excision repair at low doses and interferes with SOS repair at higher doses.

Fong et al. (1980) examined the effect of sodium arsenate on the frequency of UVC-induced single-strand DNA breaks in *E. coli* (Table 6-5). The presence

TABLE 6-5. SUMMARY OF MUTAGENICITY OF ARSENIC: INTERACTIONS WITH MUTAGENS

Reference	Test System	Chemical Information	Results	Comments
Rossman et al., 1977	Interaction of UVC and arsenic in E. coli for mutation. Strain WWP_2 (trp^-, $uvrA^-$).	$NaAsO_2$ (1 mM) plus 1.25, 5.0, and 10 J/m^2 UVC	$NaAsO_2$ reduced the number of UVC-induced mutants by 30 to 40 %.	1. Suggests that arsenic interferes with SOS repair. 2. May not be relevant to mammals since this type of repair has not been found.
Rossman, 1981	Interaction of arsenic and UVC in the induction of mutations of E. coli. Strains: WP2 (trp^-) $WP2_s$ (trp^-, $uvrA^-$) WP6 (trp^-, $polA1^-$) WP5 (trp^-, $lexA^-$) WP10 (trp^-, $recA^-$)	$NaAsO_2$ (0.1, 0.25, 0.5, 0.75 mM) plus 5.6 J/m^2 in WP2. Na_2HAsO_4 (0.1, 0.3, 0.5 mM) plus 5.6 J/m^2 in WP2. $NaAsO_2$ (0.2 mM) plus 5.6 J/m^2 in WP2, 0.6 J/m^2 in $WP2_s$, 1.2 J/m^2 in WP6, 0.6 J/m^2 in WP5, 0.6 J/m^2 in WP10 Source: Fisher Chemical Co.	Arsenite increased UVC mutagenesis in WP2 at doses up to 0.25 mM and then decreased mutation frequency at higher doses. This increase was not seen with arsenate. The effect with arsenite was seen only in excision repair-proficient strains.	1. Observations indicate that arsenic may interfere with excision repair at lower doses and with SOS repair at higher doses.

TABLE 6-5. (continued)

Reference	Test System	Chemical Information	Results	Comments
Fong et al., 1980	Induction of single-strand (S.S) DNA breaks in E. coli after exposure to UVC light (alkaline sucrose sedimentation). Strains used: WP2-wild type WP6-(polA), lacks DNA polymerase used in repair WP2-(uvrA), deficient in excision repair.	$NaAsO_2$ (1,2,3,4, 5 mM)	1 mM arsenic inhibited the induction of S.S. breaks in WP2 and WP6 after exposure to UVC (40 J/m^2 and 10 J/m^2, respectively). 3 mM arsenic prevented the rejoining of S.S. breaks after UVC (5 J/m^2) in WP2 (uvrA) cells.	1. Arsenic prevents enzymatic incision in DNA after exposure to ultraviolet light. 2. Authors speculate this may result from arsenic-induced depletion of cellular ATP. 3. Arsenic may inhibit post-replicational repair since it prevented rejoining of S.S. breaks in cells deficient in excision repair.
Jung et al., 1969	Inhibition of unscheduled DNA synthesis (UDS) in human epidermal cells seen in biopsies derived from seven normal volunteers after UV irradiation.	Na_2HAsO_4 (10^{-5}, 10^{-6} M)	Arsenic inhibited UVC-induced UDS.	1. Tissue biopsies were incubated with arsenic for either 1 hr or 4 hrs prior to UVC exposure. 2. There were no dose- or incubation time-related effects on inhibition of UVC-induced UDS. 3. Actual numbers were not shown.

TABLE 6-5. (continued)

Reference	Test System	Chemical Information	Results	Comments
Rossman, 1983 (progress report)	Mutation in V79 cells. Interaction of UVC and arsenite.	Arsenite	No interaction	1. No data provided.
Poma et al., 1981a (abstract)	Interaction between arsenic and ethyl methanesulfonate in the induction of chromosome aberrations in vivo in Swiss-albino mice: bone marrow, and spermatogonia.	Arsenic (12 mg As/kg) EMS (200 mg/kg) pre- or post-treatment.	No interaction	1. No experimental details, work described in an abstract.
Sram, 1976	Chromosomal aberrations in bone marrow cells of ICR mice. Each dose group consisted of 5 female mice. Animals sacrificed 24 hours after a single dose of TEPA, scored 250 metaphases/group (assume 50/animal).	$NaAsO_2$ in drinking water for 8 weeks. 10 mg/l (7.7×10^{-5} M) 100 mg/l (7.7×10^{-4} M) TEPA 2 mg/kg	$NaAsO_2$ alone did not appear to induce aberrations although the spontaneous rate was not clearly indicated. The lower dose of arsenic in drinking water did not affect the frequency of TEPA-induced aberrations. The higher dose of arsenic resulted in a synergistic increase in the aberration rate.	1. This study was lacking in experimental details.

TABLE 6-5. (continued)

Reference	Test System	Chemical Information	Results	Comments
Sram, 1976	Interaction of $NaAsO_2$ and TEPA for dominant lethals in ICR mice; each treated and control group consisted of 20 males and 40 females/week. Mating continued for 3 to 8 weeks after the application of TEPA.	$NaAsO_2$ in drinking water for 8 weeks/ generation, males were exposed for 4 generations prior to mating. 10 mg/l (7.7×10^{-5} M) 100 mg/l (7.7×10^{-4} M) TEPA 2 mg/kg	$NaAsO_2$ alone did not appear to induce dominant lethals, although it is not clear what the spontaneous rate was. There appeared to be a positive interaction between TEPA and the higher exposure to arsenic.	1. This study was badly lacking in experimental details. 2. It was not indicated at what time after TEPA administration the increase in dominant lethals was seen, thus it is not known which germ cell stage was affected.

of strand breaks in DNA was measured by alkaline sucrose sedimentation. One mM arsenite was found to inhibit the induction of strand breaks in WP2 (wild type) and WP6 polA (lacks DNA polymerase I) after exposure to UVC. The presence of 3 mM arsenate in growth medium prevented the rejoining of strand breaks after UVC exposure in WP2 uvrA cells (excision repair-deficient). The authors interpreted these observations to suggest: (1) that arsenic prevents enzymatic incision of DNA after UVC exposure (UVC alone does not cause strand breaks), and (2) that arsenic may inhibit post-replicational repair since it prevented rejoining of breaks in cells deficient in excision repair. The authors further speculated that the inhibition of enzymatic incision may result from arsenic-induced cellular depletion of ATP.

6.4.2 Mammalian Cells In Vitro

The interaction of sodium arsenate and UVC on levels of unscheduled DNA synthesis (UDS) was measured in cells from human skin biopsies taken from seven volunteers (Jung et al., 1969; Table 6-5). Arsenate was tested at two concentrations (10^{-5}, 10^{-6}M) and for two preincubation periods (1 and 4 hrs). Arsenic was reported to inhibit the level of UVC-induced UDS, although there were no dose- or time-related effects. The actual numbers were not reported in the paper.

Rossman (1983) examined the effect of arsenite on UVC-induced HGPRT mutations in V79 cells. Although no data were provided in this report, the outcome was reported to be negative.

6.4.3 Mammalian Cells In Vivo

The interaction of arsenic and ethylmethanesulfonate (EMS) on levels of chromosome aberrations in vivo was examined in bone marrow and spermatogonial cells of Swiss-albino mice (Poma et al., 1981a). The arsenic dose was 12 mg As/kg combined with either pre- or post-treatment with 200 mg/kg of EMS. No

interactions were reported. It should be cautioned that this information has only been reported in abstract form.

Sram (1976) examined the effects of including sodium arsenite in drinking water (7.7×10^{-5}, 7.7×10^{-4} M) on frequencies of tris (1-aziridinyl) phosphine oxide (TEPA)-induced (2 mg/kg) chromosomal aberrations in ICR mouse bone marrow cells. Animals were given arsenic-laced water for 8 weeks, were injected with TEPA, and killed after 24 hours. A total of 250 cells per dose group (5 animals per dose) were scored. Sodium arsenite alone did not appear to induce aberrations, although the spontaneous rate was not clearly indicated. The lower dose of arsenic in drinking water did not affect the frequency of TEPA-induced aberrations. The higher concentration of arsenic resulted in a synergistic increase in the aberration rate. This study was, unfortunately, lacking in experimental details.

Sram (1976) did essentially the same study for the examination of dominant lethality in ICR mice. Animals were maintained for 4 generations prior to mating on arsenic-laced drinking water (7.7×10^{-5}, 7.7×10^{-4} M). TEPA was again given as a single dose of 2 mg/kg. Each treated animal and a control group of 20 males was mated with 40 females per week. The matings continued for 3 to 8 weeks after mutagen application. Sodium arsenite alone did not appear to induce dominant lethals, although the spontaneous rate was not clearly indicated. The lower dose of arsenic in drinking water did not affect the frequency of TEPA-induced dominant lethals. The higher concentration of arsenic resulted in a synergistic increase in the dominant lethal rate. It was not indicated at what time after TEPA administration the increase in dominant lethals occurred; thus, it is not known which germ cell stage was affected. This study also failed to provide experimental details.

6.5 POSSIBLE MECHANISMS OF ACTION

Arsenic is unusual in several respects. First, unlike the overwhelming majority of clastogenic agents, arsenic does not appear to directly damage DNA. Rather, it seems to have its effect through some interference with DNA synthesis. This contention is supported by the observations that arsenic induces chromosomal aberrations and SCE only when it is present during DNA replication. Incubation and removal of arsenic before DNA synthesis has no effect (Nordenson et al., 1981; Crossen, 1983).

Second, arsenic is highly unusual in that it induces chromosomal aberrations and SCE while it fails to induce gene mutations. In this regard, it is like diethylstibesterol, which is another highly unusual carcinogen. X-irradiation, although capable of producing chromosome aberrations as well as gene mutations, is much more potent for the former endpoint. There is a small possibility, however, that the discrepancy for arsenic may be founded on an artifact. Protocols for gene mutation assays generally involve cellular incubation with the test agent for relatively short time periods (2 to 3 hours), while protocols for aberrations often involve the presence of the test agent for one or two entire cell cycles (12 to 48 hours). Thus, in the latter protocol, arsenic would be present for at least an entire S phase for all cells, whereas, when tested for gene mutations, arsenic would be present for only a small fraction of the S phase in approximately one-third to one-half of the cells. Since the evidence available suggests that arsenic has its effect only during DNA replication, this may account for the discrepancy.

Arsenic has long been known to be a sulfhydryl reagent capable of inhibiting a number of thiol-dependent enzyme systems, trivalent forms being much more potent than pentavalent forms (Leonard and Lauwerys, 1980). Thus, one possible mechanism of action for arsenic would be the inhibition of DNA repair enzymes. The work of Rossman (1981) in bacteria and Jung (1969) in human

skin cells *in vitro* lends support to this hypothesis. Also, the observations of Sram (1976) on the interactions of arsenic with TEPA for the induction of chromosomal aberrations and dominant lethals support such a contention. The potencies of trivalent and pentavalent arsenicals as sulfhydryl reagents are similar to their potencies as clastogens and SCE-inducing agents. Observations which counter this hypothesis are the reports by Rossman that arsenic has no effect on the frequency of UVC-induced mutations in mammalian cells *in vitro* and the fact that arsenic does not affect the frequency of EMS-induced aberrations *in vivo* (Poma et al., 1981a).

Another possible mechanism for the action of arsenic may be through its occasional incorporation into the DNA backbone in place of phosphorus. There are several lines of evidence to support this mechanism. First, for this to occur, arsenic would have to be present during DNA synthesis and would have no effect on non-dividing cells. Second, such a mechanism could explain why arsenic is clastogenic (such a bond would be weaker than the normal phosphodiester bond) but does not induce gene mutation. Third, arsenic has been shown to cause strand breaks in DNA (Fornace and Little, 1979). X-irradiation, a potent clastogen and poor inducer of gene mutations, also predominantly causes strand breaks as its major DNA lesion. An argument against such a mechanism is the observation that the trivalent forms are more potent than pentavalent forms, while pentavalent arsenic should be more likely to substitute for phosphorus in DNA. Therefore at present, there is no single, unambiguous explanation for the mechanisms by which arsenic breaks chromosomes or induces SCE.

7. ARSENIC CARCINOGENICITY

The case for the association of inorganic arsenic with skin and lung cancer as well as other visceral carcinomas has been extensively reviewed (Arsenic NAS, 1977; IARC, 1973 and 1980; NIOSH, 1975; Hernberg, 1977; Sunderman, 1976, Pelfrene, 1976; Kraybill, 1978; Wildenberg, 1978; Pershagen and Vahter, 1979; WHO, 1981). The following chapter is divided into three major sections discussing human studies, animal studies and quantitative carcinogenic risk estimates.

7.1 HUMAN STUDIES

The literature on arsenic carcinogenicity in humans is summarized in Table 7-1. This subsection on human studies will first focus on clinical pathophysiological aspects of arsenic carcinogenesis, followed by pertinent epidemiological studies of arsenic-induced carcinogenesis.

7.1.1 Clinical Aspects of Human Arsenic Carcinogenesis

In man, chronic exposure to arsenic induces a characteristic sequence of changes in skin epithelium, proceeding from hyperpigmentation to hyperkeratosis which may be histologically described as showing keratin proliferation of a verrucose nature with derangement of the squamous portions of the epithelium or may even be described in some cases as squamous cell carcinomas.

Late onset skin cancers, associated with arsenic exposure, appear to be of two histopathological types: squamous carcinomas in the keratotic areas and basal cell carcinomas. In one study dealing with skin cancer after prolonged use of Fowler's solution (Neubauer, 1947), the ratio of types was approximately 1:1.

Arsenic-associated skin cancers differ from those of ultraviolet light etiology by occurring on areas generally not exposed to sunlight, e.g. palms and soles, and occurring as multiple lesions (Arsenic. NAS, 1977; Pershagen

TABLE 7-1. SUMMARY OF CASE REPORTS AND EPIDEMIOLOGIC STUDIES OF CANCER OR PRECANCEROUS LESIONS IN PERSONS EXPOSED TO ARSENIC

Media	Study Population	Author(s)	Type of Study	Results	Highlights and Deficiencies
Air	Smelter workers-Tacoma, Washington (Analysis of deaths for 1946-1960)	Pinto and Bennett (1963)	Proportionate mortality	No difference in lung cancer proportionate mortality between exposed and unexposed workers.	Workers leaving the plant before retirement were not included. In the classification of workers by exposure, the "non-exposed" group apparently were exposed since they also had high levels of arsenic in the urine.
	Smelter workers-Tacoma, Washington (follow-up from 1950-1971)	Milham and Strong (1974)	Cohort	40 observed lung cancer deaths versus 18 expected ($P < 0.001$).	Urinary arsenic levels of persons living around the smelter decreased with distance from the smelter.
	Smelter workers-Tacoma, Washington (follow-up from 1949-1973)	Pinto et al. (1977)	Cohort	32 observed respiratory cancer deaths, versus 10.5 expected ($P < 0.05$). Dose response seen by urinary arsenic levels and by duration and intensity of exposure.	Study consisted of only pensioners.
	Smelter workers-Tacoma, Washington (Follow-up from 1941-1976)	Enterline and Marsh (1982)	Cohort	104 respiratory cancer deaths observed versus 52.5 expected ($P < 0.01$). Dose response found by intensity and duration of exposure.	Short-term high-intensity arsenic exposures appeared to have a greater effect than did long-term low-intensity exposures; SO_2 exposure was found to have little or no effect.
	Smelter workers-Anaconda, Montana (Follow-up from 1938 to 1963)	Lee and Fraumeni (1969)	Cohort	147 respiratory cancer deaths observed versus 44.7 expected ($P < 0.01$). Dose response found by intensity and duration of exposure.	A dose response was found between exposure to sulfur dioxide and respiratory cancer mortality. Exposure to sulfur dioxide could not be separated from exposure to arsenic, however.
	Smelter workers-Anaconda, Montana (Follow-up from 1964 to 1977)	Lubin et al. (1981)	Cohort	146 respiratory cancer deaths versus 88.7 expected ($P < 0.01$).	Exposure to sulfur dioxide was not found to have an independent effect on cancer risk.
	Sample of 1800 of the smelter workers-Anaconda, Montana (Follow-up from 1938-1977)	Welch et al. (1982); Higgins et al. (1982)	Cohort	24 respiratory cancer deaths versus 4.6 expected ($P < 0.01$) in the heavy exposure category. Dose response found by intensity (both time-weighted average and ceiling level categories) of exposure.	Analysis of lung cancer mortality by SO_2 exposure found that SO_2 did not play an important role in the respiratory cancer process.

TABLE 7-1. (continued)

Media	Study Population	Author(s)	Type of Study	Results	Highlights and Deficiencies
Air	Smelter workers-Anaconda, Montana (Follow-up from 1938 to 1977)	Lee-Feldstein (1983)	Cohort	302 respiratory cancer deaths observed versus 105.8 expected ($P < 0.01$). Dose response found by duration and exposure.	
	Lung cancer from the parish where the Ronnskar smelter is located	Axelson et al. (1978)	Case-control	For smelter workers, the lung cancer mortality odds ratio was 4.6; there also was a significantly ($P < 0.02$) elevated risk of leukemia and myeloma among smelter workers.	Exposure to sulfur dioxide did not appear to be associated with lung cancer.
	Lung cancer deaths in the city of Saganoseki-machi, Japan	Kuratsune et al. (1974)	Case-control	58% of lung cancer cases were found to be former smelter workers versus 15.8% in controls.	The cause of death listed on the death certificate was validated using detailed pathologic analysis.
	Copper smelters in Sagnoseki-machi, Japan	Tokudome and Kuratsune (1976)	Cohort	29 trachea, lung, and bronchus cancer deaths versus 2.44 expected ($P < 0.01$); 3 observed colon cancer deaths versus 0.59 expected ($P < 0.05$). A lung cancer dose response was seen by length of employment and level of exposure.	The latent period ranged from 13 to 50 years, with an average of 37.6 years.
	Smelter workers in Magna, Utah	Rencher et al. (1977)	Proportionate mortality and cohort	7 percent of the deaths were lung cancer deaths compared to 0 to 2.2 percent for other factory workers and 2.7 percent for the State; the lung cancer death rate was found to be 10.1 per 10,000 versus 2.1 and 3.3 per 10,000 for mine workers and the State, respectively.	
	Residents living near a smelter in El Paso. Texas	Rom et al. (1982)	Case-control	No association was found between lung cancer and distance from the plant.	Effects of migration, smoking and occupation were not considered.

TABLE 7-1. (continued)

Media	Study Population	Author(s)	Type of Study	Results	Highlights and Deficiencies
Air	Residents of Deer Lodge and Silver Bow Counties, Montana	Newman et al. (1976)	Ecological correlation	There was an increase found in the incidence of lung cancer among men. In one of the cities there was also an increase in lung cancer among women.	No adjustment was made for cancer cases which may be occupational.
	All counties in the United States with smelters	Blot and Fraumeni (1975)	Ecological correlation	Average lung cancer mortality rates were significantly elevated for both males and females in 36 counties with smelters processing copper, lead, or zinc ores.	
	Residents near a smelter in Utah	Lyon et al. (1977)	Case-control	No association between cancer and distance from the smelter was found.	Lymphoma cases which may have an association with arsenic exposure were used as controls. Effects of smoking, migration, and occupation were not considered.
	Residents near Ronnskarverken smelter in northern Sweden	Pershagen et al. (1977)	Ecological correlation	A significantly higher mortality rate for lung cancer was noted for men in the exposed area. The increase was no longer significant when occupational cases were excluded, however.	When excluding occupational cases of lung cancer from the study population, lung cancer cases for a comparable occupational group were not excluded from the comparison population.
	Population surrounding an arsenical pesticide facility	Matanoski et al. (1976, 1981)	Ecological correlation	The lung cancer mortality for males in the census tract in which the plant was located was 3-4 times higher than the control tracts ($P < 0.05$).	The difference in the lung cancer mortality rate in the index tract could not be explained by occupation.
	Arsenical sheep dip manufacturing workers	Hill and Faning (1948)	Proportionate mortality	29.3 percent of deaths were due to lung cancer versus 12.9 percent of deaths among workers in the same geographic area who were not exposed to arsenic ($P < 0.05$). The excess in cancer deaths was mainly due to an excess in lung cancer and skin cancer.	

TABLE 7-1. (continued)

Media	Study Population	Author(s)	Type of Study	Results	Highlights and Deficiencies
Air	Arsenical pesticide manufacturing workers	Ott et al. (1974)	Proportionate mortality and cohort	16.2% and 3.5% of deaths in the exposed group were from cancer of the respiratory system and from lymphatic and hematopoietic cancers, except leukemia, respectively, versus 5.7 and 1.4% in the controls; the cohort mortality study found 20 respiratory cancer deaths and 5 deaths of the lymphatic and hematopoietic tissues versus 5.8 and 1.3 expected, respectively (both significant at $P < 0.01$).	A respiratory cancer mortality dose response was not found below an average dosage of 3890 mg of arsenic, but above that dosage there was a good dose response. It should be noted, however, that all of the respiratory cancer at or below 3890 mg had less than one year of exposure. Thus, it is unlikely that those deaths were due to arsenic exposure.
	Retirees of an arsenical pesticide plant in Baltimore, Maryland (follow-up from 1960 to 1972)	Baetjer et al. (1975)	Proportionate mortality and cohort	The proportionate mortality ratio (PMR) was 6.58 for respiratory cancer ($P < 0.05$); for cause-specific mortality the observed-to-expected ratios were 16.67 for respiratory cancer and 50 for lymphatic cancer (both with $P < 0.05$).	The cohort study was limited to pensioners only.
	Retirees of an arsenical pesticide plant in Baltimore Maryland (follow-up 1946 to 1977)	Mabuchi et al. (1979)	Cohort	12 observed lung cancer deaths versus 3.6 expected ($P < 0.05$); a dose response by duration of employment was seen for those with exposure of high intensity.	
	Wenatchee Valley orchard workers in the state of Washington	Nelson et al. (1973)	Cohort	No difference was found between the cohort and the state of Washington for overall cancer mortality or for lung cancer mortality.	
	German vintners	Roth (1958)	Proportionate mortality	Of 47 autopsies among vintners with chronic arsenic intoxication, 64% of the deaths were due to cancer, 60% to lung cancer; 6 of the 47 and 13 of the 47 were reported to have liver and skin tumors, respectively.	No controls were used. There was no indication of how the autopsy cases were selected.

TABLE 7-1. (continued)

Media	Study Population	Author(s)	Type of Study	Results	Highlights and Deficiencies
Water	Residents of a section of Taiwan with high levels of arsenic in the drinking water	Tseng et al. (1968); Tseng (1977)	Cross-sectional	A skin cancer prevalence rate of 10.6/1000 for those drinking well water was found compared to 0/1000 for a control area. The skin cancer rate followed a dose response by arsenic concentration in the water.	
	Sample of inhabitants of Antofagasta, Chile	Borgono and Greiber (1972)	Cross-sectional	Abnormal skin pigmentation and hyperkeratosis were found in Antofagasta where high arsenic levels in the water were reported. No skin cancers were reported, however.	
	Residents of certain departments in the province of Cordoba, Argentina, exposed to high levels of arsenic in the water	Bergoglio (1964)	Proportionate mortality	The proportion of cancer deaths was higher than for the province as a whole (23.84% versus 15.3%, $P < 0.05$). Of the cancer deaths, respiratory cancer was reported to be 35% and skin cancer 2.3%.	The data were apparently not age-adjusted. No comparison was made of the percentage of respiratory and skin cancer deaths in the affected departments with the respective proportion for Cordoba Province.
	Patients at a dermatology clinic in eastern Argentina	Arguello et al. (1938)	Case reports	The largest proportion of cases in the clinic (82%) came from areas with the highest incidence of chronic endemic regional arsenical intoxication.	The study was not population-based.
	Residents in an area of Lane County, Oregon	Morton et al. (1976)	Cross-sectional	The prevalence of skin cancer was not found to be associated with arsenic concentrations in the water.	The sample size was relatively small.
	Residents of Hinckley and Deseret, Utah, where relatively high arsenic contamination of the drinking water supplies existed and Delta, Utah, which had very little arsenic contamination of the water supply	Southwick et al. (1981)	Cross-sectional; mortality comparison	There was no dermatological evidence of arsenic ingestion in Hinckley or Deseret. No evidence of unusual cancer mortality patterns in Hinckley was found.	Sample size was very small-only 145 in the exposed group, 105 in the controls. The town of Hinckley is rather small for a mortality analysis. The population was only 400 in 1970.

TABLE 7-1. (continued)

Media	Study Population	Author(s)	Type of Study	Results	Highlights and Deficiencies
Water	353 cases of Blackfoot disease and 353 controls matched for sex and age in an area of Taiwan with an endemic arsenic contamination of the water supply	Ch'i and Blackwell (1968)	Case-control	Significantly ($P < 0.01$) more cases than controls were found to consume deep well water (known to be contaminated with arsenic) and population had a low socioeconomic status.	
	Two persons living in an area of Taiwan with endemic high levels of arsenic in the water supply	Astrup (1968)	Case report	Both individuals had developed Blackfoot disease.	
Water, soil, dust	One female child	Falk et al. (1981b)	Case report	Child, with a history of pica, developed hepatic angiosarcoma with associated congenital dysplasia of the liver and an infantile benign hemangioendothelioma suggesting pre-natal as well as post-natal etiological factors.	
Milk	A group of children in Japan	Yamashita et al. (1972)	Cohort	Hyperpigmentation and depigmentation were found to be prevalent in about 15 percent of the survivors approximately 15 years after exposure.	There was no comparison group.
Arsenical medicinals	Patients being treated with arsenical medicinals	Hutchinson (1888)	Case reports	Six patients treated with arsenical medicinals exhibited the keratotic lesions associated with arsenical poisoning.	
Arsenical medicinals	Patients being treated for skin diseases and various internal disorders with arsenical medicinals.	Neubauer (1947)	Case reports	143 individuals with epitheliomas and who had taken arsenical medicinals.	

TABLE 7-1. (continued)

Media	Study Population	Author(s)	Type of Study	Results	Highlights and Deficiencies
Arsenical medicinal	Patients treated with Fowler's solution (an arsenical medicinal) by a private practitioner	Fierz (1965)	Cohort	106 of the 262 patients reporting for physical examination reported hyperkeratosis; 21 cases of skin cancer were also found. The response increased with increasing dose.	Less than 45% of the cohort presented themselves for physical examination, and the author himself reported that the patients reporting for examination were not a representative sample. Furthermore, no controls were used.
Arsenical medicinal	Patients treated with arsenical medicinals	Reymann et al. (1978)	Cohort	Of 389 persons treated with arsenical medicinals, 41 internal malignant neoplasms were found to occur versus 44.6 expected. No increase in internal malignant neoplasms was found by dose.	There was no control group. Internal organs presumably include the lung, and there was no control for smoking, a major confounder with regard to lung cancer.
Arsenical medicinal (Fowler's Solution)	Patients treated with Fowler's solution	Cuzick et al. (1982)	Cohort	A statistically significant association of ingestion of Fowler's solution with deaths from internal malignancies was not found. A subset of 142 of the 487 in the cohort was examined and 49% were found to show dermal signs of arsenicism including skin cancer (11%).	In the subset of 142, deaths from internal malignancies occurred only in those who had previously demonstrated dermal signs of arsenicism, leading the authors to conclude that perhaps persons who show signs of arsenicism are at a greater risk of death from internal malignancies.
Arsenical medicinal (Fowler's Solution)	Male patient	Regelson et al. (1968)	Case report	Hemangioendothelial sarcoma of the liver.	
Arsenical medicinals (Fowler's Solution)	27 cases exposed to arsenic either via arsenical drugs or via occupation	Sommers and McManus (1953)	Case reports	Skin carcinomas were reported in all cases; visceral cancers were reported for some of the cases.	
Arsenical medicinal	Male patient	Nurse (1978)	Case report	Adenocarcinoma of the kidney	Patient treated with a variety of other drugs before developing kidney cancer.

TABLE 7-1. (continued)

Media	Study Population	Author(s)	Type of Study	Results	Highlights and Deficiencies
Arsenical medicinal	2 male patients 1 female patient	Knoth (1966)	Case reports	Female developed mammary carcinoma and skin cancer; 1 male patient developed a reticulosarcoma of the glans penis; 1 male developed skin cancer.	
Arsenical medicinals, occupational exposure, and air (occupational) exposure	16 vintners who were arsenical pesticide users; patient who took arsenical medicinals	Braun (1958)	Case reports	Skin and visceral cancers were reported among the vintners; skin and lung cancers were reported for one patient taking an arsenical medicinal; skin cancer was reported for the other patient who took an arsenical medicinal.	
Arsenical medicinals (Fowler's Solution)	2 male patients	Morris et al. (1974)	Case reports	One patient developed skin pigmentation, skin tumors, carcinoma of the larynx, and a probable bronchial carcinoma; the other developed skin pigmentation and keratosis. Both developed noncirrhotic portal hypertension.	
Arsenical medicinal (Fowler's Solution)	Female patient	Prystowsky (1978)	Case report	Woman developed nasopharyngeal cancer; also developed palmar and plantar keratosis.	
Arsenical medicinals (Fowler's (Solution)	4 male patients and 1 female patient	Popper et al. (1978)	Case reports	The cases developed angiosarcoma of the liver.	
Arsenical medicinal (Fowler's Solution)	1 male patient	Lander et al. (1975)	Case report	The patient developed angiosarcoma.	

TABLE 7-1. (continued)

Media	Study Population	Author(s)	Type of Study	Results	Highlights and Deficiencies
Arsenical medicinal (Fowler's Solution)	1 male patient	Roat et al. (1982)	Case report	The patient developed both angiosarcoma and skin cancer.	
Arsenical medicinal (Fowler's Solution)	7 male patients and 1 female patient	Falk et al. (1981a)	Case reports	The cases developed angiosarcoma.	
Wood preservative	Wood treaters in Hawaii	Gilbert et al. (1983)	Cross-sectional and cohort	No association of arsenic exposure with cancer mortality or morbidity was found.	The sample size was small (only 88 in the study cohort and 61 in the controls in the cross-sectional study; 125 in the mortality study; 182 in the morbidity study).

and Vahter, 1979; WHO, 1981; Tseng, 1977; Sunderman, 1976). This appears to be the case for medicinal (Neubauer, 1947), environmental (Tseng et al., 1968), and occupational (Roth, 1958; Braun, 1958) exposure. The time lag between initiation of exposure and occurrence of skin cancer has been reported to range from 6 to 50 years for arsenical medicinally-induced skin cancer. The minimal latency period for skin cancer in the most reliable epidemiologic study of arsenic-contaminated drinking water was reported to be 24 years.

The amount of data on the histological classification of lung tumors associated with occupational arsenic exposure is limited. Newman et al. (1976) report that arsenic-associated lung cancers are usually the poorly differentiated type of epidermoid bronchogenic carcinoma. These investigators studied worker groups with diagnosed lung cancer in copper-mining and smelting communities in Montana. Of 25 smelter workers, 4 had well-differentiated epidermoid carcinoma, 10 poorly differentiated epidermoid carcinoma, 7 small-cell undifferentiated epidermoid carcinoma and 3 acinar-type adenocarcinoma. Copper miners and "non-copper" control individuals had lung cancer profiles which were similar to each other.

The time period between initiation of exposure and the occurrence of arsenic-associated lung cancer was found in a couple of studies to be on the order of 35-45 years (Lee and Fraumeni, 1969). Recently, a latency period of <20 years was reported by Enterline and Marsh (1980; 1982) based upon their studies of copper smelter workers in Tacoma, Washington. Tokudome and Kuratsune (1976) found that the latent period for lung cancer ranged from 13 to 50 years.

The association of other visceral cancers with arsenic exposure has been noted in a number of reports and has been reviewed elsewhere (WHO, 1981; Arsenic. NAS, 1977; NIOSH, 1976; IARC, 1973). For example, hemangiosarcoma of

the liver, a rare form of cancer, has been diagnosed in workers exposed to arsenic and in non-occupationally arsenic-exposed individuals (Roth, 1958; Regelson et al., 1968; Lander et al., 1975; Falk et al., 1981a and b; Roat et al., 1982). Morris et al. (1974) have postulated that the peculiar hepatic fibrosis associated with arsenic-induced portal hypertension is a precursor state for subsequent progression to hepatic angiosarcoma. Popper et al. (1978) have noted that the hepatic fibrosis and hypertension seen in humans with Thorotrast, vinyl chloride or arsenic exposure are also induced by agents which presumably also have a role in hepatic angiosarcoma.

Other cancers noted in arsenic-exposed subjects include: lymphomas and leukemia (NIOSH, 1976; Ott et al., 1974); renal adenocarcinoma (Sommers and McManus, 1953; Nurse, 1978); and nasopharyngeal carcinoma (Prystowsky et al., 1978).

Pelfrene (1976) has criticized the reports of internal malignant neoplasms associated with arsenic exposure on the basis of the relative rarity of their detection in large-scale studies of chronic arsenic exposure such as that of Tseng (1968, 1977). More recently, Reymann et al. (1978) reported on a study of a group of 389 patients who took arsenic medicinally in the 1930s. An excess of internal cancers was not observed in the total cohort when compared with the expected incidence of malignant internal neoplasms based on the Danish Cancer Registry. The size of the cohort was probably too small to have detected an increase, however.

7.1.2 Epidemiological Aspects of Human Arsenic Carcinogenesis

7.1.2.1 Cancer of the Lung--A large number of reports are available on possible associations between occupational exposure to arsenic and cancer of the respiratory system. As is common in studies of this type, exposure data are very uncertain and the arsenic exposure is not always clearly defined regarding the physicochemical properties of the arsenic compounds. The picture is often

confused by simultaneous exposure to other agents, especially sulfur dioxide and metals. Data on smoking are often lacking or incomplete.

An excess mortality in respiratory cancer has especially been noted among workers engaged in the production and usage of pesticides, and among smelter workers.

In 1948, Hill and Faning presented data on proportional mortality rates among British workers exposed to a mixture of ingredients--including sodium arsenite, powdered sulfur and soda ash--used in the manufacture of a sheep-dip powder. Between 1910 and 1943, 75 deaths had occurred among workers in the sodium arsenite factory and 1,216 deaths had occurred among workers in the same area but without known exposure to arsenic. Proportionate mortality analysis showed that of the deaths among factory workers, 29.3 percent had died from cancer, whereas the corresponding figure for the other workers was 12.9 percent. The excess in cancer deaths among the factory workers was mainly due to an excess in lung cancer, 31.8 percent of all cancer deaths compared with 15.9 percent; and in skin cancer, 13.6 percent compared with 1.3 percent.

Among the factory workers, chemical workers, who were the workers most closely associated with arsenite production, had a higher proportion of cancer deaths than did the factory workers as a group. Furthermore, all lung cancer deaths had occurred among the chemical workers.

Arsenic in the air of the sodium arsenite factory was determined in 1945-46 (Perry et al., 1948) and concentrations up to 4 mg As/m^3 were found by sampling for 10 minutes. No data were given on the age of the deceased, and smoking habits were not recorded. The data do not allow any conclusions about exposure before 1943. Nevertheless, this study indicated that there might be an increased risk for respiratory cancer in the manufacture of arsenic-containing pesticides, and studies in two United States plants have given further support.

Ott et al. (1974) studied the mortality of workers in one of these two chemical plants. From 1919 to 1956 one unit formulated and packaged insecticides containing arsenic in the form of lead arsenate, calcium arsenate, copper acetoarsenite, and magnesium arsenate. During this period, the proportions of the different compounds varied. The main product was lead arsenate. The size of the workforce was about 30 in 1928 and 100 in 1948. Turnover was high with less than 25 percent of the men remaining with the unit for more than one year. Arsenic concentrations in air in 1943 were between 0.18 and 19 mg As/m^3 in the packaging area; in 1952 concentrations were 1.7-40.8 mg As/m^3 and 0.26-7.5 mg/m^3 in the drum dryer area and packaging area, respectively. By combining job classifications and air arsenic data, four exposure classifications were obtained with estimated arsenic exposures (8-hr TWA) of 5, 3, 1, and 0.1 mg/m^3. The total dosage was then calculated for each individual by multiplying air levels with the number of days at work and assuming that 4 m^3 were inhaled during a working day.

Mortality was studied by analysis of proportionate mortality and by a retrospective cohort analysis. Nearly 2,000 employees in the factory had died between 1940 and 1972. One hundred seventy-three were identified as having worked one or more days in the arsenical production unit and who then either worked for the company until death or died after retirement.

Ott et al. (1974), after adjusting for age and year of death, compared the differences in proportionate mortality between the study group and the controls. Among the exposed, respiratory cancer accounted for 16.2 percent of the deaths compared with 5.7 percent in the controls ($p < 0.001$). There was also a significant increase ($p < 0.05$) in deaths from lymphatic and hematopoietic cancers, except for leukemia. Table 7-2 shows the observed-to-expected ratios for respiratory cancer in relation to exposure. (In the original table, dosage estimates were based on 4 m^3 inhaled per 8 hr and expressed as the natural logarithms.

TABLE 7-2. OBSERVED AND EXPECTED DEATHS DUE TO RESPIRATORY MALIGNANCIES, BY EXPOSURE CATEGORY

TWA Concentration x months of exposure	Average dosage mg	No. of total deaths†	Respiratory Malignancy Deaths			
			Observed*	Expected	Ratio	Observed / Expected
<1	105	26	1 (1)	1.77		.6
1-1.9	316	17	2 (2)	1.01		2.0
2-3.9	630	24	4 (4)	1.38		2.9
4-5.9	1050	22	3 (3)	1.36		2.2
6-11.9	1991	27	3 (3)	1.70		1.8
12-23.9	3890	18	2 (2)	.97		2.1
24-59.9	8833	13	3 (1)	.77		3.9
60-95.9	16257	13	5 (0)	.79		6.3
96+	74332	13	5 (0)	.72		7.0

†n = 173, 138 workers had less than one year of exposure.

*Number in brackets shows respiratory cancer deaths in workers exposed less than one year.

Source: Modified from Ott et al. (1974), and Blejer and Wagner (1976).

In the present table, dosage is expressed in mg and is based on 10 m^3 inhaled air.) There is no tendency towards a dose-response relationship at total exposures from 105 to 3890 mg, but a sharp increase is noted at higher dosages. Furthermore, Blejer and Wagner (1976) reported that of the 173 deaths, 138 had occurred among workers with less than one year of exposure. In that group, 16 deaths were due to respiratory cancer. As seen in Table 7-2, 15 of those deaths occurred in the six groups with average total exposures estimated to be from 105 to 3890 mg. There are no quantitative data on other compounds that these workers might have been exposed to during their total time with the company; however, it is known that in addition to the arsenic-containing insecticides, the plant processed and packaged several other products, the most important of which were powdered sulfur and dry lime sulfur.

The retrospective cohort analysis was based on a roster of 603 workers who had worked for at least one month in the actual unit between 1940 and 1973. Workers leaving the company before retirement as well as workers who had been exposed to asbestos were not included in the analysis. It was stated that virtually all men with at least one year of exposure had been identified. Person-years, by 10-year age groups, for five calendar year groups were calculated and expected number of deaths were calculated by using United States white male mortality data. Table 7-3 shows that by this analysis a significant increase ($p < 0.01$) in deaths due to respiratory cancer was found among exposed workers. There was also a significant increase ($p < 0.01$) in the number of deaths due to malignant neoplasms in lymphatic and hematopoietic tissues, except leukemia.

A chemical plant in Baltimore was the subject of two studies concerning the working environment and one study concerning the outer environment. This plant started producing arsenic acid in the early 1900s and in the early

TABLE 7-3. OBSERVED AND EXPECTED DEATHS FOR SELECTED CAUSES IN RETROSPECTIVE COHORT ANALYSIS (1940-1973)

	Observed deaths	Expected deaths (U.S. white males)	Ratio of observed to expected deaths
All causes	95	113.5	.84
Malignant neoplasms, total	35	19.4	1.80
Respiratory system	20	5.8	3.45†
Digestive organs & peritoneum	7	6.3	1.11
Lymphatic & hematopoietic tissues except leukemia	5	1.3	3.85†
All other sites	3	6.0	.50
Diseases of cardiovascular system	41	58.5	.70
Emphysema, chronic bronchitis, & asthma	4	2.8	1.43
All external causes	9	12.7	.71
All other causes	6	20.1	.30

† $p < 0.01$

Source: Ott et al. (1974).

1950s production of arsenical pesticides started. Lead arsenate, calcium arsenate and sodium arsenate were among the compounds produced. Production terminated in 1974 (Matanoski et al., 1976). The plant also produced chlorinated hydrocarbons and organic phosphates. Data on air concentrations of arsenic are lacking.

In the first study, Baetjer et al. (1975) reported on both the proportionate mortality and age-specific death rates of workers who had retired between 1960 and 1972 and generally had at least 15 years' employment. Seventeen of 22 deaths among male white workers and two of five among female workers were due to malignant neoplasms. The female deaths did not appear to be related to occupational exposure, whereas, the male deaths did. Of the 17 malignant neoplasms in males, 10 were in the respiratory tract, 3 were lymphosarcomas, and the remaining 4 were of other tissues. The proportionate mortality analysis, based on mortality data for the city of Baltimore, showed an observed/expected ratio of 6.58 for respiratory cancer ($p < .05$) and 15.79 for cancer of the lymphatic and hematopoietic system ($0.1 < p < 0.05$). The age-specific death rate analysis showed that deaths from respiratory cancer were 16.67 times the expected, and, that for lymphosarcomas, the observed number was 50 times that of the expected number. The authors reported that observed and expected rates for non-cancer deaths did not differ significantly ($p < 0.05$).

In a second study (Mabuchi et al., 1979), a follow-up was made of workers employed from 1946 to 1974. Since exposure data were lacking, an attempt was made to classify workers according to exposure to arsenicals and non-arsenicals. A roster of 3,141 workers was obtained. Since 2,189 workers had been employed for less than 4 months, a 20 percent random sample was drawn from that population and together with the remaining 952 workers constituted the study popula-

tion: 1,050 males and 343 females, mainly white. Exposure assessments were made, and the workers were categorized into one of six exposure groups.

Of the study population, 240 had died: 197 males and 43 females. Expected deaths were calculated from the city of Baltimore statistics. The observed/expected ratios for lung cancer were analyzed by exposure, year of first employment, and duration of employment. A statistically significant increase in lung cancer mortality (SMR = 336, $p < 0.05$) was found among "predominantly arsenical production" workers. There was a clear lung cancer mortality dose response among these workers by duration of exposure. Those employed 15-24 years and 25+ years both had statistically significant ($p < 0.05$) lung cancer SMRs (1365 and 2750, respectively). Interestingly, statistically significantly elevated SMRs were only found in "predominantly arsenical production" workers, but not in workers engaged entirely in arsenical production. Further analysis revealed that the proportion of workers engaged entirely in arsenical production for 5 years or more was relatively low (1 percent), while the proportion of workers exposed predominantly, but not entirely, to arsenic for 5 years or more was much higher (29 percent). This difference in duration of exposure may have accounted for the absence of excess lung cancer mortality among the workers engaged entirely in arsenical production. Data on smoking were not obtained.

Occupational exposure to arsenical pesticides has been common among vintners and agricultural workers. Exposure has mainly been to lead arsenate. In a study of orchard workers who used lead arsenate in the Wenatchee Valley in the state of Washington, Nelson et al. (1973) found a deficit of lung cancer mortality for the period 1938-68 when compared with mortality for the state of Washington.

Because the results of this study were at variance with previous evidence on the long-term effects of arsenic exposure, NIOSH reviewed data from other

sources and used alternative procedures in an attempt to verify the findings. Analysis of respiratory cancer mortality data by occupational category for the state of Washington for the period 1950-71 found that orchardists had 19 percent more deaths from respiratory cancer than expected. An analysis of cancer mortality rates for 1950-69 for the counties comprising the locale from which the orchardist sample was drawn by Nelson et al. found that males had a 7 percent higher respiratory cancer rate than expected among males. The county from which most of the orchardists were drawn had a 31 percent excess ($P < 0.01$) of lung cancer mortality. Thus, it was NIOSH's (1975) conclusion that the Nelson et al. report did not accurately depict the cancer experience of persons exposed to lead arsenate spray in the Wenatchee Valley.

Several studies in Germany indicate that workers exposed to arsenic trioxide when spraying vineyards had a high mortality in cancer, especially lung cancer. In one report (Roth, 1958), it was stated that of 47 autopsies among vintners with chronic arsenic intoxication, 30 (64 percent) were due to cancer, and 18 to lung cancer (60 percent of all cancer deaths). The author did not state how the cases were selected, nor were controls used in the study.

Gilbert et al. (1983) studied a group of 182 workers in Hawaii exposed for at least 3 months during the period 1960-1981 to the wood-treating chemicals chromated-copper-arsenate (CCA), pentachlorophenol (penta), tributyl tin oxide (TBTO) and lindane. The study was divided into two parts: (1) a cohort comparison study of 88 workers and 61 controls and (2) a historic prospective study which consisted of a morbidity and a mortality analysis of the entire cohort.

In the cohort comparison study, 61 controls were matched on the basis of age, sex, race, level of physical activity, and weight to 88 wood treatment

workers who were "qualified and agreed to participate in the study." Controls were recruited from among the membership of carpenters', ironworkers', masons', plumbers', and stevedores' unions and from the names of friends and relatives referred to the study by participating members of the occupational cohort. Fourteen of the controls were reported to be carpenters and 13 of them had had exposure to either CCA or penta or both. Their urine arsenic levels, however, were reported not to differ significantly from those of other controls. The exposed group and the control group were each given a comprehensive health examination consisting of a questionnaire and clinical and laboratory tests including analysis of a urine sample for penta, arsenic, copper, chromium, and tin levels. Only penta was found to be significantly elevated in the urine of the exposed group over that of the controls. The authors reported that there were no "clinically significant" differences between the exposed group and the controls. No significant differences were found between the wood treaters and controls with respect to educational level, smoking history, or alcohol consumption.

The historical prospective study identified three cases of cancer, one by means of the questionnaire in the cross-sectional study and the other two by means of the Hawaii Tumor Registry. One of the cancer cases was a bladder cancer case; the other two were colorectal cancer cases. For the mortality analysis, the vital status of 125 of the 182 workers (69 percent) was able to be determined. Of these 125, six deaths occurred, five from cardiovascular disease, the other from an unknown cause. The authors calculated that eight deaths would have been expected in this group, three of which would have been from cancer. The authors did not state the basis of the expected number of cancer deaths.

There are limitations in the study design and sample size of this study which make the results with regard to the evaluation of a cancer risk among

the wood treaters inconclusive. A cohort comparison study on the basis of a single medical examination is an inappropriate approach to determine if a cancer risk exists in the wood treater group, particularly when the group consists primarily of persons who are currently employed as wood treaters (60 of 88 were current employees). Most persons who have developed cancer will either have died or left the work force. In addition, the sample size (88 current or former wood treaters and 61 controls) would have been too small to detect an excess cancer risk. Also, it should be noted that the inclusion in the controls of 13 carpenters who had been exposed to arsenic-treated wood certainly presents a potential bias, despite the fact that the authors claimed that the levels of arsenic in the urine of these 13 were not significantly different from those in other controls. In this regard it should be noted that no effort had apparently been made to restrict the intake of seafood or other foods or liquids, which might have elevated urine arsenic levels, prior to collection of the urine samples. The mean level of urinary arsenic in both the study group and in the controls was significantly ($P < 0.01$) higher than what the authors reported would be a normal level.

The historic prospective study also had limitations. Again, the sample size was too small to adequately determine whether an excess risk of cancer existed in the study cohort. Only 125 were included in the mortality study and only 182 were included in the morbidity study. Arsenic exposure via inhalation and ingestion is known to be associated with lung and nonmelanoma skin cancer, respectively. Nonmelanoma skin cancer is rarely fatal and thus, an excess risk of skin cancer would not have been detected in such a small mortality study. The Hawaii Tumor Registry, which was one of the primary sources of information used to identify cancer cases for the morbidity study, does not even report nonmelanoma skin cancer.

There is also a question of whether the authors had sufficiently allowed for a cancer latency period in their study. The authors did not indicate the length of follow-up of the cohort members. Some indication is provided, however, in the data reported by the authors on the length of employment of the 88 workers in the study cohort of the cohort comparison study. These workers were part of the population in the incidence and mortality studies. Of the 88 workers, 60 had worked 10 years or less and 80 had worked 15 years or less at the time of the physical examination in 1981. Twenty-two of the study cohort in the cohort comparison study were former employees. At the minimum, assuming that the workers had had no breaks in employment, 58 of 125 (46 percent) in the mortality study would have been followed for only 15 years or less and 38 of 125 (30 percent) would have been followed for only 10 years or less. In the morbidity study, if, again, no breaks in employment of the workers are assumed, 58 of 182 (32 percent) would have been followed for only 15 years or less and 38 of 182 (21 percent) would have been followed for only 10 years or less. In conclusion, this study is inadequate to conclude whether an excess risk of cancer exists in the wood treater population in Hawaii.

Occupational exposure to arsenic also occurs in smelters where exposure is predominantly to arsenic trioxide. Several studies have been done on mortality among workers at the copper smelter in Tacoma, Washington. Pinto and Bennett (1963) reported on the proportionate mortality of 229 workers from 1946 to 1960. Workers leaving the plant before retirement were not included. The proportionate mortality of the smelter workers was compared with that of males in the state of Washington in 1958. Of all cancer deaths, the respective proportions of lung cancer were 41.9 and 23.7 percent, respectively. The authors then classified the smelter workers according to arsenic exposure and did not find any difference between exposed and non-exposed. However, the "non-exposed" had elevated arsenic levels in urine, suggesting possible exposure.

More extensive studies have since been published, showing an increase in lung cancer among arsenic-exposed workers (Milham and Strong, 1974; Pinto et al., 1977; Pinto et al., 1978; Enterline and Marsh, 1980; Enterline and Marsh, 1982).

Milham and Strong (1974) examined county records from 1950 to 1971 to find the number of deaths due to respiratory cancer among county residents employed at the smelter. Expected number of cases were calculated for the smelter population by using the 1960 age-cause specific mortality statistics for white males in the United States. Forty deaths were observed and 18 were expected.

The two papers by Pinto et al. (1977, 1978) refer to the same study and the following is based on the 1978 paper. The cohort studied consisted of 527 men who were living pensioners on January 1, 1949 or who became pensioners before January 1, 1973. Complete job histories were obtained for 525 men. The average duration of employment was 28 years, ranging from 7 to 54 years and beginning in 1910. Death certificates were obtained for all 324 men who had died during the observation period (1949-1973). Expected numbers of deaths were calculated from statistics of the state of Washington.

An exposure index was constructed by using data on urinary levels of arsenic obtained in 1973. Mean urinary concentrations were calculated for 32 departments, and the individual exposure index was obtained by multiplying urinary arsenic level with years of work in a department. If an individual had worked in more than one department, the index values were added. By dividing the exposure index by the total number of years in the smelter, an index of intensity of exposure was obtained, i.e., the average urinary arsenic level. These indices were created to enable interdepartmental comparisons and did not reflect past exposure since air analysis in the 1930s to 1940s indicated

that exposure might have been 5-10 times higher at that time. It may have been still higher in 1910.

Data were also obtained on smoking habits from all men still alive and from relatives of men who had died since January, 1961. Table 7-4 (Pinto et al., 1978) shows that there was a significant increase ($p < 0.05$) in deaths from all causes, in cancer deaths in general, and, specifically, in deaths from respiratory cancer. Almost all of the excess mortality could be explained by the increase in lung cancers which could not be explained by smoking.

Table 7-5 shows respiratory cancer deaths in relation to exposure index (a value which reflects both the duration and intensity of exposure). An increase in SMR with exposure is seen. Table 7-6 shows that both duration and intensity of exposure contributed to the excess in respiratory cancer. As stated above, the urine values are relative and do not reflect the actual exposure.

It was also shown that the main excess occurred in ages 65-74 years, whereas at higher ages the lung cancer rate was closer to expected rates.

More recently, Enterline and Marsh (1980, 1982) conducted additional studies on workers at this same copper smelter in Tacoma. A cohort of 2802 males who worked a year or more during the period 1940-1964 was identified. Since a one-year work exposure was required for eligibility into the cohort, actual follow-up did not start until 1941 and extended through 1976. In the cohort, the vital status of 51 could not be verified, leaving 2751 persons. In that group, 1061 deaths had occurred. There was a significant increase in total cancer mortality which wholly depended on an increase in deaths from lung cancer. Arsenic exposure was estimated for each man on the basis of a representative average urinary arsenic level for workers in a given department. Using this representative value, an individual value was calculated for each

TABLE 7-4. OBSERVED AND EXPECTED DEATHS AND STANDARDIZED MORTALITY RATIOS FOR SELECTED CAUSES OF DEATH OF 527 MALES OF COHORT UNDER STUDY*

Cause of death	Disease Classification†	Observed	Expected	SMR
All Causes		324	288.7	112.2‡
Cancer	140-205	69	46.5	148.4‡
Digestive	150-159	20	16.4	122.0
Respiratory	160-164	32	10.5	304.8‡
Lymph, etc.	200-203, 205	2	2.1	95.2
Urinary	180,181	3	3.3	90.9
All Other Cancers		12	14.2	84.5
Stroke	330-334	43	38.0	113.2
Heart Disease	400-443	144	132.3	108.8
Coronary Heart Disease	420	120	110.2	108.9
All Other Heart Disease		24	22.1	108.6
Respiratory Disease	480-493, 500-502	11	10.8	101.8
All Other Causes		57	61.8	92.2

*Cohort consisted of living male pensioners from a copper-smelting plant who were living January 1, 1949, and whose causes of death were noted through December 31, 1973.

†Numbers from rubrics of 7th Revision of International Classification of Diseases.

‡P<.05

Source: Pinto et al. (1978).

TABLE 7-5. OBSERVED AND EXPECTED RESPIRATORY CANCER DEATHS AND STANDARDIZED MORTALITY RATIOS BY ARSENIC EXPOSURE INDEX

Exposure index	Mean index	No. of men	Respiratory Cancer Deaths		
			Observed	Expected	SMR
Under 2,000	1,514	36	1	0.9	111.1
2,000-2,999	2,513	109	4	2.1	190.5
3,000-5,999	4,317	205	11	3.9	282.0*
6,000-8,999	7,473	109	7	2.3	304.3*
9,000-11,999	10,135	38	4	0.7	571.4*
12,000 and over	14,712	29	5	0.6	833.3*

*p <.05

Source: Pinto et al. (1978).

TABLE 7-6. OBSERVED AND EXPECTED RESPIRATORY CANCER DEATHS AND STANDARDIZED MORTALITY RATIOS BY INTENSITY AND DURATION OF EXPOSURE TO ARSENIC

Intensity of exposure (µg/liter urine)	Duration of exposure					
	less than 25 years			25 years and more		
	Observed	Expected	SMR	Observed	Expected	SMR
50-199	2	2.1	95.2	10	3.6	277.8*
200-349	4	1.5	266.7	8	2.2	363.6*
350 and over	3	0.5	600.0*	5	0.6	833.3*

*P<.05

Source: Pinto et al. (1978).

man for each year of employment in a given department, and a total exposure estimate per individual was made by summing values across all jobs and all years of employment.

This method of estimating exposure differed from earlier methods employed by Enterline and co-workers (Pinto et al., 1977, 1978) in that estimates of historic exposure, based upon simple linear interpolations and extrapolations of actual data from 1948-52 and 1973-75, were used to characterize exposure by department, rather than by 1973 urinary measurements. Use of this new method of analysis partially helped to eliminate exposure underestimates of workers employed in the early years of the smelter operation. However, the present method did not totally eliminate this bias because urinary arsenic levels were only determined for workers starting in 1948. For workers exposed prior to 1948 (approximately 80 percent of the present study cohort), urinary arsenic values for 1948-52 were assumed to apply. Furthermore, the average urinary arsenic level for some departments may have been based on only a few samples, thereby limiting the usefulness of the departmental average as a representative measure of any given worker's urinary arsenic level. The authors did note that in areas of the smelter where arsenic levels were reported to be high, workers tended to be measured more often for urinary arsenic. Thus, averages for those areas were, in fact, more representative.

Using this time-weighted measure of exposure, a life table method for accumulative dose, a 10-year lag period and a standard population of mortality rates in the state of Washington, the authors reported that SMRs for respiratory cancer ranged from 155 in the lowest exposure category to 246 in the highest category. Table 7-7 shows the relationship between the time-weighted estimates of arsenic exposure lagged 0 and 10 years and respiratory cancer. This relationship was much weaker than that previously reported by Pinto et al. (1977, 1978). Enterline and Marsh noted that results from the two sets of

TABLE 7-7. RESPIRATORY CANCER DEATHS AND SMRs BY CUMULATIVE ARSENIC EXPOSURE LAGGED 0 AND 10 YEARS, TACOMA SMELTER WORKERS

Cumulative Exposure (μg/As/1) (urine-years)	Lag			
	0 Lag		10-Year Lag	
	Observed Deaths	SMR	Observed Deaths	SMR
<500 (302)	8	202.0	10	155.4
500-1500 (866)	18	158.4	22	176.6*
1500-3000 (2173)	21	203.2**	26	226.4**
3000-5000 (4543)	26	184.1**	22	177.6*
7000+ (13457)	31	243.4**	24	246.2**

* $p<0.05$

**$p<0.01$

()Mean of class interval

Source: Enterline and Marsh (1982).

studies were not totally comparable due not only to the differences in the exposure estimates noted above, but also to differences in follow-up periods. In earlier reports, the follow-up started after exposure stopped at retirement, whereas in the present study, follow-up started at various points in the work experience of the workers, allowing for follow-up and dose accumulation to proceed concurrently. When the authors analyzed a subsample of the present study cohort, consisting of 582 workers retired at age 65 and over (paralleling the experimental design of the earlier studies), a stronger dose-response relationship was, in fact, observed.

Table 7-8 shows the respiratory cancer deaths and SMRs by duration of exposure and time since first exposure. From Table 7-8, it appears that neither duration of exposure nor long latent periods made strong contributions to excess respiratory cancer. The authors suggested that this may have been due to the high SMRs observed shortly after termination of employment but not noted thereafter; thus, for workers with less than 10 years of exposure the

TABLE 7-8. RESPIRATORY CANCER DEATHS AND SMRs BY DURATION OF EXPOSURE AND LATENCY, TACOMA SMELTER WORKERS

Duration (years)	Latency (Years) <10 Observed Deaths	<10 SMR	10-19 Observed Deaths	10-19 SMR	20-29 Observed Deaths	20-29 SMR	30+ Observed Deaths	30+ SMR	Total Observed Deaths	Total SMR
<10	1	55.6	10	265.4*	17	210.1**	12	137.9	40	178.9**
10-19	-	-	6	156.4	8	278.0*	4	137.9	18	187.2*
20-29	-	-	-	-	13	197.0*	13	265.3**	26**	226.1*
30+	-	-	-	-	-	-	20	221.3**	20	221.3**
Total	1	55.6	16	210.4*	38	216.3**	49	191.8**	104	198.1**

* $p < 0.05$

** $p < 0.01$

Source: Enterline and Marsh (1982).

SMR is highest 10-19 years after date of hire; for workers employed 10-19 years, the SMR is highest 20-29 years after date of hire, etc. This high relative risk of lung cancer mortality in the decade following termination of employment, which essentially disappears in the following 20 years, prompted the authors to suggest that arsenic may be a promoter rather than an initiator. However, when the authors reanalyzed the data according to a method which followed workers only from the point of termination or retirement, both duration of exposure and intensity of exposure contributed more strongly to respiratory cancer mortality (Table 7-9). The difference in the two analyses led the authors to suggest that the weak dose-response relationship observed in the first analysis may have resulted from a tendency for workers in high-exposure jobs to leave employment more quickly than those in low-exposure jobs.

In studying the interactive effects of sulfur dioxide, the authors did not find significant differences in respiratory cancer incidence in two departments which both had high arsenic exposures (7500 $\mu g/m^3$) but differing SO_2 exposures, one having low to moderate exposures (520 ppm) and the other having essentially none. Because the respiratory cancer SMRs were quite similar in the two departments, the authors suggested that SO_2 exposure did not play an important role in respiratory cancer excess at that particular smelter.

In discussing their overall study results, Enterline and Marsh noted that, in this particular case, a dose response was not observed when dose was measured in terms of cumulative dose. The results seen in Table 7-8 suggest that short exposures seemed to have a disproportionately greater effect than long exposures and that effects of early exposure tended to diminish with time. Table 7-9 suggests that short high-intensity exposures may have a greater effect than longer-term, more low-level exposures. The fact that different results are obtained when different exposure/follow-up methods are

TABLE 7-9. RESPIRATORY CANCER DEATHS AND SMRs BY DURATION AND INTENSITY OF EXPOSURES, TACOMA SMELTER WORKERS

Duration of exposure (years)	Intensity estimate: Low† No. at risk	Low† Observed deaths	Low† Expected§ deaths	Low† SMR	High++ No. at risk	High++ Observed deaths	High++ Expected§ deaths	High++ SMR
<10	687	15	8.83	169.9	824	25	12.26	203.9**
10-19	149	7	2.61	268.2*	168	11	3.42	321.6**
20-29	225	10	3.59	278.6**	171	16	2.77	577.6**
30+	159	9	2.98	302.0**	165	11	3.17	347.0**
Total	1220	41	18.01	227.7**	1328	63	21.62	291.4**

* $p < 0.05$.

** $p < 0.01$.

† low = <290 µg/As/ℓ urine (mean 163).

++ high = ≥290 µg/As/ℓ urine (mean 477).

§ Based on Washington State white males.

Source: Enterline and Marsh (1982).

employed suggests that choice of experimental design has a possible influence on results. The possibility that some workers may have simply been more susceptible than others may also have accounted for the dose-response relationships observed in this study.

Because the authors suggested that the role of arsenic in the carcinogenesis process may have been as a promoter rather than an initiator, the significance of cumulative exposure to arsenic as a measure of dose would be questionable in regard to the induction of respiratory cancer as observed in this study. The role of arsenic as an initiator as well as a promoter cannot be ruled out, however. Until further research is done, the authors' conclusions from this study remain speculative.

Mortality of workers in a smelter in Magna, Utah, was studied by Rencher et al. (1977). Average hourly air concentrations of arsenic in 12 work areas were between zero and 22 mg/m^3 in 1975 (NIOSH, 1975). However, exposure before 1959 had likely been higher, since a processing of ore with a relatively low arsenic content began in that year. In the period 1959 to 1969, 965 deaths had occurred among all current or former employees, and death certificates were obtained for virtually all deceased. The proportionate mortality for smelter workers was compared with that for mine workers, concentrator workers, refinery workers, and office workers, and for the population above 20 years of age for the entire state of Utah in 1968. Among the smelter workers, 7 percent of the deaths were due to respiratory cancer, whereas the percentage for the other factory employees varied from 0 to 2.2 percent and was 2.7 percent for the state. Data on smoking were obtained for all smelter workers and for subsamples of the other employee groups and indicated that nonsmoking smelter workers had the same percentage of deaths from lung cancer as mine and concentrator workers who smoked. By applying lifetable methods, age-adjusted

death rates were obtained. For smelter workers, a death rate for lung cancer of 10.1 per 10,000 was obtained compared with 2.1 and 3.3 per 10,000 for mine workers and the state population, respectively. Causes of death were compared with a cumulative exposure index obtained by multiplying the number of days spent in each department by the average exposure level and then summing. The average exposure to arsenic as well as sulfur dioxide, sulfates, lead, and copper was found to be higher for the lung cancer cases than for other causes of death.

In addition to these studies, a large study by Lee and Fraumeni (1969) involving 8,047 white males was conducted at the Anaconda Copper Smelter in Montana from 1938 to 1956.* Data were obtained on time, place, and duration of employment for each individual, all subjects having worked at least 12 months in the smelter during the indicated study period. Follow-up was from 1938 to 1964. Death certificates were obtained, and the lifetable method was used to compute the expected number of deaths, using mortality rates of the state of Montana. The smelter workers were classified into 5 cohorts, based on total years of smelter work and the time period in which the years were worked: (1) 15 or more years worked before 1938; (2) 15 or more years worked between 1938 and 1963; (3) 10-14 years; (4) 5-9 years; and (5) 1-4 years. An attempt was also made to classify the workers according to exposure to arsenic and sulphur dioxide. Exposure to arsenic for more than 12 months had occurred among 5,185 men. These workers were divided into three groups; heavy, medium, and light exposures. This division was based on exposure times and place at work. Arsenic concentrations in air were primarily determined from a

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*While the original Lee and Fraumeni study reported on the mortality experience of male smelter workers in unidentified states, subsequent analyses of these workers indicate that they were employed solely at the Anaconda smelter in Montana.

1965 survey by Public Health Service officials (NIOSH, 1975). These air data are shown in Table 7-10.

According to a former public health official associated with this survey, actual measurements were collected during two different periods--one in 1965 and one "about five to six years earlier"--and at several locations within given departments (Archer, 1983; personal communication). It is impossible, however, to determine how the values listed in Table 7-10 are distributed over these different time periods and locations. Further, it is also impossible to determine the number of hours sampled at a given location. Therefore, the arithmetic means used by Lee and Fraumeni to characterize heavy, medium and light exposures can only be viewed as very rough estimates of arsenic exposure, their primary value being in their relative scale of measurement.

In Table 7-11 it is seen that heavy and medium exposures resulted in significant increases in SMR for respiratory cancer. The SMR was highest (800) in workers belonging to cohort 1 (more than 15 years of smelter work before 1938), and then decreased to 263 among workers with 1-14 years of smelter work. Among the workers with light exposure, the SMR was 250, 310, and 214 in cohorts 1, 2, and 3-5, respectively. Among the smelter workers with less than 12 months' exposure to arsenic, the SMR was 286.

Lee and Fraumeni also looked at factors that possibly had confounding effects on their study results. Smoking histories were not recorded; however, based upon information obtained from other studies, Lee and Fraumeni concluded that smoking alone could not have accounted for the excess respiratory cancer mortality of the magnitude observed in their study.

In contrast to smoking, the authors did note a positive relationship between exposure to sulfur dioxide and respiratory cancer mortality; however, they found it difficult to separate the relationship of arsenic from sulfur

TABLE 7-10. 1965 SMELTER SURVEY ATMOSPHERIC ARSENIC CONCENTRATIONS (mg As/m^3)

"Heavy exposure area" as classified by Lee and Fraumeni

Arsenic Roaster Area — Mean: 1.47

0.10	0.20	Median: 0.185
0.10	0.22	
0.10	0.25	
0.10	0.35	
0.10	1.18	
0.10	5.00	
0.17	12.66	

"Medium exposure area" as classified by Lee and Fraumeni

Reverberatory Area — Mean: 1.56

0.03	0.93	Median: 0.88
0.22	1.00	
0.23	1.27	
0.36	1.60	
0.56	1.66	
0.63	1.84	
0.66	1.94	
0.76	2.06	
0.78	2.76	
0.78	3.40	
0.80	4.14	
0.83	8.20	

Treater Building and Arsenic Loading — Mean: 1.50

0.10	0.48	Median: 0.295
0.10	0.62	
0.10	3.26	
0.11	7.20	

"Light exposure areas" as classified by Lee and Fraumeni

Copper Concentrate Transfer System — Mean: 0.70

0.25	Median: 0.65
0.65	
1.20	

Samples from Flue Station — Mean: 0.17

0.10	Median: 0.17
0.24	

Reactor Building — Mean: 0.004

0.001	0.003	Median: 0.002
0.002	0.009	
0.002	0.010	
0.002		

Source: National Institute of Occupational Safety and Health (1975).

TABLE 7-11. OBSERVED AND EXPECTED DEATHS FROM RESPIRATORY CANCER, WITH STANDARDIZED MORTALITY RATIOS (SMR), BY COHORT AND DEGREE OF ARSENIC EXPOSURE, 1938-63

Cohort	Respiratory cancer mortality	Maximum exposure to arsenic (12 or more months)* Heavy	Medium	Light
All cohorts combined	Observed	18	44	45
	Expected	2.7	9.2	18.8
	SMR	667†	478†	239†
1	Observed	8	22	14
	Expected	1.0	3.3	5.6
	SMR	800†	667†	250†
2	Observed	6	12	9
	Expected	0.9	2.2	2.9
	SMR	667†	545.†	310†
3-5‡	Observed	4	10	22
	Expected	0.9	3.8	10.3
	SMR	444§	263§	214†
Number of persons in arsenic category*		402	1,526	3,257

*The remaining 2,862 men in the study worked less than 12 months in their category of maximum arsenic exposure and had an SMR of 286†.

†Significant at the 1% level.

‡Cohorts 3, 4, and 5 were combined, since observed and expected deaths were small for each cohort alone.

§Significant at the 5% level.

Source: Lee and Fraumeni (1969).

dioxide. Most of the work areas having heavy arsenic exposure were also areas having medium sulfur dioxide exposure; conversely, all work areas with heavy sulfur dioxide exposure were areas of medium arsenic exposure. The authors did note, however, that persons with the heaviest exposure to arsenic and moderate or heavy exposure to sulfur dioxide were those most likely to die of respiratory cancer in this particular instance.

Since the Lee and Fraumeni study, additional research has been conducted on the employees of the Anaconda smelter. Lubin et al. (1981) studied 5403 of these employees. These workers had all been employed for 12 months or more between January 1, 1938, and December 31, 1956, and were known to be alive as of December 31, 1963. Essentially, this cohort was equivalent to the surviving members from the Lee and Fraumeni cohort.

Exposure was from date hired to December 31, 1963; follow-up was from 1964 to 1977. Classification of exposure categories was similar to that of Lee and Fraumeni. However, unlike the study of Lee and Fraumeni, a cumulative arsenic exposure index was calculated for each worker. This index was derived by, first, weighting the three exposure categories and then multiplying the number of years an individual worked in a given category by this weight and summing over categories. The weights were derived from mean airborne dust concentrations taken during 1943 to 1958, which averaged 11.3, 0.58 and 0.29 mg As/m^3 in the respective heavy, medium and light categories. These values differed from those used by Lee and Fraumeni to group departments (Table 7-9). It should be noted that the exposure estimates used by Lee and Fraumeni were based upon more recent monitoring data primarily collected in 1965. Lubin et al. reduced weights in the heavy category by a factor of 10 in order to account for the wearing of respirators as was observed "at least in recent years." SMRs were calculated by comparisons to U.S. white males.

The mortality experience of workers during the years 1964 to 1977 was similar to that of the workers studied by Lee and Fraumeni during the period 1938-1963. Excess deaths from respiratory cancer corresponded to areas of highest arsenic levels. The authors noted an overall strong gradient in risk associated with the indices of cumulative arsenic exposure. However, the authors also noted that this gradient was less clear when weighting of the high-exposure category was reduced ten-fold to account for respirator usage. According to Welch et al. (1982), however, respirator usage was not common prior to 1964.

Some study differences were noted by Lubin et al. between their respective study and that of Lee and Fraumeni. Differences in excess respiratory cancer--65 percent in the more recent period versus a three-fold excess in the earlier period--were partially attributed to differences in respiratory cancer rates observed between the two comparison populations. Respiratory cancer rates in the general populace have increased in recent years; therefore, comparisons to recent populations will produce lower relative risks than comparisons to past general populations in which the rates of respiratory cancer were lower. The authors also noted that the comparison populations differed in composition. Lee and Fraumeni used white males in the state of Montana as their standard population, whereas Lubin et al. used U.S. white males. As noted in this study, as well as elsewhere (Welch et al., 1982; Higgins et al., 1982), death rates for specific causes of death (inclusive of respiratory cancer) have been reported to be lower in Montana. Finally, the authors suggested the possibility that individuals most susceptible to lung cancer contracted the disease in the earlier period and were, thus, lost to the study follow-up due to death.

In looking at SO_2 exposures, the authors were unable to totally separate the possible interactive effects of SO_2 with arsenic. However, they did note

that after controlling for arsenic, no significant increase in mortality could be associated with heavy or medium SO_2 exposures, whereas the association with arsenic exposure persisted after controlling for SO_2. This finding is consistent with that of other researchers studying smelter populations (Enterline and Marsh, 1982; Welch et al., 1982; Higgins et al., 1982).

In an update of the earlier study co-authored with Fraumeni, Lee-Feldstein (1983) observed the mortality experience of the same Anaconda workers (with the exception of two women) from 1938 to 1977. The workers (8045) were assigned to one of five cohorts on the basis of total years of employment. Cohort 1 worked 25+ years; cohort 2, 15-24 years; cohort 3, 10-14 years; cohort 4, 5-9 years, and cohort 5, 1-4 years. SMRs were calculated by comparison to the combined white male populations in the states of Idaho, Wyoming and Montana.

Of the thirteen specific causes of death considered, tuberculosis, digestive and respiratory cancer, vascular lesions of the CNS, diseases of the heart, emphysema, and cirrhosis of the liver showed a significant excess of observed deaths over that expected; however, only excesses in respiratory cancer showed a positive gradient with length of employment when comparing cohorts 1 through 5. The ratio of observed to expected mortality from respiratory cancer was approximately 5.1, 4.5 and 2.3 in the heavy, medium and light arsenic-exposure groups, respectively. This was in accord with the earlier results of Lee and Fraumeni, except that the ratio of observed respiratory cancer deaths to that expected in the heavy exposure category in the earlier study was 7.

Brown and Chu (1983c) discussed the Lee-Feldstein (1983) data with regard to its implications on the multistage theory of cancer. They indicated that analysis of the data suggests that arsenic acts as a late-stage carcinogen

because: (1) there was an increasing excess lung cancer mortality risk with increasing age at initial exposure, and (2) the excess mortality was independent of time after exposure stopped.

Higgins et al. (1982) and Welch et al. (1982) reported on a sample of 1800 workers at the Anaconda smelter. Compared to the 8047 workers studied by Lee and Fraumeni, this cohort of 1800 workers included all the workers originally designated in Lee and Fraumeni's heavy exposure category (277) and a random sample (20 percent) of the remaining known workers. The date of entry into the study cohort ranged from 1938 to 1956, providing the individual had one year of work experience. Unlike other studies on these workers, smoking histories on the 1800 workers were obtained either by direct questioning or by proxy respondent. SMRs were based on comparisons to white males both in the state of Montana and the United States.

From industrial hygiene records for the period 1943 to 1965, estimates of airborne arsenic concentrations within 35 smelter departments were provided. A total of 818 samples were collected from 18 departments and departmental averages were calculated from these measurements. The remaining 17 departments were estimated by analogy with those that were known. The departments were then grouped into four categories in which arsenic exposure was characterized as low ($<100\ \mu g/m^3$), medium ($100\text{-}499\ \mu g/m^3$), high ($500\text{-}4999\ \mu g/m^3$) or very high ($>5000\ \mu g/m^3$).

Workers were assigned to these categories based upon estimations of both time-weighted average (TWA) arsenic exposure levels and ceiling levels. TWA values were individually calculated based upon the time that a worker spent in a given department and the average arsenic concentration estimated for that department. This quantity was summed across all departments the individual worked in and was divided by total time worked to yield a TWA. TWA arsenic

exposures were calculated at entry into the study cohort and at the beginning of January, 1964, corresponding to the end of the follow-up period used by Lee and Fraumeni. TWA differences between these two periods could have increased, decreased, or remained the same depending on the work history of an individual worker. In contrast, ceiling levels were defined as the highest level to which an employee was exposed for a period of 30 days or more. Ceiling levels were calculated at entry into cohort, at the beginning of 1964 and at the beginning of 1978. Unlike a TWA value, a worker's ceiling level could only increase or remain the same from point of entry into the cohort.

Data were analyzed according to five different exposure/follow-up methods which varied in the amount of overlap allowed between exposure and follow-up periods. Method I, the primary method used by the authors, included each worker's arsenic exposure up to the date he entered the cohort. Follow-up was from entry to 1978; thus, there was no overlap of the two periods. Method IV--exposure from date hired to 1964, follow-up from 1964 to 1978--also had no overlap. Methods II and V had complete overlap--exposure from date hired to 1964, follow-up from 1938 to 1964 and exposure from date hired till termination, follow-up from 1938 to 1978, respectively. Method III had partial overlap--exposure from date hired to 1964, follow-up from 1938 to 1978. Except where specifically noted, results were given according to Method I.

The results of the study supported the thesis that exposure to arsenic was strongly related to respiratory cancer mortality in workers at the Anaconda smelter. SMRs for the total cohort for all causes of death were identical when compared to either the state of Montana or U.S. white males (both SMRs = 133, significant at 0.01 level); however, SMRs for specific causes were somewhat higher when compared to Montana males than when compared to U.S. males. Exposure to arsenic appeared to be the principal factor in the observed

increased risk for respiratory cancer, the study cohort having 3 times the expected death rate for white men living in Montana. Exposure to other occupational contaminants, such as sulfur dioxide and asbestos, did not appear to account for respiratory cancer excess, while smoking explained only a small fraction of the excess.

Of particular note were the differing respiratory cancer results obtained under the two categories of arsenic exposure (Tables 7-12 and 7-13). The SMR for men in the lowest TWA category was elevated, although not significantly so, whereas the SMRs in the other TWA categories were significantly elevated. Mortality for respiratory cancer by ceiling arsenic exposure showed that SMRs were only signficantly elevated in the high and very high categories, whereas they were close to expectation in the two lower exposure categories. Date of hire showed a definite relationship to mortality from respiratory cancer. Workers who were employed in the early years of the smelter operation--from 1884 to 1938, but particularly prior to 1923, when a selective floatation process which markedly improved fume and dust recovery was introduced--had higher SMRs, indicating that the overall higher arsenic exposures in the early years were associated with higher death rates from respiratory cancer. Age at hire did not seem to have a confounding effect, although the authors did note that the SMRs for respiratory cancer showed more fluctuation with age than did all causes of death.

Tables 7-14 and 7-15 show comparisons of TWA and ceiling respiratory cancer mortality as analyzed by the different exposure/follow-up methods. The authors noted that, while there was some variation in the SMRs derived from the different methods, the same basic pattern of increasing respiratory cancer SMRs with increasing TWA and ceiling arsenic exposures could be seen for each method. The authors indicated that none of the exposure/follow-up methods found a significantly ($P < 0.05$) increased respiratory cancer risk for ceiling level

TABLE 7-12. MORTALITY FOR ALL CAUSES AND RESPIRATORY CANCER FROM 1938 TO 1978 BY TIME-WEIGHTED AVERAGE (TWA) ARSENIC EXPOSURE AS OF ENTRANCE INTO COHORT

TWA Arsenic ($\mu g/m^3$)	N	Person-Years	All Causes			Respiratory Cancer		
			Obs	Exp	SMR	Obs	Exp	SMR
<100	547	13152	219	196.7	111*	11	7.9	138
100-	542	14157	216	178.0	121**	22	7.3	303**
500-	565	13460	292	184.7	158**	29	7.7	375**
5000-	146	3552	89	56.1	159**	18	2.6	704**

* Significant at 0.05 level

** Significant at 0.01 level

Source: Higgins et al. (1982).

TABLE 7-13. MORTALITY FOR ALL CAUSES AND RESPIRATORY CANCER BY CEILING ARSENIC EXPOSURE AS OF ENTRANCE INTO COHORT

Ceiling Arsenic ($\mu g/m^3$)	N	Person-Years	All Causes			Respiratory Cancer		
			Obs	Exp	SMR	Obs	Exp	SMR
<100	445	10591	165	152.1	108	8	6.2	129
100-	276	7083	80	80.5	99	4	3.4	116
500-	833	20757	416	288.5	144**	41	11.8	348**
>5000	246	5889	155	94.4	164**	27	4.1	662**

* Significant at 0.05 level

** Significant at 0.01 level

Source: Higgins et al. (1982).

TABLE 7-14. RESPIRATORY CANCER MORTALITY BY METHOD OF ANALYSIS AND TWA ARSENIC CATEGORY

TWA Arsenic ($\mu g/m^3$)	METHOD OF ANALYSIS I[a]				III[b]				IV[c]			
	N	Obs	Exp	SMR	N	Obs	Exp	SMR	N	Obs	Exp	SMR
<100	547	11	7.9	138	522	5	7.9	63	354	4	4.8	84
100-	542	22	7.3	303**	580	28	7.8	359**	410	16	5.1	313**
500-	565	29	7.7	375**	515	29	7.1	408**	313	9	4.2	216*
≥5000	146	18	2.6	704**	183	18	2.7	673**	111	9	1.6	573**

*Significant at 0.05 level

**Significant at 0.01 level

[a]Exposure from date hired to cohort entry. Follow-up from cohort entry to 1978.

[b]Exposure from date hired to 1964. Follow-up from cohort entry to 1978.

[c]Exposure from date hired to 1964. Follow-up from 1964 to 1978.

Source: Higgins et al. (1982).

TABLE 7-15. RESPIRATORY CANCER MORTALITY BY METHOD OF ANALYSIS AND CEILING ARSENIC CATEGORY

Ceiling Arsenic ($\mu g/m^3$)	METHOD OF ANALYSIS															
	I[a]				III[b]				IV[c]				V[d]			
	N	Obs	Exp	SMR	N	Obs	Exp	SMR	N	Obs	Exp	SMR	N	Obs	Exp	SMR
<100	445	8	6.2	129	275	3	4.0	75	178	3	2.3	130	267	3	3.9	77
100-	276	4	3.4	116	218	2	2.5	79	152	0	1.6	-	210	2	2.4	83
500-	833	41	11.8	348**	970	41	13.8	298**	656	20	8.7	230**	969	41	13.7	300**
≥5000	246	27	4.1	662**	337	34	5.2	652**	202	15	3.0	496**	354	34	5.5	617**

*Significant at 0.05 level

**Significant at 0.01 level

[a]Exposure from date hired to cohort entry. Follow-up from cohort entry to 1978.

[b]Exposure from date hired to 1964. Follow-up from cohort entry to 1978.

[c]Exposure from date hired to 1964. Follow-up from 1964 to 1978.

[d]Exposure from date hired to 1978. Follow-up from cohort entry to 1978.

Source: Higgins et al. (1982).

categories less than 500 $\mu g/m^3$ of arsenic (Table 7-15). For the respiratory cancer SMR analysis by TWA exposure, a significantly ($P < 0.05$) elevated SMR was not found in the lowest dose category. In the 100-499 $\mu g/m^3$ TWA exposure category, there was a significantly ($P < 0.05$) elevated respiratory cancer SMR (Table 7-14). The respiratory cancer SMR in this category would not have been significant, however, if those respiratory cancer deaths with <500 $\mu g/m^3$ ceiling arsenic exposure had been excluded from the analysis. The authors concluded that if a worker in the study had not been exposed to <500 $\mu g/m^3$ ceiling level, he would have had little, if any, excess cancer risk.

A number of criticisms have been made of this study (48 FR 1864), a few of which bear mentioning at this point. The representativeness of the exposure estimates as they relate to overall exposure conditions in the smelter and specifically to the cohort's TWA and ceiling exposures has been criticized. The authors noted that individual worker exposure estimates, based upon area measurements rather than personal samples, would not likely have great precision. Furthermore, estimates of analogy--as in 17 of the departments--weaken the reliability of overall exposure estimates, although areas that were thought to be "problem" areas of high exposure were areas that were generally measured. The extent to which respirator usage was an effective protective measure is also unknown. In interviews with former workers, however, indications were that the use of respirators was not widespread or regular during the period prior to 1964. Collectively, the authors stated that exposure estimates probably tended to affect results such that exposure values were underestimated from 1884 to 1938, were reasonable for 1938 to 1964, and were overestimated for the period after 1964.

The authors found that workers who had not experienced a ceiling level of 500 $\mu g/m^3$ of arsenic did not have an elevated risk of lung cancer. However, the number of lung cancer deaths that could be predicted using a linear dose-

response model (see Section 7.3.1) in the group of workers with <500 $\mu g/m^3$ arsenic ceiling exposure would not be significantly different than the number of lung cancer deaths actually found. This was determined using the linear risk model (Section 7.3.1) and data obtained from Higgins and made available by Consultants in Epidemiology and Occupational Health (1982) on the cross-tabulation of the number of workers in cumulative and ceiling exposure categories. Higgins et al. are presently undertaking a study of the entire Anaconda cohort; however, results of this study will not be forthcoming until late 1984.

In foreign smelters, an excess in lung cancer mortality has also been found. The Rönnskär smelter in Sweden, which has been processing arsenic-rich ores since the 1920s, has been the subject of several studies. Axelson et al. (1978) conducted a case-control study of mortality from respiratory cancer in relation to employment at that smelter. In the parish surrounding the smelter, 369 deaths have been recorded in the registers for men aged 30-74 years during the years 1960 to 1976. Causes of death were obtained in all cases. Smoking habits were obtained from medical files. Cases were defined as subjects who died of malignant tumors of the lung, other cancers, cardiovascular disease, cerebrovascular disease, and cirrhosis of the liver. The control group was made up of persons from the same parish who died from causes other than the above, excluding 44 persons with diabetes, mental deficiency and unclear diagnoses. Attempts were made to assess exposure and four exposure groups were constructed, based on intensity and duration of exposure and time between initiation of exposure and death. It was found that occupational exposure to arsenic was associated with a significant increase in deaths from lung cancer. For the three exposure groups with at least 3 months of exposure occurring 5 years

prior to death, the lung cancer mortality ratio was 4.6. In these groups, there was an increase with exposure intensity. For the fourth group in which either persons were not exposed or the first exposure was for a period less than 3 months and/or death occurred within 5 years of this first exposure, a risk of respiratory cancer was not found.

Other agents, including sulfur dioxide, did not seem to be associated with lung cancer in this study. In 83 percent of the exposed lung cancer cases there was a history of smoking. A study of smoking habits by Pershagen (1978) showed that the excess lung cancer mortality could not be explained by smoking habits.

Because a high lung cancer mortality rate was noted among males in Saganoseki-machi, Japan, for the period 1967-69, Kuratsune et al. (1974) did a case-control study of lung cancer cases in that town. The nineteen cases of lung cancer for the period 1967-69 were compared with nineteen controls randomly selected from deaths of diseases other than cancer of the lung, skin, or bladder for the 1967-69 period. Smoking and drinking habits, residential and occupational histories, and exposure to atomic bomb radiation were the factors compared. Fifty-eight percent of lung cancer cases were found to be former smelter workers vs. 15.8 percent in the controls ($p < 0.01$). The relative risk was reported to be 9.0 (confidence limits not reported). No difference was found between the cases and controls for smoking habits, residential history, drinking habits, or atomic bomb radiation.

Tokudome and Kuratsune (1976) did a cohort study of 2765 male workers, including 839 copper smelter workers at the metal refinery in Saganoseki-machi, Japan. Deaths which occurred between 1949 and 1971 were analyzed in the

study. The expected number of deaths was calculated using mortality data for Japanese males. A significantly increased mortality was noted for lung cancer (SMR = 1189; observed = 29; expected = 2.44; $p < 0.01$) and colon cancer (SMR = 508; observed = 3; expected = 0.59; $p < 0.05$). A dose response was demonstrated between lung cancer mortality and the degree of exposure measured by length of employment and level of exposure. A very high excess mortality from lung cancer (SMR = 2500; 10 observed; 0.4 expected; $p < 0.01$) was found among smelter workers who had worked in the heaviest exposure category and who had been employed over 15 years before 1949. The latent period in this study ranged from 13 to 50 years.

Studies have also been performed to see if there is any increase in lung cancer among residents in areas surrounding smelters. Lyon et al. (1977) compared the incidence of lung cancer and lymphoma in Utah residents from 1970-1975 in relation to the distance of these residents from a smelter and found no association. It should be noted that distance from the smelter was based on address at the time of diagnosis; nothing regarding the length of time lived near the smelter was factored into the analysis. Furthermore, use of lymphoma cases as controls is questionable since lymphomas may also be associated with arsenic (Ott et al., 1974). Thus, the conclusion of the study that there was no association between lung cancer and distance from the smelter is questionable.

In a more recent study, Rom et al. (1982) compared lung cancer with breast and prostate cancer in residents living near a non-ferrous smelter in El Paso, Texas. The study period ranged from 1944-1973. Similar to methods used by Lyon et al. (1977), comparisons were made in relation to distance from the smelter. Breast and prostate cancer were chosen as control cancers because they have no known association with arsenic exposure. The authors reported

that the distribution of lung cancer cases (575) and control cancer cases (1490) was roughly the same for the different distances studied. No association between lung cancer and distance from the smelter was found, nor were there any associations for race, age or sex. However, the authors did note that they were unable to control for such factors as smoking, occupation and migration and were unable to obtain environmental exposure measurements over most of the years studied.

In Montana, the studies by Newman et al. (1976) showed that there was an increase in the incidence of lung cancer among men in cities where copper smelters are located. In one of the cities there was also an increased incidence of lung cancer among women. It was not stated to what extent occupational exposure had caused the increase, and there was no control for smoking.

In the Blot and Fraumeni study (1975), the cancer mortality in 71 counties with smelters and refineries was studied from 1950 to 1969. Comparisons were made with the remaining 2,985 counties in 48 states. In 36 counties with smelters processing copper, lead, or zinc ores, lung cancer mortality was significantly higher both among males ($p < 0.01$) and females ($p < 0.05$). For all 36 counties with these industries the median SMR was 112 for males and 110 for females. Although occupational cancers were included in the analyses and, therefore, contributed to some of the excess risk, the number of workers in the smelter industry generally comprised a small fraction of the total population (less than 1 to 3 percent); thus, it was unlikely that occupational exposures alone accounted for the observed excess mortality in males or the increased risk for females. Although this study is suggestive of a lung cancer effect in populations surrounding smelters, it is unknown if the lung cancer cases were even exposed to arsenic. Thus, the results, although suggestive, are inconclusive.

In the Baltimore, Maryland area, Matanoski et al. (1976, 1981) studied cancer mortality in areas near the earlier mentioned pesticide facility. They found an excess of all cancers and respiratory cancers among males in the area nearest to the factory but not among females. Soil arsenic levels generally corresponded to lung cancer and all cancer incidences, with the highest average of arsenic in the soil (63 ppm) reported in the area with the greatest cancer risk. The authors were unable to account for the differences noted between males and females, but suggested that smoking may have contributed to these differences. Other environmental factors and/or occupational exposure may have also influenced cancer mortality excess. Further environmental sampling of arsenic and conducting of community surveys were recommended to address these unknown factors.

Pershagen et al. (1977) studied cancer deaths in the area surrounding the Rönnskär smelter in Sweden. From 1961 to 1975 there was a significant excess of respiratory cancers in the male population (SMR = 250) compared to residents in an area without known emissions of arsenic but in which the same age distribution and occupational profiles applied. When the occupationally exposed cases were excluded, significant increases in respiratory cancers were no longer detected (SMR 173); however, the male population still showed a tendency to excess lung cancers. No similar occupational group was excluded from the comparison population, however. There was no tendency to an increase in lung cancer among women.

7.1.2.2 Cancer of the Skin and Precancerous Skin Lesions--An elevation in the proportionate mortality of skin cancer was reported by Hill and Faning (1948) for factory workers manufacturing sodium arsenite and by Roth (1957, 1958) for German vintners. In addition, an increased incidence of skin cancer has been reported after long-term oral exposure to arsenic.

In Taiwan a large population had long-term exposures to inorganic arsenic in drinking water. Exposure started in 1910-20 when water was obtained from deep wells, 100-200 m. below the surface. Already in the 1920s, vascular changes began to appear, and in the 1950s, the first epidemiological studies were conducted. The arsenic content of the water varied from 0.01 to 1.82 mg/l (Ch'i and Blackwell, 1968; Astrup, 1968; Tseng et al., 1968; Tseng, 1977), generally being 0.4 - 0.6 mg/l, whereas water from shallow wells or other surface waters generally contained from near zero to 0.15 mg As/l.

Tseng et al. (1968) and Tseng (1977) have reported the results from a large-scale epidemiologic survey of arsenic-related diseases in an area with high arsenic concentrations in drinking water. The population at risk was 103,514 persons. Thirty-seven villages with a population of 40,421 were surveyed house-to-house. Examinations were made with special attention to pigmentation, hyperkeratosis, and cancer of the skin. Four hundred twenty-eight cases of arsenical skin cancer were found, resulting in a rate of 10.6/1000. No cases were under 20 years of age. The prevalence rate increased markedly with age except for females >70. Over 10 percent of the people >59 were affected by skin cancer. The overall male/female ratio was 2.9:1, with males having a higher rate in all age groups >29.

The villages were divided into 4 exposure levels: <0.3, 0.3-0.6, $\geq$0.6, and undetermined, based on their water arsenic content. There was a clear cut ascending gradient of prevalence from low to high in each of 3 age groups (Table 7-16).

Hyperpigmentation (melanosis) was found in 18.4 percent of the total population: 19.2 percent for males and 17.6 percent for females. Usually the prevalence was higher for males than females. The rates increased steadily with age for males and did likewise for females until a peak was reached at 50-59, followed by a gradual decline.

TABLE 7-16. PREVALENCE OF SKIN CANCER (per 1000) BY AGE AND ARSENIC EXPOSURE (ppm)

Arsenic content of drinking water (ppm)	Age 20-39	40-59	>60
<.3	1.3	4.9	27.1
0.3 - 0.6	2.2	32.6	106.2
>0.6	11.5	72.0	192.0

Source: Adapted from Tseng et al. (1968).

The overall prevalence rate for keratosis was 7.1 percent - 7.5 percent for males and 6.8 percent for females. Males had higher rates in the greater than-49-year group. The prevalence increased for both males and females up to age 70 and then declined.

As was the case for skin cancer, the prevalence rates for hyperpigmentation and keratosis suggested that positive correlations existed between these conditions and the arsenic content of the water in the artesian wells; the greater the arsenic content, the higher the prevalence.

In the total survey of 40,421 people, 7418 cases of hyperpigmentation, 2868 of keratosis, 428 of skin cancer, and 360 of Blackfoot disease (see Section 5.2.2) were found. Many of these occurred in combination in the same individual.

The data were examined by comparing expected (based on overall rates) and observed rates for various combinations of the 4 end points. The obtained ratios indicated quite strongly that a common underlying cause existed for the 4 conditions, presumably chronic arsenicism.

A control population of 7500 persons from nonendemic areas was examined in the same way as the arsenic-exposed persons. Four thousand, nine hundred

and seventy-eight people lived on Matsu Island; its water supply was from shallow wells and no arsenic was detectable by the analytic methods used in the main series. The remaining portion of control population members came from 5 villages on Taiwan whose water source was shallow wells with arsenic levels between 0.001-0.017 mg/ℓ (ppm). No cases of melanosis, keratosis, or skin cancer were observed in the entire control population.

Although age at onset of the conditions was difficult to assess, some information on latency was obtained. "We know from the study that the youngest cancer patient was 24, the youngest with hyperpigmentation was 3, and the youngest with keratoses was 4." This meant that hyperpigmentation could occur in patients who were exposed from birth for at least 3 years, keratosis for 4 years, and cancer for 24 years (Tseng et al., 1968).

While the Taiwanese data collected in the late 1960's strongly implicated arsenic as the etiological source of the observed diseases, recent findings have called to question the hypothesis of arsenicism as sole causative source in the induction of cardiovascular effects. The discovery by Lu et al. (1977b, 1978) of fluorescent compounds identified as alkaloids--either lysergic acid, dihydrolysergic acid or a derivative of ergotamine tartfate--has opened the possibility that other toxic mechanisms may have been involved. Ergotamine-like compounds in combination with high alkalinity, characteristic of these waters, have been shown to cause gangrene (Lu et al., 1977a,b; 1978). Whether these compounds have a confounding effect on skin cancer is presently unknown.

In addition, recent analyses by Irgolic (1982) on a limited number of samples have shown the water samples to contain predominantly pentavalent arsenic and no organic arsenicals. Samples taken from two wells in the Yenshei Province of Taiwan were collected in plastic cubitainers. Two samples each of unpreserved water and water preserved either by addition of 0.1 weight percent

of ascorbic acid or by acidification of 0.1 M HNO_3 were sent to the U.S. for analysis a few days after collection. Treatment of samples by HNO_3 or ascorbic acid was done immediately upon collection (Irgolic, 1983; personal communication). Samples were analyzed during a two-week period after arrival in the U.S., the total time lapse between collection and analyses ranging from one to three weeks. The results of the analyses can be seen in Table 7-17. Additional water samples collected from other parts of Taiwan also contained pentavalent arsenic. However, these samples were less reliable in that the collection period was unknown, and, upon arrival in the U.S., these samples had a yellowish hue with some flocculated matter present (Irgolic, 1982).

Several questions still remain to be answered in regard to water-usage patterns of the Taiwanese. For instance, it is not clear how quickly the water drawn from the wells was consumed; nor is it clear how much of the water was consumed in tea or other beverages where cooking preparations, such as boiling, would have altered the chemical form of the arsenic. These questions need to be answered in light of the possible effect these answers might have on interpreting the observed skin cancer incidence.

Ch'i and Blackwell (1968) conducted a case-control study in the area of Taiwan studied by Tseng et al. The authors compared a variety of factors between 353 cases of Blackfoot disease and 353 controls matched for sex and age. Socioeconomic status, occupation, cigarette smoking, diet, and consumption of deep well water which was arsenic-contaminated were the factors compared. Two factors were found to be significantly different between the cases and controls. Significantly ($P < 0.01$) more cases than controls were found to consume deep well water and to have a lower socioeconomic status. Though the author concluded that the primary contributing cause of Blackfoot disease was consumption of deep well water, the socioeconomic differences cannot be completely discounted.

TABLE 7-17. RESULTS OF TOTAL ARSENIC ANALYSES AND ARSENITE AND ARSENATE DETERMINATIONS IN THE YENSHEI WATER SAMPLES*

Sample	Ascorbic Acid 0.1%	0.1 M HNO_3	Un-preserved	TOTAL ARSENIC, ppm HG[a]	TOTAL ARSENIC, ppm ICP[b]	Arsenite, ppm by HG	Arsenate, ppm by HG
Well I	-	+	-	0.84±0.02	0.73±0.01	-	-
	+	-	-	0.88±0.01	0.72±0.01	0.024±0.001	0.85±0.01
	-	-	+	0.85±0.01	0.73±0.01	0.022±0.001	0.83±0.08
Well II	-	+	-	1.05±0.08	0.95±0.01	-	-
	+	-	-	1.16±0.03	0.96±0.01	-	-
	-	-	+	1.11±0.02	0.98±0.01	0.024±0.01	1.08±0.02

*Average ± average deviation of at least three determinations per sample.

[a]HG = Hydride generation technique.

[b]ICP = Inductively coupled argon plasma emission spectrometry.

Source: Irgolic (1982).

Other studies have also explored the relationship of arsenic to skin cancer and various skin lesions. Similar chronic effects as seen in Taiwan have been reported in other countries.

In Antofagasta, Chile, a new water supply was put into service in 1958. In the 1960s, physicians began noticing dermatological manifestations and even deaths, especially among children. In an investigation of skin pigmentation in 27,088 school children from the province of Antofagasta, an overall incidence of 12 percent was reported (Borgono and Greiber, 1972). It was discovered that the drinking water contained 0.8 mg As/l. Borgono and Greiber compared 180 inhabitants of Antofagasta with a community without exposure to arsenic via drinking water. Abnormal skin pigmentation was reported to be present in 80 percent and hyperkeratosis in 36 percent of the Antofagasta inhabitants, whereas none was found in the control group ($p \leq 0.05$).

In 1970, a water treatment plant was installed and there was a considerable drop in arsenic. According to Borgono et al. (1977), there were no skin lesions in children born since the water treatment began. However, it should be noted that in this more recent study the sample size of children born since the water treatment plant began was small (306) and no comparison population was studied. Therefore, any conclusions associating the lack of dermatological manifestations with the decrease in arsenic must take into account the small sample size. In regard to skin cancer, the follow-up may not have been long enough to detect a difference.

In addition to the work of Borgono and co-workers, Zaldivar and Guillier published a series of papers on the Antofagasta situation (Zaldivar, 1974; Zaldivar, 1977; Zaldivar and Guillier, 1977). The first of these (Zaldivar, 1974) describes a study on a total of 457 patients (208 males and 249 females) bearing cutaneous lesions (leukoderma, melanoderma, hyperkeratosis, and squamous cell carcinoma). The cases were collected both by the author and the

local hospital during the period 1968 to 1971. Children 0 to 15 years of age accounted for 69.2 percent of the male cases and 77.5 percent of the female cases. The average incidence/100,000 for cases with cutaneous lesions in 1968 to 1969 were 145.5 and 168.0 for males and females, respectively. By 1971 the incidence rates had dropped to 9.1 and 10.0 for males and females, respectively. The decline in morbidity was so rapid that a conclusion that arsenic was the cause of the skin lesions would have to be considered suspect.

The existence of arsenical waters in an eastern area of the province of Cordoba, Argentina, has been known for many decades (Arguello et al., 1938; Bergoglio, 1964). Effects noted on the population from this area include hyperpigmentation, keratosis, and skin and respiratory cancer. A large area of the province, mainly in the east and somewhat to the south, is the focal point for chronic endemic regional arsenical intoxication (CERAI) (Arguello et al., 1938). This CERAI is due to the ingestion of well water coming from the uppermost sheet of underground water--the principal source of arsenic--as well as to the ingestion of arsenic from the wells, which varies among wells throughout the region. The concentration also varies with rainfall. Vanadium is also elevated in areas with high arsenic content. A later report (Bergoglio, 1964) indicates that progress had been made in improving the hygienic condition of the drinking water.

Arguello et al. (1938) summarized the early history of investigations (1913 to mid-1938) into the health outcomes associated with the ingestion of arsenic-contaminated water. They also reported the results of an investigation of a large series of epitheliomas collected from mid-1932 to September 1938 at the dermatosyphilology clinic of a medical school in the arsenic-contaminated area. The series consisted of 323 cases of epithelioma of which 39 or 12.1 percent were cases with clinical evidence of CERAI.

Patients exhibiting CERAI had characteristic cutaneous lesions, represented by the symmetrical palmo-plantar keratoderma and melanoderma, although the latter symptom was seen less frequently. Foot and hand keratoderma were seen in 100 percent of the CERAI patients. Appearance usually occurred 2 to 3 years after the onset of intoxication. A prodrome of the keratosis is the appearance of an erythema in the same location, and a subjective crawling sensation and local fever. Otherwise, it is a state of dryness which precedes the keratosis.

Arguello et al. (1938) also reported that most patients also had hyperhidrosis and abnormalities of pigmentation. The melanoderma appeared early in the process and was variable among patients. It was described as small dark spots ranging in diameter from 1 to 10 mm. They had a tendency to coalesce and appeared predominantly on the trunk in the areas not exposed to the sun. Atropy was associated with telangiectasia and loss of color, or leukoderma, between the hyperpigmented areas (the "raindrop" appearance cited by Reynolds, 1901).

Geographically, the largest proportion of cases in the clinic came from the areas with the highest incidence of CERAI. Because the authors' data are not population-based, however, it cannot be stated that the incidence of skin cancer is significantly increased in these areas. The authors reported that the hands and feet were the locations of choice for the arsenical epitheliomas (38.5 percent vs 3.9 percent) compared to the nonarsenical epitheliomas. An example of this was seen in the head where 81.6 percent of the nonarsenical epitheliomas occurred versus 15.4 percent for arsenical epitheliomas.

Bergoglio (1964) did a proportionate mortality study of residents of certain departments (counties) in the Province of Cordoba, Argentina, where endemic arsenic levels in the water supply are reported to be very high. The

proportion of cancer deaths was higher in those departments than for the province as a whole (23.84 percent versus 15.3 percent; $P < 0.05$). Of the cancer deaths, respiratory cancer constituted 35 percent and skin cancer 2.3 percent. From the description by the author, it can probably be inferred that these data are not age-adjusted. No comparison is made of the percentage of respiratory and skin cancer deaths in the affected departments with the respective proportion for Cordoba Province.

Morton et al. (1976) investigated the relationship of skin cancer morbidity and the ingestion of arsenic-contaminated drinking water in Lane County, Oregon. The southcentral region of Lane County is underlaid by an arsenic-rich stratum called the Fisher formation, which is known to produce high arsenic levels in waters from wells drilled into the land. An extensive search of the pathology records of medical providers in Lane County, Oregon, was conducted in 1972 for the occurrence of skin cancer during the years 1958 to 1971. Cases were thoroughly screened to eliminate duplications and were then coded to 1970 census tract numbers according to the residential address at the time of diagnosis. Water samples were obtained in all census tracts at selected points in all municipalities and water districts in the county, as well as from single-family water sources. The single-family water sources were neither randomly nor uniformly distributed throughout the county but instead were heavily concentrated in the regions believed to have water arsenic problems. Water samples collected during 1968 to 1974 were compiled into mean concentrations for each census tract and census tract region. The authors stated that it seemed reasonable to assume that the samples were representative of the earlier time periods as well.

The skin cancer data were expressed in four sets of rates because of the availability of 4 sets of population estimates. Overall mean annual incidence

rates for the entire 1958 to 1971 period used mean population estimates based on all four sets of denominators. Census tract regions were devised to simplify analysis and presentation. Table 7-18 presents the water arsenic level obtained. As can be readily seen, the South rural area had a much greater arsenic exposure than any of the other sections of the county. Figure 7-1 contrasts the parts of the county underlaid by the Fisher formation, and subsequent higher arsenic levels, with the parts of the county experiencing higher squamous cell skin cancer. Relatively little concordance is noted. A multiple regression analysis performed by the authors demonstrated essentially no relation between skin cancer and water arsenic. It should be noted that water arsenic levels in this study varied from 0 to 2150 ppb. The authors point out that the Lane County water arsenic levels were much lower than those reported for Taiwan and Antofagasta. In particular, only 5 percent of the Lane County samples contained 100 or more ppb of arsenic in contrast to 48 percent of the samples in that range in the Taiwan data.

Similar findings were reported by Southwick et al. (1981) in a study conducted on residents of West Millard County, Utah. As an area in which naturally occurring arsenic in public drinking water had been reported, West Millard provided an "excellent opportunity to study the effects of arsenic exposure on a homogeneous, stable population with a predominantly 'Mormon lifestyle'" (Southwick et al., 1981). The exposed communities of Hinckley and Deseret had average arsenic concentrations of 0.18 mg/l and 0.27 mg/l, respectively (based upon monthly water samples taken between May 1976 to May 1977). The control community of Delta had average arsenic concentrations of 0.02 mg/l. All drinking water in the study communities came from wells and the predominant species of arsenic was reported as the pentavalent form (85 percent).

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TABLE 7-18. LANE COUNTY WATER ARSENIC LEVELS 1974-1978

Geographic region	Arsenic, ppb			1970 Population served by water districts	
	mean*	range	no. of samples	number	% of area residents
Rural	16.5+	0-2150	491	29,470	44
North	7.6	0-24	29	3,644	39
East	11.8	0-70	80	7,383	49
South	33.0	0-2150	186	12,713	59
Midwest	9.7	0-107	159	1,260	10
Coast	4.7	<1-13	37	4,470	54
Urban	4.8	0-860	67	135,260	91
NE Springfield	3.9	0-8	14	16,235	92
SW Springfield	6.0	0-30	4	18,460	96
S Eugene	5.3	0-750	10	29.230	88
W Eugene	6.5-	0-860	20	16,470	96
NW Eugene	3.8	<1-8	6	20,730	85
N Eugene	3.8	0-8	8	11,690	81
Core Eugene	4.0	<1-8	5	22,445	100
Lane County	8.6	0-2150	558	164,730	76

*Values with terminal digit of 5 indicate direction from which rounded, e.g., 0.51 - 0.5+, 0.49 - 0.5.

Source: Morton et al. (1976).

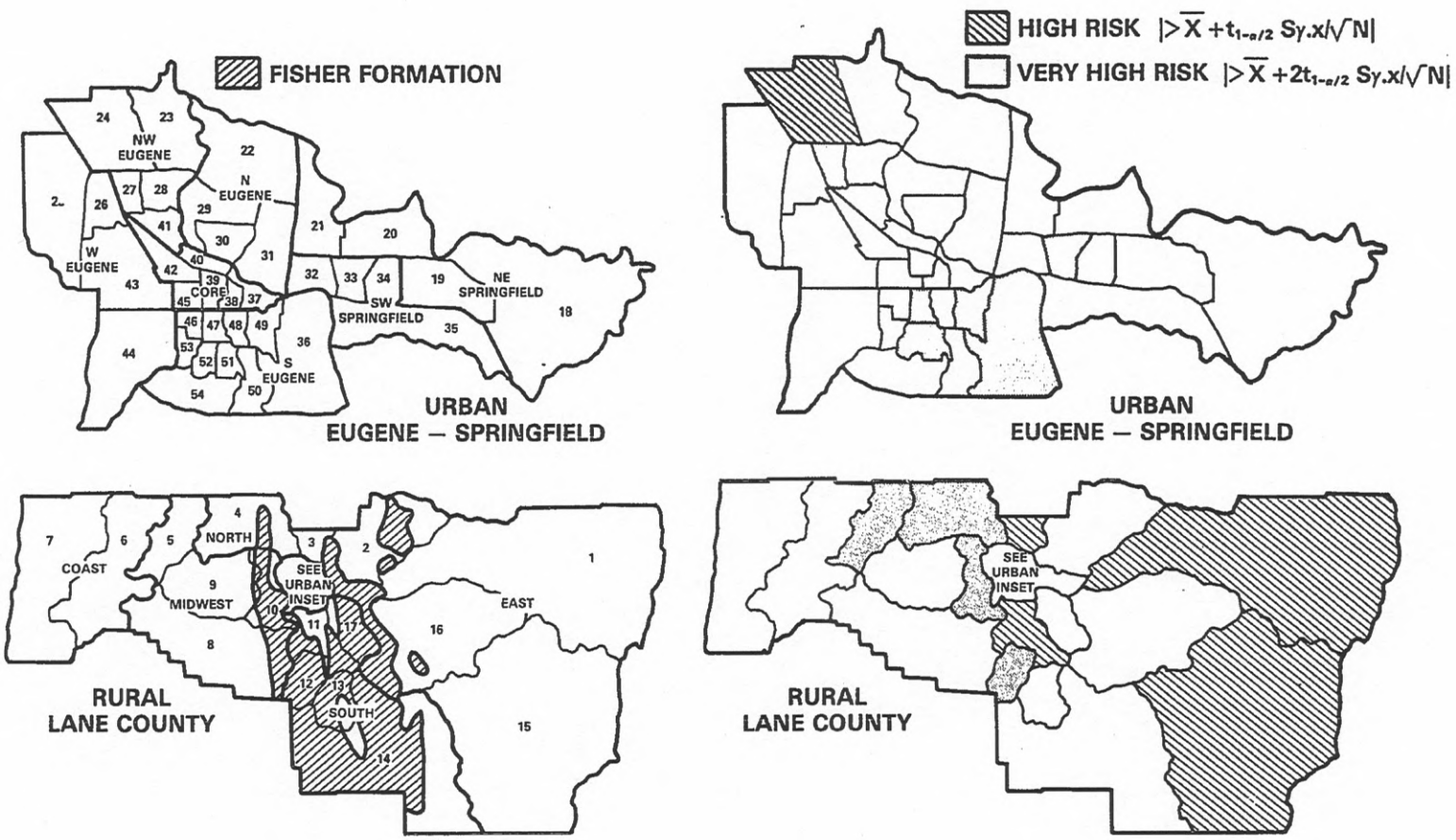

Figure 7-1. Comparison of census tracts experiencing exposure to the Fisher formation and exhibiting high skin cancer occurrence.

Source: Morton et al. (1975).

All study participants from the exposed communities were required to be five years of age or older and to have been residents of Hinckley or Deseret for at least the previous five years. Control participants were selected at random from age and sex categories matched to the exposed participants. Control participants were required to have lived their entire lives either in Delta or communities where arsenic in drinking water did not exceed the national standard of 0.05 mg/l.

Physical examinations were conducted to detect signs and symptoms associated with chronic arsenic poisoning. A total of 250 people participated in these examinations (145 exposed, 105 control); not all of these participated in each part of the examination, however. No explanation was provided by the authors as to the differences in participation rate for different parts of the examination. Urine and hair samples were collected from 94 and 74 percent of the participants, respectively. Dermatological examinations were conducted on 249 individuals. Neurological and hematological examinations were also conducted and are discussed in Sections 5.2.1 and 5.2.4, respectively. In addition, the incidence of cancer and vascular diseases in the study population was compared to other counties in the state of Utah.

The study results showed a clear relationship between the amount of arsenic consumed in drinking water and the amount measured in hair and urine. Differences between exposed and control populations were statistically significant.

Of the 249 participants examined for dermatological signs of arsenic toxicity (palmar and plantar keratosis and hyperkeratosis, tumors, diffuse pigmentation, arterial insufficiency), only 12 showed such signs and no participant had more than one sign. The 12 individuals were not clustered among the more heavily exposed, and when the dermatological signs were regressed

against annual arsenic dose and the log of the dose, no significant associations were found.

Age-adjusted cancer incidence rates showed Hinckley to have a somewhat lower cancer incidence than Delta. Cancer death rates, 1956 to 1976, showed Hinckley to have the highest rate (138 per 100,000) when compared to 42 other Utah communities. Table 7-19 shows age-specific death rates for Utah and three Millard County communities. (Fillmore is the County seat; comparisons to Deseret were not made due to the community's small population). Between 1956 and 1976, 14 cancer deaths were reported for Hinckley. All of these deaths occurred in individuals 45 years or older and the cancers were types most frequently reported for Utah: lung, breast, large intestine, prostate, stomach, leukemia, kidney, uterus, bone and connective tissue. Hinckley had generally lower death rates for cardiac and vascular diseases than did the control community of Delta. The authors noted that no unusual death patterns likely to be associated with arsenic exposure were seen in Hinckley.

Certain weaknesses exist with this study, most notably, that of a small study population from which to derive meaningful statistical analyses. Furthermore, children and adults were not treated separately. In regard to sample size, the authors felt that the small sample size was somewhat compensated by the homogeneity and stability of the predominantly nonsmoking population. Data on food consumption were also missing which might have influenced urinary arsenic levels. This, in turn, may have resulted in overstating the strength of the dose-response relationship for urinary arsenic and arsenic in drinking water. It should also be noted that some participants were reported to have an average daily water consumption greater than 8ℓ, which seems very high, even

TABLE 7-19. AGE-SPECIFIC DEATH RATES FOR UTAH AND THREE MILLARD COUNTY COMMUNITIES (DEATHS/100,000/YEAR)

Community Characteristics	Age Groups and (Number of Deaths)					
	0-4	5-14	15-24	25-44	45-64	65+
CANCER						
State	7 (158)	6 (274)	6 (223)	19 (875)	149 (4749)	558 (7680)
Fillmore	0	14 (1)	0	17 (1)	196 (13)	706 (25)
Delta	0	0	22 (1)	61 (4)	189 (11)	986 (29)
Hinckley	0	0	0	0	390 (6)	1053 (8)
CARDIOVASCULAR						
State	1 (25)	0.4 (18)	1 (34)	18 (840)	275 (8788)	2079 (28587)
Fillmore	0	0	0	17 (1)	392 (26)	1638 (58)
Delta	0	0	0	30 (2)	344 (20)	1599 (47)
Hinckley	0	0	0	0	325 (5)	1316 (10)
CEREBROVASCULAR						
State	1 (24)	0.5 (23)	1 (36)	4 (201)	52 (1651)	797 (10965)
Fillmore	0	0	0	0	60 (4)	1017 (36)
Delta	0	0	0	0	34 (2)	1088 (32)
Hinckley	0	0	0	0	0	789 (6)
ARTERIOSCLEROSIS						
State	0	0.07 (3)	0.2 (7)	0.5 (21)	13 (406)	202 (2781)
Fillmore	0	0	0	0	15 (1)	311 (11)
Delta	0	0	0	0	17 (1)	272 (8)
Hinckley	0	0	0	0	65 (1)	395 (3)
AGE GROUP SIZE						
State	119,004	224,417	175,607	227,502	159,613	68,759
Fillmore	157	347	202	293	332	177
Delta	202	400	224	330	291	147
Hinckley	40	108	57	79	77	38

Death rates from 1956-1975 for cancer, cardiovascular disease, cerebrovascular disease, and arteriosclerosis, showing numbers of deaths and the average size of the age group.

Source: Southwick et al. (1981).

taking into account the hot summers. In reporting on the lack of arsenic-related effects in this study population compared to others (Tseng et al., 1968; Borgono and Greiber, 1972; Borgono et al., 1977; Zaldivar, 1977; Zaldivar and Guiller, 1977), the authors did note that populations in Taiwan and Antofagasta were exposed to considerably higher concentrations of arsenic in their drinking water.

Interestingly, the importance attached to the fact that no adverse effects were seen in this group of individuals exposed to drinking water arsenic levels four times that allowed by the Interim Primary Drinking Water Regulations (0.05 mg As/l) is somewhat compromised by the very characteristics of the population that make it useful for epidemiological study. The fact that this study population is so homogeneous and stable and, therefore, lends itself to a relatively well controlled statistical analysis, also makes it less useful in terms of being representative of the overall population of the U.S. For this reason, any generalizations that might be drawn from this study population are subject to limitations.

In addition to exposures via drinking water, food exposures and therapeutic exposures have also caused skin lesions and cancers. Hyperpigmentation and depigmentation of the skin were found to be common among the survivors of the Morinaga milk poisoning in 1955. A follow-up study conducted on the exposed children when they were 17-20 years of age showed the prevalence of lesions to be 15 percent (Yamashita et al., 1972). It is not known if any skin cancers have developed.

Hutchinson (1888) first reported on a possible association of skin cancer with the use of arsenical medicines. Prior to that, the association between these arsenical agents and keratotic lesions had been recognized. In his classic paper, Hutchinson reported on 6 patients with case histories who

exhibited the keratotic lesions associated with arsenical poisoning. He felt that the clinical series supported two principal conclusions:

1. Prolonged internal use of arsenic may seriously affect the nutrition of the skin and that use may produce warty or corn-like indurations.

2. Continued use of arsenic may result in a tendency for these "arsenic corns" to grow downward and pass into epithelial cancer.

Neubauer (1947) later compiled a series of reports on 143 cases of medicinal arsenical epitheliomas. He excluded five categories of cases reported in the literature to keep the series consistent with regard to diagnosis of case and history of arsenical use. Seventy-one percent of the patients being treated with arsenical medicine were patients suffering from skin diseases, especially psoriasis (54 percent). In contrast, only a small percentage of the cases reported came from patients treated with arsenic for various internal disorders. In nearly all cases the drugs used were inorganic and almost all were trivalent. The most commonly used arsenical was potassium arsenite. No externally applied arsenic-related skin cancer case was reported in the series.

The elapsed time from the beginning of administration of the arsenical drug to the beginning of the epitheliomatous growth was variable, but averaged 18 years regardless of the type of lesion. In cases with keratosis, the latent period to the onset of keratosis was about half the latent period to the onset of the epithelioma, i.e., about 9 years. Thirty-three percent of the patients were 40 or younger. Of the 143 patients, 13 had or developed miscellaneous cancers at other sites, but such cases were not reported systematically.

Fierz (1965) reported a follow-up study of patients treated with arsenic by a private practitioner. An accurate assessment of the total arsenic intake

in terms of the amount of Fowler's Solution administered was available to the investigator from patient records. The follow-up examination was conducted under the auspices of a local polyclinic. Fourteen hundred fifty patients were identified as having received arsenic treatment, and invitations were mailed for them to come for a free follow-up medical examination. During the period March 1963 to April 1964, 262 patients presented themselves for examination. Two hundred eighty patients were not located while 100 patients actively refused to participate. Only patients under 65 years of age were invited to participate in the study. The author admits that the patients reporting for examination were not a representative sample. In fact, he categorizes them into three groups which range the spectrum of likely biases. There were patients satisfied with the results of the arsenic treatment and wishing to express thanks, patients in whom disturbing side effects were occurring, and finally patients who were still suffering from the initial disease and who were eager to get a consultation.

Arsenic treatment was prescribed for individuals suffering primarily from three main skin diseases: psoriasis (64 patients), neurodermatitis (62), and chronic eczema (72). In addition, treatment was also prescribed for 64 patients suffering from assorted skin diseases other than those listed above.

Fierz noted that the arsenic treatment showed good success. Of the 64 cases of psoriasis, 55 reported a favorable effect while taking the drops. Forty-eight of 62 patients with neurodermatitis reported a favorable effect. This effectiveness was the cause for the patients' reliance on the drug.

Upon examination, 106 of 262 patients (40.4 percent) reported hyperkeratoses, although frequently a detailed examination was necessary to find the changes. Hyperkeratoses were round, superficially verrucose papules, 1 to 3 mm in diameter. The number and the exact presentation of the hyperkeratoses varied from case to case.

In the series, 21 cases of skin cancer were found comprising 8 percent of the total subjects. As was in the case of hyperkeratosis, some variability was observed in the expression of the skin cancers. Multiple basal cell carcinoma was the most frequent histologic type observed, occurring in 48 percent of the cancer patients. The basal cell carcinomas appeared morphologically as polycyclic, sharply bounded erythemas with slight infiltration. In 13 of the 21 cancer cases, multiple carcinomas were observed, a much higher proportion than had been observed with other causes of skin cancer. Of the 21 patients with carcinomas, 16 showed distinctly developed arsenic warts on the palms and soles simultaneously with the skin tumors.

Both hyperkeratosis and skin cancer were found to vary with increasing arsenic intake. Above 400 ml of Fowler's solution, more than 50 percent of the patients studied showed hyperkeratosis. As the dose increased there was a corresponding increase in the simultaneous occurrence of hyperkeratosis of the palms and soles. Only 2/15 cases of hyperkeratosis with intakes of up to 250 ml had a simultaneous presentation, while 16/27 had a simultaneous presentation with intake of 250 to 500 ml.

As with the hyperkeratosis, skin cancer increased with increasing arsenic doses. Below 500 ml only basal cell carcinomas were found; spindle cell carcinomas were only found above that dose. The latency period for hyperkeratosis was at a minimum 2.5 years; skin cancer, however, had a minimum latency period of 6 years with a mean latency period of 14 years.

Cuzick et al. (1982) conducted a mortality analysis of a cohort of 478 patients given Fowler's solution to determine if persons taking the solution were at an increased risk of internal malignancies. The cohort consisted of 213 males (45 percent) and 265 females (55 percent) who took Fowler's solution for various lenghts of time ranging from 2 weeks to 12 years (mean duration,

8.92 months) during the period of 1945-1969. Follow-up was until January 1, 1980; the mean follow-up time for the entire cohort was 20.3 years. The median cumulative dose of arsenic was reported as 448 mg, with most patients consuming arsenic at a rate of about 250 mg/month.

Within the defined risk period, 139 patients died, 265 patients were known to be alive and at risk, 29 had passed 85 years of age, 19 had emigrated, and 26 could not be traced. Because of the unreliability of the expected values in the open-ended group beyond 85 years of age, deaths and person-years at risk after age 85 were ignored. Persons who emigrated were censored as of the date of emigration.

A subset of 142 of the cohort were physically examined during 1969-70, and the presence of arsenical keratoses, hyperpigmentation, and skin cancer was recorded. No signs of internal malignancy were clinically apparent at the time of examination. This subset was chosen because the individuals were known to be alive and were able to be traced.

The results showed that risk ratios were similar for both males and females. No signs of internal malignancy were clinically apparent in the patients given physical examinations, and mortality was not found to be significantly increased for any internal malignancies in the cohort, although it was somewhat elevated for death from bladder cancer (observed = 3, expected = 1.19, P = 0.12). The ratio of observed-to-expected deaths from all neoplasms, from cancer of the digestive organs, from cancer of the respiratory organs, and from all causes was analyzed by cumulative dose level. No trend by cumulative dose level was found; however, the risk ratios were low for deaths from all neoplasms, digestive cancers, and respiratory cancers in the lowest dose group, with the risks for deaths from all neoplasms being significantly ($p < 0.05$) lower than expected. A significant positive trend in the ratio of

observed-to-expected mortality for all neoplasms was found for dose in the period 5-9 years from first exposure, but this trend was not found in other time intervals since first exposure.

Of the subset of 142 patients examined for skin manifestation of arsenicism, their overall mortality was consistent with the remainder of the cohort. Within this group, 45 percent had keratosis, 14 percent had hyperpigmentation, and 11 percent were found to have skin cancer. The authors did not indicate what the expected proportions of patients with these signs would be. Some patients showed 2 or all 3 signs of arsenicism, and 49 percent showed at least one of the signs. The appearance of signs was dose- and age-related. Patients with signs had higher median doses (672 mg) than those without any signs (448 mg), and this was significant ($P < 0.001$) by the Wilcoxon rank-sum test. Forty percent of patients with signs had cumulative doses above 1000 mg, whereas only 22 percent of the patients without arsenical signs had cumulative doses above 1000 mg. On the average, patients with signs were 7 years older and had received their first exposure 6 calendar years earlier than those without signs. Within the group with exposures > 1000 mg, those with signs were, again, an average of 7 years older, and they had their first exposure 3 years earlier. It is interesting to note that all seven of the subsequent deaths from internal malignancy in this subgroup had been identified as showing signs of arsenicism. No deaths from cancer occurred in the group without physical signs.

In summary, this study provided little evidence that ingestion of arsenic is related to a risk of mortality from internal malignancies. Non-fatal skin cancer was found, however, to be related as a function of dose to ingestion of Fowler's solution. The authors indicated that perhaps persons who demonstrate signs of arsenicism following arsenic exposure retain arsenic longer than those

who do not show signs, which may suggest that persons who demonstrate signs of arsenicism are at a greater risk of internal malignancies. This was suggested by the fact that all of the deaths from internal malignancies in the subset of individuals that was examined for signs of arsenicism occurred in individuals who demonstrated such signs.

Knoth (1966) also reported on two patients treated with arsenical medicinals and who developed skin cancer. Roth (1958) reported that of 47 autopsy cases of vintners with chronic arsenic intoxication, 13 had skin tumors.

Gilbert et al. (1983) conducted a study on wood treaters in Hawaii who were occupationally exposed to arsenic (see Section 7.1.2.1 for complete discussion of study). The authors found no evidence of risk of skin cancer, but inadequacies in the study design and the small sample size limit the ability to draw valid conclusions from the data.

7.1.2.3 Other Cancers--Whereas there are many studies suggesting that there is an association between inhalation exposure and respiratory cancer and oral exposure and skin cancer, respectively, there are no consistent data with regai to cancer in internal organs.

Reymann et al. (1978) have investigated the relationship between the intake of arsenic for medicinal purposes and subsequent internal neoplasms. Study subjects were identified by examining the files of a dermatology clinic in Denmark for the years 1930 to 1939. Two rosters of study subjects were generated: 1) persons treated with arsenic for multiple basal cell carcinoma, Bowen's disease, psoriasis, verruca planus, and lichen planus, and 2) persons with keratoses from the first roster plus 30 other persons identified as having keratoses. The first roster of 413 persons comprised the basic study population; 24 persons were excluded for various reasons, resulting in a final study population of 389 persons. The malignancy histories of both populations

were traced through the years 1943-1974 in the Danish Cancer Registry. For each person a length-of-observation period was determined and an expected number of internal malignant neoplasms was determined using the former data.

In the main study population, 41 cases were observed versus 44.6 cases expected. Therefore, no increased incidence of internal malignancies was noted in the arsenic-treated patients. However, examination of the data by individual skin disease categories showed that women with multiple basal cell carcinoma had a significantly higher incidence of internal cancer. The same trend, although not significant, was observed in female patients exhibiting verruca planus. Next, an analysis was made of a possible dose-response relationship using duration of treatment as the exposure variable. The categories were low, medium and high, based on <1 month, 1-3 month, and >3 month duration of standard dose administration (6-8 mg As_2O_3). No relationship between dose and internal organ cancer was noted for the total population or by sex. In addition, the form of arsenic administered did not seem to affect the incidence of internal cancer, nor was any effect noted due to period of observation. Reymann et al. did not provide a definition of the term "internal cancer." It is presumed that the authors included lung cancer in their definition. If so, the authors did not provide any adjustment for smoking. Regardless, the sample size of 389 persons is probably too small to detect an excess in the incidence of internal cancer, even if lung cancers were excluded.

The keratosis group was not analyzed in the same way. Eight of the 19 men with keratosis died before 1974. Four of these were due to cancer of the internal organs. Expected deaths were 1.9. Similarly, 5 deaths due to cancer of the internal organs were observed in the 34 women with keratosis compared with 3.3 expected. Together there were 9 deaths due to cancer of the internal organs compared to 5.2 expected. Although the figure is almost doubled, it is

still not significant. On the average, the patients with keratosis received higher doses of arsenic than the other patients.

Hemangioendothelioma and reticulosarcoma of the liver has been reported by Roth (1958) to occur among German vintners exposed occupationally to arsenic. The same type of malignancy occurrence has also been reported in isolated cases by other authors (Pershagen and Vahter, 1979). Higgins et al. (1982) reported increased mortality for cirrhosis of the liver and urinary cancer in workers at the Anaconda Montana smelter.

More recently, Falk and coworkers (1981a) described a nationwide (U.S.) review of deaths from hepatic angiosarcoma during the years 1964-1974. Of 168 confirmed cases included for survey, a group of seven cases with a history of prolonged use of Fowler's solution was found. Taken with the data of Roth, chronic arsenic exposure, mainly via ingestion, appears to be associated with this very rare liver cancer.

In a review of four cases of hepatic angiosarcoma, Falk et al. (1981b) determined that one case, that of a child, involved environmental arsenic exposure in a copper-smelting community in Arizona. Since this child had a history of pica, the usual exposure routes were augmented by further arsenic intake.

Roat et al. (1982) reported a case of hepatic angiosarcoma in a subject who, 33 years earlier, had ingested Fowler's solution for the relatively short period of 6 months. The pre-existence of skin cancer in this subject, from age 25, of the type associated with arsenic exposure, was further support of an arsenic association.

Knoth (1966) reported on two patients who had been treated with arsenical medicinals and developed tumors at sites other than the skin or lung. One of the patients was a 61-year old woman who had been treated with an arsenical

medicinal and developed mammary carcinoma. The other case was that of a 53-year old male who had been treated with an arsenical medicinal for cirrhosis vulgaris and developed a reticulosarcoma of the glans penis.

In the studies by Ott et al. (1974), an increased proportionate mortality due to malignant neoplasms of lymphatic and hematopoietic tissues was found. Axelson et al. (1978) found an increased risk of leukemia and myeloma in a case-control study of workers exposed at a smelter.

7.2 ANIMAL STUDIES

While arsenic carcinogenicity in test animals has not been observed in most studies, some recent reports have noted positive results. The literature on experimental inorganic arsenic carcinogenesis, as summarized in Table 7-20 and as reviewed by scientific bodies (NAS, 1977; NIOSH, 1975; IARC, 1973 and 1980) and individuals (Sunderman, 1976; Wildenberg, 1978; Pershagen and Vahter, 1979) supports this conclusion.

In light of the presently recognized anomalous metabolizing of inorganic arsenic by rats, studies which used rats as the experimental subjects should be viewed cautiously. Studies on other animal models have generally resulted in negative findings. A few of these studies are discussed below, but most have been summarized in Table 7-20.

In a study by Baroni et al. (1963), Swiss mice were given either arsenic trioxide dissolved in drinking water (concentration of 100 mg/ℓ) ad libitum for the duration of the 70-week experiment; or, sodium arsenate in a concentration of 15.8 gm/ℓ in a 2.5 percent solution of Tween 60 in water, applied twice weekly for the duration of the experiment. Each compound was tested alone, in combination with skin applications of croton oil (to test for initiating action), and after initiation with a single skin application of 7,12-dimethylbenz(a)anthracene or with administration of urethan by stomach tube

TABLE 7-20. SUMMARY TABLE OF EXPERIMENTAL STUDIES OF ARSENIC CARCINOGENESIS

Route	Species (Strain)	Compound	Vehicle	Results*	Reference	Remarks
Oral	Mice (C57B16)	As_2O_3	Tap water or 12% aqueous ethanol	-	Hueper and Payne, 1962	Shortened life span of treated (aq. ethanol) vs. control.
Oral	Mice (Swiss)	As_2O_3	Drinking water	-	Baroni et al., 1963	
Oral	Mice (Swiss)	$NaAsO_2$	Drinking water	-	Kanisawa and Schroeder, 1967	Shortened life span, low dose.
Oral	Mice (NMRI)	As_2O_3	Drug (Psor-Intern) or Fowler's solution	+(?)	Knoth, 1966	Significance cannot be determined, uncomplete reporting by author.
Oral	Mice (C3H/St, female)	$NaAsO_2$	Drinking water	-	Schrauzer and Ishmael, 1974	
Oral	Rats (not specified)	$Pb_3(AsO_4)_2$ $Ca_3(AsO_4)_2$	Not specified	-	Fairhall and Miller 1941	Poor survival in treated. As reviewed by IARC (Vol. 23, 1980)
Oral	Rats (Bethesda Blacks)	As_2O_3	Tap water or aqueous ethanol (12%)	-	Hueper and Payne, 1962	
Oral	Rats (Osborne-Mendel)	$NaAsO_2$ Na_3AsO_4	Diet	-	Byron et al., 1967	Reduced survival at highest dose.
Oral	Rats (Long Evans)	$NaAsO_2$	Drinking water	-	Kanisawa and Schroeder, 1969	Low dose.
Oral	Rats (Wistar)	$Pb_3(AsO_4)_2$ Na_3AsO_4 $Pb_3(AsO_4)_2$ + NDEA Na_3AsO_4 + NDEA	Diet Diet Diet Diet	- - - -	Kroes et al., 1974	High mortality and 2 tumors (incidence not reported observed in lead arsenate group).

TABLE 7-20. (continued)

Route	Species (Strain)	Compound	Vehicle	Results*	Reference	Remarks
Oral	Dog	$NaAsO_2$ or Na_3AsO_4	Diet	-	Byron et al., 1967	Weight loss, early mortality, short duration of experiment.
Inhalation	Mice (not specified)	$NaAsO_2$	Aqueous aerosol	-	Berteau et al., 1978	Reported in an abstract form, high incidence in controls.
Intratracheal instillation	Rats (Wistar King) male	(1) As_2O_3	Not specified	-	Ishinishi et al., 1977	
		(2) Copper ore (3.95% Arsenic)		-		
		(3) Flue dust		-		One tumor observed in treated, not significant.
Intratracheal instillation	Rats (Wistar King) male	As_2O_3	Aqueous solution	-	Ishinishi et al., 1976	One tumor observed in treated, not significant.
Intratracheal instillation	Rats (BDIX)	$Ca_3(AsO_4)_2$	Bordeaux mixture (contains $CuSO_4$ and $Ca(OH)_2$)	+	Ivankovic et al., 1979	Results cannot be attributed to arsenic alone.
Intratracheal instillation	Golden Hamsters (males)	As_2O_3 ± BP	Carbon carrier + dilute H_2SO_4	+	Pershagen et al., 1983	Adenomas significantly greater than controls ($p < 0.01$). Carcinomas in 3 treated animals vs. 0 in controls.
Intratracheal instillation	Golden Hamsters (female)	As_2O_3	Phosphate buffer	+	Ishinishi and Yamamoto, 1983	As_2O_3 was tumorigenic in a dose-response fashion.

TABLE 7-20. (continued)

Route	Species (Strain)	Compound	Vehicle	Results*	Reference	Remarks
Intratracheal instillation	Rats	Ore dust containing As at two levels of content	Not specified	+	Chung and Liu, 1982	Possible confounding effects of other elements present, unknown. No apparent differences in lung cancer with different As levels in dust.
Skin painting (application)	Mice (not specified)	$KAsO_2$ and As_2O_3	Ethanol	-	Leitch and Kennaway, 1922	Neubauer (1947) failed to confirm this observation.
Skin painting (application)	Mice (S)	$KAsO_2$ followed by croton oil in acetone	Methanol	-	Salaman and Roe, 1956	As reviewed by IARC (Vol. 23, 1980).
Skin painting (application)	Mice (Rockland all-purpose)	(1) $KAsO_2$ followed by croton oil in benzene	80% ethanol	-	Boutwell, 1963	As reviewed by IARC (Vol. 23, 1980).
Skin painting (application)	Mice (Rockland all-purpose)	(2) DMBA followed by $KAsO_2$ in 80% ethanol	acetone	Not carcinogenic	Boutwell, 1963	
Skin painting (application)	Mice (Swiss)	(1) Na_3AsO_4	Water containing Tween 60	-	Baroni et al., 1963	
		(2) Na_3AsO_4 followed by croton oil and DMBA	Water containing Tween 60	No promotional activity observed		
Subcutaneous injection	Mice (Swiss) female Progeny	Na_3AsO_4 Na_3AsO_4	Water Water	+ +	Osswald and Goerttler, 1971	

TABLE 7-20. (continued)

Route	Species (Strain)	Compound	Vehicle	Results*	Reference	Remarks
Subcutaneous implant	Rats (random-bred) male albino	$Ca_3(AsO_4)_2$	Paraffin pellets	-	Arkhipov, 1968	As reviewed by IARC (Vol. 23, 1980).
Subcutaneous injection	Rats (random-bred) male albino	$Ca_3(AsO_4)_2$	Sunflower oil	-	Arkhipov, 1968	
Subcutaneous injection (pre-natal + post-natal)	Mice (CFLP)	As_2O_3	Aqueous solution	+	Rudnai and Borzsony, 1981	Histological description of tumors poor.
Intravenous injection	Mice (Swiss) female	Na_3AsO_4	Water	+	Osswald and Goerttler, 1971	
Intramuscullary injection	Rats (Osborne-Mendel)	Arsenic	Metallic	-	Hueper, 1954	
Intramuscullary injection	Rabbits	Arsenic	Metallic	-	Hueper, 1954	
Oral	Mice (Swiss)	As_2O_3 and croton oil, DMBA or urethan	Drinking water	-	Baroni et al., 1963	
Oral	Mice (STS)	Arsanilic acid or $KAsO_2$ followed by DMBA (skin) then croton oil (skin) in benzene	Diet	-	Boutwell, 1963	As reviewed by IARC (Vol. 23, 1980).

(*) + statistically significant excess tumors observed over controls

\- no statistically significant excess tumors of treated vs. control or no tumors observed

(to test for promoting action). All tests failed to show any carcinogenic activity of the two compounds under the given experimental conditions.

Kanisawa and Schroeder (1969) treated Swiss mice with sodium arsenite (equivalent to 5 µg/ml As) in drinking water for the 30-month duration of their study. In the treated animals, the authors noted 6 malignant and 11 combined malignant and benign tumors out of 103 animals versus 15 malignant and 50 combined malignant and benign tumors out of 170 control animals; thus, the results were negative for showing any carcinogenic effect of sodium arsenite in this study.

In a study of Leitch and Kennaway (1922; as reported in IARC, 1980), 100 mice were given skin applications of a solution of potassium arsenite in ethanol containing 1.8 percent arsenic trioxide (later reduced to 0.12 percent due to a high death rate), thrice weekly for 3 months. Of the 33 mice that lived for 3 months, only one developed a metastasizing squamous cell carcinoma.

In certain animal systems, positive carcinogenic responses have been reported, however. For example, Osswald and Goerttler (1971) exposed pregnant Swiss mice to daily parenteral dosing of sodium arsenate (0.5 mg/kg, solution of 0.005 percent arsenate salt) for a total of 20 injections. Part of the offspring groups received 20 injections of the same level subcutaneously at weekly intervals. Leukemia or lymphoma was seen in 46 percent of the mothers (11/24) at the end of 2 years versus none in the controls. Of the treated offspring, 41 percent (17/41) of the males and about half of the females (24/50) developed leukemia versus only 3 of 55 male and female control offspring (approximately 6 percent). IARC (1973) has criticized this study for the absence of exposure of controls to the appropriate vehicle solution.

Knoth (1966) noted a significant frequency of tumors in 30 mice exposed to Fowler's solution orally (one drop/week, 20 weeks, approximately 5.3 mg As

total),including adenocarcinomas of the skin, lung, and lymph nodes. The absence of experimental details makes critical assessment of this study difficult.

Some recent animal studies have employed different exposure conditions than have been employed in the past. Berteau et al. (1978) have exposed a tumor-susceptible strain of female mice to a respirable aerosol of inorganic arsenic (1 percent aqueous solution of sodium meta-arsenite, 20 to 40 minutes daily, 5 days/week, 55 weeks total). The 30 exposed mice showed neither gross nor histological evidence of neoplasia.

In a two-part study, Ishinishi et al. (1977) examined the carcinogenic and co-carcinogenic effects of various arsenic compounds on male Wistar-King rats. In the first part of the study, arsenic trioxide, an arsenic-containing copper ore (containing 3.95 percent arsenic) or metal refinery flue dust (containing 10.5 percent arsenic) were administered to 51 rats via 15 weekly intratracheal instillations. The rats were observed over their lifespan. Of the 25 surviving rats, one adenocarcinoma was seen in the group receiving flue dust. One lung metastasis from osteosarcoma of the femur and one adenoma was reported in the group exposed to the copper ore. No malignant tumors were reported in the group receiving arsenic trioxide; however, one adenoma was reported for this group. All groups displayed squamous cell metaplasia in the airway and osteometaplasia in the alveolus of the lung.

In the second part of the study, 87 rats were instilled with each of the above compounds suspended in a saline solution containing benzo[a]pyrene (B[a]P) or with B[a]P, alone. Control rats (23) were instilled with the saline solution. Of the 34 surviving exposed rats, one adenocarcinoma was seen in the group receiving B[a]P plus copper ore. All exposed groups had squamous cell carcinomas of the lung. Of particular interest to the authors, was the noted co-carcinogenic effect of arsenic trioxide with B[a]P; rats in

this group exhibited a 43 percent incidence rate (3/7) for squamous cell carcinomas. This compared with a 14 percent (1/7) incidence rate in animals given B[a]P, alone. No benign or malignant tumors were seen in the 7 surviving control rats. Again, squamous cell metaplasia or osteometaplasia were seen in all groups.

The results indicated a positive interaction between arsenic trioxide and B[a]P; however, the authors noted that the numbers of surviving animals were too small to permit drawing any firm conclusions from the study.

In another study, Ishinishi et al. (1980) gave 30 male adult Wistar rats intratracheal instillations of arsenic trioxide in suspension for 15 weeks. Of the 19 rats that survived, only one malignant squamous cell carcinoma was observed over lifetime. No tumors were found in the controls.

Ivankovic and co-workers (1979) exposed rats, via intratracheal instillation, to a pesticide mixture corresponding to that used in the past for vineyard treatment and consisting of a mixture of copper (II) sulfate, calcium hydroxide and calcium arsenate. Of 25 rats exposed to approximately 0.07 mg arsenic, 10 died from lung necrosis or pneumonia. In the survivors, 9 animals (60 percent) showed multi-focal bronchogenic adenocarcinomas and bronchiolar/alveolar cell carcinomas.

This study appears to offer experimental evidence that the vineyard pesticide mixture, employed as such, could have been carcinogenic to vine dressers working with the material. One difficulty with this study is an ambiguity regarding its full significance for the general issue of arsenic-inducing carcinogenic effects by itself. Clearly, the high mortality rate, 40 percent, and the known toxicity of Bordeau mixture (copper sulfate plus calcium hydroxide) to animals (Pimentel and Marques, 1969) and man (Villar, 1974, Pimentel and Marques, 1969) suggest carcinogenesis; however, it is impossible

to clearly ascribe such activity to arsenic alone given the presence of other compounds within the mixture. In their studies, Ivankovic et al. (1979) did not include animal groups exposed to calcium arsenate alone or to Bordeau mixture alone.

Pershagen et al. (1983, in press) have studied the pulmonary carcinogenicity of arsenic trioxide alone and in combination with benzo(a)pyrene in male golden hamsters given 15 weekly intratracheal instillations of 3 mg As/kg and/or 6 mg/kg B[a]P. In this study, a carbon dust carrier with dilute sulfuric acid was employed to enhance retention of arsenic. Carcinomas of larynx, trachea, bronchi and lungs were found in 3 animals given just arsenic versus a zero response in controls. The incidence of adenomas, papillomas and adenomatoid lesions was higher in arsenic versus control groups ($p < 0.01$). While the carcinomas in the arsenic group did not reach statistical significance, the significantly higher incidence of the adenomas, papillomas, and adenomatoid lesions support the authors' conclusion that the carcinomas were not a chance finding. The use of the carrier to enhance lung retention of arsenic appears to be the key to the results in this study. By itself, the oxide of arsenic is rather rapidly cleared from the lung (see below).

Rudnai and Borzsony (1981) reported that a combination of pre- and postnatal exposure of CFLP mice to injected arsenic trioxide (1.2 µg As/g, days 15-18 of gestation; 5 µg As/animal for 3 days post-birth) resulted in a 63 percent lung tumor incidence at 1 year of age versus approximately 18 percent in controls. In this study, a detailed histological description of the tumors was not given, but it can be assumed that both adenomas and adenocarcinomas were observed.

Chung and Liu (1982) reported that the repeated intratracheal instillation of ore dust containing arsenic in rats resulted in a lung cancer incidence

rate of approxiamtely 15 percent (6/41) over a period of 3 years, while controls (N=18) showed no lung tumors. There was extensive metastasis in one animal. In this study, two compositions of metal content in ores were used, with the arsenic varying by 8-fold. The lung cancer rate for the two forms of ore dust were comparable, despite the 8-fold difference in arsenic, i.e., there was no simple dose response. On the other hand, the ores contained variable amounts of iron and lead, which may have affected both the dose response and, possibly, the actual incidence of the lung cancers.

Ishinishi and Yamamoto (1983) exposed female golden hamsters to arsenic trioxide by intratracheal instillation of a suspension in phosphate buffer, 15 times weekly, for 4 months, at a total dose of 5.3 mg As. A second group was given a total dose of 3.8 mg As. All animals were followed over their entire life span. The incidence of lung tumors (adenomas) for the combined exposure groups was approximately 17 percent versus no tumors in surviving controls. While the sample size was small, there was the suggestion of a dose response across the two exposure levels (3/10 for the higher dose; 1/10 for the lower dose). These data suggest that arsenic trioxide is tumorigenic in the golden hamster and may be carcinogenic.

Recently, both Inamasu et al. (1982) and Pershagen et al. (1982) have studied the effects of intratracheal instillation of calcium arsenate (see Section 4.1.1 for complete discussion of studies). Inamasu et al. gave single intratracheal instillations of arsenic trioxide or calcium arsenate to male Wistar rats. Pershagen et al. instilled male Syrian golden hamsters with four weekly suspensions of arsenic trioxide, arsenic trisulfide and calcium arsenate. The results of both studies showed that arsenic trioxide was rapidly cleared from the lungs, whereas calcium arsenate was slowly eliminated. The differences in clearance appeared to be related to solubility, with the less soluble calcium arsenate exhibiting the slowest clearance.

These recent findings might help to explain the differences noted above in the earlier studies of Ishinishi et al. (1977; 1980) and Ivankovic et al. (1979). In regard to the Ivankovic study, it may be that the calcium arsenate, of itself, contributed to the high mortality rate observed in the exposed rats.

Schrauzer and co-workers (Schrauzer and Ishmael, 1974; Schrauzer et al., 1977; Schrauzer et al., 1978) have reported experimental results using oral arsenic and the tumorigenic effect of the agent on spontaneous mammary adenocarcinomas in an inbred strain of mice (C_3H/St Mice). These workers noted that while arsenic retards the overall incidence of tumor formation (10 or 80 ppm As), it stimulates the growth of tumors that otherwise occur. When these animals were exposed to only 2 ppm As (arsenite) in drinking water, compared to levels of 10 or 80 ppm, there was no effect on frequency of tumors, although the same enhanced tumor growth was seen as before with levels of 10 or 80 ppm As (Schrauzer et al., 1978). Furthermore, a higher incidence of multiple tumors of the mammary gland was observed, as was the abolishing of the anticarcinogenic effect of selenium in this system when both elements were given together.

In support of the positive responses noted in the above animal studies, Dipaolo and Casto (1979) reported the transformation of cultured Syrian hamster embryo cells by direct exposure to sodium arsenate (NA_2HAsO_4). In their assay, 300 cells from secondary cultures of Syrian hamster embryo cells (HEC) were plated in complete medium with 20 percent serum in 50-mm plastic Petri dishes along with 6×10^4 HEC cells which had been irradiated as confluent monolayer cultures. Sodium arsenate at concentrations of 0 µg/ml (control), 2.5 µg/ml and 5.0 µg/ml in complete medium (with a final concentration of acetone less than 0.02 percent) were added 24 hours later. Dishes were fixed and stained nine days after seeding. Colonies were scored blind by two observers.

For the two sodium arsenate concentrations, the authors reported that the number of transformations were 1.16 and 2.08/dish, respectively, or 1.74 and 4.13 percent, respectively, on the basis of transformed colonies relative to total colonies scored. The authors also reported that typical colonies scored as transformed after direct treatment with a metal carcinogen were identical to those obtained with other chemical carcinogens. In addition, the authors claimed (data not shown) that when 2.5 µg benz(a)pyrene per ml of medium were used, the transformation frequency, on a colony basis, was 4 to 6 percent.

7.3 QUANTITATIVE CARCINOGEN RISK ESTIMATES

7.3.1 Introduction

This quantitative section deals with the unit risk for arsenic in air and water and the potency of arsenic relative to other carcinogens that the Carcinogen Assessment Group (CAG) of the U.S. Environmental Protection Agency has evaluated. The unit risk estimate for an air pollutant is defined as the lifetime cancer risk occurring in a population in which all individuals are exposed continuously from birth throughout their lifetimes to a concentration of 1 $\mu g/m^3$ of the agent in the air they breathe. The unit risk estimate for water is defined similarly, but with a water concentration of 1 µg/ℓ. Unit risk estimates are used for two purposes: (1) to compare several agents with each other in terms of carcinogenic potency, and (2) to give a crude indication of the human health risks that might be associated with exposure to these agents, if the actual exposures are known.

The data used for quantitative estimates can be of two types: (1) lifetime animal studies, and (2) human studies where cancer risk has been associated with exposure to the agent. It is assumed, unless evidence exists to the contrary, that if a carcinogenic response occurs at the dose levels used in a study, then responses at all lower doses will occur with an incidence that can be determined by an appropriate extrapolation model.

There is no solid scientific basis for any mathematical extrapolation model that relates carcinogen exposure to cancer risks at the extremely low concentrations which must be dealt with in evaluating environmental hazards. For practical reasons, such low levels of risk cannot be measured directly either by animal experiments or by epidemiologic studies. It is necessary, therefore, to depend on current knowledge of the mechanisms of carcinogenesis for guidance as to the correct risk model to use.

At the present time, the dominant view is that most cancer-causing agents also cause irreversible damage to DNA--a position supported by the fact that a large proportion of agents that cause cancer are also mutagenic. There is reason to expect that the quantal type of biological response, which is characteristic of mutagenesis, is associated with a linear non-threshold dose-response relationship. Indeed, there is substantial evidence from mutagenesis studies with both ionizing radiation and a wide variety of chemicals that this type of dose-response model is the appropriate one to use in estimating cancer risks from environmental exposures. This is particularly true at the lower end of the dose-response curve. At higher doses, there can be an upward curvature, probably reflecting the effects of multistage processes on the mutagenic response. The linear non-threshold dose-response relationship is also consistent with the relatively few epidemiologic studies of cancer responses to specific agents that contain enough information to make the evaluation possible (e.g., radiation-induced leukemia, breast and thyroid cancer, skin cancer induced by arsenic in drinking water, liver cancer induced by aflatoxins in the diet). There is also some evidence from animal experiments that is consistent with the linear non-threshold model (e.g., the initiation stage of the two-stage carcinogenesis model in rat liver and mouse skin).

Because of these factors, the linear non-threshold model is considered to be a viable possibility for the true dose-response relationship and, unless

direct evidence to the contrary is presented, it is used as the primary basis for risk extrapolation at low levels of exposure.

The quantitative aspect of carcinogen risk assessment is included here because it may be of use in setting regulatory priorities, evaluating the adequacy of technology-based controls, and other aspects of the regulatory decision-making process. However, the imprecision of presently available technology for estimating cancer risks to humans at low levels of exposure should be recognized. At best, the linear extrapolation model used here provides a rough but plausible estimate of the upper limit of risk--that is, with this model it is not likely that the true risk would be much more than the estimated risk, but it could be considerably lower. The risk estimates presented below should not be regarded, therefore, as accurate representations of true cancer risks even when the exposures involved are accurately defined. The estimates presented may, however, be factored into regulatory decisions to the extent that the concept of upper-risk limits is found to be useful.

7.3.2 Unit Risk for Air

7.3.2.1 Methodology for Quantitative Risk Estimates--The methodologies used to arrive at quantitative estimates of risk must be capable of being implemented using the data available in existing epidemiologic studies of exposure to airborne arsenic. In order to extrapolate from the exposure levels and temporal exposure patterns in these studies to those for which risk estimates are required, it will be assumed that the age-specific mortality rate of respiratory cancer per year per 100,000 persons for a particular 5-year age interval, i, can be represented using either of two models:

$$a_i(D) = a_i[1 + a'D^k] \qquad (1)$$

(a relative or multiplicative risk model), or

$$a_i(D) = a_i + 100{,}000a'D^k \qquad (2)$$

(an absolute or additive risk model). With either model, a_i is the age-specific mortality rate per year of respiratory cancer in a control population not exposed to arsenic, a' is a parameter representing the potential of airborne arsenic to cause respiratory cancer, and D is some measure of the exposure to arsenic up to the ith age interval. For example, D might be the cumulative dose in $\mu g/m^3$ years, the cumulative dose neglecting exposure during the last 10 years prior to the ith age interval, or the average dose in $\mu g/m^3$ over some time period prior to the ith age interval. The forms to be used for D will be constrained by the manner in which dose was treated in each individual epidemiologic study. The parameter k determines the shape of the dose-response curve. Attention will be given particularly to the values k = 1 and k = 2. If k = 1, the age-specific incidence rates vary linearly with the dose level (a linear model), and if k = 2 they vary quadratically. At low exposures the extra lifetime probability of respiratory cancer mortality will vary correspondingly (e.g., linearly for k = 1 and quadratically for k = 2).

The dose-response data available in the epidemiologic studies for estimating the parameters in these models consists primarily of a dose measure D_j for the jth exposure group, the person-years of observation Y_j, the observed number of respiratory cancer deaths O_j, and the number E_j of these deaths expected in a control population with the same sex and age distribution as the exposure group. The expected number E_j is calculated as

$$E_j = \sum_i Y_{ji} a_i / 100{,}000, \qquad (3)$$

where Y_{ji} is the number of person-years of observation in the ith age category and the jth exposure group ($Y_j = \sum_i Y_{ji}$). This is actually a simplified representation, because the calculation also takes account of the change in the

age-specific incidence rates with absolute time. The expected number of respiratory cancer deaths for the ith exposure group is

$$E(O_j) = \sum_i Y_{ji} a_i (1 + a' D_j^k)/100{,}000$$

$$= E_j (1 + a' D_j^k) \qquad (4)$$

under the relative risk model, and is

$$E(O_j) = \sum_i Y_{ji} (a_i + 100{,}000 a' D_j^k)/100{,}000$$

$$= E_j + a' Y_j D_j^k \qquad (5)$$

under the absolute risk model. Consequently, with either model, $E(O_j)$ can be expressed in terms of quantities typically available from the published epidemiologic studies. Note that person-years of observation are not required if the multiplicative model is used.

Making the reasonable assumption that O_j has a Poisson distribution, the parameters a' and k can be estimated from the above equations using the method of maximum likelihood. Once these parameters are estimated, the age-specific mortality rates for respiratory cancer can be estimated for any desired exposure pattern.

To estimate the corresponding additional lifetime probability of respiratory cancer mortality, let $b_1, \ldots, b_{18}$ be the mortality rates, in the absence of exposure, for all cases per year per 100,000 persons for the age intervals 0-4, 5-9,..., 80-84, and 85+, respectively; let $a_1, \ldots, a_{18}$ represent the corresponding rates for malignant neoplasms of the respiratory system. The probability of survival to the beginning of the ith 5-year age interval is estimated as

$$\prod_{j=1}^{i-1} [1 - 5b_j/100,000]. \qquad (6)$$

Given survival to the beginning of age interval i, the probability of dying of respiratory cancer during this 5-year interval is estimated as

$$5a_i/100,000. \qquad (7)$$

The probability of dying of respiratory cancer given survival to age 85 is estimated as a_{18}/b_{18}. Therefore, the probability of dying of respiratory cancer in the absence of exposure to arsenic is estimated as

$$P_0 = \sum_{i=1}^{17} [5a_i/100,000) \prod_{j=1}^{i-1} (1 - 5b_j/100,000)] \qquad (8)$$

$$+(a_{18}/b_{18}) \prod_{j=1}^{17} (1 - 5_{bj}/100,000)$$

Here the mortality rates a_i apply to the target population for which risk estimates are desired, and consequently will be different from those in (1)-(5), which applied to the epidemiologic study cohort. If the 1976 U.S. mortality rates (male, female, white, and non-white combined) are used in this expression, then $P_0 = 0.0451$.

To estimate the probability P_{EP} of respiratory cancer mortality when exposed to a particular exposure pattern EP, the formula (8) is again used, but a_i and b_i are replaced by $a_i(D_i)$ and $b_i(D_i)$, where D_i is the exposure measure calculated for the ith age interval from the exposure pattern EP. For example, if the dose measure used in (1) is cumulative dose to the beginning of the ith age interval in $\mu g/m^3$-years, and the exposure pattern EP is a

lifetime exposure to a constant level of 10 μg/m^3, then $D_i = (i-1)(5)(10)$, where the 5 accounts for the fact that each age inverval has a width of 5 years. The additional risk of respiratory cancer mortality is estimated as

$$P_{EP} - P_0. \qquad (9)$$

If the exposure pattern EP is constant exposure to μg/m^3, then $P_{EP} - P_0$ is called the "unit risk."

This approach can easily be modified to estimate the extra probability of respiratory cancer mortality by a particular age due to any specified exposure pattern. It is also clear that the applications of the approach are not limited to respiratory cancer.

7.3.2.2 Risk Estimates from Epidemiologic Studies--Prospective studies of the relationship between mortality and exposure to airborne arsenic have been conducted for the Anaconda, Montana smelter (Lee and Fraumeni, 1969; Lee-Feldstein, 1983; Higgins et al., 1982; Brown and Chu, 1983 a, b, c); and the Tacoma, Washington smelter (Pinto et al., 1977; Enterline and Marsh, 1982).

The study of Lee-Feldstein (1983) reported on an additional 14 years of follow-up of the cohort of 8047 studied by Lee and Fraumeni (1969), and used essentially the same methods of analysis as the earlier study. Therefore, it will not be necessary to consider the Lee and Fraumeni study in any detail in this report. Higgins et al. (1982) followed for an additional 14 years a sample of 1800 men from the cohort studied by Lee and Fraumeni, but used different exposure classifications and different methods of analyses.

Brown and Chu (1983 a, b, c), in a series of papers, arranged the Anaconda smelter data in such a manner that a mathematical model could be derived from it to account for the effect of the timing of exposure as predicted by the multistage model.

Whereas Pinto et al. (1977) studied a cohort from the Tacoma smelter consisting of 527 men followed only after retirement, the study by Enterline and Marsh (1982) involved 2802 men and included follow-up prior to retirement. Consequently, the Enterline and Marsh study appears to provide a stronger basis for quantitative risk assessment than the Pinto et al. study.

In addition to studies of copper smelter workers, there have also been studies of workers exposed to arsenicals in the production or use of pesticides. Ott et al. (1974) studied the mortality experience of workers exposed to lead arsenate and calcium arsenate.

7.3.2.2.1 The Lee-Feldstein (1983) study. This study included 8047 white males who were employed as smelter workers for 12 months or more before 1957, and whose mortality experience was observed from 1938 through 1977. Altogether, the study involved 192,476 person-years of follow-up and 3550 deaths, including 302 from respiratory cancer (Table 7-21). Expected numbers of cancer deaths were calculated on an age-adjusted basis using the combined mortality experience of the white male population of Idaho, Wyoming, and Montana. As Table 7-21 indicates, malignant neoplasms of the digestive and respiratory tracts had SMRs of 125 and 285, respectively, both of which were significant at the 1 percent level (SMR = [observed/expected][100]).

Workers were categorized both by duration of employment and level of exposure to airborne arsenic in order to determine the effect of these parameters upon mortality. For each year of the study period, workers were assigned to one of five groups on the basis of total years of smelter employment completed (Table 7-22). Work areas in the smelter were divided into heavy, medium, or light exposure areas. Based upon this division, workers were categorized into heavy, medium, or light exposure groups, as determined by their maximum exposure for 12 or more months. The results for respiratory cancer based upon these categorizations are given in Table 7-23.

TABLE 7-21. OBSERVED AND EXPECTED DEATHS DUE TO SELECTED CAUSES, WITH STANDARDIZED MORTALITY RATIOS (SMRs) AMONG SMELTER WORKERS, 1938-77

Cause of Death	List No.[a]	Number of deaths		SMR[b]
		Observed	Expected	
Tuberculosis	001-019	53	27.93	190[c]
Respiratory	001-008	47	25.51	184[c]
Other	010-019	6	2.42	248
Malignant neoplasms	140-199	609	370.74	164[c]
Digestive	150-159	167	133.58	125[c]
Respiratory	160-164[d]	302	105.81	285[c]
Other	140-148, 165-170, 177-181, 190-199	140	131.35	107
Vascular lesions of central nervous system	330-334	262	211.56	124[c]
Diseases of heart	400-443	1366	1056.55	129[c]
Influenza and pneumonia	480-483, 490-493	88	76.05	116
Emphysema (1963-77 only)	527	90	34.58	260[c]
Cirrhosis of liver	581	76	36.53	208[c]
Accidents	800-962	288	280.27	103
Motor vehicle	810-825, 830-835	106	115.55	92
Other	800-802, 840-862	182	164.72	110
Suicide and homicide	963-964, 970-979, 980-985	83	86.08	98
All other causes	Residual	606[e]	548.50	
Total		3522	2728.79	129[c]

[a]Seventh revision of International Lists of Diseases and Causes of Death.

[b]SMR = (observed/expected) x 100.

[c]Significant at 1% level. Bailar and Ederer (1964)

[d]Among the 302 deaths from respiratory cancer, the site was lung and bronchus (162,163) in 289 cases, larynx (163) in 9, mediastinum (164) in 3 and (160) in 1.

[e]Includes 19 emphysema deaths occurring in the years preceding 1963, for which emphysema death rates are not available from individual states.

Source: Lee-Feldstein (1983).

TABLE 7-22. DESCRIPTION OF LENGTH OF EMPLOYMENT GROUPS, WITH NUMBERS OF SMELTER WORKERS, NUMBERS OF DEATHS, PERSON-YEARS AT RISK, AND DURATION OF SMELTER EMPLOYMENT (BASED ON TOTAL WORK EXPERIENCE THROUGH SEPT. 30, 1977)

Length of employment group[a]	Number of persons[b]	Number of deaths	Number of person-years of follow-up[c]
1 (25 or more years)	1899	1169	27,053
2 (15 to 24 years)	1138	586	26,556
3 (10 to 14 years)	678	328	19,734
4 (5 to 9 years)	1082	433	30,854
5 (1 to 4 years)	3248	1006	88,279
TOTAL	8045	3522	192,476

[a]Employees in all cohorts were living on Jan. 1, 1938.

[b]Group assignment of each person here was based on his status at the termination of employment or on September 30, 1977 (whichever date was earlier).

[c]Represents cumulative follow-up experience over the study period, 1938-77, with a total of 67,569 person-years of follow-up in the period 1964-77. Individuals were initially counted at risk upon completing 1 year of employment or on Jan. 1, 1938, if employed at least a full year before that date. In each calendar year of the study period, employees were counted in the group reflecting their cumulative work experience to date.

Source: Lee-Feldstein (1983).

Exposure to airborne arsenic was estimated from 702 samples collected at 56 sampling stations during the years 1943-1958 (Morris, 1975). Morris estimated that airborne levels averaged 11.27, 0.58, and 0.27 mg/m^3 in the heavy, medium, and light exposure areas, respectively. Respirators were used with varying degrees of faithfulness in the high exposure areas; consequently, average individual exposures in these areas were probably much less than 11.27 mg/m^3. A rough estimate is that use of respirators reduces the exposure levels by a factor of 10 (OSHA, 1978).

TABLE 7-23. OBSERVED AND EXPECTED DEATHS FROM RESPIRATORY CANCER, WITH PERSON-YEARS OF FOLLOW-UP, BY COHORT AND DEGREE OF ARSENIC EXPOSURE

	Maximum Exposure to Arsenic (12 or more months)[a]					
	Heavy		Medium		Light	
Years of Exposure	Obs/Exp[b]	P-Y[c]	Obs/Exp	P-Y	Obs/Exp	P-Y
25 years+	13/2.5	2400	49/7	6837	51/16.3	14573
15-24	9/1.3	2629	13/4.0	6509	16/8.6	12520
Less than 15 years	11/2.4	6520	31/9.3	24594	69/31	78245

[a]The 1562 men who worked less than 12 months in their category of maximum arsenic exposure were not included in this table.

[b]Observed/Expected.

[c]Person-years of follow-up furnished by Dr. Lee-Feldstein (personal communication).

Source: Adapted from Lee-Feldstein (1983).

The Lee-Feldstein (1983) study has a number of features which support its use in making quantitative estimates of respiratory cancer risk from airborne arsenic. It was a large study that involved observations of a considerable number of respiratory cancer deaths. A substantial amount of follow-up was conducted of persons who had been exposed for 15 years or more. Estimates of exposure levels and work histories are available for estimating individual exposures and for determining dose response.

It would have been more appropriate for making quantitative estimates of risk to have categorized workers by their individual cumulative or average exposures, rather than by their maximum exposures for 1 year or more. In developing the quantitative estimates, it will be assumed that a worker's average exposure during work hours was equal to the exposure for the category to which he was assigned. However, because these assignments were based upon

maximum exposures for at least a 12-month period, this approach tends to overestimate exposures, and consequently, to underestimate the carcinogenic potency of arsenic.

Because smoking is also an important risk factor for respiratory cancer, it would have been very useful to have smoking histories for the workers. Higgins et al. (1982) collected some limited smoking data for this cohort. Higgins and co-workers suggest that the smelter workers smoked somewhat more than the average U.S. white male population, but the difference was not enough to have a major effect upon the outcome of the study.

Development of risk estimates: The data from the Lee-Feldstein (1983) study used in the risk assessment are listed in Table 7-24. The relative risk (observed/expected) from this table are graphed in Figure 7-2, and the absolute risks ([observed-expected/person-years) in Figure 7-3. It is clear from these graphs that the risk for the high-exposure group exposed for greater than 25 years is not commensurate with the risks for the other groups. Because of this, and also because the exposures in the high exposure groups are much more uncertain than those of the other groups, it was decided to estimate risk using only the low and medium exposure groups. Results of applying chi-square goodness-of-fit tests of the relative and absolute risk models with $k = 1$ and $k = 2$ are recorded in Table 7-25. The maximum likelihood estimates of the carcinogenic potency parameter a' are also listed in this table. The maximum likelihood fits of these models are graphed in Figures 7-2 and 7-3. All of the fits are poor (p less than 0.0001) with the exception of that for the absolute-risk model; this latter fit is marginally acceptable ($p = 0.025$).

The unit risk (additional risk of respiratory cancer death from lifetime exposure to 1 $\mu g/m^3$ airborne arsenic) obtained from the absolute-risk model with $k = 1$ is also listed in Table 7-25. This risk was estimated by applying (2), (8), and (9) with D_i based upon a constant exposure of 1 $\mu g/m^3$.

TABLE 7-24. DOSE-RESPONSE DATA FROM LEE-FELDSTEIN (1983) USED FOR RISK ASSESSMENT

Cohort	Maximum Exposure to Arsenic	Cumulative Exposure[a] ($\mu g/m^3$-years)	Person-Years of Observation[b]	Observed Deaths	Expected Deaths
1	Heavy	36064	2400	13	2.5
(25 + years	Medium	18560	6837	49	7.0
(of exposure)	Light	9280	14573	51	16.3
2					
(15-25	Heavy	22250	2629	9	1.3
years of	Medium	11600	6509	13	4.0
exposure)	Light	5800	12520	16	8.6
3					
(less than	Heavy	5973	6520	11	2.4
15 years of	Medium	3074	24594	31	9.3
exposure)	Light				

[a]Exposures are in $\mu g/m^3$-years estimated as (air concentration)(duration). For light, medium, and heavy exposures, air concentration was estimated as 290, 580, and 1127 $\mu g/m^3$, respectively (OSHA, 1978). Duration was estimated as follows (cf. Table 7-22):

Cohort 1: Persons in this cohort had at least 25 years' exposure. If all had worked continuously throughout follow-up, average duration would have been 25 + 27053/1899 = 39 years. Therefore the midpoint (39 + 25)/2 = 32 years was used.

Cohort 2: The midpoint of the employed interval, i.e., (15 + 25)/2 = 20 years was used.

Cohort 3: A weighted average of the midpoints of the employment intervals, i.e.,

$$\frac{(3)\ (88279) + (7.5)(30854) + (12.5)(19734)}{88279 + 30854 + 19734} = 5.3 \text{ years was used.}$$

[b]Furnished by Dr. Lee-Feldstein.

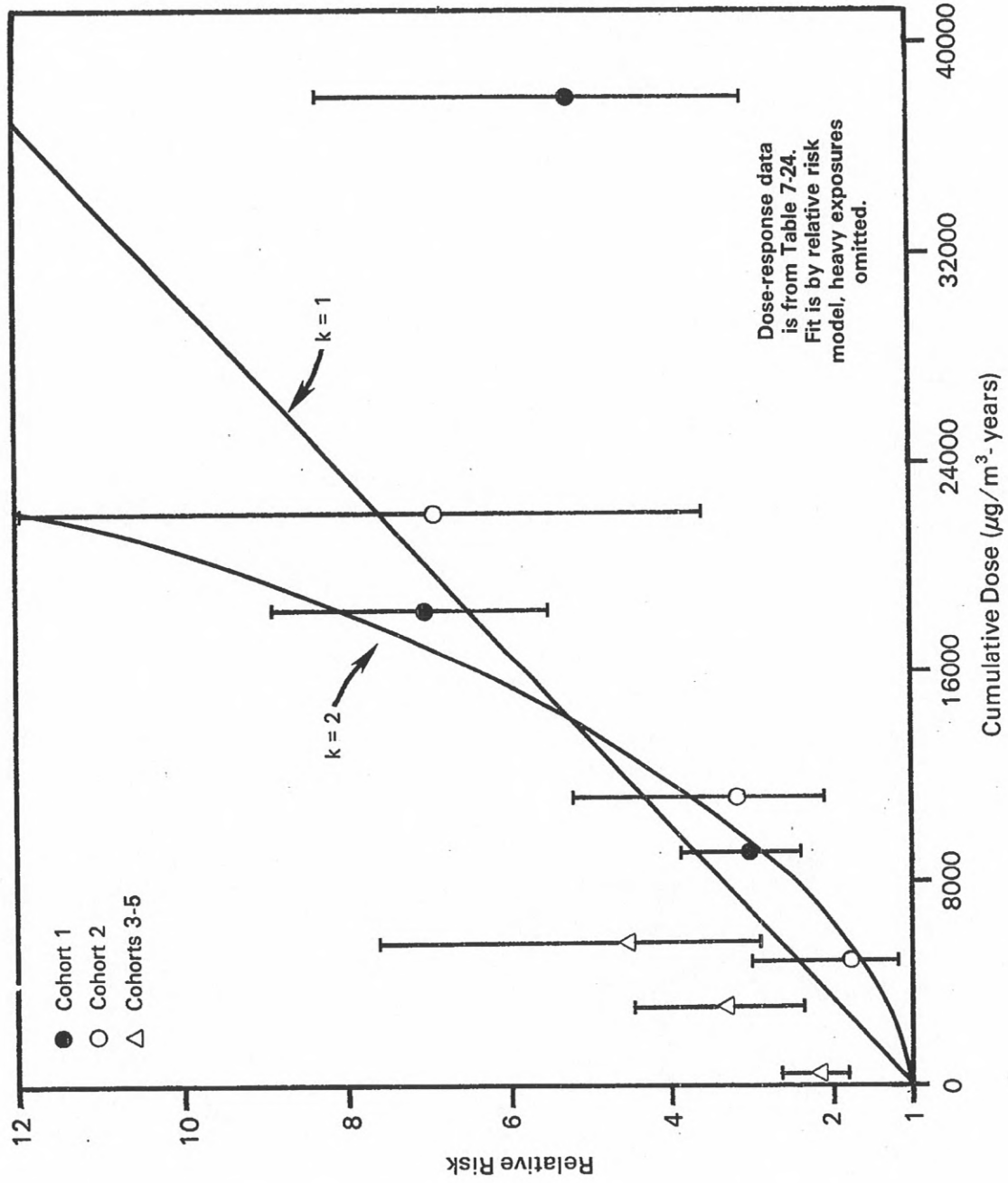

Figure 7-2. Relative risks and 90% confidence limits for data of Lee-Feldstein (1983).

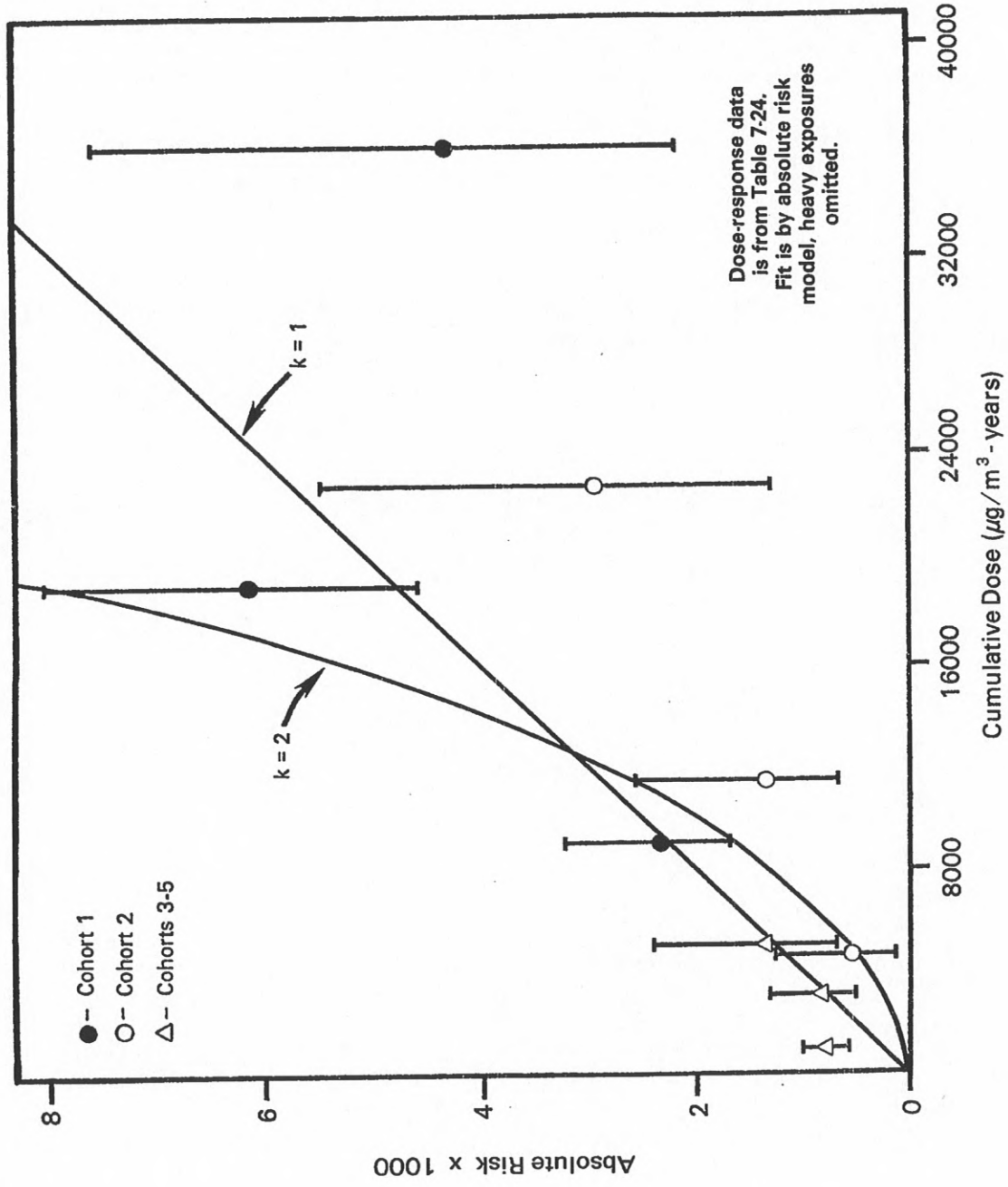

Figure 7-3. Absolute risks and 90% confidence limits for data of Lee-Feldstein (1983).

TABLE 7-25. SUMMARY OF QUANTITATIVE RISK ANALYSES

Exposed Population	Study and Data Source	Model	Results of Goodness-of-Fit Test: k	Carcinogenic Potency (a')[a]	x^2 (d.f.)	p-value	"unit" risk[b]
Anaconda smelter workers	Lee-Feldstein Table 7-24 (heavy exposure omitted)	absolute risk	1	2.48(-7)	12.7(5)	0.025	2.80(-3)
			2	2.09(-11)	60(5)	0.00001	lack of fit[d]
		relative risk	1	3.00(-4)	28(5)	0.00004	lack of fit
			2	2.09(-8)	79(5)	0.00001	lack of fit
	Higgins et al. Table 7-26	absolute risk	1	2.36(-7)	1.2(3)	0.75	4.90(-3)
			2	1.74(-11)	10.3(3)	0.017	1.05(-4)
		relative risk	1	3.17(-4)	2.57(3)	0.46	4.03(-3)
			2	2.18(-8)	15.4(3)	0.0015	lack of fit
	Brown & Chu Tables 7-27 and 7-29	absolute risk	1	9.45(-16)	7.01(7)	0.41	1.25(-3)
ASARCO smelter workers	Enterline & Marsh Table 7-33 (zero lag)	absolute risk	1	6.04(-7)[c]	5.5(4)	0.24	6.81(-3)
			2	1.43(-10)	20.7(4)	0.0003	lack of fit
		relative risk	1	4.6(-4)	11.6(4)	0.02	5.44(-3)
			2	1.01(-7)	23.4(4)	0.00011	lack of fit
	Enterline & Marsh Table 7-33 (10-year lag)	absolute risk	1	8.85(-7)	7.0(4)	0.14	7.60(-3)
			2	2.01(-10)	26.1(4)	0.00003	lack of fit
		relative risk	1	5.13(-4)	14.5(4)	0.006	lack of fit
			2	1.06(-4)	28.9(4)	0.00002	lack of fit
Dow pesticide manufacture workers	Ott et al. Table 7-34 (high exposure omitted)	relative risk	1	9.2(-4)	5.0(7)	0.66	1.36(-2)
			2	1.58(-7)	9.4(7)	0.23	7.68(-4)

[a] Potencies are in different units, depending upon model used (see text), and consequently are not comparable.

[b] Additional lifetime risk of respiratory cancer mortality from lifetime environmental exposure to 1 $\mu g/m^3$ arsenic.

[c] 6.04(E-7) means 6.04×10^{-7}.

[d] p-value of chi-square goodness-of-fit test is less than 0.01.

Specifically,

$$D_i = 4.56[(i-1) + 2.5] \quad (10)$$

was used, which represents the cumulative exposure in $\mu g/m^3$ resulting from a constant exposure to $\mu g/m^3$ from birth to the midpoint of the ith 5-year age interval. The factor 4.56 is needed to account for the fact that the workers in the occupational study used to estimate the carcinogenic potency of arsenic were only exposed during work hours. Assuming that workers were exposed for an average of 8 hours per day, 240 days per year, an environmental exposure to 1 $\mu g/m^3$ for 1 year is equivalent to an occupational exposure to

$$(1\ \mu g/m^3)(24\ \text{hours}/8\ \text{hours})(365\ \text{days}/240\ \text{days}) = 4.56\ \mu g/m^3 \quad (11)$$

for 1 year.

7.3.2.2.2 The Higgins et al. (1982) study. Higgins et al. conducted additional independent follow-up through 1977 of a sample of 1800 men from the Anaconda smelter cohort studied by Lee and Fraumeni (1969). The sample included all of the men classified in the heavy exposure category by Lee and Fraumeni (1969), as well as a random sample of 20 percent of the remaining cohort. There were 80 deaths from respiratory cancer in the sample. Expected numbers were based upon the mortality rates of Montana white males, except for "all respiratory diseases"; U.S. white males were the referenced population for the latter category.

Higgins et al. also reviewed the industrial hygiene data and calculated average concentrations for the period 1943-1965 for 18 departments. No measurements were available for 17 departments, and average concentrations were estimated for these. These estimates were coupled with work histories

updated through 1978 to obtain exposure measures for each individual in the study. Three types of individual exposure measures were considered: ceiling, time-weighted average (TWA), and cumulative. Ceiling exposures were estimates, in $\mu g/m^3$, of the highest exposure a man experienced for 30 days or more. TWA exposures were estimates, in units of $\mu g/m^3$, of the time-weighted average exposures during the period of employment. Cumulative exposures were estimates of total exposure in units of $\mu g/m^3$-years.

Higgins et al. investigated 5 combinations of follow-up and time period during which exposure was assessed: I. Exposure was assessed up to the date a worker entered the study and follow-up was from entry into the study through 1978; II. Exposure was assessed up to 1964 and follow-up was also through this date; III. Exposure was assessed through 1964 and follow-up was through 1978; IV. Exposure was assessed through 1964 and follow-up was from 1964 through 1978; V. Exposure was assessed through 1978 and follow-up was also through 1978. These different methods were considered principally because of the perceived difficulties of overlapping exposure and follow-up periods. Thus, with methods I and IV, exposure and follow-up periods were disjoint, whereas with methods II and V they coincided.

The analyses based upon ceiling exposures are not considered suitable for quantitative risk assessment because it seems extremely unlikely that respiratory cancer risk would be a function of peak exposures for any 30-day period, regardless of the other exposures that might have been experienced. This is also the case with the TWA analyses, because the exposures were averaged only over the period of employment, without regard to the duration of employment. If either of these dose measures were appropriate, it would mean, for example, that exposure to 500 $\mu g/m^3$ for 1 month would produce the same risk as exposure to 500 $\mu g/m^3$ for 30 years--which seems highly unlikely.

Thus, the analyses of Higgins et al. which appear to be most appropriate for developing quantitative estimates are those based upon cumulative exposure. This particular type of analysis was applied only to method V and applied only in Higgins (1982). The results of this analysis for lung cancer are listed in Table 7-26.

TABLE 7-26. RESPIRATORY CANCER MORTALITY 1938-1978 FROM CUMULATIVE EXPOSURE TO ARSENIC FOR 1800 MEN WORKING AT THE ANACONDA COPPER SMELTER[a]

Cumulative Exposure $\mu g/m^3$-years	Person-Years of Observation	Observed Deaths	Expected Deaths
0-500[b] (250)	13845.9	4	5.8
500-2000 (1250)	10713.0	9	5.7
2000-12000 (7000)	11117.8	27**	6.8
≧ 12000 (16000)	9015.5	40**	7.3

[a]From Higgins (1982), Table 6.

[b]Numbers in parenthesis indicate assumed average exposures.

**Significant at 0.01 level.

Information on the smoking habits of 80.6 percent of the 1800 men was obtained from questionnaires administered directely to those still living and to close friends or relatives of those who were deceased. Sixteen percent of the smelter workers were "non-smokers" compared with 24-36 percent of U.S. males from 1955 through 1978. Thus, it appears that the smelter workers smoked somewhat more than the average U.S. male. However, no confounding was detected between arsenic exposure and smoking; 15.1 percent of those in the "heavy" exposure group were non-smokers, versus 16.3 percent in the other

exposure groups. Significant increases in respiratory cancer were observed even among non-smokers exposed to high levels of arsenic.

Development of risk estimates: The relative risks (observed/expected) from Table 7-26 are graphed in Figure 7-4, and the absolute risks ([observed-expected]/person-years) in Figure 7-5. Results of applying chi-square goodness-of-fit tests of the relative- and absolute-risk models with $k = 1$ and $k = 2$ are recorded in Table 7-25. The maximum likelihood estimates of the carcinogenic potency parameter a' are also listed in Table 7-25. The maximum likelihood fits of those models are graphed in Figures 7-4 and 7-5. The fits for $k = 1$ are both excellent, with the absolute-risk model providing a slightly better fit than the relative-risk model ($p = 0.75$ vs. $p = 0.46$). The fits for $k = 2$ are much less adequate ($p = 0.017$ for the absolute-risk model and $p = 0.0015$ for the relative-risk model).

The unit risks (defined as the additional risk of respiratory cancer death from lifetime exposure to 1 $\mu g/m^3$ airborne arsenic) obtained from the absolute- and relative-risk models with $k = 1$ are also listed in Table 7-25.

These risks were estimated by applying (1) or (2), (8), and (9) with D_i based upon a constant exposure of 1 $\mu g/m^3$. Specifically,

$$D_i = (4.56)(72) \qquad (12)$$

was used, which represents the average lifetime cumulative exposure in $\mu g/m^3$ resulting from a constant exposure to 1 $\mu g/m^3$. Average lifetime exposure is used because it seems most commensurate with the treatment of exposure by Higgins et al.; in their analysis all of the person-years attributable to a single worker were placed into a single exposure category based upon total lifetime exposure, and consequently person-years of observation were placed into exposure categories according to exposures which had not yet occurred. It

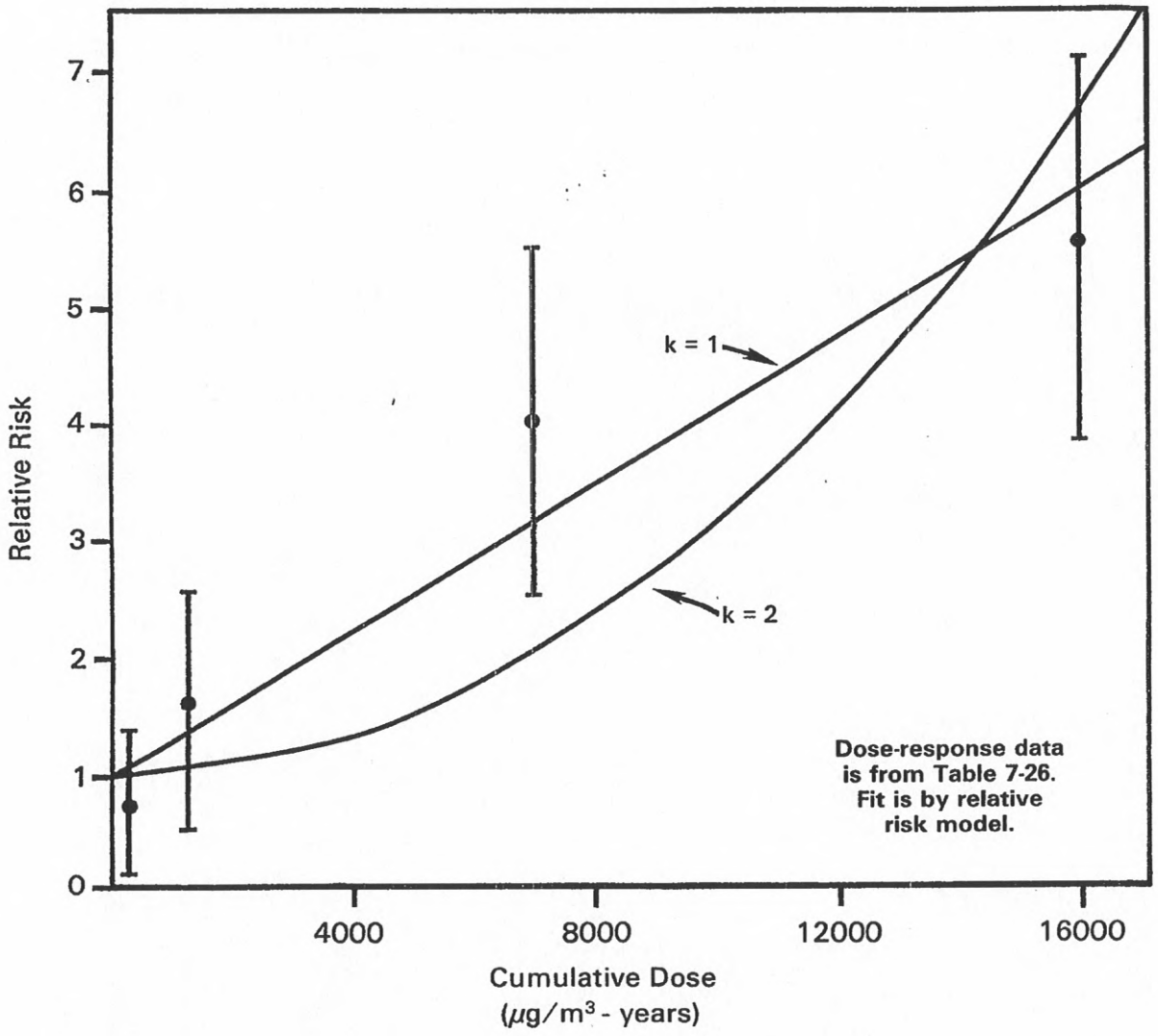

Figure 7-4. Relative risks and 90% confidence limits for data of Higgins (1982).

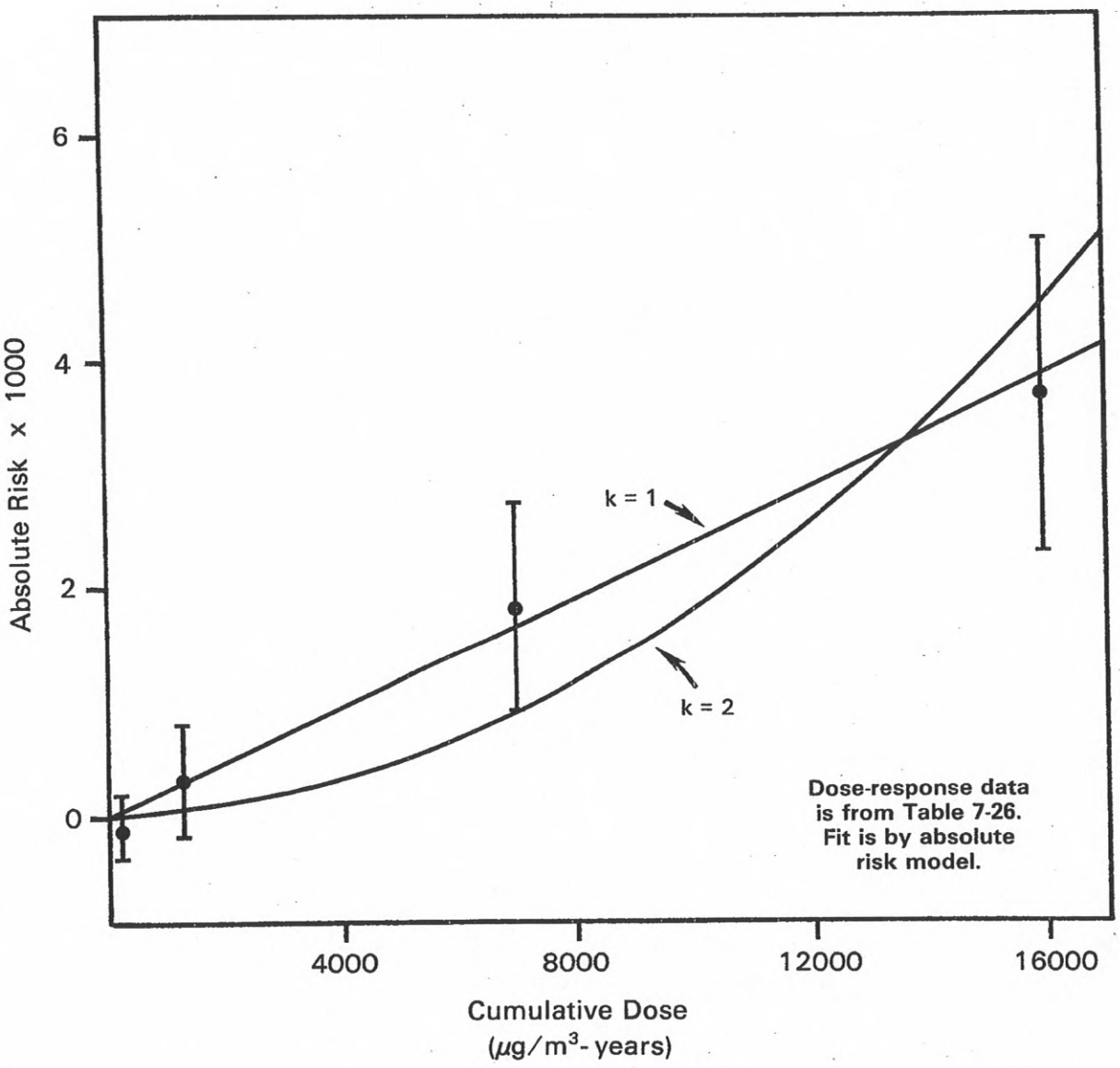

Figure 7-5. Absolute risks and 90% confidence limits for data of Higgins (1982).

would have been more appropriate for purposes of quantitative risk assessment had exposures been related to each 5-year age interval (as was done in the analysis of Enterline and Marsh, 1982) rather than to the total observation period of an individual. The factor 4.56 converts from occupational to environmental exposures and is explained at equation (11).

7.3.2.2.3 The Brown and Chu estimates from the Anaconda data. Development of Risk Estimates. As noted by Whittemore (1977) and Day and Brown (1980), the multistage theory for the carcinogenic process predicts that the carcinogenic response is a function of the following factors:

(1) exposure rate

(2) duration of exposure

(3) age at initial exposure

(4) time since cessation of exposure.

Brown and Chu (1983a) discuss in detail the ways in which these factors influence the age-specific carcinogenic rate at various stages of the carcinogenic process.

Using the updated Anaconda copper smelter workers cohort originally studied by Lee and Fraumeni (1969) and recently extended through 1977 by Lee-Feldstein (1983), Brown and Chu (1983b) concluded that airborne arsenic most probably acted on a late stage of the carcinogenic process. As a result, they hypothesized that the carcinogenic risk from arsenic exposure could be quantified by assuming a multistage model in which only the penultimate stage is affected by exposure. Under this assumption, the risk may be expressed in the form

$$r(d, t_o) = C[(d + t_o)^{k-1} - t_o^{k-1}] \qquad (13)$$

where d is the duration of exposure, t_o is the age at initial exposure, and C and k are unknown parameters. The parameter C depends upon the exposure rate, and the parameter k upon the time effect of exposure.

Brown and Chu (1983b) noted a deviation from this model on the part of workers who left employment at the copper smelter before the age of 55. As a result, the mortality experience of that group after leaving employment was not included in the analysis.

In order to estimate the unknown parameters C and k, the basic mortality data were arranged in the three-way table reproduced as Table 7-27. The three classifications used in this table are as follows:

(1) Level of exposure, corresponding to Lee and Fraumeni (1969)--classified into heavy, medium, and light exposure groups;

(2) Duration of employment, classified into the following five subgroups; 0-9, 10-19, 20-29, 30-39, and 40+ years;

(3) Age at initial employment, classified into the following five subgroups; 20, 20-29, 30-39, 40-49, and 50+ years.

For each of the 3 x 5 x 5 = 75 cells in the table, the following three variables were given:

Obs = observed number of respiratory cancer deaths;

Exp = expected number of respiratory cancer deaths (based upon the U.S. white male age-specific calendar-time-specific respiratory cancer mortality rates); and

Pyr = person-years of observation

A single individual could supply information for more than one cell as his duration of employment increased over the follow-up period. The person-year weighted average duration of employment, and age at initial employment, were calculated for each cell.

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Assuming that age at initial exposure is equivalent to age at initial employment, and that duration of employment and exposure are equivalent, Brown and Chu (1983c) fitted equation 13 to the data in Table 7-27. They used the maximum likelihood method, assuming a binomial distribution where Obs is the number of positive responses, Pyr is the sample size, and the rate of response is $p = Exp/Pyr + r(\bar{d},\bar{t}_o)$, where $\bar{d},\bar{t}_o$ are the averages for each cell. Using this approach, the value for k is estimated to be 6.8, and c = .603, 1.42, 1.74×10^{-13} for the light, medium, and heavy exposure categories, respectively.

Brown and Chu (1983c) did not attempt to give an exposure rate estimate to the heavy, medium, and light exposure groups of Lee and Fraumeni, (1969). One reason for this was that "heavy" and "medium" were defined as "having worked at least one year in a heavy or medium exposure area." The "total time worked" was not necessarily an indication of the total time worked in a heavy or medium exposure area. As a result, the use of the exposure rate in the areas defined as medium or heavy would tend to overestimate the true average exposure over an individual's working history. This bias did not exist for those in the light exposure group, since almost all of their working time was spent in light exposure areas. In addition, these low environmental exposures are of greater utility in estimating risks.

As a result of these factors, only the light exposure group was used to obtain a dose-response model. In this group, Brown and Chu (1983c) estimated that the respiratory cancer rate for an individual first exposed at age t_o for a duration of d years would be

$$r(d,t_o) = .603 \times 10^{-13} [(d + t_o)^{5.8} - t_o^{5.8}]. \qquad (14)$$

Only limited information exists concerning the time-weighted exposure of workers in the light exposure areas. Arsenic concentrations in several light

TABLE 7-27. OBSERVED AND EXPECTED LUNG CANCER DEATHS AND PERSON-YEARS BY LEVEL OF EXPOSURE, DURATION OF EMPLOYMENT, AND AGE AT INITIAL EMPLOYMENT

Age at Initial Employment		Duration of Employment (years) 0-9	10-19	20-29	30-39	40+
High Exposure Level Group						
<20	Obs	0	0	0	3	0
	Exp	0.001	0.009	0.065	0.249	0.193
	Pyr	206	408	588	499	172
20-29	Obs	0	0	2	0	2
	Exp	0.008	0.051	0.164	0.277	0.082
	Pyr	624	637	495	308	64.4
30-39	Obs	0	0	3	0	0
	Exp	0.030	0.077	0.106	0.053	0.001
	Pyr	398	207	155	59.1	0.86
40-49	Obs	0	0	0	0	0
	Exp	0.083	0.054	0.034	0.007	0.0
	Pyr	210	80.0	49.1	6.88	0.0
50+	Obs	0	0	0	0	0
	Exp	0.066	0.027	0.0	0.0	0.0
	Pyr	78.0	23.2	0.0	0.0	0.0
Medium Exposure Level Group						
<20	Obs	0	0	1	4	1
	Exp	0.010	0.039	0.171	0.591	0.597
	Pyr	1801	1763	1500	1206	579
20-29	Obs	0	0	2	4	7
	Exp	0.035	0.118	0.331	0.717	0.514
	Pyr	2636	1622	1099	951	654
30-39	Obs	0	0	1	3	0
	Exp	0.167	0.473	0.329	0.161	0.045
	Pyr	1939	1137	438	194	68.2
40-49	Obs	0	0	1	3	0
	Exp	0.167	0.414	0.098	0.010	0.0
	Pyr	1190	448	98.9	12.1	0.0
50+	Obs	1	0	0	0	0
	Exp	0.262	0.076	0.011	0.0	0.0
	Pyr	295	71.2	14.5	0.0	0.0

TABLE 7-27. (continued)

Age at Initial Employment		Duration of Employment (years) 0-9	10-19	20-29	30-39	40+
Low Exposure Level Group						
<20	Obs	0	0	1	1	3
	Exp	0.056	0.117	0.478	1.59	1.57
	Pyr	8524	5249	4038	3175	1376
20-29	Obs	0	0	2	5	6
	Exp	0.115	0.334	0.892	1.74	0.796
	Pyr	9951	4724	2965	2117	834
30-39	Obs	0	3	1	0	1
	Exp	0.390	0.802	0.937	0.662	0.062
	Pyr	5218	2218	1364	715	74.6
40-49	Obs	2	1	1	1	0
	Exp	1.29	1.18	0.344	0.035	0.001
	Pyr	3703	1319	386	52.7	2.00
50+	Obs	3	2	0	0	0
	Exp	1.62	0.385	0.041	0.0	0.0
	Pyr	1945	371	65.4	0.0	0.0

Source: Brown and Chu (1983a).

exposure areas, as given in a NIOSH criteria document (1975), are shown in Table 7-28.

In the absence of information to the contrary, it is assumed that the person-hours spent in each area are equal. Thus an estimate of the time-weighted average for workers in the light exposure category is

$$1/3 \times .7 + 1/3 \times .17 + 1/3 \times .004 = .291 \text{ mg As/m}^3.$$

Under the linear assumption, equation 14 may be expressed in terms of mg As/m^3 working exposure by dividing by .291, which gives the result

$$r(d,t_o) = 2.07 \times 10^{-13} [(d + t_o)^{5.8} - t_o^{5.8}]. \qquad (15)$$

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TABLE 7-28. ARSENIC EXPOSURES: 1965 SMELTER SURVEY ATMOSPHERIC ARSENIC CONCENTRATIONS (mg/As/m^3)

"Heavy exposure area" as classified by Lee and Fraumeni

Arsenic Roaster Area		Mean: 1.47
0.10	0.20	Median: 0.185
0.10	0.22	
0.10	0.25	
0.10	0.35	
0.10	1.18	
0.10	5.00	
0.17	12.66	

"Medium exposure areas" as classified by Lee and Fraumeni

Reverberatory Area		Mean: 1.56
0.03	0.93	Median: 0.88
0.22	1.00	
0.23	1.27	
0.36	1.60	
0.56	1.66	
0.63	1.84	
0.66	1.94	
0.76	2.06	
0.78	2.76	
0.78	3.40	
0.80	4.14	
0.83	8.20	
Treater Building and Arsenic Loading		Mean: 1.50
0.10	0.48	Median: 0.295
0.10	0.62	
0.10	3.26	
0.11	7.20	

"Light exposure areas" as classified by Lee and Fraumeni

Copper Concentrate Transfer System		Mean: 0.70
0.25		Median: 0.65
0.65		
1.20		
Samples from Flue Station		Mean: 0.17
0.10		Median: 0.17
0.24		
Reactor Building		Mean: 0.004
0.001	0.003	Median: 0.002
0.002	0.009	
0.002	0.010	
0.002		

Source: Table X-3, NIOSH Criteria Document (1975).

In this case, exposure is expressed in mg As/m^3 per 8-hr working day. To change the relationship so that it expresses the risk due to a lifetime of continuous exposure to 1 ug As/m^3, we assume 240 days worked per year, one mg As/m^3 on the job gives the same cumulative exposure as 10^3 x $1/3 \times \frac{240}{365} = 219$ µg As/m^3 continuous exposure.

The age-specific rate due to a continuous 1 µg As/m^3 exposure is obtained by substituting $t_o = 0$ and $d = t$ = age into equation (15) and dividing by 219 to arrive at the correct number of exposure units. This gives the result

$$r(t) = 9.45 \times 10^{-16}\ t^{5.8}. \qquad (16)$$

The unit risk is approximately equivalent to the risk of induced respiratory cancer in the median life span. Based upon 1976 U.S. vital statistics, the median life span is 76.2 years, so that the unit risk is expressed approximately as

$$p \simeq \int_0^{76.2} 9.45 \times 10^{-16}\ t^{5.8} = \frac{9.45}{6.8}\ (76.2)^{6.8} \times 10^{-16} = 8.71 \times 10^{-4}. \qquad (17)$$

An additional approximation consistent with the previous unit calculations is obtained by assuming that

$$r(t) = 9.45 \times 10^{-16}\ \left[\frac{t_j + t_{j-1}}{2}\right]^{5.8} \quad t_{j-1} < t < t_j \qquad (18)$$

where t_j are the ages at the interval boundaries given in U.S. vital statistics records. This assumes that the age-specific death rate due to the exposure is constant throughout the interval and equal to the true value at the midpoint of the interval. Under this approximation, using 1976 vital statistics, the unit risk is estimated to be $P \simeq 1.25 \times 10^{-3}$.

Evaluation of Goodness-of-Fit. It is desirable to assess whether the data for the low-exposure group is consistent with the model utilized to estimate the unit risk. However, two factors tend to create a situation that would decrease this goodness-of-fit and bias the results. First, the exact values for each cell of $\bar{d}$, $\bar{t}_o$ are presently not available. Second, the value of k was determined on the basis of all three exposure groups, and does not give as good a fit as would be obtained using the low-exposure group alone.

Brown states (personal communication, 1983) that the exact values of $\bar{d}, \bar{t}_o$ are very close to the midpoint of the interval, and that the values of k appear to be statistically consistent between exposure groups. Thus, distortions of the data because of the use of midpoint values and average k, although inevitable, are not appreciable.

The expected number of cases in each cell are calculated using the relationship

$$E = Exp + Pyr \times .603 \times 10^{-13} [(d + t_o)^{5.8} - t_o^{5.8}], \qquad (19)$$

in which Exp and Pyr are taken from Table 7-27 and d, t_o are the midpoints of the intervals. These results are shown in Table 7-29. A standard chi-square goodness-of-fit test is then run, resulting in a chi-square value of $X^2_{21} = 13.85$ with 23.2 = 21 degrees of freedom and an associated p-value of .88. Unfortunately, due to the low expected number of cases in many of the cells, the X^2 approximation is of questionable validity for this situation.

To obtain a more stable approximation, cells with low frequency that are as close as possible to each other are usually combined. It is important to have some criteria for combining the data that do not depend upon inspection of the data itself. Two methods of combining the data are used here. The first is across columns (duration exposed), so that the maximum number of

TABLE 7-29. OBSERVED AND EXPECTED NUMBER OF RESPIRATORY CANCER DEATHS FOR EACH CELL IN THE LOW-EXPOSURE GROUP OF TABLE 7-27

	d				
t_o	5	15	25	35	45
18	0 .088	0 .314	1 1.20	1 3.504	3 3.836
25	0 .258	0 .858	2 2.145	5 4.358	6 3.321
35	0 .723	3 1.641	1 2.556	0 2.791	1 .497
45	2 2.023	1 2.508	1 1.428	1 .371	0 .026
55	3 2.582	2 1.234	0 .418		

$X^2_{21} = 13.85$, $p = .88$

cells are obtained, with the constraints that combined cells must have at least three expected cases, and that all cells combined are consecutive within a row. The second approach uses the same technique within a column (age first exposed). The results are shown in Tables 7-30 and 7-31 respectively, giving chi-square values of 7.01 and 7.61, with p-values of .41 and .38. Thus the assumed model is shown to be consistent with the observed low-exposure data.

7.3.2.2.4 The Enterline and Marsh (1982) study. This study included all men (2802 in all) employed at the Tacoma, Washington copper smelter for a year or more during 1940-1964. Their mortality experience was observed through 1976. The study involved over 70,000 person-years of observation, and 104 deaths from cancer of the respiratory system were recorded (Table 7-32). Respiratory cancer deaths had an SMR of 189.4, which was significantly increased at the 1 percent level. Expected deaths for Table 7-32 were based upon U.S. white

TABLE 7-30. CELLS FROM TABLE 7-29 COMBINED WITHIN ROWS TO OBTAIN CELLS WITH THREE OR MORE EXPECTED RESPIRATORY CANCER DEATHS

	d				
t_o	5	15	25	35	45
18				2 5.106	3 3.836
25			2 3.261	5 4.358	6 3.321
35			4 4.920		1 3.288
45					5 6.356
55			5 4.234		

$X^2 = 7.01$, $p = .41$

TABLE 7-31. CELLS FROM TABLE 7-29 COMBINED WITHIN COLUMNS TO OBTAIN CELLS WITH 3 OR MORE EXPECTED RESPIRATORY CANCER DEATHS

	d				
t_o	5	15	25	35	45
18				1 3.504	3 3.836
25			3 3.345	5 4.358	
35					
45				1 3.162	7 3.844
55	5 5.674	6 6.555	2 4.402		

$X^2 = 7.61$, $p = .38$

TABLE 7-32. OBSERVED DEATHS AND SMRs FOR 2802 SMELTER WORKERS WHO WORKED A YEAR OR MORE 1940-64, FOLLOWED THROUGH 1976, BY CAUSE OF DEATH

Cause of death (7th revision code)	Observed Deaths	SMR
All causes of death	1061	103.2
Tuberculosis (001-019)	4	27.6**
Malignant neoplasms (140-148)	231	123.6**
Buccal cavity and pharynx (140-148)	7	110.7
Digestive organs & peritoneum (150-159)	65	108.9
Esophagus (150)	3	66.2
Stomach (151)	17	122.1
Large intestine (153)	21	120.4
Rectum (154)	9	122.4
Biliary passages and liver (155-156)	3	64.1
Pancreas (157)	11	106.0
All other digestive organs (residual)	1	71.6
Respiratory system (160-164)	104	189.4**
Larynx (161)	2	67.7
Bronchus, trachea, and lung (162-163)	100	194.9**
All other respiratory system (residual)	2	305.0
Prostate (177)	11	79.0
Testes and other genital (178-179)	1	92.6
Kidney (180)	6	133.3
Bladder and other urinary organs (181)	4	63.0
Malignant melanoma of skin (19)	0	--
Eye (192)	1	492.7
Central nervous system (193)	3	59.8
Thyroid gland (194)	0	--
Bone (196)	2	175.0
Lymphatic & haematopoietic (200-205)	17	93.8
Lymphosarcoma and reticulosarcoma (200)	4	93.2
Hodgkins' disease (201)	2	83.9
Leukemia and aleukemia (204)	6	78.7
Other lymphopoietic tissue (202, 203, 205)	5	130.4
Other malignant neoplasms (residual)	10	82.3
Benign neoplasms (210-239)	2	78.6
Diabetes mellitus (260)	12	84.8
Stroke (333-334)	91	111.4
Heart disease (400-443)	412	92.5
Hypertension without heart disease (444-447)	1	18.8
Nonmalignant respiratory disease (470-527)	60	108.6
Influenza and pneumonia (480-493)	24	92.9
All other respiratory diseases (residual)	36	122.4
Ulcer of stomach and duodenum (540-541)	7	75.5
Cirrhosis of liver (581)	22	101.9
Chronic nephritis (592)	6	87.5
External causes of death (800-998)	81	94.2
Accidents (899-962)	61	100.6
Suicides (963, 970-979)	17	84.8
Other external causes (residual)	3	56.2
Other causes of death (residual)	85	86.1
Unknown causes	47	--

* $p < .05$, ** $p < .01$
Source: Enterline and Marsh (1982).

male mortality rates. The respiratory cancer SMR increases to 198.1 when Washington State mortality rates are applied.

Enterline and Marsh estimated individual exposures to airborne arsenic using individual work histories, urine arsenic measurements, and an estimated correlation between exposure to airborne arsenic and resulting levels of arsenic in urine. Average urine arsenic levels were available by department for the years 1948-52, 1973, 1974, and 1975. Linear interpolations were used to estimate levels between 1952 and 1973. Levels during 1949-1952 were assumed to hold prior to that time. By coupling these data with employee work histories, Enterline and Marsh estimated individual cumulative exposures for various times in units of μg-years/ℓ urinary arsenic.

Pinto et al. (1977) compared airborne concentrations of arsenic with urinary arsenic levels for 24 workers wearing personal air samplers for 5 successive days. A regression analysis of these data showed a highly significant linear correlation between airborne and urinary arsenic ($p < 0.01$). Average airborne arsenic in units of $\mu g/m^3$ was estimated to be 0.304 times average urinary arsenic levels in units of μg/ℓ.

To investigate dose-response, Enterline and Marsh divided the total person-years of observation into 5 groups by cumulative arsenic exposure (0 lag), and also by cumulative arsenic exposure up to 10 years prior to the year of observation (10-year lag). In this type of analysis, as a worker continues to be exposed to arsenic, he or she will contribute person-years to progressively higher exposure categories. The numbers of respiratory cancer deaths and corresponding expected numbers for each of these groups are given in Table 7-33. In this table, urinary arsenic levels provided by Enterline and Marsh have been converted to airborne exposures in $\mu g/m^3$-years, using the factor 0.304 estimated by Pinto et al. (1977). The observed numbers of cancers are all significantly increased at the higher exposure levels.

TABLE 7-33. DATA FROM TABLE 8 OF ENTERLINE AND MARSH (1982) WITH PERSON-YEARS OF OBSERVATION ADDED

Cumulative Exposure[a] µg/m³-years	Person-Years of Observation[b]	Observed Deaths	Expected Deaths
	0 Lag		
91.8	10902	8	4.0
263	21642	18	11.0
661	14623	21	10.3
1381	13898	26	14.1
4091	9398	31	12.7
	10-Year Lag		
91.8	27802	10	6.4
263	16453	22	12.5
661	11213	26	11.5
1381	9571	22	12.4
4091	5423	24	9.7

[a]Exposures are in µg/m³-years estimated by the formula (I µg/l-years) (0.304) where I is mean urinary exposure index from Enterline and Marsh (1982) Table 8 and 0.304 is the relation between urinary and airborne arsenic estimated by Pinto et al. (1977).

[b]Furnished by Dr. Enterline (personal communication).

Although the Enterline and Marsh (1982) study is not as large as that of Lee-Feldstein (1983), it does involve a sizable number of respiratory cancer deaths (104). Workers were followed for an extended period--an average of 25 years per individual. Several features of the analysis render it more amenable to quantitative risk estimation than the analysis used by Lee-Feldstein. Enterline and Marsh made estimates of individual exposure histories, whereas Lee-Feldstein did not. The type of dose-response analysis used by Enterline and Marsh is also more suitable for quantitative risk estimation. The exposure estimates based on a 10-year lag probably yield a more realistic dose response than those that do not utilize a lag. Because the latency period for respiratory cancer is generally greater than 10 years (cf. Doll and Peto,

1978), exposure during the last 10 years prior to observation would not be expected to affect respiratory cancer mortality.

By applying urinary arsenic measurements made during the years 1948-52 to earlier years, Enterline and Marsh probably underestimated exposures prior to 1948. This would result in an overestimate of the carcinogenic potency of arsenic. A calculation by Enterline and Marsh of SMRs by both year of hire and cumulative exposure indicates that workers in a given cumulative exposure category tend to have at least roughly comparable SMRs irrespective of the year of hire. This suggests that exposure estimates for earlier years are not greatly in error. However, further investigation of this problem would be useful.

Because smoking is also an important risk factor for respiratory cancer, it would have been helpful if data on smoking habits had been available for analysis. Pinto and Enterline (undated) report on smoking histories obtained in 1975 from 550 active employees at the Tacoma smelter. Of these employees, 59.6 percent were active smokers, compared to 45.4 percent in 1970 for U.S. males aged 21-64. If this excess of smokers holds in general for the smelter workers, then a small fraction of the excess in respiratory cancer could have been due to smoking.

Development of risk estimates: The data from Table 7-33 were used for quantitative risk assessment. The relative risks (observed/expected) from this table are graphed in Figures 7-6 and 7-7, and the absolute risks ([observed- expected]/person-years) in Figures 7-8 and 7-9. Although there is no clear trend of increasing SMRs with increasing exposures, such a trend is present for absolute risk. Results of applying chi-square goodness-of-fit tests of the relative- and absolute-risk models with $k = 1$ and $k = 2$ are recorded in Table 7-25. The maximum likelihood estimates of the carcinogenic

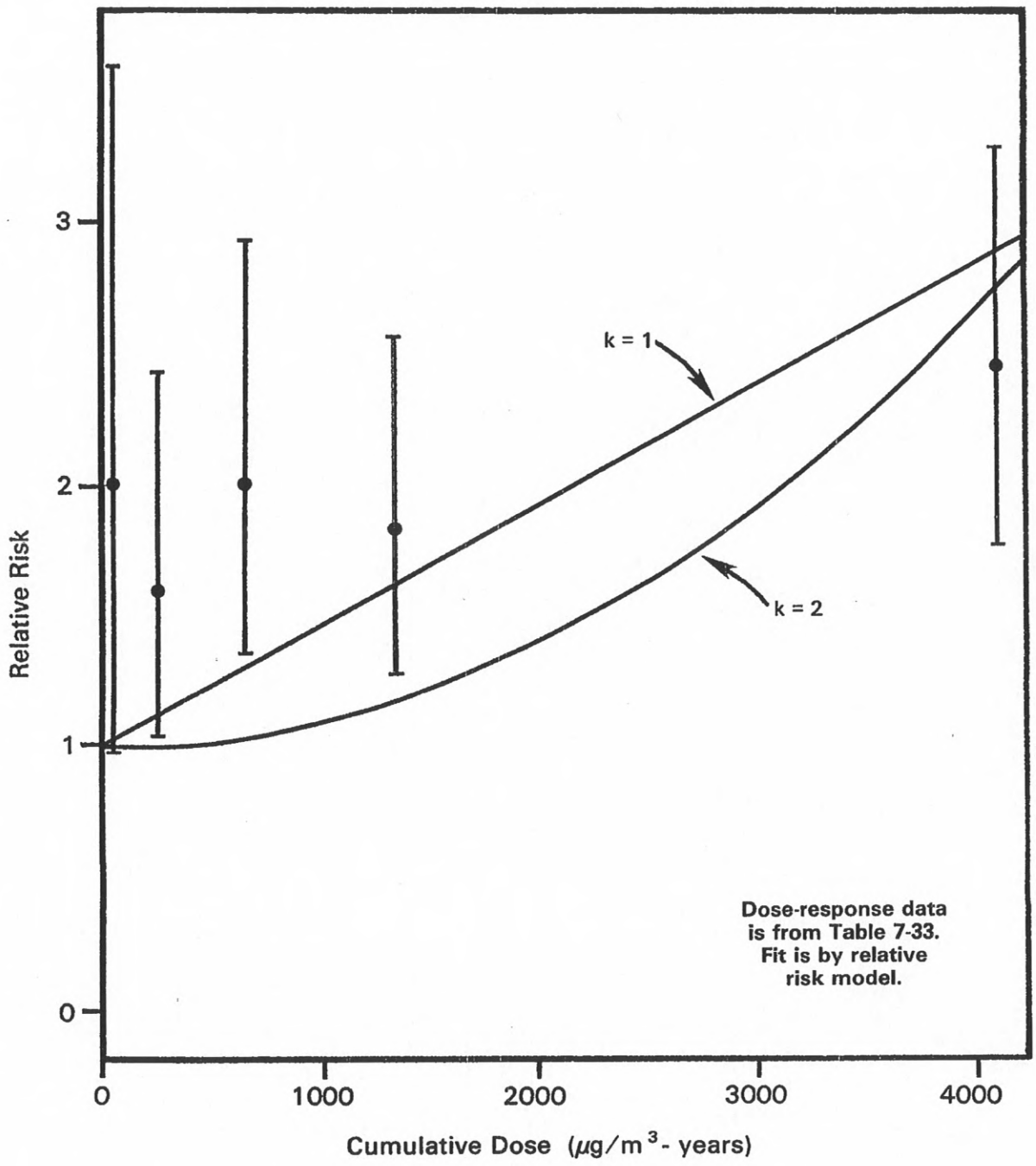

Figure 7-6. Relative risks and 90% confidence limits for zero-lag data of Enterline and Marsh (1982).

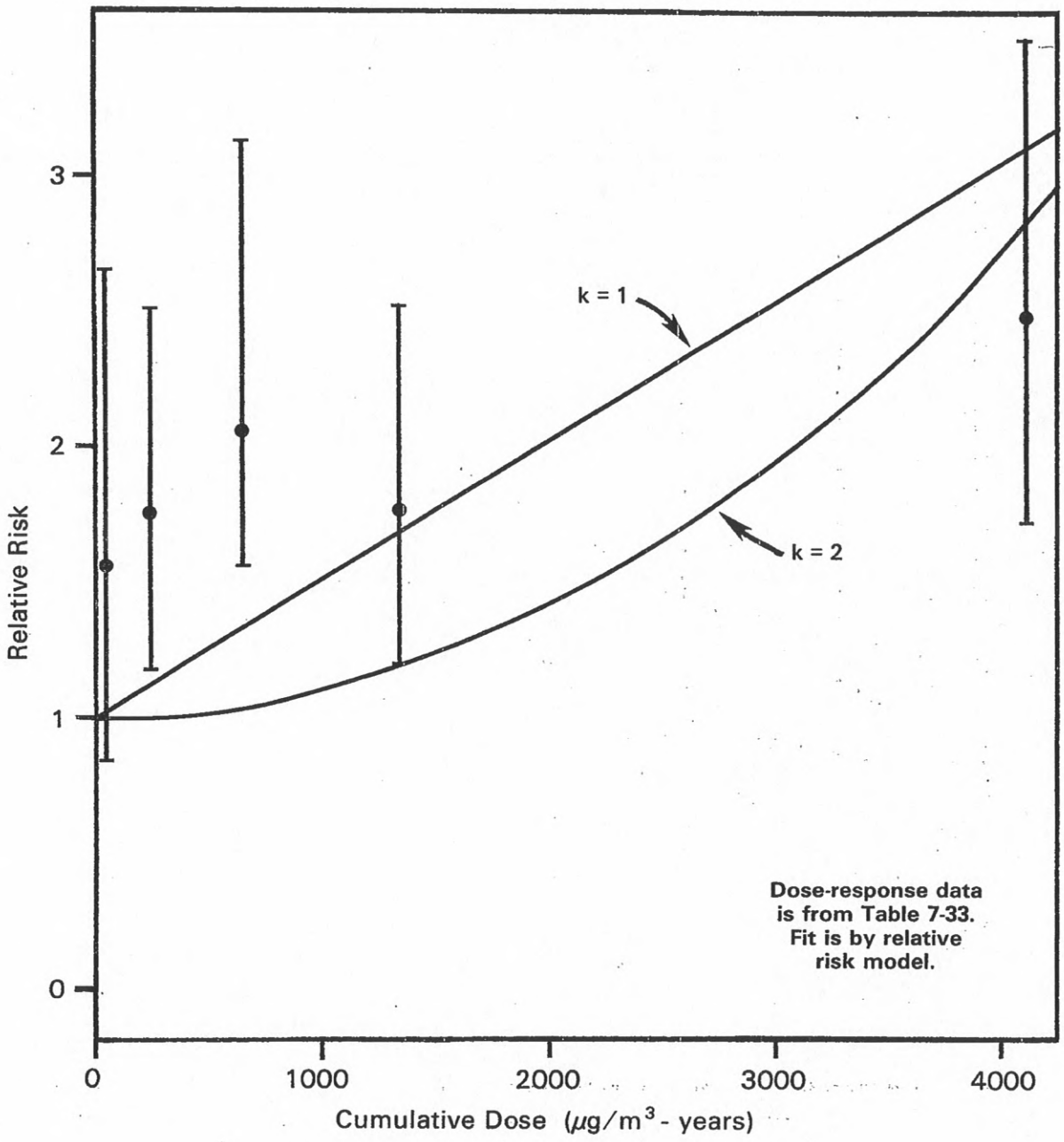

Figure 7-7. Relative risks and 90% confidence limits for 10 year lag data of Enterline and Marsh (1982).

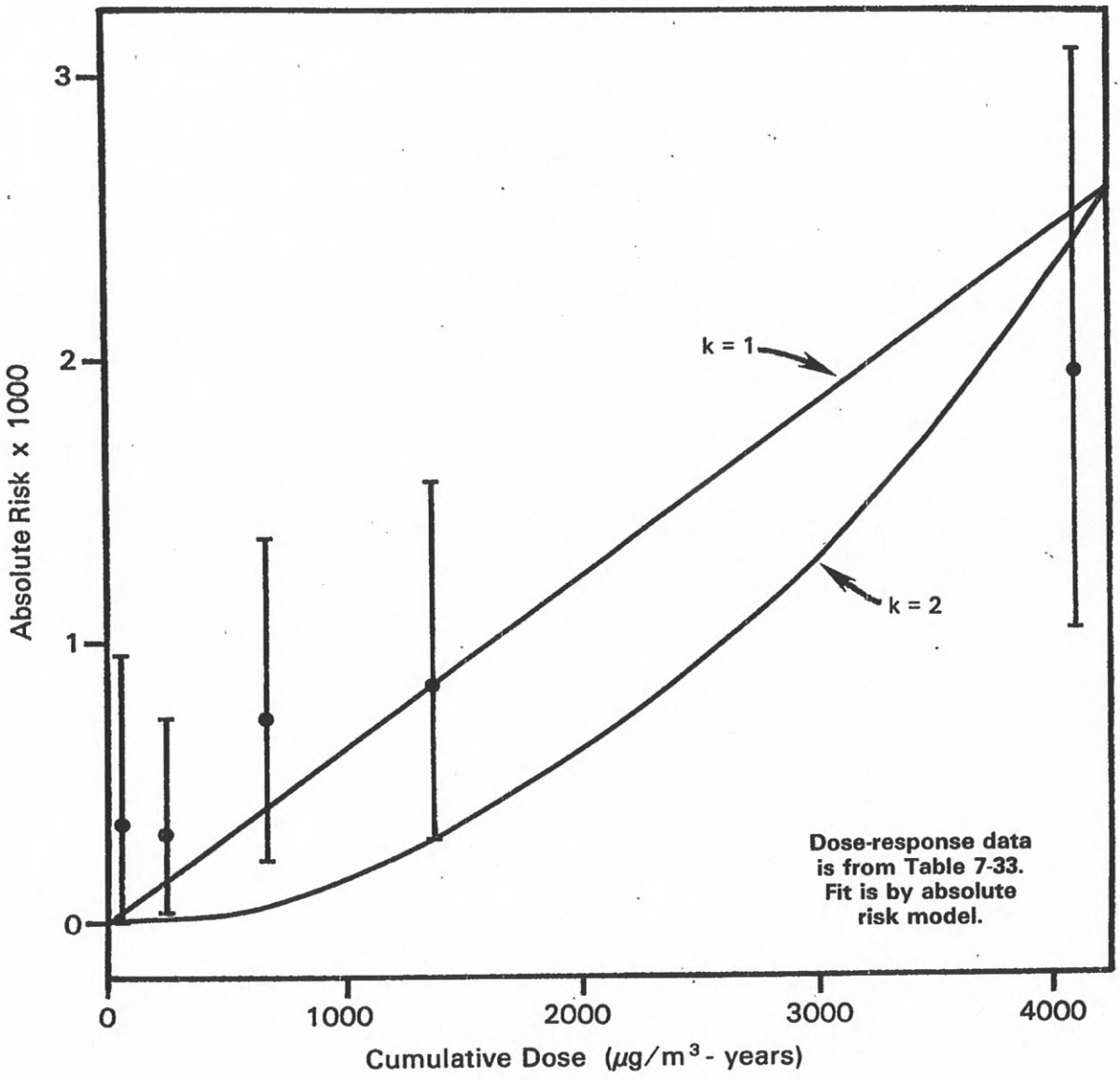

Figure 7-8. Absolute risks and 90% confidence limits for zero-lag data of Enterline and Marsh (1982).

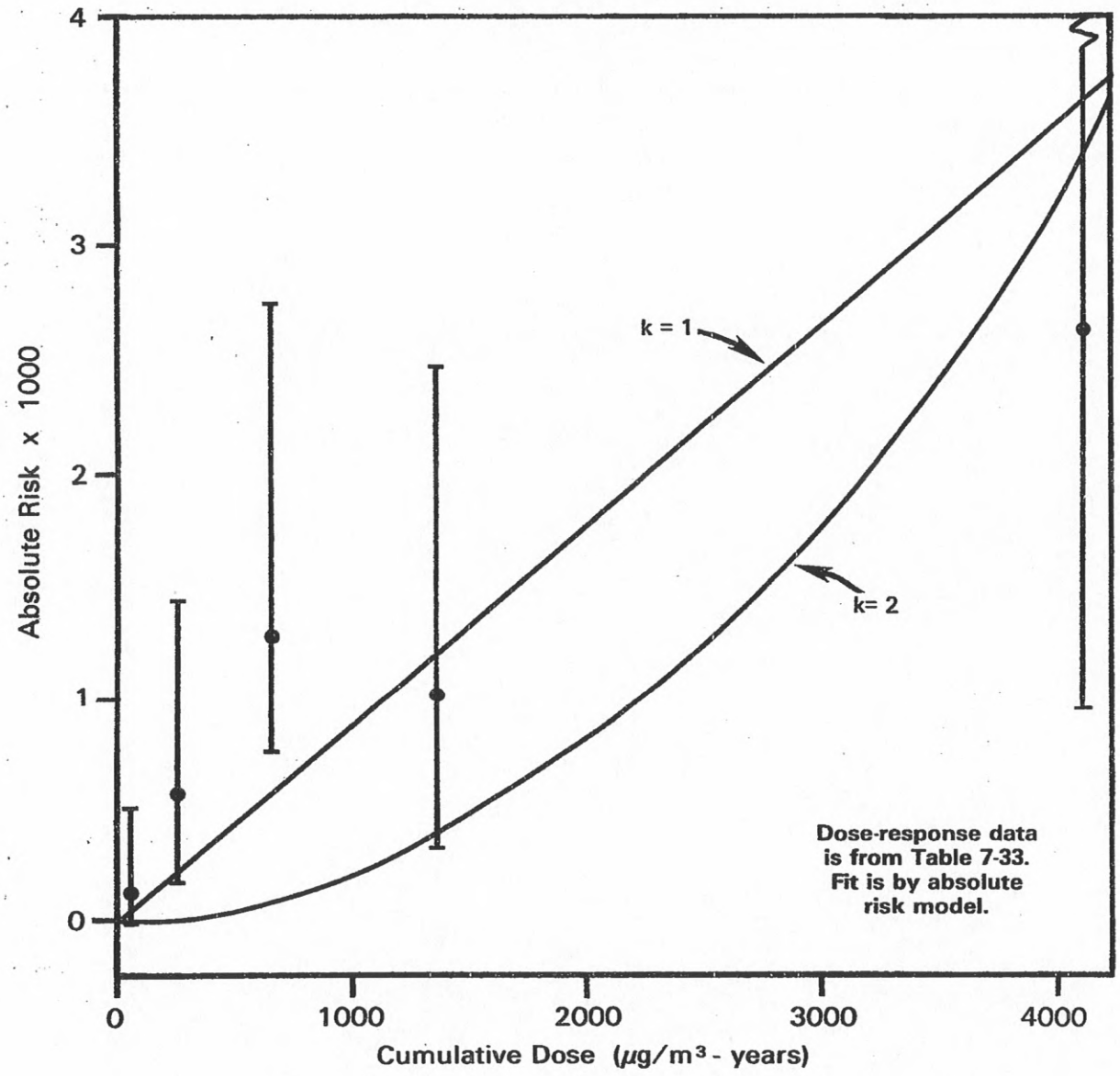

Figure 7-9. Absolute risks and 90% confidence limits for 10 year lag data of Enterline and Marsh (1982).

potency parameter a' are also listed in Table 7-25. The maximum-likelihood fits of these models are graphed in Figures 7-6 through 7-9. The quadratic fit (k = 2) is poor for both the absolute- and relative-risk models with either 0 lag or 10-year lag data (p less than 0.001 in each case). The linear fits to the relative-risk models are also relatively poor (p = 0.02 for the 0 lag data and 0.006 for the 10-year lag data). On the other hand, the linear fits of the absolute-risk model are all acceptable (p = 0.24 for 0 lag data and 0.14 for 10-year lag data).

The unit risks (additional risks of respiratory cancer death from lifetime exposure to 1 $\mu g/m^3$ airborne arsenic) obtained from each of the fits for which the chi-square p-value is 0.01 or higher, are also listed in Table 7-25. These risks were estimated by applying (1) or (2), (8), and (9) with D_i based upon a constant exposure of 1 $\mu g/m^3$. Specifically,

$$D_i = 4.56[5(i-1) + 2.5] \qquad (17)$$

was used for the 0 lag data, and

$$D_i = 4.56[5(i-1) - 7.5] \qquad (18)$$

was used for the 10-year lag data. These D_i represent the cumulative exposure in $\mu g/m^3$ resulting from a constant exposure to 1 $\mu g/m^3$ from birth to the midpoint of the ith 5-year age interval. The factor 4.56 converts from occupational to environmental exposures, and is explained at equation (11).

7.3.2.2.5 The Ott et al. (1974) study. Ott et al. (1974) compared the age-specific death patterns of 174 decedents exposed to arsenic in the production of pesticides to those of 1809 decedents who were not exposed to arsenicals. By fitting the death patterns of the unexposed decedents to a mathematical function, an estimate was obtained of the probability that a death at a parti-

cular age and during a particular epoch was due to respiratory cancer. This function was used to estimate expected respiratory cancer deaths in various exposure categories for the exposed decedents. Cumulative exposures were estimated for exposed decendents, using work histories and estimates of average exposures in various jobs. The exposure estimates were made by industrial hygienists familiar with the processes. Expected cancer deaths were compared with observed to obtain observed-to-expected ratios. Table 7-34 shows the results of Ott et al.'s dose-response analysis. The data in this table are all reproduced directly from Table 4 of Ott et al. (1974), except for the cumulative exposures. Average total exposures in mg provided by Ott et al. were converted to cumulative exposures in $\mu g/m^3$ years by multiplying by the factor

$$\frac{1000\ \mu g/mg}{(4\ m^3/day)(21\ days/mo)(12\ mo/year)} \qquad (19)$$

TABLE 7-34. DATA FROM TABLE 4 OF OTT ET AL. (1974)

Cumulative Exposure[a] $\mu g/m^3$-years	Observed Deaths	Expected Deaths
41.8	1	1.77
125	2	1.01
250	4	1.38
417	3	1.36
790	3	1.70
1544	2	0.97
3505	3	0.77
6451	5	0.79
29497	5	0.72

[a]Exposures are in $\mu g/m^3$-years estimated by:

$$\frac{d\ mg \times 1000\ \mu g/mg}{(4\ m^3/day)(21\ days/month)(12\ months/year)}$$

where d is average total exposure from Table 4 of Ott et al.

The values included in this factor are not in doubt because use of the factor simply negates the calculation of total exposure made by Ott et al.

Decedent studies such as this are more subject to bias then prospective studies such as those of Lee-Feldstein (1983) and Enterline and Marsh (1982). If, for example, in some age category arsenic exposure increased the mortality from some other disease in addition to respiratory cancer, an analyis of decedents might show an artificially low effect of arsenic upon respiratory cancer for this age group (because there might be an artificially large number of total deaths). It is also of some concern that Ott et al. did not clearly describe how the study cohort was defined.

This study involved primarily short-term exposures, as less than 25 percent of the decedents had worked with arsenicals for more than one year. Thus, this study is less appropriate for estimating risks from lifetime environmental exposure than a comparable study involving longer exposures. The study also was quite small; only 28 respiratory cancer deaths occurred among exposed decedents.

Development of risk estimates: The dose-response data in Table 7-34 were used in an assessment of risk. Because of the nature of the study, only a relative risk model could be applied to these data. The dose-response for relative risk is graphed in Figure 7-10. The response in the most highly exposed group falls far below that predicted by the lower-dose data and is omitted from Figure 7-10. This is possibly due to the fact that some of the more highly exposed workers wore respirators. Because of this shortfall in response, and also because the exposures to this group were the furthest from the low-level environmental exposures of interest, the data from the highest exposure group were omitted from the analysis.

Results of applying chi-square goodness-of-fit tests of the relative-risk model with $k = 1$ and $k = 2$ are listed in Table 7-25. The maximum-likelihood

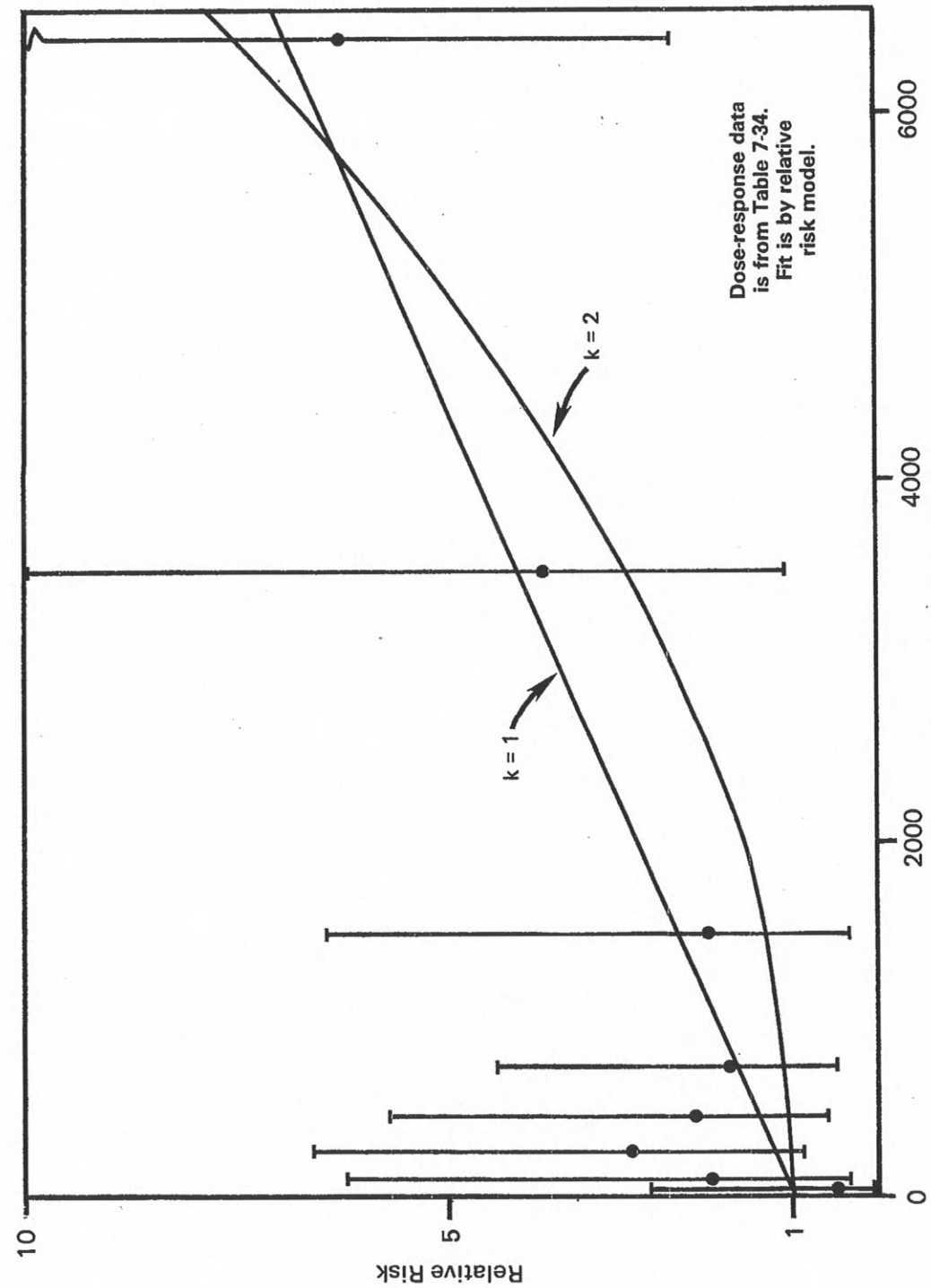

Figure 7-10. Relative risks and 90% confidence limits for data of Ott et al. (1974) with highest exposure group omitted.

estimates of the carcinogenic potency parameter a' are also listed in this table. The maximum-likelihood fits are graphed in Figure 7-10. Both of these fits are acceptable ($p = 0.66$ for $k = 1$ and $p = 0.23$ for $k = 2$), although the data appear to be more linear than quadratic. It should be kept in mind that the sample size was quite small in this study, and consequently a wide range of curve shapes would probably provide an acceptable fit.

The risk estimation method described in the previous section is based upon the life table method of analysis, and does not seem particularly appropriate for a decedent analysis. Because the method employed by Ott et al. seems to estimate a relative probability of respiratory cancer death, it was decided to estimate the extra lifetime probability of respiratory cancer death from lifetime exposure to d $\mu g/m^3$ airborne arsenic, using the expression

$$P_0(1 + a'[(72)(4.56)d]^k) - P_0 = P_0 a'[(72)(4.56)]^k. \qquad (20)$$

Here P_0 is the lifetime probability of respiratory cancer mortality given by (8), and is equal to 0.0451 if 1976 U.S. mortality rates are used. The factor 72 represents life expectancy in the U.S. in years. The factor 4.56 converts from occupational to environmental exposures, and is explained at equation (11). Thus, the term in the square brackets in (20) represents the average total exposure over a life span in $\mu g/m^3$ years, which is the same as the measure used in estimating the potency a'.

7.3.2.3 Discussion--Table 7-25 summarizes the fits of both absolute- and relative-risk models, with either $k = 1$ or $k = 2$, to dose-response data from 4 different studies. Table 7-25 also displays the carcinogenic potencies a'. It should be noted that the potencies estimated from different models are in different units, and are therefore not comparable.

In every case, a linear model ($k = 1$) fitted the data better than the corresponding quadratic model ($k = 2$). In every case but two, the fits of the

quadratic model could be rejected at the 0.01 level. The two exceptions involved the two smallest data sets (Higgins et al. absolute risk, and Ott et al.) and in the former case the fit was very marginal (p = 0.017). On the other hand, for each data set a linear model provided an adequate fit. Also, in every case, an absolute-risk linear model fit the data better than the corresponding relative-risk linear model. The p-values for the fits of the absolute-risk linear model ranged from 0.025 to 0.75.

The estimated unit risk is presented for each fit for which the chi-square goodness-of-fit p-value is greater than 0.01. The unit risks derived from linear models--8 in all--range from 0.0013 to 0.0136. The largest of these is from the Ott et al. study, which probably is the least reliable for developing quantitative estimates, and which also involved exposures to pentavalent arsenic, whereas the other studies involved trivalent arsenic. The unit risks derived from the linear (k = 1) absolute-risk models are considered to be the most reliable; although derived from 5 sets of data involving 4 sets of investigators and 2 distinct exposed populations, these estimates are quite consistent, ranging from 0.0013 to 0.0076.

To establish a single point estimate, the geometric mean for data sets is obtained within distinct exposed populations, and the final estimate is taken to be the geometric mean of those values. This process is illustrated in Table 7-35.

The final estimate is 4.29×10^{-3}, where exposure is in $\mu g/m^3$ of continuous exposure. Based upon an assumed 20 m^3 tidal volume of air and a 30 percent absorption rate, this amounts to a unit risk of $4.29 \times 10^{-3} \div (.3 \times 20 \times .001/70) = 50.1$ in units of mg/kg absorbed dose per day.

Although the estimates derived from the various studies are quite consistent, there are a number of uncertainties associated with them. The estimates

TABLE 7-35. COMBINED UNIT RISK ESTIMATES FOR ABSOLUTE-RISK LINEAR MODELS

Exposure Source	Study	Unit Risk	Geometric Mean Unit Risk	Final Estimated Unit Risk
Anaconda smelter	Brown & Chu	1.25×10^{-3}		
	Lee-Feldstein	2.80×10^{-3}	2.56×10^{-3}	
	Higgins	4.90×10^{-3}		4.29×10^{-3}
ASARCO smelter	Enterline & Marsh	6.81×10^{-3}		
		7.60×10^{-3}	7.19×10^{-3}	

were made from occupational studies that involved exposures only after employment age was reached. In estimating risks from environmental exposures throughout life, it was assumed, through either the relative-risk model (1) or the absolute-risk model (2), that the increase in the age-specific mortality rates of lung cancer was a function only of cumulative exposures, irrespective of how the exposure was accumulated. Although this assumption provides an adequate description of all of the data, it may be in error when applied to exposures that begin very early in life. Similarly, the linear models possibly are inaccurate at low exposures, even though they provide excellent descriptions of the experimental data.

The risk assessment methods employed were severely constrained by the fact that they were based only upon the analyses performed and reported by the original authors--analyses that had been performed for purposes other than quantitative risk assessment. For example, although other measures of exposure might be more appropriate, the analyses were necessarily based upon cumulative dose, since that was the only usable measure reported. Given greater access to the data from these studies, other dose measures, as well as models other than the simple relative-risk and absolute-risk models, could be

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studied. It is possible that such wide analyses would indicate that other approaches are more appropriate than the ones applied here.

7.3.3 Unit Risk for Water

The best data available for making quantitative cancer risk estimates for ingestion of arsenic in water are the data collected by Tseng et al. (1968). They surveyed a stable population of 40,421 individuals who lived in a rural area along the southwest coast of Taiwan and who were known to have consumed drinking water containing arsenic. The occurrences of skin cancer among this population, and the arsenic concentrations in their drinking water, were measured. Since the population was stable, the study can be viewed as a lifetime feeding study, and the data may be used to predict the lifetime probability of skin cancer caused by the ingestion of arsenic.

A model estimating the cancer rate as a function of drinking water arsenic concentration was generated using information from the above study in its published form, which is a summary of data collected by the investigators. If the original data had been available, a more exact mathematical analysis would have been possible.

Doll (1971) has suggested that the relationship between the incidence of some site-specific cancers, age, and exposure level of a population may be expressed as:

$$I(x,t) = kBx^m t^{k-1} \qquad (21)$$

where x is the exposure level (which can be measured by the water concentration in ppm), t is the age of the population, and B, m, k are unknown parameters.

However, the data collected by Tseng et al. (1968) was obtained at one point in time, and since skin cancer has only a marginal effect on the death

rate, the obtained rates may be viewed more accurately as the probability of having contracted skin cancer by time t. The relationship between this probability, often referred to as the cumulative probability density or prevalence F(x,t), and the incidence or age-specific or hazard rate, may be expressed as:

$$F(x,t) = 1 - \exp\left[-\int_0^t I(x,s)\, ds\right]. \qquad (22)$$

Utilizing equation (21) as the form of the incidence rate, the prevalence may be expressed as

$$F(x,t) = 1 - \exp\left(-Bx^m t^k\right), \qquad (23)$$

which is a Weibull distribution.

In Table 7-36, adapted from information in Tseng, et al. (1968), estimates are given of F(x,t) for different age and water concentration groupings for males. The prevalence for females is less than for males, and therefore is not used to estimate risk.

To use this data, specific values for x and t had to be obtained for the intervals. Where the intervals were closed, the midpoint was utilized. For the greater than 0.6 ppm group, the midpoint between 0.6 and the greatest recorded value, 1.8, was taken, resulting in 1.2 ppm. For age 60 or greater, a value of 70 was utilized somewhat arbitrarily, being the same increase over the lower level as that in the other two age intervals. The values for (x,t) to relate to the prevalence estimates are shown in parentheses in Table 7-36.

From equation (23) it follows that

$$\ln(-\ln[1-F(x,t)]) = \ln(B) + m\ln(x) + k\ln(t), \qquad (24)$$

which is multiple-linear in form. Estimating the parameters by the usual least-square techniques, the following relationship is obtained:

TABLE 7-36. AGE-EXPOSURE-SPECIFIC PREVALENCE RATES FOR SKIN CANCER

Exposure in ppm[3]	AGE 20-39 (30)	AGE 40-59 (50)	AGE ≥60 (70)
0 - 0.29 (0.15)	0.0013	0.0065	0.0481
0.30 - 0.59 (0.450)	0.0043	0.0477	0.1634
≥0.6 (1.2)	0.0224	0.0983	0.2553

*Source: Tseng et al. (1968).

[a]Range given by authors. Midpoint is in parentheses.

$$\ln(- \ln[1 - F(x,t)]) = 17.548 + 1.192 \ln(x) + 3.881 \ln(t), \quad (25)$$

which is an excellent fit, having a multiple correlation coefficient of 0.986 and a standard error on the exposure regression m of .138.

Equation (25) may be expressed as

$$F(x,t) = 1\text{-}\exp\text{-}[2.429 \times 10^{-8}(X^{1.192})(t^{3.881})]$$
$$= 1\text{-}\exp\text{-}[X^{1.192}\ H(t)] \quad (26)$$

If the parameter m = 1.192 were in fact equal to 1, then for a given value of t, equation (26) would be "one-hit" in form.

To test this hypothesis (i.e., Ho: m = 1) the student "t" test is used, giving the result:

$$t_6 = \frac{1.192 - 1}{0.138} = 1.391,$$

which is not significant at the 0.1 level. Thus, there is insufficient evidence to reject the hypothesis that the dose-response relationship is "one-hit" even at the 0.1 level. However, a quadratic model would be rejected at the $p<.001$ level.

Fixing m = 1, the following relationship is obtained:

$$F(x,t) = 1 - \exp[-g(t)x] \qquad (27)$$

Transforming this equation to its linear form (as in equation 23) and obtaining the least-square linear estimates of B and v, it is found that:

$$g(t) = \exp(-17.5393)\, t^{3.853}, \text{ where } B = 2.41423 \times 10^{-8}, \; k = 3.853.$$

The data used to obtain these estimates are shown in Table 7-37, and the goodness-of-fit is illustrated in Figure 7-11.

TABLE 7-37. DATA UTILIZED TO OBTAIN PREDICTOR EQUATION AND FIGURE 7-11

ppm Arsenic	Age at Medical Examination	Skin Cancer Prevalence Rate		Transformed Skin Cancer Prevalence Rate	
		F(x,t)		$-\ln(-\ln[1-F(x,t)])=$ $-17.5393 + 3.853\ln t + \ln x$	
x	t	Observed Rate	Expected Rate	Observed	Expected
0.15	30	0.0013	0.0031	6.64474	6.33160
	50	0.0063	0.0127	5.03269	4.36341
	70	0.0481	0.0455	3.00993	3.06695
0.45	30	0.0043	0.0053	5.44699	5.23299
	50	0.0477	0.0375	3.01849	3.26480
	70	0.1634	0.1304	1.72368	1.96834
1.20	30	0.0224	0.0141	3.78739	4.25216
	50	0.0983	0.0969	2.26844	2.28397
	70	0.2553	0.3110	1.22155	0.98751

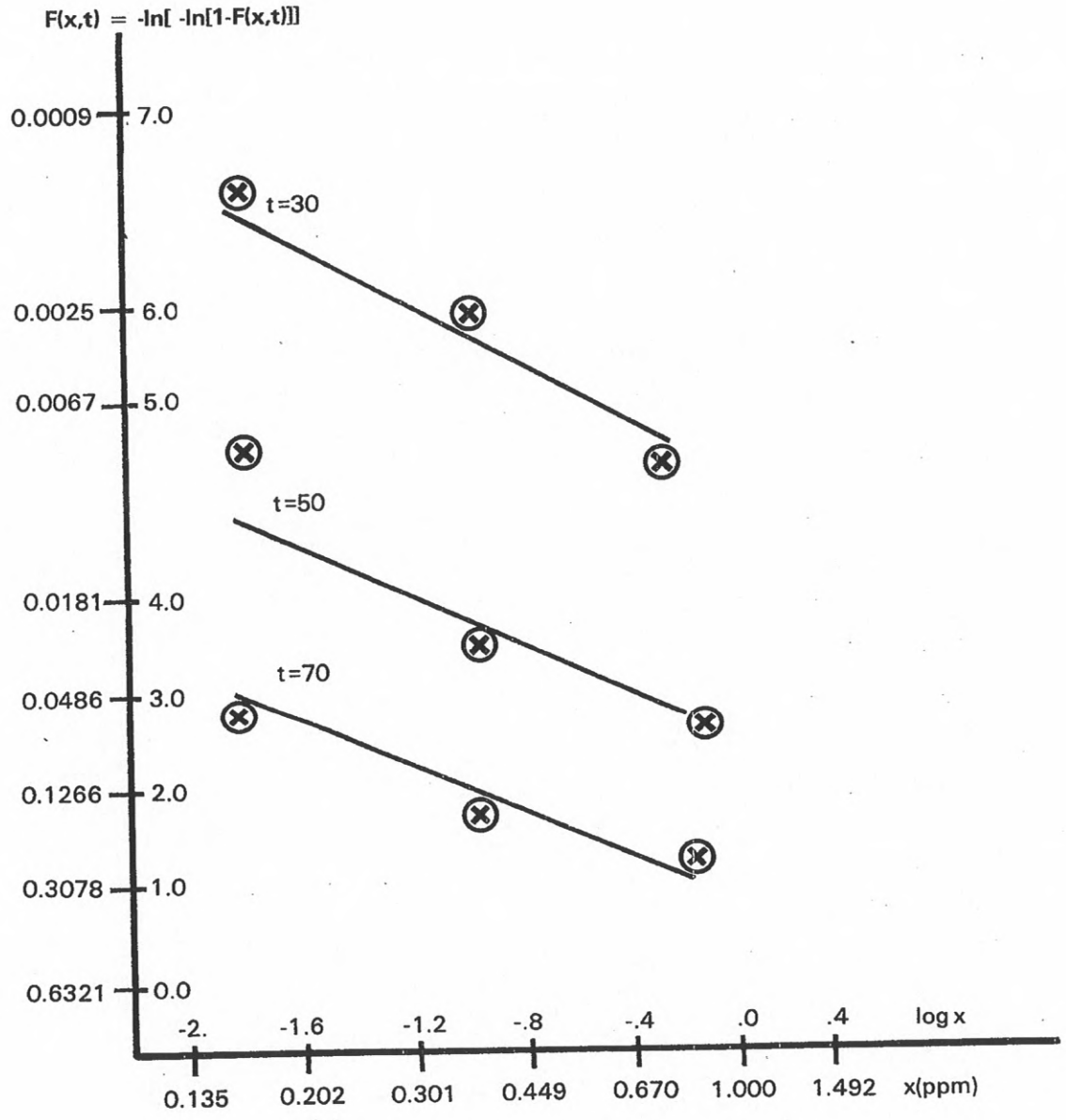

Figure 7-11. Relationship between transformed prevalence and log ppm arsenic in water, log age.

The function

$$F(x,t) = 1-\exp[-2.41423 \times 10^{-8} \times t^{3.853}], \qquad (28)$$

is the probability of contracting skin cancer by age t, given that an individual had a life-time exposure to x ppm in his drinking water (and lived until age t).

To obtain a unit risk estimate, lifetime risk is assumed to be approximately equal to the risk to the median life span in the absence of competing risk. The unit risk is thus obtained by substituting x = 1 and t = 76.2 (the median U.S. life span based upon 1976 vital statistics data) into equation (28). This gives the result

$$P(1) \tilde{-} 1-\exp[-2.414 \times 10^{-8} \times 76.2^{3.853}] = .350 \qquad (29)$$

The exponent is the slope estimate for cancer risks at low doses, so that:

$$P(x) \tilde{-} .430\ x \qquad \text{for small } x, \text{ where } x \text{ is in ppm.} \qquad (30)$$

To express the unit in mg/kg/day exposures, it is assumed that two liters of water are consumed per day by an individual weighing 70 kg. Under the assumption that 100 percent of the arsenic is absorbed through the gut, the slope in units of mg/kg/day absorbed dose is $.430 \div (.2 \div 70) = 15.8$.

A number of potential factors exist that could possibly make the Taiwanese data unsuitable as surrogate data for the U.S. population. Among them are racial, dietary, and nutritional differences. Also, exposure to ergotamine was confounded with arsenic exposure in the well water--a fact which also could have modified the results. However, there is no direct evidence demonstrating the role of these agents in the carcinogenic response to ingested arsenic. Furthermore, a recent extensive review by Andelman and Barnett (1983)

of the arsenic dose-response model developed here, demonstrates that presently there is no quantitative evidence that is inconsistent with the model. The Andelman and Barnett study also showed that there does not appear to be any population in the U.S. that could be studied that would have a reasonable power to contradict the hypothesis that the Taiwanese dose-response model is consistent with the U.S. dose response.

7.3.4 Relative Potency

One of the uses of the concept of unit risk is to compare the relative potencies of carcinogens. To estimate relative potency on a per-mole basis, the unit risk slope factor is multiplied by the molecular weight, and the resulting number is expressed in terms of $(mMol/kg/day)^{-1}$. This is called the relative potency index.

Figure 7-12 is a histogram representing the frequency distribution of potency indices of 52 chemicals evaluated by the CAG as suspect carcinogens. The actual data summarized by the histogram are presented in Table 7-38. Where human data were available for a compound, they were used to calculate the index. Where no human data were available, animal oral studies and animal inhalation studies were used, in that order. Animal oral studies were selected over animal inhalation studies because they have been made on most of the chemicals, thus allowing potency comparisons by route.

The potency index for arsenic, based on the Tseng et al. study, is 2.25×10^3 $(mMol/kg/day)^{-1}$. This is derived by means of the slope estimate from the Tseng et al. study, which is $15(mg/kg/day)^{-1}$.

Multiplication by the molecular weight of 149.8 gives a potency index of $2.25 \times 10^{+3}$. Rounding off to the nearest order of magnitude gives a value of 10^{+3}, which is the scale presented on the horizontal axis of Figure 7-12. The index of $2.25 \times 10^{+3}$ lies at the bottom of the first quartile of the 52 suspect carcinogens.

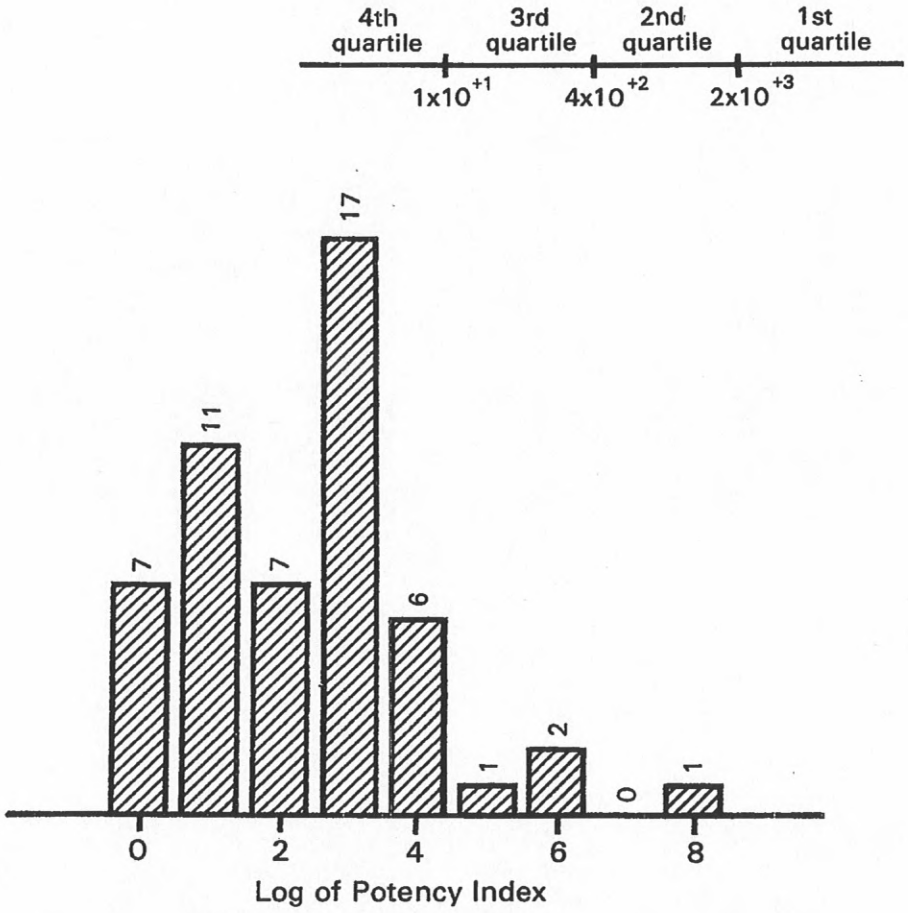

Figure 7-12. Histogram representing the frequency distribution of the potency indices of 52 suspect carcinogens evaluated by the Carcinogen Assessment Group.

TABLE 7-38. RELATIVE CARCINOGENIC POTENCIES AMONG 52 CHEMICALS EVALUATED BY THE CARCINOGEN ASSESSMENT GROUP AS SUSPECT HUMAN CARCINOGENS

Compounds	Slope (mg/kg/day)-1	Molecular Weight	Potency Index	Order of Magnitude (log_{10}) Index
Acrylonitrile	0.24(W)	53.1	$1x10^{+1}$	+1
Aflatoxin B_1	2924	312.3	$9x10^{+5}$	+6
Aldrin	11.4	369.4	$4x10^{+3}$	+4
Allyl Chloride	$1.19x10^{-2}$	76.5	$9x10^{-1}$	0
Arsenic	15(H)	149.8	$2x10^{+3}$	+3
B[a]P	11.5	252.3	$3x10^{+3}$	+3
Benzene	$5.2x10^{-2}$(W)	78	$4x10^{0}$	+1
Benzidine	234(W)	184.2	$4x10^{+4}$	+5
Beryllium	4.86	9	$4x10^{+1}$	+2
Cadmium	6.65(W)	112.4	$7x10^{+2}$	+3
Carbon Tetrachloride	$1.30x10^{-1}$	153.8	$2x10^{+1}$	+1
Chlordane	1.61	409.8	$7x10^{+2}$	+3
Chlorinated Ethanes				
1,2-dichloroethane	$6.90x10^{-2}$	98.9	$7x10^{0}$	+1
1,1,2-trichloroethane	$5.73x10^{-2}$	133.4	$8x10^{0}$	+1
1,1,2,2-tetrachloroethane	0.20	167.9	$3x10^{+1}$	+1
Hexachloroethane	$1.42x10^{-2}$	236.7	$3x10^{0}$	0
Chloroform	$7x10^{-2}$	119.4	$8x10^{0}$	+1
Chromium	41	104	$4x10^{+3}$	+4
DDT	8.42	354.5	$3x10^{+3}$	+3
Dichlorobenzidine	1.69	253.1	$4x10^{+2}$	+3
1,1-dichloroethylene	1.04(I)	97	$1x10^{+2}$	+2
Dieldrin	30.4	380.9	$1x10^{+4}$	+4

TABLE 7-38. (continued)

Compounds	Slope (mg/kg/day)-1	Molecular Weight	Potency Index	Order of Magnitude (log_{10}) Index
Dinitrotoluene	0.31	182	$6x10^{+1}$	+2
Diphenylhydrazine	0.77	180	$1x10^{+2}$	+2
Epichlorohydrin	$9.9x10^{-3}$	92.5	$9x10^{-1}$	0
Bis(2-chloroethyl)ether	1.14	143	$2x10^{+2}$	+2
Bis(chloromethyl)ether	9300(I)	115	$1x10^{+6}$	+6
Ethylene Dibromide (EDB)	8.51	187.9	$2x10^{+3}$	+3
Ethylene Oxide	0.63(I)	44.0	$3x10^{+1}$	+1
Formaldehyde	$2.14x10^{-2}$(I)	30	$6x10^{-1}$	0
Heptachlor	3.37	373.3	$1x10^{+3}$	+3
Hexachlorobenzene	1.67	284.4	$5x10^{+2}$	+3
Hexachlorobutadiene	$7.75x10^{-2}$	261	$2x10^{+1}$	+1
Hexachlorocyclohexane				
technical grade	4.75	290.9	$1x10^{+3}$	+3
alpha isomer	11.12	290.9	$3x10^{+3}$	+3
beta isomer	1.84	290.9	$5x10^{+2}$	+3
gamma isomer	1.33	290.9	$4x10^{+2}$	+3
Nickel	1.15(W)	58.7	$7x10^{+1}$	+2
Nitrosamines				
Dimethylnitrosamine	25.9(not by q_1^*)	74.1	$2x10^{+3}$	+3
Diethylnitrosamine	43.5(not by q_1^*)	102.1	$4x10^{+3}$	+4
Dibutylnitrosamine	5.43	158.2	$9x10^{+2}$	+3
N-nitrosopyrrolidine	2.13	100.2	$2x10^{+2}$	+2
N-nitroso-N-ethylurea	32.9	117.1	$4x10^{+3}$	+4
N-nitroso-N-methylurea	302.6	103.1	$3x10^{+4}$	+4
N-nitroso-diphenylamine	$4.92x10^{-3}$	198	$1x10^{0}$	0
PCBs	4.34	324	$1x10^{+3}$	+3
Phenols				
2,4,6-trichlorophenol	$1.99x10^{-2}$	197.4	4x10	+1

TABLE 7-38. (continued)

Compounds	Slope (mg/kg/day)-1	Molecular Weight	Potency Index	Order of Magnitude (log_{10}) Index
Tetrachlorodioxin	$4.25x10^{5}$	322	$1x10^{+8}$	+8
Tetrachloroethylene	$5.31x10^{-2}$	165.8	$9x10^{0}$	+1
Toxaphene	1.13	414	$5x10^{+2}$	+3
Trichloroethylene	$1.26x10^{-2}$	131.4	$2x10^{0}$	0
Vinyl Chloride	$1.75x10^{-2}$(I)	62.5	$1x10^{0}$	0

Remarks:

1. Animal slopes are 95% upperlimit slopes based on the linear multistage model. They are calculated based on animal oral studies, except for those indicated by I (animal inhalation), W (human occupational exposure), and H (human drinking water exposure). Human slopes are point estimate, based on the linear non-threshold model.

2. The potency index is a rounded-off slope in (mMol/kg/day)-1 and is calculated by multiplying the slopes in (mg/kg/day)-1 by the molecular weight of the compound.

3. Not all the carcinogenic potencies presented in this table represent the same degree of certainty. All are subject to change as new evidence becomes available.

Ranking of the relative potency indices is subject to the uncertainty involved in comparing estimates of potency for different chemicals based on different routes of exposure to different species, and using studies of different quality. Furthermore, all the indices are based on estimates of low-dose risk using linear extrapolation from the observational range. Thus, these indices are not valid for the purpose of comparing potencies in the experimental or observational range if linearity does not exist there.

7.3.5 Summary and Conclusions of the Carcinogenicity of Arsenic

7.3.5.1 Qualitative Summary--Human studies of the effects of arsenic from smelters, drinking water, pesticide manufacturing plants, and medicinals have

been conducted. These are summarized in Table 7-1. Studies of five independent smelter worker populations have all found an association between occupational arsenic exposure and lung cancer mortality. Several of the smelter studies have found a dose response both by intensity and by duration of exposure. The risk of lung cancer mortality in the high dose group of one study of smelter workers in Japan was found to be 10 times that expected. Some of the recent data from these smelter studies suggest that, if the multistage theory of carcinogenesis is correct, arsenic may act as a late-stage carcinogen. It is also possible to hypothesize from some of the data that arsenic may be a promoter. Either of these hypotheses, however, requires further study. In addition, some studies of communities surrounding smelters have found an association between geographic proximity to the smelter and lung cancer mortality.

Both proportionate mortality and cohort studies of pesticide manufacturing workers have demonstrated an excess of lung cancer deaths among workers in that occupation. One study of the population around a pesticide manufacturing plant found that residents of the area surrounding the plant were also at an excess risk of lung cancer. Several case reports of arsenical pesticide applicators have also shown an association between arsenical exposure and lung cancer.

A study of 40,000 persons in Taiwan exposed to arsenic in the drinking water found a significant excess prevalence of skin cancer over that of 7,500 other Taiwanese and residents of Matsu Island who drank water relatively free of arsenic. Water supplies in Chile and Argentina were also reported to be the cause of arsenic-induced skin cancers. In contrast, studies of populations in the United States exposed to relatively high levels of arsenic in the drinking water by U.S. standards did not find any excess of skin cancer.

The difference in response between the Taiwanese and the United States studies may reflect the fact that the drinking water in the study area in Taiwan

contained much higher levels of arsenic than did the drinking water in the United States. Furthermore, the Taiwanese waters also contained ergotamine-like compounds. Other differences between the two study areas include differences in socioeconomic status, with the Taiwanese who developed skin cancer belonging to a rather low socioeconomic strata which could have had ramifications in terms of diet, personal hygiene and medical care. Racial differences may have also contributed to the differences between the study results. In addition to these physical and cultural differences, the U.S. studies were limited by small sample sizes and would not have detected the risk from skin cancer that would have been predicted, on the basis of arsenic ingestion, from a linear model of the Taiwanese data.

Persons exposed to arsenical medicinals have also been shown to be at a risk of skin cancer.

Using the International Agency for Research on Cancer (IARC) classification scheme for evaluating carcinogens, the evidence for arsenic as a human carcinogen is considered sufficient. This is evidenced by the high relative risks, the consistency in findings in different studies, and the specificity of tumor sites (i.e., skin and lungs).

Consistent demonstration of arsenic carcinogenicity in test animals, using different chemical forms, routes of exposure, and various experimental species, has not been observed. Nevertheless, recent data indicate that tumorigenicity and possibly carcinogenicity can be demonstrated in animals if the retention of arsenic in the lung is increased. The additional observation that calcium arsenate is only slowly cleared from the lung, strongly suggests that this agent may be carcinogenic. In support of the recent animal studies, is the observation that cultured Syrian hamster embryo cells can be transformed by direct exposure to sodium arsenate.

7.3.5.2 Quantitative summary--Unit risks are estimated for both air and water exposures to arsenic. The air estimates were based on data obtained in five separate studies involving three independently exposed worker populations. Linear and quadratic dose-response models in both the absolute and relative form are fitted to the worker data. It was found that for the models that fit the data at the P = .01 or better level that the corresponding unit risk estimates ranged from 1.05×10^{-4} to 1.36×10^{-2}. However, linear models fit better than quadratic models and absolute better than relative models. Also it was felt that exposure to trivalent arsenic was more representive of low environmental exposure than pentavalent arsenic. Restricting unit risk estimates to those obtained from linear absolute models where exposure was to trivalent arsenic gives a range of 1.25×10^{-3} to 7.6×10^{-3}. A weighted average of the five estimates in this range gave a composite estimate of 4.29×10^{-3}.

An extensive drinking water study of the association between arsenic in well water and an examination for skin cancer of a population who lived in a rural area of Taiwan was used to estimate the unit risk for ingestion. Using the male population who appeared to be more susceptible, it was estimated that the unit risk associated with drinking water contaminated with 1 µg/ℓ of arsenic was 4.3×10^{-4}. To compare the air and water unit risks, the exposure units in both cases were converted to mg/kg/day absorbed doses, resulting in unit risk estimates of 50.1 and 15.0, respectively.

The potency of arsenic compared to other carcinogens is evaluated by noting that an arsenic potency of $2.25 \times 10^{+3}$ $(\text{mMol/kg/day})^{-1}$ lies in the first quartile of the 52 suspect carcinogens that have been evaluated by CAG.

7.3.5.3 Conclusions--Skin cancer and lung cancer have been shown by numerous epidemiologic studies to have an association with arsenic exposure. Arsenic

has not definitively been found to be a carcinogen in animal studies, however. In applying the IARC criteria for evaluating a substance as to the weight of evidence for human carcinogenicity, arsenic would be placed in group 1, which IARC characterizes as "carcinogenic to humans."

Using the linear absolute risk model, the composite estimate for cancer risk due to a lifetime exposure to 1 $\mu g/m^3$ trivalent arsenic in the air is estimated to be 4.29×10^{-3}. The unit risk due to lifetime exposure to 1 $\mu g/\ell$ of arsenic in drinking water is estimated to be 4.3×10^{-4}. On the basis of mg/kg/day absorbed dose, the unit-risk slope estimates for air and water are 50.1 and 15, respectively. While it is unlikely that the true risks would be higher than these estimates, they could be substantially lower. Compared to other compounds on a mole unit basis, the carcinogenic potency for arsenic falls towards the lower end of the first quartile.

8. ARSENIC AS AN ESSENTIAL ELEMENT

Mertz (1970) has set forth a set of logical criteria which trace elements should obey in order to be considered physiologically essential for man and/or animals. One of the most obvious of these, and one which should be readily demonstrable, is that the element meet a unique requirement physiologically, and, consequently, that a deficiency in that element be associated with deleterious effects.

In the case of arsenic, early reports attempting to show a nutritional requirement for the element in animals were inconclusive (Arsenic. NAS, 1977; Underwood, 1977). Part of the problem was undoubtedly technical in nature, i.e., the difficulty of carrying out such studies in an experimental environment where rigorous exclusion of a ubiquitous element from the diet is necessary. More recently, however, several carefully controlled studies have been reported to have demonstrated nutritional essentiality for arsenic in at least some mammalian species.

Nielsen et al. (1978) have noted that deprivation of pregnant rats of arsenic-supplemented diets resulted in offspring showing such post-weaning effects as slow growth, enlarged spleens, and increased red cell osmotic fragility. Greater perinatal mortality among pups from arsenic-deprived dams was also noted in a second experimental group.

In a recent review by Uthus et al. (1983), the authors reported on studies with chicks that suggest that arsenic influences arginine metabolism. It was reported that arsenic deprivation influenced the effects of dietary arginine, manganese and zinc, the fluctuations of which variously affected growth, kidney arginase, plasma alkaline phosphatase, plasma urea, plasma uric acid

and hematocrit. The authors suggested that the four components interacted to affect the conversion of arginine into urea and ornithine.

Anke et al. (1978) studied the nutritional requirements for arsenic using goats and mini-pigs and a semi-synthetic diet containing less that 50 ppb arsenic. Effects attributed to arsenic deficiency in both species were seen not only in the adult animals but in their offspring. Arsenic deficiency increased the mortality of adult goats as well as altered the mineral profiles for copper and manganese in the carcass. Significant reproductive effects for both arsenic-deficient goats and mini-pigs included reduction of the normal litter size. Furthermore, the mortality of kids and piglets from the arsenic-deficient groups was significantly higher than controls. Manganese levels were elevated in arsenic-deficient kids and piglets, but no perturbation of hematological indices (hemoglobin, hematocrit or mean corpuscular concentration) was noted. This is in contrast to the experimental observations with rats (Nielsen et al., 1974), where decreased hematocrits, elevated iron content in spleen and increased osmotic fragility of cells are seen. Given the fact that the rat is known to be an anomalous animal model for arsenic metabolism (see Chapter 4), this difference is probably peculiar to this species.

Schwartz (1977) has noted growth effects of arsenite on rats fed an arsenic-supplemented diet, with an optimal effect seen at 0.25 to 0.5 ppm. Interestingly, this worker noted that pentavalent arsenic as sodium arsenate is less effective.

Remaining to be independently demonstrated is a physiological role for arsenic, the existence of any specific carrier agent in the body, or arsenic essentiality in man.

A feature of essential element metabolism is homeostatic control of levels and movement of a particular element in vivo. From the information

considered earlier, there is no effective absorption barrier for most soluble inorganic arsenicals, but efficient excretory mechanisms (kidney, hair) and biotransformation appear to provide some control over any absorption-excretion balance.

9. HUMAN HEALTH RISK ASSESSMENT FOR ARSENIC

This portion of the report places the information in the earlier Chapters into a quantitative perspective with regard to non-occupational population exposure and health effects of arsenic germane to such a population.

Data for levels of arsenic encountered by humans in air, water, food and other sources, such as cigarette smoking, were set forth in Chapter 3 and are combined with data on rates of intake and rates of absorption to provide information on the total assimilation of arsenic on a daily basis. Health effects of arsenic most germane to non-occupational population exposures are then summarized. Generally, these are chronic effects associated with long-term intake of relatively low levels of arsenic. In the case of hazardous wastes, however, some health effects of concern may be associated with acute exposures; therefore, acute and sub-acute effects must also be considered.

The section dealing with dose-effect/dose-response data includes consideration of various indices of internal exposure followed by quantitative data for intake and population response.

Populations at risk, identified at least along qualitative lines, are included for discussion.

9.1 AGGREGATE EXPOSURE LEVELS TO ARSENIC IN THE U.S. POPULATION

Among individuals of the general population (not occupationally exposed to arsenic), the main routes of exposure to arsenic are typically via ingestion of food and water, with lesser exposures occurring via inhalation. Representative intake figures are presented in Table 9-1. Intake by inhalation is augmented among smokers in proportion to the level of smoking.

TABLE 9-1. ROUTES OF DAILY HUMAN ARSENIC INTAKE

Route/level	Rate	Total intake	Absorbed amount
Ambient air/0.006 μg/m^3[a]	20 m^3	0.12 μg	0.036 μg[b]
Drinking water/≤ 10 μg/liter	2 liters	≤ 20 μg	≤ 20 μg[c]
Food/50 μg daily (elemental As)	--	50 μg	40 μg[d]
Cigarettes/6 μg in mainstream smoke/pack[e]	1/2 pack	3 μg	0.9 μg[f]
	1 pack	6 μg	1.8 μg[f]
	2 pack	12 μg	2.7 μg[f]
Total: ≤ 60 μg nonsmokers			

[a] National average for 1981 (see Section 3.3.1)
[b] Assumes 30 percent respiratory absorption (see Chapter 4).
[c] Assumes total absorption (see Chapter 4).
[d] Assumes 80 percent absorption (see Chapter 4).
[e] Assumes 20 percent of cigarette content in inhaled smoke (see Chapter 4).
[f] Assumes 30 percent absorption of inhaled amount (see Chapter 4).

Assuming a daily ventilation rate of 20 m^3, and a national population inhalation average of 0.006 μg/m^3/As, the total daily inhalation exposure for arsenic can be projected to be approximately 0.12 μg. Assuming 30 percent absorption, approximately 0.03 μg of arsenic would be absorbed on a daily average.

Contribution of tobacco-borne arsenic to the respiratory burden would depend upon the rate of cigarette smoking. If one assumes a mass of 1 gram/cigarette and an average tobacco value of 1.5 ppm, this yields 1.5 μg arsenic/cigarette. With 20 percent of this amount in mainstream smoke, the inhaled amount for each pack of cigarettes would be approximately 6 μg arsenic, and of this amount, 40 percent would be deposited in the respiratory tract (see Chapter 4). Assuming an absorption of 75 percent of the deposited fraction, one arrives at an absorption of approximately 2 μg/pack of cigarettes or a

factor of 10 to 100 times greater than intake for nonsmokers in given ambient air settings. One may assume that the rates of absorption for trivalent and pentavalent arsenic in the respiratory tract are equivalent.

Since drinking water arsenic is mainly in a soluble form (arsenate or arsenite), virtually all of it is absorbed in the GI tract (see Chapter 4). Thus, assuming an average daily consumption of two liters of water containing at most 10 µg As/liter as an outside high figure, one can estimate that the total arsenic absorbed from drinking water would be approximately 20 µg/day. Most individuals would, in reality, take in much less than this amount, while those in the Western U.S. with well water supplies much higher in arsenic content would assimilate proportionately more.

Food arsenic values taken from the 1974 FDA survey indicate a daily total dietary intake of approximately 50 µg elemental arsenic. Based on information presented in Chapter 4, the major portion (80 percent) of food arsenic would be absorbed resulting in a net daily food arsenic absorption of 40 µg total.

Thus, a non-smoker would have a total daily absorption from all exposure media of approximately 60 µg arsenic/day or less. Of this, the diet would be the major contributor, assuming levels in water much below 10 µg/liter. For cigarette smokers, one would add 2 µg arsenic/pack of cigarettes smoked daily.

If one views aggregate intake not in terms of total arsenic intake but in terms of toxicologically significant forms of the element, then much of the dietary fraction, for reasons given earlier, such as complex organoarsenicals being present, becomes relatively less important than the forms in water and air as well as in cigarette smoke. Arsenic forms in such media include: pentavalent arsenic in most water supplies; variable mixtures of tri-and pentavalent arsenic in ambient air; and probably an arsenic oxide in cigarette smoke. From this view point, utilizing the examples already given above, non-

smokers would absorb 20 μg or less daily of toxicologically significant arsenic. Heavy smokers having otherwise very low air and water exposure, conceivably could receive their major exposure via cigarettes.

9.2 SIGNIFICANT HUMAN HEALTH EFFECTS ASSOCIATED WITH AMBIENT EXPOSURES

9.2.1 Acute Exposure Effects

Serious acute effects and late sequelae from exposure to arsenic will appear after single or short-term respiratory or oral exposures to large amounts of arsenic. Available data indicate that inorganic trivalent compounds of arsenic are generally more acutely toxic than inorganic pentavalent compounds, which in turn are more toxic than organic arsenic compounds. Serious effects will also appear after long-term exposure to respiratory or oral doses of arsenic.

The acute symptoms following oral exposure consist of gastrointestinal disturbances, which may be so severe that secondary cardiovascular effects and shock may result and cause death. Also, direct toxic effects on the liver, blood-forming organs, the central and peripheral nervous systems, and the cardiovascular system may appear. Some symptoms, especially those from the nervous system, may appear a long time after exposure has ceased and may not be reversible, whereas the other effects seem to be reversible. Infants and young children especially are susceptible with regard to effects on the central nervous system. The Japanese follow-up after the Morinaga milk poisoning showed that persisting damage, especially mental retardation and epilepsy, is a late sequela in children of short-term oral exposure to large doses of inorganic arsenic. Among adults, the central nervous system is not as susceptible, but peripheral neuropathy has been a common finding.

Both in adults and children, acute oral exposure has resulted in dermal changes, especially hyperpigmentation and keratosis, as a late sequela.

Acute inhalation exposures have also resulted in irritation of the upper respiratory tract, even leading to nasal perforations.

Direct dermal exposure to arsenic may lead to dermal changes; allergic reactions may also be involved.

9.2.2 Chronic Exposure Effects

Both carcinogenic and non-carcinogenic effects are associated with long-term exposures, which do not cause any obvious immediate effects. For the purpose of this document, such chronic effects will be discussed in sequence as follows:

1. Respiratory tract cancer
2. Skin cancer
3. Non-cancerous skin lesions
4. Peripheral neuropathological effects
5. Cardiovascular changes

Cancer of the respiratory system is clearly associated with exposure to arsenic via inhalation. This association has been especially noted among workers engaged in the production and usage of pesticides and among smelter workers. While it is not known to what extent exposure to other compounds in industrial atmospheres has contributed to the excess of lung cancer, the Carcinogen Assessment Group (CAG) has concluded that there is sufficient evidence that inorganic arsenic compounds are lung carcinogens in humans.

Cancer of the skin has been found as a dose-related effect in a population in Taiwan, with lifetime exposure to arsenic in well water. It has also been found among people treated with large doses of arsenite for skin disorders. Skin cancer often has a long latency period on the order of decades, the latency time decreasing with increasing intensity of exposure. The CAG has concluded that there is sufficient evidence that inorganic arsenic compounds are skin carcinogens in humans.

Hyperkeratosis and hyperpigmentation, sometimes with precancerous changes, have been a common finding in persons ingesting arsenic. These skin lesions, as well as the manifest cancer, develop on skin surfaces usually unexposed to sunlight. In studies in the United States, an association between skin lesions or skin cancer has not been demonstrated. These studies have been limited, however, by sample sizes too small to be able to detect the dose response seen in studies outside the U.S.

The effects on the peripheral nervous system range from sensory disturbances to motor weakness and even paralysis. The more severe signs have been noted in subacute poisonings, but more subtle changes after long-term low-level exposure have been found by using electromyography or measuring nerve conduction velocity. These subclinical effects are slow in recovery and may persist for years after cessation of exposure. In a study in Canada, electromyographic (EMG) changes were noted when water concentrations of arsenic exceeded 0.05 mg/l.

Cardiovascular effects have been noted especially in Taiwan, where Blackfoot disease (peripheral vasculopathy) occurred after long-term exposure to arsenic in well water. However, the presence of ergotamine-like compounds raises the possibility of vascular effects from these agents. Peripheral vascular changes were also found among German vintners who were exposed both occupationally, by spraying arsenic-containing pesticides, and orally, by drinking wine with elevated arsenic levels. Studies on occupationally-exposed persons have been inconclusive in showing that arsenic causes an increase in mortality from cardiac disease.

9.3 DOSE-EFFECT/DOSE-RESPONSE RELATIONSHIPS

9.3.1 General Considerations

This section generally attempts to define, as presently feasible, human dose-effect/dose-response relationships for health effects of likely greatest

concern at ambient environment exposure levels for arsenic in the United States. As such, the present section highlights mainly the quantitative carcinogenic risk estimates that were derived in Section 7.3.

The general question of how to define and employ a dose factor in attempts at quantitative assessments of human health risk for any toxicant is highly dependent upon: 1) the available information on the body's ability to metabolize the agent, and 2) the assessment of the relative utility of various internal indices of exposure.

The time period over which a given total intake occurs is highly important. For example, intake of one gram of arsenic over a period of years would be quite different pathophysiologically from assimilating this amount at one time, the latter probably having a lethal outcome. This time-dependent behavior is related in part to the relative ability of the body to detoxify inorganic arsenic by methylation as a function of both dose and time.

In cases of acute and sub-acute exposure, indicators of internal exposure such as blood or urine arsenic levels are probably appropriate for assessing the intensity of exposure.

With chronic, low-level exposure, however, the available data would indicate that the total amount assimilated is probably more important than an indicator concentration without knowledge of the total exposure period. An added problem is the background level of arsenic found in these indicators due to dietary habits. For example, in acute exposures, levels in blood or urine would be greatly elevated over background values while low-level chronic exposures would only result in moderate increases over background.

In regard to hair arsenic levels as an indicator of internal arsenic exposure, no reliable methods exist for distinguishing external contamination levels from those accumulated via absorption and metabolic distribution. Hair arsenic levels cannot, therefore, be employed as reliable indicators of either

current or cumulative long-term exposures for individual subjects, but rather may provide only a rough overall indication of group exposure situations.

Given the above considerations and limitations concerning the use of blood, urinary or hair arsenic concentrations as internal indices of cumulative, long-term low-level arsenic exposures of concern here, the dose-effect/dose-response relationships summarized below are done so mainly in terms of external arsenic exposure levels via either inhalation or ingestion.

9.3.2 Effects and Dose-Response Relationships

It is difficult to define a precise acute lethal dose of arsenic for man, because such exposure situations rarely allow accurate determination of the effective amounts. However, for trivalent arsenic, the figure is believed to range from 70 - 180 milligrams.

For subacute exposure, it appears that for children, about one gram assimilated over a period of 3-4 weeks will induce death with severe effects in survivors, while for adults, that dose will occasion significant clinical effects. In one poisoning episode, intake of approximately 50 milligrams over a period as short as two weeks resulted in clinically demonstrable effects in adults.

9.3.2.1 Respiratory Cancer--A considerable number of studies have shown associations between occupational exposure to arsenic and cancer of the respiratory system. The best information available for making quantitative risk estimates for lung cancer are derived from 5 sets of data involving 4 sets of investigators and 2 distinct exposed populations. The 4 sets of investigators are Brown and Chu (1983a,b,c), Lee-Feldstein (1983) and Higgins (1982)--who conducted studies on workers at the Anaconda smelter in Montana--and Enterline and Marsh (1982)--who conducted a study on the workers at the ASARCO smelter in Tacoma, Washington.

Using an absolute-risk linear model and the data from the four smelter studies, the lifetime lung cancer risk, due to continuous exposure of 1 μg/As/m^3, was estimated to range from 1.25×10^{-3} to 7.6×10^{-3}. A weighted average of the five estimates* in this range gave a composite estimate of 4.29×10^{-3} (see Section 7.3.2.3). This represents a plausible estimate of the upper limit of risk--that is, the true risk would not likely be more than the estimated risk, but it could be substantially lower.

9.3.2.2 Skin Cancer--Chronic arsenic exposure, both occupational and non-occupational, is associated with a distinctive hyperkeratosis, which is usually followed by a later onset of skin cancer. The best data available for making quantitative risk estimates for skin cancer are the data collected by Tseng et al. (1968). In this study, the authors surveyed a stable population of 40,421 individuals who lived in a rural area along the southwest coast of Taiwan and who were known to have consumed drinking water containing arsenic. The occurrences of skin cancer among this population and the arsenic concentrations in their drinking water were measured. Since the population was stable, the data obtained from the study lends itself to predictions of lifetime probability of skin cancer caused by the ingestion of arsenic.

Using an absolute-risk linear model and the data from Tseng et al., the lifetime skin cancer risk from drinking water containing 1 μg/liter of arsenic was estimated to be 4.3×10^{-4} (see Section 7.3.3). It is not likely that the true risk for skin cancer would be more than this estimated risk, but it could be considerably lower.

9.3.2.3 Non-cancerous Skin Lesions -- As noted above, in man, chronic oral exposure to arsenic induces a sequence of changes in skin epithelium, proceeding from hyperpigmentation to hyperkeratosis, characterized as keratin proliferation

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*Two risk estimates were derived from the Enterline and Marsh study based upon exposure periods lagged 0 and 10 years. See Table 7-25.

of a verrucose nature and leading, in some cases, to late onset skin cancers. These effects have been noted both in populations which have ingested arsenic via drinking water and among people treated with large doses of arsenite for skin disorders. In a report by Pershagen and Vahter (1979), the authors, using the data from a patient population exposed to arsenic via Fowler's solution (Fierz, 1965), noted an increase in prevalence of hyperkeratosis with increasing dose of arsenic. The U.S. EPA is presently examining this information, along with information from other studies, in order to determine whether quantitative dose-response relationships, similar to those seen for skin cancer, can be established for these precancerous skin lesions.

9.3.2.4 Peripheral Neuropathological Effects and Cardiovascular Changes -- While the qualitative evidence for peripheral neurological effects and cardiovascular changes in arsenic-exposed populations is incontrovertible, the data are insufficient to establish quantitative dose-response relationships at the present time.

9.4 POPULATIONS AT SPECIAL RISK TO ARSENIC EXPOSURE

In reviewing the literature dealing with the acute, subacute and chronic effects of arsenic in children and adults, the evidence suggests that children may be at special risk for the effects of inorganic arsenic under conditions of acute or subacute exposure.

In earlier sections, reference was made to the outbreak of pediatric poisoning by arsenic in Japan due to the presence of arsenic in infant milk formula (Hamamoto et al., 1955). From the clinical reports published at the time of the mass poisoning as well as those from follow-up studies, a number of signs of central nervous system involvement were noted both at the time of the episode and much later, with the follow-up studies showing behavioral problems, abnormal brain wave patterns, marked cognitive deficits, and severe hearing loss in some of those children who survived the acute episode. Some

of these same tardive effects have also been noted in adults but appear to be a much less constant feature of arsenic-induced neurotoxic effects than are the peripheral neuropathies.

Because children consume more water per body weight than do adults, the daily intake of arsenic via drinking water per kilogram body weight would be greater in children. This may have implications regarding chronic exposure effects in children. Zaldivar (1977) developed a regression equation describing this relationship. It should be noted, however, that serious health effects due to chronic exposure of arsenic in drinking water have not been found at a greater frequency in children than adults.

Individuals residing in the vicinity of certain arsenic-emitting sources, e.g., certain types of smelters, may be at risk for increased arsenic intake because of both direct exposure to arsenic in air and indirect exposure via arsenic secondarily deposited from air onto soil or other human exposure media. The relative contribution of such indirect exposures to increased risk of these individuals for arsenic health effects is difficult to define due to the lack of information on this subject. However, it is most likely minimal in relation to the direct effects arising from inhalation of arsenic, including lung cancer.

As a large class of the general population at risk for increased arsenic intake, one would have to include cigarette smokers. However, it is not clear to what extent some increased arsenic intake from tobacco smoke poses a specific heightened health effect risk, although it is clear that internal indicator levels, e.g. blood arsenic, are somewhat elevated in the case of cigarette smokers relative to nonsmokers.

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March 7, 1991

M E M O R A N D O M

To: Orvil Green

From: Robert Wilkosz RW
Tim Teater TT

Subject: Request for layman's explanation of URF & TLV

Attached, per your request is a draft explanation of URF and TLV/100 concepts as utilized in TAP NSR. This, of course, represents our tox. based views of what will do the job. We defer this draft to you for final decision as to what a layman might understand.

In developing emissions limits for new permitted facilities, the Idaho Air Quality Bureau (IAQB) uses the terms Unit Risk Factors and Threshold Limit Values. The following is an explanation of these terms and how they are used.

UNIT RISK FACTOR

A unit risk factor (URF) is used to describe the possibility of developing excess cancers over a average 70 year lifetime. This is based on being exposed to concentration of one microgram of a carcinogenic (cancer causing) substance in one cubic meter (1 $ug/m^{3)}$ of air over the 70 years. The term excess cancers means cases of cancers in excess of what would be normal for a given population. For example, if there was normally 5 cases of a given type of cancer in Anytown USA before a given exposure to some substance and 7 after the exposure, there would be 2 excess cancers.

Inhalation URFs are developed by the U.S. Environmental Protection Agency for carcinogenic substances. Each URF represents months of research and often years of policy process. Teams of toxicologists gathered all the toxicological information for each known or suspected carcinogen that could be found around the world. The available data were then rated or point factored per the quality of the research involved. A URF then is a probability statement derived from this process. Each URF was proposed by EPA

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and extensively reviewed and debated in public by scientists, health officials and industry representatives. Every URF represents a consensus of the best science and health opinion of the potency of a given carcinogen.

URFs are usually expressed as a number times 10 to some negative power. For example, benzine, an organic hydrocarbon found in various petroleum products and cigarette smoke has a unit risk factor of 8.3×10^{-6}. This means that there are 8.3 chances in one million of getting cancer if a person is exposed to 1 ug/m^3 24 hours a day for 70 years.

Another example would be asbestos. Asbestos has a URF of 2.3×10^{-1}. That means that if exposed to 1 ug/m^3 concentration for 70 years, the chances of getting cancer would be 2.3 in 10.

Within IAQB New Source Review (NSR) policy, URFs are used to calculate acceptable ambient levels for a given carcinogen. IAQB generally establishes that an ambient concentration which causes no more excess cancers than one in a million (1×10^{-6}) is acceptable. Once an acceptable ambient level is established, IAQB can then back calculate via engineering equations to an acceptable emission rate (in pounds per hour) for a given stack.

THRESHOLD LIMIT VALUE

Threshold Limit Value (TLV) is a time weighted exposure limit developed by the Occupational and Safety Administration and or the American Council of Government Industrial Hygienists. This value is used to limit the exposure of informed workers to a given toxic substance in the work place. The value is based on exposure of adult males working an eight hour shift. The IAQB uses TLV information to screen proposed new source emissions levels. The IAQB divides the TLV first by a value of 10 due to the fact that an ambient air exposure of a carcinogen means people are usually living under that exposure longer than eight hours out of 24. This value is then again divided by 10 to compensate for the fact that not everyone who is potentially exposed is an adult male. Other people may be more sensitive. The TLV thus is divided by a total of 100 for use in setting an acceptable ambient level.

For example, the TLV for cyanide is 5 milligrams per cubic meter (mg/m^3). An acceptable ambient level under IAQB policy would be 5 divided by 100 or 0.05 mg/m^3. For another example, the TLV for Lindane (an insecticide) would be 0.5 mg/m^3 concentration. The acceptable ambient level would be 0.5 divided by 100 or 0.005 mg/m^3.

As with carcinogens, the TLV derived acceptable ambient levels are used by the IAQB engineers to back calculate an acceptable stack emission rate for any proposed new source. A more pointed treatment these concepts can be found in The Toxic Air Pollutant NSR Policy Summary or the more thorough Draft Guidance Manual for Obtaining a Permit to Construct, Modify or Operate an Air Pollution Source.

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Volume I: Human Health Evaluation Manual
(Part F, Supplemental Guidance for Inhalation Risk Assessment)

Final

Office of Superfund Remediation and Technology Innovation
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LIST OF ACRONYMS

µg	Microgram
µm	Micrometer
ADAF	Age Dependent Adjustment Factor
AT	Averaging Time
ATSDR	Agency for Toxic Substances and Disease Registry
BMCL	Benchmark Concentration, Lower confidence limit
BMD	Benchmark Dose
BW	Body Weight
CA	Contaminant Concentration in Air
CERCLA	Comprehensive Environmental Response, Compensation, and Liability Act
CSF	Cancer Slope Factor
DAF	Dosimetric Adjustment Factor
ED	Exposure Duration
EC	Exposure Concentration
EF	Exposure Frequency
EPA	Environmental Protection Agency
ER	Extra-respiratory
ET	Exposure Time
ETh	Extrathoracic
F_r	Fractional Deposition in region r
F_{total}	Total particle deposition in respiratory tract
$H_{b/g\text{-}animal}$	Animal Blood:Gas Partition Coefficient
$H_{b/g\text{-}human}$	Human Blood:Gas Partition Coefficient
HEAST	Health Effects Assessment Summary Table
HEC	Human Equivalent Concentration
HI	Hazard Index
HQ	Hazard Quotient
ICRP	International Commission for Radiological Protection
IR	Inhalation Rate
IRIS	Integrated Risk Information System
IUR	Inhalation Unit Risk
kg	Kilogram
LEC_{10}	Lower limit on Effective Concentration, using a 10 percent response level
LOAEL	Lowest Observable Adverse Effect Level
ME	Microenvironment
MF	Modifying Factor
mg	Milligram
MOA	Mode of Action
MRL	Minimal Risk Level
MW	Molecular Weight
NCEA	National Center for Environmental Assessment
NOAEL	No Observable Adverse Effect Level
ORD	Office of Research and Development
OSRTI	Office of Superfund Remediation and Technology Innovation

LIST OF ACRONYMS (CONT.)

OSWER	Office of Solid Waste and Emergency Response
PBPK	Physiologically Based Pharmacokinetic
POD	Point of Departure
ppm	Parts Per Million
PPRTV	Provisional Peer Reviewed Toxicity Value
PRG	Preliminary Remediation Goal
PU	Pulmonary
Q-alv	Alveolar ventilation rate
QSAR	Quantitative Structure-Activity Relationship
RAGS	Risk Assessment Guidance for Superfund
RBC	Risk-Based Concentration
RfC	Reference Concentration
RfD	Reference Dose
RGDR	Regional Gas Dose Ratio
RDDR	Regional Deposited Dose Ratio
RME	Reasonable Maximum Exposure
SA	Surface Area
SSL	Soil Screening Level
STSC	Superfund Health Risk Technical Support Center
TB	Tracheobronchial
TOT	Total Respiratory System
UF	Uncertainty Factor
V_e	Minute Volume

1. INTRODUCTION

The Environmental Protection Agency's (EPA's) Superfund Program has updated its approach for determining risk from inhaled chemicals to be consistent with the inhalation dosimetry methodology described in *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry* (USEPA, 1994; hereafter, the *Inhalation Dosimetry Methodology*).[1] This document provides Superfund site risk assessors with guidance that should help more consistently address the *Inhalation Dosimetry Methodology*.

This document outlines recommended processes consisting of a series of steps as well as recommended equations for EPA Regions to consider when estimating inhalation exposure and risk at Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) sites. This guidance is intended to provide a recommended methodology for consistently addressing the inhalation pathway in risk assessments for Superfund sites.

Some of the statutory provisions described in this document contain legally binding requirements. However, this document does not substitute for those provisions or regulations, nor is it a regulation itself. Thus, it cannot impose legally binding requirements on EPA, States, or the regulated community, and may not apply to a particular situation based upon the circumstances. Any decisions regarding a particular remedy selection decision will be made based on the statute and regulations, and EPA decisionmakers retain the discretion to adopt approaches on a case-by-case basis that differ from this guidance where appropriate. EPA may change this guidance in the future.

1.1 Background

EPA's *Risk Assessment Guidance for Superfund (RAGS), Part A* (USEPA, 1989; hereafter, *RAGS, Part A*) outlined a previously recommended approach for conducting site-specific baseline risk assessments for inhaled contaminants.[2] According to the original RAGS approach, the inhalation exposure estimate was typically derived in terms of a chronic, daily "air intake" (mg/kg-day) using the following general approach. The intake of the chemical was estimated as a function of the concentration of the chemical in air (CA), inhalation rate (IR), body weight (BW), and the exposure scenario. Age-specific values for BW and IR were used when evaluating childhood exposures. Table 1 presents the *RAGS, Part A* equation for calculating intake for inhalation exposure. Inhalation toxicity values were "converted" into similar units for the risk quantification step. Cancer risk was estimated by multiplying the chronic daily intake of the chemical from the air by the "inhalation cancer slope factor" (CSF_i); the Hazard Quotient (HQ) for non-cancer effects was estimated by dividing the intake of the chemical by an "inhalation reference dose" (RfD_i).[3]

The approach outlined in *RAGS, Part A* was developed before EPA issued the *Inhalation Dosimetry Methodology*, which describes the Agency's refined recommended approach for interpreting

[1] The *Inhalation Dosimetry Methodology* can be found at the following web address: http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=71993.

[2] See sections 6.6.3, 7.2.3, 7.3.3, and 8.2 of *RAGS, Part A*.

[3] EPA defines an HQ in *RAGS, Part A* as: "The ratio of a single substance exposure level over a specified time period (e.g., subchronic) to a reference dose (RfD) for that substance derived from a similar exposure period" (USEPA, 1989).

inhalation toxicity studies in laboratory animals or studies of occupational exposures of humans to airborne chemicals. Under the *Inhalation Dosimetry Methodology*, the experimental exposures are typically extrapolated to a Human Equivalent Concentration (HEC), and a reference concentration (RfC) is typically calculated by dividing the HEC by uncertainty factors (UFs). As described in the Agency's *Guidelines for Cancer Risk Assessment* (USEPA, 2005a), the HEC developed in accordance with the *Inhalation Dosimetry Methodology* typically is also used in developing an inhalation unit risk (IUR) for cancer risk assessment (which may also be called an inhalation cancer slope factor).[4] The procedure that was used to calculate the published RfC or IUR is described in the Integrated Risk Information System (IRIS) profile or other toxicological reference document for a chemical.

TABLE 1
RAGS, PART A EQUATION DESCRIBING THE ESTIMATION OF INHALATION EXPOSURE

Equation	Location in RAGS, Part A
Intake (mg/kg-d) = CA x (IR/BW) x (ET x EF x ED)/AT	Exhibit 6-16, Page 6-44
Key: CA (mg/m^3) = contaminant concentration in air; IR (m^3/hr) = inhalation rate; BW (kg) = body weight; ET (hours/day) = exposure time; EF (days/year) = exposure frequency; ED (years) = exposure duration; and AT (days) = averaging time (period over which exposure is averaged).	

The Superfund Program has updated its inhalation risk paradigm to be compatible with the *Inhalation Dosimetry Methodology*, which represents the Agency's current methodology for inhalation dosimetry and derivation of inhalation toxicity values.[5] This document recommends that when estimating risk via inhalation, risk assessors should use the concentration of the chemical in air as the exposure metric (e.g., mg/m^3), rather than inhalation intake of a contaminant in air based on IR and BW (e.g., mg/kg-day).

1.2 Purpose and Scope

The intake equation described above (*RAGS, Part A*, Exhibit 6-16) is not consistent with the principles of EPA's *Inhalation Dosimetry Methodology* because the amount of the chemical that reaches the target site is not a simple function of IR and BW. Instead, the interaction of the inhaled contaminant with the respiratory tract is affected by factors such as species-specific relationships of exposure concentrations (ECs) to deposited/delivered doses and physiochemical characteristics of the inhaled contaminant. The *Inhalation Dosimetry Methodology* also considers the target site where the toxic effect occurs (e.g., the respiratory tract or a location in the body remote from the portal-of-entry) when applying dosimetric adjustments to experimental concentrations (USEPA, 1994). Therefore, this *RAGS, Part A* equation is not recommended for estimating exposures to inhaled contaminants.

---

[4] The phrase "inhalation cancer slope factor," as used in this guidance, refers generally to the risk per a measure of inhalation exposure. Inhalation exposure in cancer bioassays or occupational studies from which slope factors may be derived is most commonly expressed as an exposure concentration (e.g., µg agent/m^3 air). Please note that this differs from past use of the phrase "inhalation cancer slope factor" or "CSF_i" by the Superfund program to refer to a cancer slope expressed as an "inhalation intake" (e.g., *RAGS, Part A* (USEPA, 1989)).

[5] For additional information about the Superfund program's adoption of the *Inhalation Dosimetry Methodology*, please refer to the summary of a 2003 Superfund workshop on inhalation risk assessment: http://www.epa.gov/oswer/riskassessment/pdf/finalinhalationriskworkshop.pdf.

The purpose of this document is to provide a recommended approach for developing the information necessary to assist risk assessment and risk management decision-making at waste sites involving potential risks from inhalation exposures.[6, 7] This includes providing equations that may be used in conducting baseline risk assessments and in calculating risk-based concentrations (RBCs). It is intended that *RAGS, Part F* will replace those portions of *RAGS, Part A*, which addressed inhalation risk.

1.3 Effects on Other Office of Superfund Remediation and Technology Innovation Guidance

EPA recommends that the intake equation presented in *RAGS, Part A* (USEPA, 1989, Exhibit 6-16) should no longer be used when evaluating risk from the inhalation pathway. Implementation of a risk assessment approach consistent with the *Inhalation Dosimetry Methodology* will also affect the following guidance documents: *RAGS, Part B*, Section 3.3: Volatilization and Particulate Emission Factors (USEPA, 1991); and the Office of Solid Waste and Emergency Response's (OSWER's) *Draft Guidance for Evaluating the Vapor Intrusion to Indoor Air Pathway from Groundwater and Soils* (USEPA, 2002a; hereafter the *Vapor Intrusion Guidance*). EPA no longer recommends using the equations in Section 3.3 of *RAGS, Part B* nor the inhalation toxicity values generated using simple route-to-route extrapolation, such as those presented in the 2002 draft *Vapor Intrusion Guidance* and related documents.[8]

This guidance does not affect the equations pertaining to risk from inhaled chemicals in the *Soil Screening Guidance* (USEPA, 1996), Section 2.4, or the *Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites* (USEPA, 2002b), Sections 4.2.3, 5.3.2 and Appendix B, other than to clarify that the IURs and RfCs used in the equations are based on continuous exposure (24 hours per day). If the exposure scenario of interest is less than 24 hours per day, the scenario-specific exposure time (ET) in hours per day should be used in the equations and the averaging time should be in units of hours (see Equations 6 and 8 in this document). *RAGS, Part D* (USEPA, 2001) is also not affected by *RAGS, Part F*, as it includes sufficient flexibility to accommodate the revisions described in this guidance. In addition, the screening values presented on the "Regional Screening Levels for Chemical Contaminants at Superfund Sites" screening level/preliminary remediation goal table are consistent with *RAGS, Part F* (USEPA, 2008a).[9] Readers can contact EPA headquarters with questions about the compatibility of specific Superfund documents with *RAGS, Part F*.

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[6] Note that the assessment of risk from inhaled nanoparticles is outside the scope of this document.

[7] If a site contains asbestos contamination, risk assessors should contact EPA's Technical Review Workgroup for Metals and Asbestos for assistance.

[8] Related documents include the *Johnson and Ettinger (1991) Model for Subsurface Vapor Intrusion into Buildings* spreadsheet models (http://www.epa.gov/oswer/riskassessment/airmodel/johnson_ettinger.htm) and the accompanying *User's Guide for Evaluating Subsurface Vapor Intrusion into Buildings* (USEPA, 2004a).

[9] This table can be found on EPA Regions 3, 6, and 9 websites (http://www.epa.gov/reg3hwmd/risk/human/rb-concentration_table/index.htm; http://www.epa.gov/earth1r6/6pd/rcra_c/pd-n/screen.htm; and http://www.epa.gov/region09/waste/sfund/prg/index.html).

2. BACKGROUND ON DERIVATION OF INHALATION TOXICITY VALUES

For all exposure routes, there are generally two approaches for deriving toxicity values. One involves the derivation of a reference value (e.g., RfC or RfD), while the other involves derivation of a predictive cancer risk estimate (e.g., an oral or inhalation CSF, such as an IUR). For the inhalation route, both approaches rely on EPA's *Inhalation Dosimetry Methodology* for the extrapolation of experimental concentrations to HECs. This extrapolation is described in Section 2.1 and its subsections. The approaches for deriving a toxicity value from the HEC are described in Sections 2.2 and 2.3 and differ depending on the type of toxicity value (e.g., RfC, IUR). This information is provided for background purposes only. **The procedures outlined in Section 2 are typically performed by IRIS chemical managers or by inhalation toxicologists at the National Center for Environmental Assessment's (NCEA's) Superfund Health Risk Technical Support Center (STSC) rather than as part of a baseline risk assessment.**

2.1 Application of Inhalation Dosimetry

The *Inhalation Dosimetry Methodology* recognizes a hierarchy of approaches that can be used for determining the HEC that is used to derive the RfC or IUR. Generally, the preferred approach is to use physiologically-based pharmacokinetic (PBPK) models.[10] With sufficient data, a PBPK model is capable of calculating the amount of the chemical that reaches the target organ in an animal from any exposure scenario and then estimating what human exposure would result in this same amount of chemical reaching the target organ (i.e., the HEC). PBPK models can also be used to derive continuous ECs from human and animal studies with less-than-continuous exposures. Because constructing a valid PBPK model is an information-intensive process that typically requires substantial chemical-specific data, this approach has rarely been used (USEPA, 2004b); an example can be found in the IRIS file for vinyl chloride (USEPA, 2000a). In cases where a complete PBPK model is not available, an intermediate model relying on certain chemical-specific data may be used (USEPA, 1994).[11]

If the database to support the preferred approach is inadequate, an alternative approach, called the Default Chemical Category-Specific Method can be used. This method incorporates the use of limited or categorical chemical-specific and physiological information. The default method is discussed below, followed by the procedures outlined in the *Inhalation Dosimetry Methodology* for deriving the RfC and IUR as they apply to the interpretation of animal and human data.

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[10] EPA defines PBPK models in the IRIS glossary as a model that estimates the dose to a target tissue or organ by taking into account the rate of absorption into the body, distribution among target organs and tissues, metabolism, and excretion (USEPA, 2008b). For further information about PBPK modeling, please refer to *Approaches for the Application of Physiologically Based Pharmacokinetic Models and Supporting Data in Risk Assessment* (USEPA, 2006a).

[11] The *Inhalation Dosimetry Methodology* recognizes the existence of alternate approaches in addition to the two presented in this guidance. The PBPK approach is generally preferred. In the absence of such a model, alternate models may be more optimal than the default approach when default assumptions or parameters can be replaced by more detailed, biologically-motivated descriptions or actual data, respectively. For instance, a model may be considered more optimal if it incorporates chemical or species-specific information or if it accounts for mechanistic determinants. See Table 3-6 in the *Inhalation Dosimetry Methodology* for more details on the hierarchy of approaches (EPA, 1994, page 3-40).

2.1.1 Default Approach - Extrapolation from Experimental Animal Data

The default method involves a two-step procedure that uses limited or categorical chemical-specific and physiological information to calculate the HEC. First, the chosen point of departure (POD) from the experimental data for a chemical is adjusted to derive a concentration intended to represent an equivalent dose under conditions of continuous exposure (7 days a week, 24 hours a day).[12] In the second step, this concentration is then multiplied by a Dosimetric Adjustment Factor (DAF) to generate the HEC. Further details on each step are outlined below.

2.1.1.1 Duration Adjustment to Continuous Exposure

Most of the inhalation studies of laboratory animals used to derive RfCs and IURs involve an exposure regimen of four to six hours per day, five to seven days per week, for 13 weeks or more (equivalent to 10 percent or more of the lifetime of the animal). The POD concentration from an animal study is mathematically adjusted to reflect an equivalent dose under conditions of continuous exposure.[13] Adjustment of duration to a continuous exposure scenario is regularly applied as a default procedure to studies with repeated exposures but not to single-exposure inhalation toxicity studies in animals (USEPA, 1994). Operationally, this is accomplished by applying a c x t product (where "c" is concentration, and "t" is duration of exposure) for both the number of hours in a daily exposure period and the number of days per week that the exposure is experienced. For example, if exposure in a particular study was 6 hours per day, 5 days per week, the experimental exposure is multiplied by 6/24 x 5/7 to calculate an equivalent continuous exposure. The general equation provided in the *Inhalation Dosimetry Methodology* (USEPA, 1994, Equation 4-2) for calculating duration-adjusted exposure levels in mg/m^3 for experimental animals is presented below.

$NOAEL_{[ADJ]}$ = E x D x W **(Equation 1)**

Where:
$NOAEL_{[ADJ]}$ (mg/m^3) = the NOAEL or analogous exposure level obtained with an alternate approach (e.g., LOAEL, LEC_{10}), adjusted for duration of experimental regimen;
E (mg/m^3) = the NOAEL or analogous exposure level observed in the experimental study;
D (h/h) = number of hours exposed/24 hours; and
W (days/days) = number of days of exposure/7days.

Using the example above, the assumption is that the product of c x t, not concentration alone, is associated with the toxicity observed. This is roughly equivalent to implying that if an effect occurs from a chemical at an exposure of 6 hours per day at 40 parts per million (ppm), that same effect will

[12] Examples of PODs include the no-observed-adverse-effect level (NOAEL); the lowest-observed-adverse-effect level (LOAEL); Benchmark Concentration, Lower confidence limit (BMCL); and the Lower limit on an Effective Concentration using a 10 percent response level (LEC_{10}). For definitions of the various PODs, please refer to the IRIS glossary (http://www.epa.gov/ncea/iris/help_gloss.htm).

[13] Continuous exposure refers to 24 hours per day, 7 days per week.

occur at an exposure of 24 hours per day at 10 ppm.[14] Note that this adjustment always produces a lower concentration value than that administered to experimental animals. Thus, as stated in *A Review of the Reference Dose and Reference Concentration Processes* (hereafter, the *RfD/RfC Review*), application of this procedure results in an automatic margin of protectiveness for chemicals for which concentration alone may be the more appropriate dose metric, and it reflects the maximum dose for chemicals for which total or cumulative dose is the appropriate measure (USEPA, 2002c). If a different procedure is used to calculate the continuous exposure, it should be fully discussed in the relevant technical support document for the chemical (e.g., IRIS profile, Provisional Peer Reviewed Toxicity Values (PPRTVs) Assessment). For additional discussion, including the uncertainties associated with this approach, see Section 4.3.2 of the *Inhalation Dosimetry Methodology* and Section 4.4.2.1 of the *RfD/RfC Review* (USEPA, 2002c).

2.1.1.2 Dosimetric Adjustment to Human Equivalent Concentration

Typically, the adjusted POD concentration from the animal study is next converted to an HEC using the following equation (USEPA, 1994, Equation 4-3):

$NOAEL_{[HEC]} = NOAEL_{[ADJ]} \times DAF$ **(Equation 2)**

Where:

$NOAEL_{[HEC]}$ (mg/m^3) = the NOAEL or analogous exposure level obtained with an alternate approach, dosimetrically adjusted to an HEC;

$NOAEL_{[ADJ]}$ (mg/m^3) = the NOAEL or analogous exposure level obtained with an alternate approach, adjusted for duration of experimental regimen; and

DAF = Dosimetric Adjustment Factor for the specific site of effects (e.g., respiratory tract region or extra-respiratory).

The DAF is typically based on ratios of animal and human physiologic parameters. The specific DAF used depends on the nature of the contaminant (e.g., particle or gas) and the target site where the toxic effect occurs (e.g., respiratory tract or a location in the body remote from the portal-of-entry). For example, the DAF can be based on either the Regional Gas Dose Ratio (RGDR), for gases with respiratory effects, or the Regional Deposited Dose Ratio (RDDR) for particles.

Table 2 provides information on the site of effects for the different chemical types. It also lists the physiologic parameters considered when calculating the DAF for specific regions of the body.[15] In addition, the table provides references to the equations from the *Inhalation Dosimetry Methodology* used in deriving the DAFs. Figure 1 provides a schematic of the human respiratory tract, illustrating each of the different regions.

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[14] This assumption is based on Haber's Law, which states that "the incidence and/or severity of an adverse health effect depends on the total exposure to a potentially toxic substance. Total exposure (K) is the concentration of the substance (c) times the duration time of exposure (t), (i.e., $c \times t = K$)" (Gaylor, 2000).

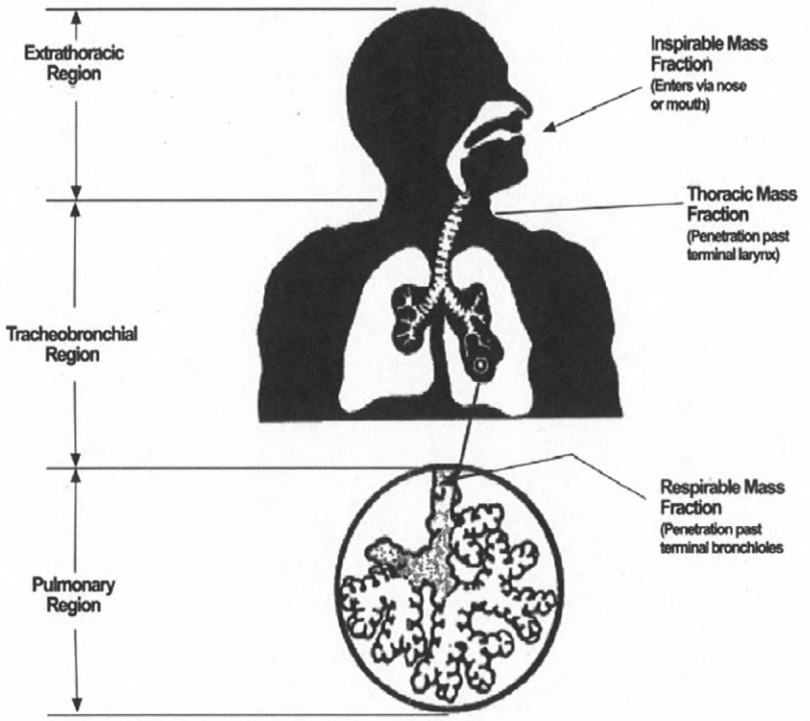
[15] The three main regions of the respiratory tract include the following: 1) Extrathoracic (includes nose, mouth, nasopharynx, oropharynx, laryngopharynx, and larynx); 2) Tracheobronchial (includes trachea, bronchi, and bronchioles); and 3) Pulmonary (includes respiratory bronchioles, alveolar ducts, alveolar sacs and the alveoli).

TABLE 2
CONTAMINANT PROPERTIES AND DOSIMETRIC ADJUSTMENT FACTORS[a]

Chemical Type	Site of Effects	Parameters Considered in Derivation of DAF for Regions of the Body[b]	DAF Equation Numbers in Inhalation Dosimetry Methodology[c]
Category 1 Gases (e.g., acrolein, hydrogen fluoride, chlorine)	Respiratory	-Minute volume (ETh, TB) -Surface area (ETh, TB, PU) -Mass transport coefficient (TB, PU) -Fraction of inhaled chemical penetrating the respiratory region (PU) -Alveolar ventilation rate (PU)	4-18 (ETh), 4-21 & 4-22 (TB), 4-28 (PU)
Category 2 Gases (e.g., acetonitrile, xylene, propanol, isoamyl alcohol)	Respiratory and Remote	-Mass transport coefficients (ETh, TB) -Blood:gas partition coefficient (ET, TB, ER) -Cardiac output (ETh, TB, ER) -Alveolar ventilation rate (PU) -Surface Area (PU) -Minute volume (ER)	4-18 (ETh), 4-21 & 4-22 (TB), 4-28 (PU), 4-48 (ER)[d,e]
Category 3 Gases (e.g., benzene, styrene)	Remote	Blood:gas partition coefficient (ER)	4-48[d]
Particles	Respiratory and Remote	-Minute volume (TOT, ER) -Surface area (TOT) -Fractional deposition of particle (TOT, ER) -Body weight (ER) -Inhaled concentration (ER)	4-14 (TOT), 4-15 (ER)

[a] Due to the complexities inherent in evaluating the health effects associated with exposure to gases, no definitive or comprehensive list of Category 1, 2, or 3 gases is available. Risk assessors should consult with an inhalation toxicologist in order to classify a specific gas as Category 1, 2, or 3, since there is overlap between the sites of effects and the parameters considered in deriving the DAF for different regions of the respiratory tract.
[b] Additional discussion of the terms used in this table can be found in the *Inhalation Dosimetry Methodology*.
[c] The *Inhalation Dosimetry Methodology* provides equations for deriving DAFs for the different contaminant categories. The equations listed in this table are the default equations for each specific region in the body.
[d] This refers to Equation 4-48 that is found on page 4-60 of the *Inhalation Dosimetry Methodology*.
[e] The equations presented for Category 2 gases in the *Inhalation Dosimetry Methodology* contain errors. Therefore, this table refers to the equations for Category 1 and 3 gases, which are expected to cover respiratory and remote effects from Category 2 gases.
Acronyms: ETh = Extrathoracic; TB = Tracheobronchial; PU = Pulmonary; ER = Extra-respiratory; TOT = Total respiratory system.

FIGURE 1
HUMAN RESPIRATORY TRACT



Source: EPA (1994), Figure 3-1, Page 3-5.

Category 1 gases are highly water-soluble and/or are rapidly irreversibly reactive in the respiratory tract (e.g., acrolein, hydrogen fluoride, chlorine). They do not significantly accumulate in the blood, and therefore their effects are usually exclusively respiratory (USEPA, 1994). The DAF for Category 1 gases consists of an RGDR and is based on the animal to human ratio of the minute volume (V_e) divided by the surface area (SA) of the region of the respiratory tract where the effect occurs.[16] See Appendix A, Sections 1, 2, and 3 of this guidance for examples of specific Category 1 DAF equations.

[16] For the purposes of this document, the V_e is defined as the total ventilation per minute and equals the product of the tidal volume (the air volume entering or leaving the lungs with a single breath) and the respiratory frequency.

Category 3 gases are relatively water-insoluble and are unreactive in the respiratory tract (e.g., benzene, styrene). Their toxicity is generally at sites remote to the respiratory tract (USEPA, 1994). The DAF for Category 3 gases is based on the ratio of the animal blood:gas partition coefficient ($H_{b/g\text{-}animal}$) and the human blood:gas partition coefficient ($H_{b/g\text{-}human}$). See Appendix A, Section 4 of this guidance for an example of a Category 3 DAF equation.

Category 2 gases are moderately water-soluble and may be rapidly reversibly reactive or moderately to slowly irreversibly reactive in respiratory tract tissue (e.g., acetonitrile, xylene, propanol, isoamyl alcohol). These gases have potential for significant accumulation in the blood, so they can exhibit both respiratory and remote toxicity (USEPA, 1994). The DAF for respiratory effects of Category 2 gases consists of an RGDR and is based on the animal to human ratio of the V_e and the SA of the region of the respiratory tract where the effect occurs, as for Category 1 gases. The DAF for extra-respiratory (ER) effects of a Category 2 gas is based on the ratio of the $H_{b/g\text{-}animal}$ and the $H_{b/g\text{-}human}$, as for Category 3 gases.

Particles also vary by solubility and reactivity. However, the default equations used to estimate the predicted regional deposition fractions for particles are based on non-soluble, non-hygroscopic particles (USEPA, 1994, Section 4.3.5.3). The DAF for a particle causing an effect in the respiratory tract is the $RDDR_r$. The $RDDR_r$ is based on the animal to human ratio of the V_e and the fractional deposition of the particle in that region (F_r), divided by the SA_r of the region where the effect occurs. This derivation, from the *Inhalation Dosimetry Methodology,* conservatively assumes that 100 percent of the deposited dose remains in the respiratory tract; clearance mechanisms are not considered. The DAF for a particle causing an ER effect, the $RDDR_{ER}$, is based on the animal to human ratio of the V_e and the total deposition of the particle in the entire respiratory tract (F_{total}), divided by BW (USEPA, 1994). The $RDDR_{ER}$ assumes that 100 percent of the deposited dose in the entire respiratory tract is available for uptake into the systemic circulation. See Appendix A, Section 5 for examples of specific particle DAF equations.

2.1.2 Default Approach - Extrapolation from Human Occupational Data

When human data are available to derive an RfC, duration adjustments are often required to account for differences in exposure scenarios (e.g., extrapolation from an 8 hour/day occupational exposure to a continuous chronic exposure). The default approach recommended by the *Inhalation Dosimetry Methodology* for adjusting the POD concentration (e.g., the no observable adverse effect level (NOAEL)) obtained from human study data is provided below in Equation 3 (USEPA, 1994, Equation 4-49).[17,18]

[17] If sufficient data are available, a PBPK model or intermediate approach using chemical-specific information may be employed in preference to the default method for extrapolating human occupational data to an HEC.

[18] EPA's IRIS glossary defines an adverse effect as the following: "A biochemical change, functional impairment, or pathologic lesion that affects the performance of the whole organism, or reduces an organism's ability to respond to an additional environmental challenge" (USEPA, 2008b).

$NOAEL_{[HEC]}$ = NOAEL x (VEho/VEh) x 5 days/7 days **(Equation 3)**

Where: $NOAEL_{[HEC]}$ (mg/m^3) = the NOAEL or analogous exposure level obtained with an alternate approach, dosimetrically adjusted to an ambient HEC;
NOAEL (mg/m^3) = occupational exposure level (time-weighted average over an 8-hour exposure period);
VEho = human occupational default minute volume over 8 hours (10 m^3); and
VEh = human ambient default minute volume over 24 hours (20 m^3).

2.2 Derivation of the Inhalation Unit Risk

The default approach for determining predictive cancer risk recommended by EPA's *Guidelines for Carcinogen Risk Assessment* (USEPA, 2005a; hereafter, *Cancer Guidelines*) is a linear extrapolation from exposures observed in the animal or human occupational study.[19] This approach involves drawing a straight line from the POD to the origin. The default linear extrapolation approach is generally considered to be conservatively protective of public health, including sensitive sub-populations (USEPA, 2005a). The slope of this line is commonly called the slope factor, and when the units are risk per $\mu g/m^3$, it is also called the IUR. EPA defines an IUR in the IRIS glossary as "the upper-bound excess lifetime cancer risk estimated to result from continuous exposure to an agent at a concentration of 1 $\mu g/m^3$ in air" (USEPA, 2008b). Equation 4 below presents a linear extrapolation from a POD of 10 percent response (LEC_{10}).[20]

$IUR = 0.1/LEC_{10[HEC]}$ **(Equation 4)**

Where: IUR $(\mu g/m^3)^{-1}$ = Inhalation Unit Risk; and
$LEC_{10[HEC]}$ ($\mu g/m^3$) = the lowest effective concentration using a 10 percent response level, dosimetrically adjusted to an HEC.

2.3 Derivation of the Reference Concentration

EPA defines an RfC in the IRIS glossary as "an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious effects during a lifetime" (USEPA, 2008b). The RfC is derived after a review of the health effects database for a chemical and identification of the most sensitive and relevant endpoint along with the principal study or studies demonstrating that endpoint. EPA Chemical Managers use UFs to account for recognized

[19] According to the *Cancer Guidelines*, "[a] nonlinear approach should be selected when there are sufficient data to ascertain the mode of action [MOA] and conclude that it is not linear at low doses and the agent does not demonstrate mutagenic or other activity consistent with linearity at low doses" (USEPA, 2005a, page 3-22). In addition, [l]inear extrapolation should be used when there are MOA data to indicate that the dose-response curve is expected to have a linear component below the POD" (USEPA, 2005a, page 3-21). This information will appear on the IRIS profile or other toxicological information source for a chemical. Chemicals with a mutagenic MOA are thought to pose a higher risk during early life. Procedures for assessing cancer risk from these chemicals are outlined in Section 5.1.

[20] The POD used in Equation 4 is an LEC_{10}, which is the lower 95 percent confidence limit on the concentration corresponding to a 10 percent response rate (i.e., the EC_{10}). Other PODs may be substituted for this value, which could be associated with alternative response levels (e.g., 1 percent, 5 percent).

uncertainties in the extrapolations from the experimental data conditions to an estimate appropriate to the assumed human scenario (USEPA, 1994). See Table 3 for a description of the standard UFs. The formula used for deriving the RfC from the HEC is provided below.

$RfC = NOAEL_{[HEC]}/(UF)$[1] **(Equation 5)**

Where:

RfC (mg/m^3) = Reference Concentration

$NOAEL_{[HEC]}$ (mg/m^3) = The NOAEL or analogous exposure level obtained with an alternate approach, dosimetrically adjusted to an HEC; and

UF = Uncertainty factor(s) applied to account for the extrapolations required from the characteristics of the experimental regimen.

[1] Some toxicological information sources for RfCs will incorporate an additional factor to account for deficiencies in the available data set, called a modifying factor (MF). In 2002, however, EPA published the *RfD/RfC Review,* which recommended that the use of MFs be discontinued because their purpose is "sufficiently subsumed in the general database UF" (USEPA, 2002c, page xviii). Therefore, RfCs published subsequent to this document will not include MFs.

TABLE 3
THE USE OF UNCERTAINTY FACTORS IN DERIVING AN INHALATION REFERENCE CONCENTRATION

Standard UFs	Processes Considered in the UF Purview
H = Human to sensitive human: Extrapolation of valid experimental results from studies using prolonged exposure to average healthy humans. Intended to account for the variation in sensitivity among the members of the human population.	-Pharmacokinetics/Pharmacodynamics -Sensitivity[2] -Differences in body weight (age, obesity) -Concomitant exposures -Activity pattern -Does not account for idiosyncrasies
A = Animal to human: Extrapolation from valid results of long-term studies on laboratory animals when results of studies of human exposure are not available or are inadequate. Intended to account for the uncertainty in extrapolating laboratory animal data to the case of average healthy humans.	-Pharmacokinetics/Pharmacodynamics -Relevance of laboratory animal model -Species sensitivity
S = Subchronic to chronic: Extrapolation from less-than-chronic exposure results on laboratory animals or humans when there are no useful long-term human data. Intended to account for the uncertainty in extrapolating from less than chronic NOAELs to chronic NOAELs.	-Accumulation/Cumulative damage -Pharmacokinetics/ Pharmacodynamics -Severity of effect -Recovery -Duration of study -Consistency of effect with duration
L = LOAEL to NOAEL: Derivation from a LOAEL instead of a NOAEL. Intended to account for the uncertainty in extrapolating from LOAELs to NOAELs.	-Severity -Pharmacokinetics/Pharmacodynamics -Slope of dose-response curve -Trend, consistency of effect -Relationship of endpoints -Functional vs. histopathological evidence -Exposure uncertainties
D = Incomplete to complete data: Extrapolation from valid results in laboratory animals when the data are "incomplete." Intended to account for the inability of any single laboratory animal study to adequately address all possible adverse outcomes in humans.[1]	-Quality of critical study -Data gaps -Power of critical study/supporting studies -Exposure uncertainties

[1] The *RfD/RfC Review* indicates that this UF accounts for the potential for deriving an underprotective RfD/RfC as a result of an incomplete characterization of the chemical's toxicity or if the existing data suggest that a lower reference value might result if additional data were available (considering both the lacking and available data for particular organ systems as well as life stage) (USEPA, 2002c).
[2] The *RfD/RfC Review* also stresses that susceptible populations and life stages are accounted for with this UF (USEPA, 2002c).
Source: USEPA, 1994, Table 4-9, page 4-77.

3. CHARACTERIZING EXPOSURE

3.1 Introduction

This section describes an approach for characterizing exposure in a baseline risk assessment that is consistent with the *Inhalation Dosimetry Methodology*. The approach involves the estimation of exposure concentrations (ECs) for each receptor exposed to contaminants via inhalation in the risk assessment. ECs are time-weighted average concentrations derived from measured or modeled contaminant concentrations in air at a site, adjusted based on the characteristics of the exposure scenario being evaluated.[21,22]

Equations for estimating ECs are provided below. This document does not provide default input values for the exposure parameters referenced in these equations. EPA recommends the use of site-specific exposure values consistent with the exposure pathways and receptors at a site wherever practicable and appropriate. If a risk assessor opts to rely on default exposure input values, current Superfund-supported values may be found at the exposure assessment portion of the Superfund website: (http://www.epa.gov/oswer/riskassessment/superfund_hh_exposure.htm).

3.2 Estimating Exposure Concentrations for Assessing Cancer Risks

The estimation of an EC when assessing cancer risks characterized by an IUR involves the CA measured at an exposure point at a site as well as scenario-specific parameters, such as the exposure duration and frequency.[23] The EC typically takes the form of a CA that is time-weighted over the duration of exposure and incorporates information on activity patterns for the specific site or the use of professional judgment. The equation for estimating an EC for use with an IUR is presented below.

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[21] The default method for deriving inhalation toxicity values also involves calculating time-weighted ECs, as discussed in Sections 2.1.1.1 and 2.1.2.

[22] The ECs in this document are in units of $\mu g/m^3$. Inhalation toxicity values presented on IRIS are typically expressed in units of $\mu g/m^3$ or mg/m^3, which are mass units. Some regulatory contexts require the use of volumetric units such as ppm. The conversion from mass units to volumetric units depends on the molecular weight (MW) of the material as well as the ambient temperature and atmospheric pressure. To convert from ppm to mg/m^3, the following equation can be used: $\frac{ppm \times MW}{V} = mg/m^3$; where MW is the molecular weight of the gas and V is the volume of 1 gram molecular weight of the airborne contaminant. This is derived by the formula V = RT/P; where R is the ideal gas constant, T is the temperature in Kelvin (K = 273.16 + T°C) and P is the pressure in mm Hg. The value of R is 62.4 when T is in Kelvin, (K = 273.16 + T°C), the pressure is expressed in units of mm Hg and the volume is in liters. The value of R differs if the temperature is expressed degrees Fahrenheit (°F) or if other units of pressure are used (e.g., atmospheres, kilopascals).

[23] ECs are typically based on either estimated (i.e., modeled) or measured contaminant concentrations in air.

EC = (CA x ET x EF x ED)/AT **(Equation 6)**

Where: EC ($\mu g/m^3$) = exposure concentration;
CA ($\mu g/m^3$) = contaminant concentration in air;
ET (hours/day) = exposure time;
EF (days/year) = exposure frequency;
ED (years) = exposure duration; and
AT (lifetime in years x 365 days/year x 24 hours/day) = averaging time

3.3 Estimating Exposure Concentrations for Calculating Hazard Quotients

When estimating ECs for non-cancer or cancer hazards characterized by an HQ, risk assessors should match each exposure scenario at a site to the appropriate EC equation, based on the scenario duration and frequency of exposure.[24] Figure 2 presents a flowchart to assist risk assessors with this process and provides recommended equations that can be used to estimate the EC for each type of scenario.[25] As shown in Figure 2, the recommended process for estimating ECs to be used in calculating an HQ involves the following three steps: 1) assess the duration of the exposure scenario; 2) assess the exposure pattern of the exposure scenario; and 3) estimate the scenario-specific EC.

3.3.1 Step 1: Assess Duration

The first step in the recommended process of estimating an EC for use in calculating an HQ involves assessing the duration of the exposure scenario at a site. Step 1 in Figure 2 indicates that the risk assessor first should decide whether the duration of the exposure scenario is generally acute, subchronic, or chronic. Toxicologists have long been aware that effects from a single or short-term exposure can differ markedly from effects resulting from repeated exposures. The response by the exposed person depends upon factors such as whether the chemical accumulates in the body, whether it overwhelms the body's mechanisms of detoxification or elimination, or whether it produces irreversible effects (Eaton & Klaassen, 2001). Therefore, ideally, the chemical-specific elements of metabolism and kinetics, reversibility of effects, and recovery time should be considered as part of this recommended process when defining the duration of a site-specific exposure scenario.

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[24] Traditionally, the HQ approach was limited to non-cancer hazard assessment. However, the HQ approach may also be appropriate for carcinogens with a non-linear mode of action. The 2005 *Cancer Guidelines* state the following on this subject: "For cases where the tumors arise through a nonlinear mode of action, an oral reference dose or an inhalation reference concentration, or both, should be developed in accordance with EPA's established practice for developing such values ... this approach expands the past focus of such reference values (previously reserved for effects other than cancer) to include carcinogenic effects determined to have a nonlinear mode of action" (USEPA, 2005a; page 3-24).

[25] Figure 2 was developed for the evaluation of inhalation exposures. While the concepts presented in this flowchart may be useful for assessing other exposure routes (e.g., oral or dermal), these other routes are beyond the scope of this document, and therefore, are not explicitly considered. Caution should be used when using Figure 2 to evaluate other exposure routes, as considerations beyond those outlined in the flowchart may apply (e.g., time to reach steady state for dermal exposures).

To the extent possible, exposure durations (EDs) evaluated in a site-specific risk assessment should be consistent with the ED represented by the toxicity value. However, frequencies or durations of human exposures often are not as clearly defined as those in animal studies with controlled exposures, particularly for intermittent exposures. For example, the emission of some volatile chemicals into the ambient air may vary with temperature and season, providing fluctuating exposures for humans living near the source. Therefore, risk assessors should use best professional judgment to determine if the ED in a given scenario is reasonably similar to the duration associated with the toxicity value. Risk assessors should describe the uncertainties associated with their choice of toxicity value in the risk characterization section of the risk assessment (see Section 9.2.2 of this document). For situations where duration-appropriate toxicity values are not available, please follow the procedures outlined in Section 4.2 and Appendix C of this document.

The specific definition for each exposure duration category may vary depending on the source of the toxicity value being used. For Tier 1 toxicity values obtained from EPA's IRIS database, acute exposures are defined as lasting 24 hours or less; subchronic exposures are defined as repeated exposures by the oral, dermal, or inhalation route for more than 30 days, up to approximately 10 percent of the human lifespan; and chronic exposures are defined as repeated exposures for more than approximately 10 percent of the human lifespan (USEPA, 2008b).[26, 27]

After deciding which duration the exposure scenario most closely matches, risk assessors should then proceed to Step 2, following the path of the selected duration. Note that if an acute duration is selected, risk assessors should proceed directly to Step 3 to estimate an acute EC for each acute exposure period.

3.3.2 Step 2: Assess Exposure Pattern

Step 2 of the recommended process for estimating an EC for use in a hazard quotient involves assessing the exposure pattern for each exposure scenario at a site. This entails comparing the exposure time and frequency at a site to that of a typical subchronic or chronic toxicity test.[28]

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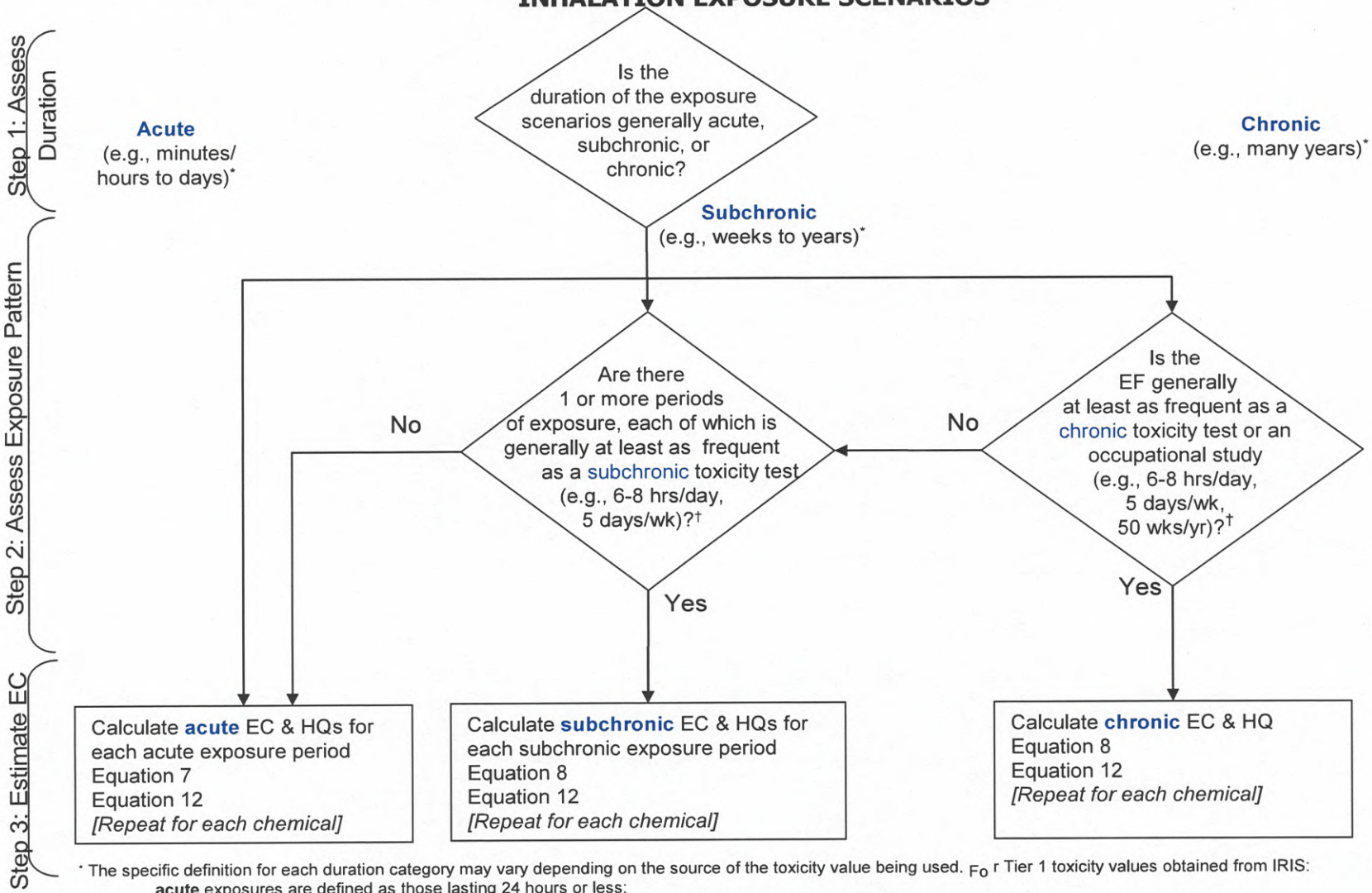
[26] Note that other sources of toxicity values may define exposures differently. For example, the Agency for Toxic Substances and Disease Registry (ATSDR) (which publishes Minimal Risk Levels (MRLs)) defines acute exposures as occurring from one to 14 days, intermediate exposures as greater than 14 to 364 days, and chronic exposures as 365 days or longer. However, the toxicity values are based on the same underlying toxicological concepts described in this section.

[27] Exposures with a duration lasting between 24 hours and 30 days should be treated as subchronic for the purposes of this document.

[28] Exposure regimens vary from study to study. Risk assessors should use best professional judgment to determine if the exposure pattern in a given scenario is reasonably similar to a typical regimen for a subchronic or chronic study.

FIGURE 2
RECOMMENDED PROCEDURE FOR DERIVING EXPOSURE CONCENTRATIONS AND HAZARD QUOTIENTS FOR INHALATION EXPOSURE SCENARIOS



* The specific definition for each duration category may vary depending on the source of the toxicity value being used. For Tier 1 toxicity values obtained from IRIS:
acute exposures are defined as those lasting 24 hours or less;
subchronic exposures are defined as repeated exposures for more than 30 days, up to approximately 10 percent of the life span in humans; and
chronic exposures are defined as repeated exposures for more than approximately 10 percent of the life span in humans (EPA, 2008b).
For the purposes of this document, short-term exposures, defined by the IRIS glossary as repeated exposures for more than 24 hours, up to 30 days, should be treated as subchronic.

† Exposure regimens vary from study to study. Risk assessors should use best professional judgment to determine if the exposure pattern in a given scenario is reasonably similar to a typical regimen for a chronic or subchronic study.

For exposure scenarios with a subchronic duration, risk assessors should follow the center path on the flowchart. Step 2 in this path asks whether there are one or more periods of exposure, each of which is generally as frequent as a subchronic toxicity test (e.g., 6-8 hours per day, 5 days per week). If the exposure scenario matches this description, risk assessors should proceed to Step 3 and estimate a subchronic EC for each subchronic exposure period. However, if the exposure pattern contains periods that are significantly shorter and/or involve significantly less frequent exposures than indicated in the flow chart, risk assessors should derive acute ECs for each of these exposure periods. If it is difficult to determine whether a specific exposure scenario is best modeled as a subchronic exposure or as a series of independent acute exposures, due to uncertainty in the time required to return to baseline following exposure, risk assessors may want to derive ECs using both approaches.

If the exposure scenario has a chronic duration, risk assessors should follow the right hand path on the flowchart. Step 2 in this path asks whether the exposure frequency (EF) is generally as frequent as a chronic animal toxicity test or a human occupational study (e.g., 6-8 hours per day, 5 days per week, for 50 weeks per year). If the exposure scenario matches this description, risk assessors should proceed to Step 3 and estimate a single chronic EC. However, if the scenario differs significantly from this pattern, risk assessors should proceed to the second question under the subchronic duration path and proceed as outlined above.

3.3.3 Step 3: Estimate Exposure Concentration

Step 3 of the recommended process involves estimating the EC for the specific exposure scenario based on the decisions made in Steps 1 and 2. For acute exposures, the EC is equal to the CA. Risk assessors can estimate an acute EC for each acute exposure period at a site using Equation 7. For longer-term exposures, risk assessors should take into consideration the exposure time, frequency, and duration for each receptor being evaluated as well as the period over which the exposure is averaged (i.e., the averaging time (AT)) to arrive at a time-weighted EC. If there are one or more exposure periods that are generally as frequent as a subchronic toxicity test, risk assessors should use Equation 8 to estimate a subchronic EC for each of these exposure periods. (Exposure periods with significantly less frequency should be treated as acute exposures.) If the exposure pattern is generally as frequent as a chronic toxicity test of an occupational study, risk assessors should use Equation 8 to estimate a single chronic EC for the duration of the exposure.

Acute Exposures

EC = CA **(Equation 7)**

Where: EC ($\mu g/m^3$) = exposure concentration;
CA ($\mu g/m^3$) = contaminant concentration in air;

Chronic or Subchronic Exposures

EC = (CA x ET x EF x ED)/AT **(Equation 8)**

Where:
EC ($\mu g/m^3$) = exposure concentration;
CA ($\mu g/m^3$) = contaminant concentration in air;
ET (hours/day) = exposure time;
EF (days/year) = exposure frequency;
ED (years) = exposure duration; and
AT (ED in years x 365 days/year x 24 hours/day) = averaging time

Note: If the duration of the exposure period is less than one year, the units in the above equation can be changed to the following: EF (days/week); ED (weeks/exposure period); and AT (hours/exposure period).

It is important to use the EC equation that most closely matches the exposure pattern and duration at a site. For instance, if the exposure pattern at a site consists of a series of short (e.g., 4-hour) periods of high exposure separated by several days of no exposure, the approach outlined above recommends estimating an acute EC for each acute exposure period. If the chronic EC equation (Equation 8) were to be used instead, the result would be an average EC value that may lead to an underestimate of risk since the inhaled concentrations could be higher than acute toxicity values during periods of exposure.

3.4 Estimating Exposure Concentrations in Multiple Microenvironments

When detailed information on the activity patterns of a receptor at a site is available, risk assessors can use these data to estimate the EC for either non-carcinogenic or carcinogenic effects. The activity pattern data describe how much time a receptor spends, on average, in different microenvironments (MEs), each of which may have a different contaminant concentration level.[29] By combining data on the contaminant concentration level in each ME and the activity pattern data, the risk assessor can calculate a time-weighted average EC for a receptor. Because activity patterns (and hence, MEs) can vary over a receptor's lifetime, EPA recommends that risk assessors pursuing the ME approach first calculate a time-weighted average EC for each exposure period characterized by a specific activity pattern (e.g., separate ECs for a school-aged child resident and a working adult resident). These exposure period-specific ECs can then be combined into a longer term or lifetime average EC by weighting the EC by the duration of each exposure period. The following sections further explain these two steps.

3.4.1 Using Microenvironments to Estimate an Average Exposure Concentration for a Specific Exposure Period

The ME approach can be used to estimate an average EC for a particular exposure period during which a receptor has a specified activity pattern. As a simplified example, a residential receptor may

[29] EPA defines a microenvironment in *Air Quality Criteria for Particulate Matter: Volume II* as a defined space that can be treated as a well-characterized, relatively homogeneous location with respect to pollutant concentration for a specified time period (e.g., rooms in homes, restaurants, schools, offices, inside vehicles, or outdoors) (USEPA, 2004b).

be exposed to a higher concentration of a contaminant in air in the bathroom for 30 minutes per day while showering, and exposed to a lower concentration in the rest of the house for the remaining 23.5 hours per day. In this case, risk assessors can use the CA value experienced in each ME weighted by the amount of time spent in each ME to estimate an average EC for the period of residency in that house using Equation 9.[30] This approach may also be used to address exposures to contaminants in outdoor and indoor environments at sites where both indoor and outdoor samples have been collected or where the vapor intrusion pathway has been characterized.

$$EC_j = \sum_{i=1}^{n} (CA_i \times ET_i \times EF_i) \times ED_j / AT_j \qquad \textbf{(Equation 9)}$$

Where:
EC_j ($\mu g/m^3$) = average exposure concentration for exposure period j;
CA_i ($\mu g/m^3$) = contaminant concentration in air in ME i;
ET_i (hours/day) = exposure time spent in ME i;
EF_i (days/year) = exposure frequency for ME i;
ED_j (years) = exposure duration for exposure period j; and
AT_j (hours) = averaging time = ED_j x 24 hours/day x 365 days/year.

3.4.2 Estimating an Average Exposure Concentration Across Multiple Exposure Periods

To derive an average EC for a receptor over multiple exposure periods, the average EC from each period (as calculated above in Equation 9) can be weighted by the fraction of the total exposure time that each period represents, using Equation 10. For example, when estimating cancer risks, the risk assessor may calculate a lifetime average EC where the weights of the individual exposure periods are the duration of the period, ED_j, divided by the total lifetime of the receptor. Alternatively, when estimating an HQ, risk assessors can use Equation 10 to calculate less-than-lifetime average ECs across multiple exposure periods. In that case, the AT will equal the sum of the individual EDs for all of the exposure periods.

$$EC_{LT} = \sum_{i=1}^{n} (EC_j \times ED_j) / AT \qquad \textbf{(Equation 10)}$$

Where:
EC_{LT} ($\mu g/m^3$) = long-term average exposure concentration;
EC_j ($\mu g/m^3$) = average exposure concentration of a contaminant in air for exposure period j;
ED_j (years) = duration of exposure period j; and
AT (years)[1] = averaging time.

[1] When evaluating cancer risk, the AT is equal to lifetime in years. When evaluating non-cancer hazard, the AT is equal to the sum of the EDs for each exposure period.

[30] If one or more MEs involve acute exposures, risk assessors should conduct a supplemental analysis comparing the CA for each of those MEs to a corresponding acute toxicity value to ensure that receptors are protected from potential acute health effects.

4. SELECTING APPROPRIATE TOXICITY VALUES

After characterizing the exposure scenarios and estimating ECs for each receptor at a site, the risk assessor should select appropriate inhalation toxicity values for each inhaled contaminant. For estimating cancer risks, this typically involves identifying and evaluating available published cancer potency estimates. For estimating HQs, this typically involves identifying and evaluating reference values that match the characterization of the exposure scenario from Figure 2 (i.e., acute, subchronic, or chronic reference values).

This section provides guidance for the selection of toxicity values appropriate for assessing risk under inhalation exposure scenarios. It describes sources for the most current inhalation data and provides guidance for proceeding when published inhalation toxicity data are not available.

4.1 Sources for Inhalation Toxicity Data

The OSWER Directive, *Human Health Toxicity Values in Superfund Risk Assessment* (USEPA, 2003), provides a recommended hierarchy of toxicological data sources to guide risk assessors when selecting appropriate toxicity values. This document sets out a recommended three-tiered framework for selecting human toxicity values. Tier 1 consists of EPA's IRIS, Tier 2 consists of EPA's PPRTVs, and Tier 3 includes other toxicity values as recommended by NCEA, such as the California EPA toxicity values, the Agency for Toxic Substances and Disease Registry's (ATSDR's) Minimal Risk Levels (MRLs), and Health Effects Assessment Summary Table (HEAST) toxicity values. Priority in Tier 3 should be given to sources that are the most current and those that are peer reviewed. Consultation with the Superfund Headquarters office is recommended regarding the use of Tier 3 values for Superfund response decisions when the contaminant appears to be a risk driver for the site.

The most up-to-date information on Superfund-supported cancer potency estimates and chronic and subchronic cancer and non-cancer reference values for inhaled contaminants are available on the Superfund risk assessment website (www.epa.gov/oswer/riskassessment/superfund_toxicity.htm). Superfund-recommended sources for acute non-cancer toxicity values can be found at www.epa.gov/oswer/riskassessment/superfund_acute.htm.[31]

In situations where the desired reference value (e.g., acute, subchronic, chronic) is not available, risk assessors may use a reference value based on the next longer duration of exposure as a conservative estimate that would be protective for a shorter-term ED (USEPA, 2002c). For example, if a risk assessor determines that an ED at a site is subchronic, but no subchronic toxicity value is available, a chronic RfC can be used to assess hazard.

EPA recommends that toxicity values published in Superfund-supported sources should generally be used in the risk equations presented in this guidance, without modification. This includes IURs on IRIS that were calculated from oral values using a default ventilation rate and BW (see Appendix B for a list of these chemicals). It is not generally appropriate to make adjustments to these values

[31] In selecting an acute toxicity value, risk assessors should consider the duration associated with their estimate of exposure (e.g., a 1-hour versus a 24-hour air sample). Use of a toxicity value specified for a longer duration than that of the exposure estimate may overestimate hazard, while the use of a shorter duration acute reference value may underestimate hazard.

based on IR and BW using the intake equation, because the amount of the chemical that reaches the target site through the inhalation pathway is not a simple function of these parameters (see Section 1.2). Use of the toxicity values listed in Appendix B should be noted in the uncertainty section of the risk assessment (see Section 9).

4.2 Recommended Procedures for Assessing Risk in the Absence of Inhalation Toxicity Values

The following section provides guidance on recommended procedures for situations where inhalation toxicity values are not available in any of the toxicity data sources described in Section 4.1.

If RfC and IUR values are not available for an inhaled contaminant, risk assessors should first contact NCEA's STSC for guidance.[32] Risk assessors working on Superfund sites can contact STSC to determine whether a provisional peer-reviewed toxicity value (PPRTV) exists for a contaminant; if not, the risk assessor, in cooperation with the appropriate EPA Regional office may request that STSC develop a PPRTV document or that STSC develop an inhalation toxicity value as a "consult". The latter would be specific to the site in question only. Additional information on STSC's current process for developing alternative toxicity values is described in Appendix C.

If STSC indicates that no quantitative toxicity information for the inhalation route is available, the risk assessor should conduct a qualitative evaluation of this exposure route. The risk assessor should discuss in the uncertainty section of the risk assessment report the implications of not quantitatively assessing risks due to inhalation exposures to chemicals lacking inhalation toxicity data. See the section on Risk Characterization (Section 9) in this guidance for more information.

Performing simple route-to-route extrapolation without the assistance of STSC is generally not appropriate because hazard may be misrepresented when data from one route are substituted for another without any consideration of the pharmacokinetic differences between the routes (USEPA, 1998). The following circumstances, outlined in the *Inhalation Dosimetry Methodology* (page 4-6), are specific examples of situations when route-to-route extrapolation from oral toxicity values might not be appropriate, even for use during screening:

- When groups of chemicals are expected to have different toxicity by the two routes – for example, metals, irritants, and sensitizers;
- When a first-pass effect by the respiratory tract is expected;
- When a first-pass effect by the liver is expected;
- When a respiratory tract effect is established, but dosimetry comparison cannot be clearly established between the two routes;
- When the respiratory tract was not adequately studied in the oral studies; and
- When short-term inhalation studies, dermal irritation, in vitro studies, or characteristics of the chemical indicate the potential for portal-of-entry effects at the respiratory tract, but studies themselves are not adequate for inhalation toxicity value development.

[32] All contact with STSC should be performed by an EPA regional risk assessor. States and other entities should first contact their EPA regional risk assessor with questions on inhalation toxicity values. Regional risk assessors can then contact STSC on their behalf.

The *Cancer Guidelines* (USEPA, 2005a) includes the following statement regarding route-to-route extrapolation:

> "When a qualitative extrapolation can be supported, quantitative extrapolation may still be problematic due to the absence of adequate data. The differences in biological processes among routes of exposure (oral, inhalation, dermal) can be great because of, for example, first-pass effects and different results from different exposure patterns. There is no generally applicable method for accounting for these differences in uptake processes in a quantitative route-to-route extrapolation of dose-response data in the absence of good data on the agent of interest. Therefore, route-to-route extrapolation of dose data relies on a case-by-case analysis of available data" (page 3-10).

5. ESTIMATING RISKS

This section provides updated equations recommended for estimating excess cancer risks and HQs from inhaled contaminants of concern at Superfund sites. Please see Section 8.2.1 of *RAGS, Part A* for further information about how to interpret calculated excess cancer risks and HQs.

5.1 Cancer Risks Characterized by an Inhalation Unit Risk

The excess cancer risk for a receptor exposed via the inhalation pathway can be estimated with the following equation:

Risk = IUR x EC **(Equation 11)**

Where: IUR $(\mu g/m^3)^{-1}$ = Inhalation Unit Risk; and
EC $(\mu g/m^3)$ = exposure concentration (See Equation 6).

When estimated ECs are above the POD used for the low dose extrapolation described in Section 2.3, a linear concentration-response relationship may not hold.[33] In such situations, the risk assessor should not use toxicity values developed through low dose extrapolation techniques. Instead, the risk assessor may report semi-quantitative risk estimates (e.g., risks are greater than 10^{-2}) or estimate risk using the original model underlying the toxicity value, which can be found in the technical support document for the value (e.g., IRIS profile, PPRTV Assessment).

When estimating cancer risks for children, risk assessors should be aware of chemicals that pose a higher risk of cancer when exposure occurs during early life. If evidence exists suggesting differences in risk across age groups for a chemical, this typically will be considered in the derivation of the toxicity value and described in the chemical's technical support document.

[33] Reviews of chemical-specific IRIS files indicate that the risk level corresponding to the concentration level above which the IUR should not be used often falls at or near 10^{-2}. However, this risk level varies by chemical and, therefore, risk assessors should refer to the toxicity value's technical support document for information on the concentration range for which the IUR was intended to be used.

Chemicals that have been determined to cause cancer by a mutagenic mode of action (MOA) are thought to pose a higher risk during early life. An EPA-recommended procedure exists for assessing risks from these chemicals. Figure 3 summarizes the recommendations of the *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* (USEPA, 2005b; hereafter *Supplemental Cancer Guidelines*) on how to adjust childhood risk calculations to account for chemicals with a mutagenic MOA for carcinogenicity. Please refer to the *Supplemental Cancer Guidelines* (USEPA, 2005b) for a list of chemicals with a mutagenic MOA that were used in the development of that document.

In addition, EPA's website for the "Handbook for Implementing the Supplemental Cancer Guidance at Waste and Cleanup Sites" contains an up-to-date list of chemicals that EPA has determined to have a mutagenic MOA (http://www.epa.gov/oswer/riskassessment/sghandbook/index.htm). As chemicals receive new assessments for mutagenicity, this information will appear in the IRIS profile or PPRTV assessment.

FIGURE 3
GUIDANCE ON ASSESSING RISK FROM EARLY-LIFE EXPOSURES FOR CHEMICALS ACTING BY A MUTAGENIC MODE OF ACTION FOR CARCINOGENICITY

If a chemical has been determined to cause cancer by a mutagenic MOA, it is possible that exposures to that chemical in early-life may result in higher lifetime cancer risks than a comparable duration adult exposure.

In risk assessments of exposure to chemicals for which a mutagenic MOA for carcinogenicity has been determined by EPA and a linear low-dose extrapolation performed, one of the following generally pertains:

1) If chemical-specific data on susceptibility from early-life exposures were available for derivation of CSFs, those slope factors are used for risk characterization, and Age Dependent Adjustment Factors (ADAFs) are not applied.
2) If chemical-specific data on susceptibility from early-life exposures were not available, the ADAFs are applied in calculating or estimating risks associated with early-life exposures (USEPA, 2005c).

If the latter case applies, the *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* (USEPA, 2005b) recommends the following default ADAFs be applied in risk assessments:

- 10-fold adjustment for exposures during the first 2 years of life;
- 3-fold adjustment for exposures from ages 2 to <16 years of age; and
- No adjustment for exposures after turning 16 years of age.

In such cases, Equation 11 can be altered to include the ADAFs in the following way:

$$\text{Risk} = (\text{IUR} \times \text{EC}_{<2} \times \text{ADAF}_{<2}) + (\text{IUR} \times \text{EC}_{2\text{-}16} \times \text{ADAF}_{2\text{-}16}) + (\text{IUR} \times \text{EC}_{>16})$$

Sources: USEPA, 2005b and USEPA, 2005c.
Note: All communications and factsheets pertaining to the implementation of the 2005 *Cancer Guidelines* can be found at www.epa.gov/osa/spc/cancer_guidelines.htm.

5.2 Hazard Quotients

The HQ for the inhalation pathway can be calculated with the following general equation:

HQ = EC/(Toxicity Value[1] x 1000 µg/mg) **(Equation 12)**

Where: HQ (unitless) = Hazard Quotient;
EC ($\mu g/m^3$) = exposure concentration (See Equations 7 or 8);
Toxicity Value (mg/m^3) = Inhalation toxicity value (e.g., RfC) that is appropriate for the exposure scenario (acute, subchronic, or chronic).

[1] Risk assessors should refer to the flowchart (Figure 2) to select an appropriate inhalation toxicity value for the exposure scenario at a site in order to calculate the HQ.

6. EXAMPLE EXPOSURE SCENARIOS

This section of the guidance includes examples of the types of exposure scenarios risk assessors may encounter when evaluating inhalation exposures at waste sites. Each scenario includes sample values for exposure parameters and reviews the process of estimating the EC and risks for cancer and other health effects. These examples are provided for illustrative purposes only and are not representative of every exposure scenario that could be encountered at a site. Furthermore, risk assessors should use site-specific values for exposure parameters if practicable when estimating ECs and risk levels or HQs. This would typically require some information on activity patterns for the specific site or the use of professional judgment. If default values are to be used for certain exposure parameters, please consult the Superfund website for up-to-date information on Superfund-recommended default exposure parameters.[34]

6.1 Residential Receptor

An example of a residential scenario could consist of inhalation exposure for up to 24 hours per day, up to 350 days per year for 6 to 30 years. When estimating cancer risk for this type of scenario, Equation 6 is recommended to calculate an EC and Equation 11 is recommended to estimate risk. For estimating hazard quotients for cancer or non-cancer effects, this scenario can be evaluated using the steps outlined in Figure 2. The duration of this scenario ranges from 6 to 30 years, which can be considered chronic (because it consists of repeated exposures for approximately 10 percent of a receptor's lifespan). The frequency of this scenario is generally as frequent as a chronic toxicity test and therefore Equation 8 is recommended to derive a chronic EC and Equation 12 with a chronic toxicity value is recommended to calculate an HQ. If information about multiple MEs is available, risk assessors should proceed according to Section 3.4 to estimate ECs to use in estimating cancer risks or HQs.

When assessing the risk under the residential scenario for children, the risk assessor should keep in mind that exposure parameters, specifically those related to activity patterns (e.g., exposure time, frequency, and duration) may be different for children and adults at the same site. For example, due

[34] http://www.epa.gov/oswer/riskassessment/superfund_hh_exposure.htm.

to outdoor play patterns, children may spend more time near the source of contamination than adults, and thus would have higher exposure time and/or exposure frequency values than adults living in the same location.[35] For indoor vapor intrusion from the subsurface, very young children might be more highly exposed due to substantial time spent indoors.

Beyond the consideration of activity patterns, MEs, and chemicals with a mutagenic MOA for carcinogenicity (as described in Section 5.1), no additional adjustments to account for specific child receptors should be made to the default values. Appendix A of this document is intended to illustrate that the use of default values sufficiently covers age-related variation in DAF or HEC values derived using the EPA *Inhalation Dosimetry Methodology's* default approach.

6.2 Commercial-Industrial/Occupational Receptor

An example of a commercial-industrial or occupational inhalation exposure scenario could be characterized by full-time workers (e.g., 8 hours per day, 5 days per week) in an indoor setting, such as an office building, exposed via vapor intrusion of subsurface contamination on a daily basis for 5 to 25 years. When estimating cancer risk for this type of scenario, Equation 6 is recommended to calculate an EC and Equation 11 is recommended to estimate risk. Following the flowchart in Figure 2, the duration and exposure pattern of this scenario would typically be considered chronic. Therefore, Equation 8 is recommended to derive a chronic EC and Equation 12 is recommended (with a chronic RfC) when calculating an HQ for cancer or non-cancer effects. If information about multiple MEs is available, risk assessors should proceed according to Section 3.4 when deriving ECs to use in estimating cancer risks or HQs. Exposure parameters should be adjusted to consider the exposure time, frequency and duration for this scenario, which may differ from a residential scenario. Risk assessors should also use appropriate exposure parameters for outdoor workers who, similar to children, may spend more time near a source of contamination than indoor workers.

6.3 Construction Worker

One example of a construction worker scenario could involve a long-term project (1-2 years) with workers exposed regularly to contaminant vapors and fugitive dust (8 hours per day, 5 days per week). When estimating cancer risk for this type of scenario, Equations 6 and 11 are recommended to calculate an EC and the risk estimate, respectively. Following the flowchart in Figure 2, the duration of this exposure scenario would typically be considered subchronic. In addition, this exposure is generally as frequent as a subchronic toxicity test. Therefore, Equation 8 is recommended to derive a subchronic EC, and Equation 12 is recommended for use with a subchronic toxicity value to calculate the HQ. If information about multiple MEs is available, risk assessors should proceed according to Section 3.4 when deriving ECs to use in estimating cancer risks or HQs.

6.4 Trespasser/Recreational Receptor

An example trespasser/recreational scenario could consist of an exposure of 1 to 2 hours per day, for 100 days per year or less. When estimating cancer risk for this type of scenario, Equations 6 and 11

[35] For additional information about early-lifestage age groups to consider when assessing children's exposure to environmental contaminants, please consult EPA's *Guidance on Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants* (EPA, 2005d).

are recommended to calculate an EC and the risk estimate, respectively. Following the steps in Figure 2 for cancer or non-cancer effects characterized by an RfC, each exposure period should be assessed separately because this exposure lasts only one to two hours each day for an average of two days per week. Therefore, Equation 7 is recommended to derive acute ECs for each exposure period. In addition, Equation 12 is recommended for use with an acute toxicity value to calculate HQs for each exposure period.

7. TARGET CONCENTRATIONS FOR SCREENING ANALYSIS OF INHALATION PATHWAYS

For purposes of this guidance, risk-based screening levels are values that may be compared to the contaminant concentration in air to help risk assessors identify potential contaminants of concern. Screening levels can also be calculated for comparison with samples from source media at a site, such as soil. Screening levels are generally not appropriate for use as clean-up levels; they are intended to aid in initial evaluation of contaminants and exposure pathways of concern prior to proceeding with a baseline risk assessment.[36] If contaminant concentrations in air exceed the risk-based screening levels appropriate for the receptor population of interest, risk assessors should gather site-specific information to determine the need for any remedial action. The following sections outline a recommended approach for calculating screening levels in air as well as source media.

7.1 Target Contaminant Concentrations in Air

The equations recommended for estimating ECs and risk (Equations 6 through 12) can be used to calculate target contaminant concentrations in air by following the four steps outlined below in Table 4.[37]

If air samples from a site are found to be below the target concentration, the risk assessor can generally conclude that this pathway does not pose an unacceptable level of risk from the contaminant. If the concentrations are found to exceed the screening levels, the risk assessor should evaluate the inhalation pathway further by gathering additional site-specific data on contaminant levels, site conditions, and receptor characteristics.

7.2 Screening Levels for Other Media

Inhalation risk-based screening levels may also be calculated for media other than air, including soils, tap water, soil gas, and ground water. The soil gas and ground water values may be derived specifically to address concerns about vapor intrusion from subsurface contamination into indoor spaces.

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[36] EPA regions, states, or other agencies may support unique screening levels for specific purposes that may differ from the method presented in this document. Generally, when using screening levels it is important that risk assessors understand the target risks, toxicity, and exposure assumptions as well as migration-attenuation assumptions on which they are based, and to apply them for their intended use.

[37] Target contaminant concentrations in air calculated according to the procedure outlined in this document are generally protective for direct inhalation exposures. This process should not be used to calculate concentrations in air to be protective of indirect exposures (e.g., ingestion of crops contaminated through air delivery or vapor phase transfer, ingestion of livestock or fish contaminated indirectly through air deposition or vapor phase transfer).

TABLE 4 RECOMMENDED PROCEDURE FOR CALCULATING RISK-BASED SCREENING CONCENTRATIONS FOR CONTAMINANTS IN AIR		
	Cancer Risk-Based	**Hazard-Based**[1]
Step 1: Select Target Levels	Select target cancer risk (e.g., 1×10^{-6}).	Select target HQ (e.g., 1).
Step 2: Identify Toxicity Value[2]	Identify inhalation cancer potency value (e.g., IUR). If none exists, proceed with hazard-based screening level calculation.	Identify inhalation reference value (e.g., RfC) to match exposure scenario (acute, subchronic, or chronic). If none exist, proceed with cancer screening level calculation.
Step 3: Calculate CA	Using target cancer risk from Step 1 along with the receptor- and scenario-specific exposure parameter values, calculate CA; the following equation is recommended: CA = (AT x Target Risk)/(IUR x ET x EF x ED)	Using target HQ from Step 1 along with the receptor- and scenario-specific exposure parameter values, calculate CA; the following equation is recommended: CA = (AT x Target HQ x RfC x 1000 µg/mg)/(ET x EF x ED)
Step 4: Select Screening Concentration	Select minimum of predicted cancer risk- and hazard-based values as screening concentrations.[3] Repeat for each receptor/scenario combination of interest.	

[1] Hazard-based screening concentrations are typically derived from reference values such as RfCs. These values may be available for non-cancer effects but may include cancer, if a nonlinear MOA is thought to operate for a chemical.
[2] If no inhalation toxicity value is available for a chemical, contact STSC for further direction on how to proceed.
[3] Screening levels estimated from the equations presented in Step 3 could yield concentrations that exceed the maximum possible vapor concentration for a chemical. In such cases, it may be useful to calculate the maximum possible vapor concentration of the pure contaminant at the temperature of interest, using the following formula: $C_{max} = S \times H \times 10^3$ L/m^3, where S = solubility at 25° C (or temperature of interest) and H (unitless) = Henry's Law Constant at 25° C (or temperature of interest). This equation is based on an established relationship (see, for example, Schwartzenbach et al. 1993), that allows the Henry's Law Constant to be estimated as the ratio of a compound's vapor pressure and aqueous solubility for compounds that are slightly to moderately soluble in water. When the dimensionless Henry's Law constant, H, is used, the relationship described above can be used to calculate the vapor concentration of a saturated solution of a given compound, assuming equilibrium between the vapor and aqueous phases.

7.2.1 Soil Screening Levels

When evaluating risk in a source medium, such as soil, it is typically possible to calculate screening levels for that medium that are expected to be protective of inhalation exposures based on the expected transfer of a contaminant from the source medium to the air. Soil Screening Levels (SSLs) can be described as "risk-based soil concentrations derived for individual chemicals of concern from standardized sets of equations. These equations combine EPA chemical toxicity data with parameters defined by assumed future land uses and exposure scenarios, including receptor characteristics and potential exposure pathways" (USEPA, 2002b). These SSLs may be used for screening analyses and may serve as the basis for the development of Preliminary Remediation Goals (PRGs). Refer to the *Soil Screening Guidance* (USEPA, 1996) and the *Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites* (USEPA, 2002b) for recommended equations that can be used to calculate SSLs for volatilization of chemicals from soil to air and for particulate emissions.

7.2.2 Tap Water Screening Values

Contaminated tap water may pose risk by the inhalation route if the contaminants present are volatile. Screening levels can be calculated for tap water that account for inhalation exposures resulting from the household use of water (e.g., showering, laundering, dishwashing). Risk assessors should consult their local EPA regional risk assessor for direction on how to calculate appropriate screening levels for tap water.

7.2.3 Soil Gas or Ground Water Screening Values for Vapor Intrusion

If there is concern at a site about the possibility of migration of vapor-forming chemicals from contaminated soil gas or ground water into the indoor air of overlying buildings ("vapor intrusion"), screening values can be calculated for these media. Risk assessors should first follow the procedure outlined in Section 7.1 and Table 4 to calculate a risk-based target concentration for the contaminant in air.

For the calculation of a soil gas screening-level concentration, the target air concentration is then divided by an assumed screening-level attenuation factor. The attenuation factor (the ratio of indoor air divided by subsurface source concentration) represents the factor by which subsurface vapor concentrations migrating into indoor air spaces are reduced due to a variety of attenuating mechanisms.

For the calculation of a ground water screening-level concentration, the target air concentration is divided by an assumed screening-level attenuation factor, and the resulting soil gas concentration is converted to a corresponding ground water concentration, assuming equilibrium between the aqueous and vapor phases at the water table.

Risk assessors should consult their local EPA regional risk assessor for direction on how to calculate appropriate screening levels for soil gas and ground water when vapor intrusion is an issue at a site.

8. DEVELOPING AGGREGATE AND CUMULATIVE RISK ESTIMATES

EPA's current approach to estimating cumulative risk or hazard at a site from multiple chemicals, set forth in *RAGS, Part A* (USEPA, 1989), is not affected by the *Inhalation Dosimetry Methodology* and therefore is not being updated at this time. In addition, the aggregation of risks and hazards across multiple exposure routes should remain unchanged. The recommended approaches for aggregating risk and hazard estimates are outlined below.

8.1 Estimating Cumulative Risks and Hazards Across Multiple Chemicals

The recommended method for estimating cumulative risk and hazard at a site from exposure to multiple chemicals is described in *RAGS, Part A*, Section 8.2.2. This method is based on the default approaches described in *Guidelines for the Health Risk Assessment of Chemical Mixtures* (USEPA, 1986). Additional information on this method was subsequently published in the *Supplementary Guidance for Conducting Health Risk Assessment of Chemical Mixtures* (USEPA, 2000b). The recommended methods to use with quantitative cancer risk estimates as well as with HQs are outlined below.

8.1.1 Cancer Risks

When evaluating predicted cancer risks from multiple contaminants, risk assessors should estimate the cancer risk for each substance and then sum these risks. This yields an estimate of total cancer risk, which represents the cumulative predicted cancer risk for the chemicals at a site.

Risk assessors should note, however, that this recommended method assumes "independence of action by the compounds involved (i.e., that there are no synergistic or antagonistic chemical interactions and that all chemicals produce the same effect, i.e., cancer)" (USEPA, 1989). In addition, this simple additive approach is generally most appropriate for total cancer risks less than 0.1. If these assumptions are incorrect, over- or under-estimation of actual multiple-substance risk could result (USEPA, 1989).

8.1.2 Hazard Quotients

When the evaluation involves multiple chemicals assessed via HQs, risk assessors typically first calculate the HQ for each substance, and then sum the individual HQ values. This generally yields an estimated hazard index (HI) for the multiple chemicals assessed via a hazard-based approach. Separate HIs should be calculated for each type of exposure period (i.e., chronic, subchronic, acute). If an HI is greater than 1, it is generally appropriate to derive separate HIs for each target organ of concern (for more information, see *RAGS, Part A*, page 8-14).[38] When multiple acute exposures are present at a site, risk assessors should evaluate each acute exposure event separately. Hazards from multiple chemicals generally should be summed only when the exposures to these chemicals occur simultaneously.[39]

8.2 Aggregating Risk and Hazard Quotients Across Exposure Routes

Guidance for combining the multi-chemical risk estimates and hazard quotients across exposure pathways is described in *RAGS, Part A*, Section 8.3 (USEPA, 1989). In order to determine whether risks or HIs should be combined across exposure pathways, risk assessors should first identify reasonable exposure pathway combinations. Then, risk assessors should examine whether it is likely that the same individuals would consistently face the reasonable maximum exposure (RME) by more than one pathway.

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[38] This recommended method assumes that "the dose for each individual component is at a level at which effects are not expected to occur, be observable, or be of concern; however, when the doses are combined, effects of concern may be expected or observed in response to the higher dose level of the mixture" (EPA, 2000b, page 12). Another assumption of the HI approach is that the compounds induce the same effect by the same mechanism of action. Therefore, "application of the HI equation to a number of compounds that are not expected to induce the same type of effects or that do not act by the same mechanism, although appropriate as a screening-level approach, could overestimate the potential for effects" (EPA, 1989, page 8-14). This is generally less of a concern if one to two substances are responsible for driving the HI above 1.

[39] In cases where a single chemical is present at a site and receptors are exposed through a series of acute exposure events, the highest single EC should be compared to an acute reference value of the appropriate duration to assess hazard.

The recommended approach for estimating excess cancer risk from exposure via multiple routes is to first estimate cancer risk from each exposure pathway and then sum across the multiple routes.[40]

For the effects assessed via a reference value, risk assessors should calculate the HI for each exposure pathway and sum across the multiple routes. Separate total HIs should be calculated for each type of exposure period (i.e., chronic, subchronic or acute). If the HI exceeds one, there may be concern for potential adverse effects and risk assessors should consider deriving separate HIs for each target organ of concern.

9. RISK CHARACTERIZATION

Risk characterization is the final, summarizing step in conducting a risk assessment. Generally, the purpose of the risk characterization section of a report is to:[41]

- Describe the key findings of the risk assessment in a transparent manner, including identifying hazard, characterizing the dose-response relationship, and describing receptor exposures;
- Identify and describe the scientific and policy assumptions used in the assessment;
- Characterize uncertainties in results; and
- Provide an overall conclusion about the risks present at a site (USEPA, 2000c).

A well-crafted risk characterization section puts risk calculations into context for risk managers so that they may effectively weigh and interpret risk assessment results (i.e., it is the interface between risk assessment and risk management). A few of the key issues and uncertainties involved in calculating risks from inhalation exposures are outlined below.

9.1 Highly Exposed or Susceptible Populations and Life Stages

EPA recommends that the risk characterization portion of the risk assessment explain any particular susceptibilities to inhaled toxicants or potential for increased inhalation exposures among the various receptor groups at a site.[42] We discuss below two possible examples, children and worker receptors, though this discussion could apply to other receptor characteristics as well (e.g., age, disease, gender, genetic characteristics).

9.1.1 Children

One population group that could potentially be more highly exposed to inhalation exposures at a site is children. As discussed in Section 6.2, exposure parameters related to activity patterns (e.g., exposure time, frequency, and duration) and MEs, may vary across age groups. For example, due to outdoor play patterns, children may spend more time near the source of contamination than adults,

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[40] Note that this approach is generally most appropriate for total cancer risks of less than 0.1 (EPA, 1989).

[41] For specific information on the format of risk characterizations, refer to *Elements to Consider when Drafting EPA Risk Characterizations* (EPA, 1995c).

[42] EPA's IRIS glossary defines susceptibility as the following: "Increased likelihood of an adverse effect, often discussed in terms of relationship to a factor that can be used to describe a human subpopulation (e.g., life stage, demographic feature, or genetic characteristic)" (EPA, 2008b).

and thus would have higher exposure time and/or exposure frequency values than adults living in the same location. Therefore, it is important to carefully describe site-specific exposures to children, and assumptions made in risk calculations.[43]

If chemical-specific data on susceptibility to the toxic effects from early life exposures are available, these data are considered when developing toxicity values that specifically address differential toxicity to the young (e.g., vinyl chloride) (USEPA, 2005c). Toxicity values derived using the default approach from the *Inhalation Dosimetry Methodology* are developed for the human population as a whole, including sensitive subgroups. Therefore, as described in Section 6 of Appendix A, no quantitative adjustment of toxicity values derived using the default approach in the *Inhalation Dosimetry Methodology* is recommended for specific age groups to account for different ventilation rates or body weights of specific age groups.

When evaluating risk to carcinogenic chemicals with a demonstrated mutagenic MOA but which lack chemical-specific information on susceptibility from early life exposures, EPA recommends a quantitative adjustment of the toxicity value to account for early life susceptibility, as described in the *Supplemental Cancer Guidelines* (see USEPA, 2005b & 2005c; and Section 5.1 of this guidance for further information).

9.1.2 Workers

Workers could have increased exposure under certain occupational scenarios. Some outdoor workers might spend more time near a source of contamination in the course of their job and this should be reflected in adjustments to the exposure parameters (e.g., ET, Exposure Frequency (EF), and ED) describing the worker exposure scenario. Toxicity values derived using the *Inhalation Dosimetry Methodology* are developed for the human population as a whole, including sensitive populations and life stages. In the default *Inhalation Dosimetry Methodology* approach, typical variation in IRs between periods of high activity and rest is considered. However, if workers have especially high levels of exertion with correspondingly high ventilation rates, these workers could be at the upper end of the risk range, particularly if they are exposed to Category 1 gases, which have direct effects in the respiratory tract. This implication should be recognized in the risk characterization section.

9.2 Uncertainties in Inhalation Risk Assessment

This guidance recommends including an assessment of the key uncertainties that may significantly impact risk estimates for inhaled chemicals. This should ensure transparency, clarity, reasonableness and consistency in risk assessments, as recommended by EPA's *Policy for Risk Characterization* (USEPA, 1995a). Other sources of uncertainty may be present and other EPA documents provide guidance on characterizing uncertainty in risk the assessment process (USEPA, 1992, 1995a, 1995b, 1995c, 1997a, 1997b). Key uncertainties related to inhalation risk assessment, which is the focus of this section, include the development of ECs, choice of toxicity value, lack of quantitative toxicity information via inhalation, and the approach to estimating and aggregating risks. According to EPA's *Guidance for Risk Characterization*, the discussion of uncertainty "should reflect the type and complexity of the risk assessment, with the level of effort for analysis and discussion of uncertainty

[43] For additional information on children's health risk assessment, please consult *A Framework for Assessing Health Risks of Environmental Exposures to Children* (EPA, 2006b).

corresponding to the level of effort for the assessment" (USEPA, 1995b). Therefore, risk assessors should provide a qualitative and/or quantitative evaluation of key uncertainties pertaining to inhalation risk, and their impact on the outcome of the assessment, consistent with the level of effort of the specific risk assessment.

9.2.1 Development of Exposure Concentrations

As described in Section 3 of this guidance, with the exception of acute exposures, time-weighted averages are typically used to represent intermittent or variable inhalation exposures to receptors at a site. This recommended approach is consistent with the duration adjustment approach (based on Haber's Law) that is generally used in deriving the toxicity values (see Section 2.1.1.1 for further information). As mentioned in Section 3, when evaluating situations in which the exposure is long-term, yet there are short periods of significantly higher exposure, those periods should also be assessed using appropriate short-term toxicity values. This ensures that periods of much higher exposure can be appropriately assessed and not "diluted out" in the assessment of longer-term exposure.

When information on multiple MEs exists at a site, risk assessors may choose to estimate ECs as outlined in Section 3.4. However, this typically requires sufficient time-activity information of receptors at a site to accurately determine the time spent in each ME. Incomplete or low quality data on time-activity pattern may introduce uncertainty into the estimation of the ECs for MEs. Risk assessors should describe the quality and completeness of these data.

The recommended method for determining the CA at a site can potentially introduce uncertainty into the EC calculations. For instance, if contaminant concentrations in air are measured, risk assessors should consider uncertainties related to how well the set of air samples available at a site represents the duration and time period being assessed as well as measurement uncertainty related to the methods and equipment used. In addition, risk assessors should describe any potential confounding of indoor air samples by other sources of contaminants (e.g., household products). If contaminant concentrations in air are modeled, (e.g., by EPA's spreadsheet models for vapor intrusion) risk assessors should address model-related uncertainties and their potential impact on the estimate of contaminant concentrations in air. Considerations of particle size at the site versus particle size used to derive the toxicity value are also important.

9.2.2 Toxicity Assessment

Section 4.1 of this document indicates that some IURs on IRIS were developed through extrapolation from oral CSFs (see Appendix B of this document). The use of toxicity values derived through simple route-to-route extrapolation introduces additional uncertainty into risk calculations. Therefore, risk assessors should indicate when extrapolated IURs are used and should characterize the potential impact of the uncertainty associated with using these values, if known.

Section 4.2 and Appendix C of this guidance recommends contacting STSC to help identify appropriate toxicity values for conducting a risk assessment at Superfund sites in the absence of published inhalation toxicity values. If STSC is unable to recommend a toxicity value, risk assessors should acknowledge the resulting uncertainty in risk associated with the chemical(s) lacking inhalation toxicity data. If STSC provides risk assessors with a toxicity value based on a PBPK

model, model uncertainty should be discussed. In addition, if STSC provides risk assessors with one or more structurally analogous chemicals, risk assessors can use toxicity data for these chemicals to help characterize the potential magnitude of the inhalation risk associated with the chemical(s) lacking data. In this case, risk assessors should acknowledge the uncertainty associated with relying on toxicity data for analogous chemicals to characterize risk at the site.

Risk assessors should also acknowledge chemicals that lack duration-appropriate toxicity values and discuss the potential impacts of substituting alternative toxicity values for HQ calculations. For instance, if the ED is determined to be subchronic but no subchronic inhalation RfC or analogous toxicity value is available for that chemical, the risk assessor should address the uncertainty associated with calculating an HQ using a toxicity value for a different duration, such as chronic, or the impact of not quantifying those risks. In addition, if risk assessors use an acute toxicity value that does not match the duration of the acute exposure being assessed, the possibility of under or overestimating hazard should be discussed.

When conducting a screening-level risk assessment using screening values such as those described in Section 7, it is important to further evaluate and clearly describe the quality and uncertainties associated with the inhalation toxicity values used in the risk assessment if measured sample contaminant concentrations at a site exceed these screening values.

9.2.3 Estimating Cancer Risks

For high exposures, for example those within the range of epidemiological studies (usually those predicted to have risks greater than 10^{-2}), the IUR derived from the linear extrapolation below the range of observation is generally not appropriate for use (see Section 5.1 of this document for further information).[44] Risk assessors should provide specific information in the risk characterization describing how these high exposures were addressed in the risk assessment. For instance, if a risk assessor chose to provide a semi-quantitative approach (e.g., indicating that risks are above 10^{-2}), this should be indicated, along with a description of the uncertainties involved in not fully quantifying risk associated with exposure to this chemical. If a risk assessor chose to use the original model in the IRIS file or other technical background document, the risk characterization section should include a description of any uncertainties in the model used and could contain examples of the risks estimated.

9.2.4 Estimating Risk and Hazard from Multiple Chemicals and Exposure Pathways

Risk assessors should also describe uncertainties involved in aggregating risk and hazard across multiple chemicals and exposure pathways. For instance, the approaches described in Section 8 of this document are associated with several assumptions (e.g., independence of action and doses for individual compounds at levels not expected to be of concern). If these assumptions are not met, aggregation may not be appropriate. This should be fully described in the risk characterization section and any uncertainties involved in the lack of quantitative information should be indicated.

[44] Also refer to Section 8.2.1 of *RAGS, Part A* for further discussion of this topic (EPA, 1989, page 8-6).

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APPENDIX A

APPENDIX A

ANALYSIS OF DEFAULT APPROACH FOR HEC DERIVATION AS COMPARED TO POPULATION- AND LIFESTAGE-SPECIFIC CALCULATIONS

NOTE: The Agency's inhalation dosimetry methodology (USEPA, 1994; hereafter, "the *Inhalation Dosimetry Methodology*") is a technical report that describes the derivation of human equivalent concentrations (HECs) from animal (or human) studies, as well as the other steps involved in developing a chronic Reference Concentration (RfC). This appendix is included to illustrate the HEC derivation using the *Inhalation Dosimetry Methodology*'s default approach (with the recommended default values for humans), and to also illustrate the impact of substituting alternate age- and activity-specific human values into the default calculations. The default approach is employed for chemicals for which more chemical-specific dosimetric and pharmacokinetic data are not available, thus precluding the use of more advanced models for deriving the HEC. The calculations in this appendix do not represent a refined or optimal model for assessing intra-human variability (e.g., age- and activity-specific risks), and are not intended to imply that risk assessors should deviate from the *Inhalation Dosimetry Methodology* by substituting alternate values into the default calculations. Age-specific data are limited. Because of these limitations, the calculations made for different ages and exposure groups in this appendix are not recommended for use in quantitative risk assessment (i.e., they are only for the purpose of illustration), but may be useful in discussions of uncertainty and variability associated with the default approach.

It is also noted that, as of this writing, the Agency is involved in a routine reevaluation of scientific advancements in the field, with consideration of the need for improvement to the *Inhalation Dosimetry Methodology*. Any revisions will consider current understanding of inhalation dosimetry and differences across and within species, as well as the Agency's risk assessment needs. In order to transparently and quantitatively address children's inhalation dosimetry and risk assessment, this guidance document will be updated (on-line) when Agency methodology updates are available that are specific to early life. Until that time, the 1994 *Inhalation Dosimetry Methodology* is the appropriate Agency methodology.

INTRODUCTION

This appendix consists of examples and discussions illustrating the current default chemical category-specific approach to inhalation dosimetry for the various categories of gases and particles as described in *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry* (USEPA, 1994; hereafter, the *Inhalation Dosimetry Methodology*). This default inhalation dosimetry approach is used to convert toxicological and epidemiological study data to an HEC that can then be used to derive chronic RfCs for the human population (inclusive of susceptible populations and life stages, such as children) and also in the development of Inhalation Unit Risks (IURs) (USEPA, 2005). The default approach does not rely on age- or activity-specific values for physiological parameters when calculating HECs; however the default approach has been designed by EPA to derive reference values that are protective across the entire population.

The appendix includes six sections. Sections 1 through 3 address Category 1 gases. These sections provide example calculations for Category 1 highly reactive, high water solubility gases that are typically absorbed in the upper airways, exhibiting adverse effects in the extrathoracic (ETh), tracheobronchial (TB), and pulmonary (PU) regions of the respiratory tract, respectively. These examples include comparisons of HEC calculations based on default parameters with those derived using age- and activity-specific parameters for the respiratory region affected. Section 4 addresses Category 3 low reactivity, limited water solubility gases that exhibit systemic effects outside the respiratory tract. Section 5 addresses changes in particle deposition in the respiratory tract across age groups. The conclusions are summarized in Section 6.

When reviewing the examples, please note the following:

- An RfC derived using the *Inhalation Dosimetry Methodology* is defined as "an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime" (USEPA, 2008).

- All examples in this appendix are based on the *Inhalation Dosimetry Methodology*. EPA is committed to periodically reviewing and updating the *Inhalation Dosimetry Methodology* to ensure that it reflects the current state of the science and that it yields toxicity values that sufficiently cover potential age- and activity-related variation in inhalation exposure. A review and update is currently underway.

- The examples in this appendix are all based on calculating HECs from a point of departure (POD) for non-cancer effects (e.g., a No Observed Adverse Effect Level (NOAEL), Lowest Observed Adverse Effect Level (LOAEL), or Benchmark Concentration, Lower confidence limit (BMCL)). These calculations could also be performed in an identical manner for carcinogens using a POD for cancer risk estimate derivation (e.g., a Lower limit on the Effective Concentration (LEC) value).

- The default animal and human values for minute volume (V_e) and surface area (SA) used in these examples were obtained from *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry* (USEPA, 1994).[45] The age- and activity-specific V_e values were obtained from the International Commission on Radiological Protection (ICRP) Publication 66, *Human Respiratory Tract Model for Radiological Protection* (ICRP, 1994).[46] Age-specific SA values used in Examples 1 and 2 were calculated using scaled estimates for the mass and thickness of respiratory region-specific target tissue from ICRP (1994); Values for Example 3 were calculated from an allometric scaling equation presented in a publication by Zeltner et al. (1987). EPA's Office of Research and Development (ORD) selected these data following review of the available physiological data for the age groups indicated in the examples.

- Chemical-specific data from the Integrated Risk Information System (IRIS) file for acrolein were used in the ETh example (Example 1). However, the other two examples, which focus on effects in the TB and PU regions, respectively, use hypothetical data for the POD because there are currently no chemicals on IRIS exhibiting Critical Effects (for RfC derivation) in those regions.[47] The conclusions of these two examples are unaffected by the use of hypothetical data because the results are driven by the values of parameters that are not chemical-specific (i.e., SA and V_e).

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[45] The minute volume is the total ventilation per minute and equals the product of the tidal volume (the air volume entering or leaving the lungs with a single breath) and the respiratory frequency.

[46] For further information on inhalation rates in humans under different scenarios, refer to Chapter 5 of EPA's *Exposure Factors Handbook* (EPA, 1997).

[47] Hypothetical examples for the TB and PU regions were included in this appendix because currently no RfCs for gases on IRIS are calculated based on animal studies showing health effects occurring in these regions of the respiratory system

1. EXAMPLE 1: CATEGORY 1 GAS, EXTRATHORACIC EFFECTS, ACROLEIN

The Dosimetric Adjustment Factor (DAF) for a Category 1 gases, the Regional Gas Dose Ratio (RGDR), is based on the animal to human ratio of the V_e divided by the SA of the region of the respiratory tract where the effect occurs. For acrolein, the effect occurs in the ETh region. The DAF is typically calculated using the following equation (USEPA, 1994, Equation 4-18):

$$RGDR_{ETh} = \frac{\left(\frac{V_e}{SA_{ETh}}\right)_{animal}}{\left(\frac{V_e}{SA_{ETh}}\right)_{human}} = \frac{\frac{0.14\,L/min}{15\,cm^2}}{\frac{13.8\,L/min}{200\,cm^2}} = 0.14 \qquad \textbf{(Equation A-1)}$$

The default *Inhalation Dosimetry Methodology*-recommended values for the V_e and SA_{ETh} of the Wistar rat (the animal in the principal study for acrolein) are 0.14 L/min (0.20 m^3/day) and 15 cm^2, respectively (USEPA, 1994). EPA's default human values are 13.8 L/min (20 m^3/day) for V_e and 200 cm^2 for SA_{ETh} (USEPA, 1994). The RGDR for the ETh region ($RGDR_{ETh}$) was calculated using these values for the rat and the human as shown in Equation A-1. In the laboratory animal study on acrolein, the LOAEL adjusted for continuous exposure ($LOAEL_{[ADJ]}$) of 0.16 mg/m^3 (USEPA, 2003) is used as the point of departure. The $LOAEL_{[HEC]}$ is the $LOAEL_{[ADJ]}$ multiplied by the $RGDR_{ETh}$.

To illustrate any potential age- or activity-related variation in the $LOAEL_{[HEC]}$ that might result from using human parameter values other than the defaults, scaled estimates for the mass and thickness of ETh target tissue from ICRP (1994) at different ages are used to calculate the SA_{ETh} values in Table A-1. Age- and activity-related V_e reported in ICRP (1994) are based on daily time-budgeted reference values. Table A-1 shows little variation in the resultant $LOAEL_{[HEC]}$ across the groups in this example. The default procedure produces the lowest $LOAEL_{[HEC]}$ value in Table A-1 and is, therefore, sufficient to cover all of these groups.

TABLE A-1 COMPARISON OF THE HEC-DEFAULT (EPA, 1994) WITH EXAMPLE $LOAEL_{[HEC]}$ VALUES FOR HUMANS OF DIFFERENT AGES AND ACTIVITY PATTERNS FOR THE EXTRATHORACIC REGION					
	Total $V_{e\,(human)}$ (L/min)[a]	$SA_{ETh\,(human)}$ (cm^2)[b]	$(V_e/SA_{ETh})_{human}$ (L/min-cm^2)	$RGDR_{ETh}$	$LOAEL_{[HEC]}$ (mg/m^3)
Outdoor Worker, Male	17.5	470	0.037	0.25	0.04
Sedentary Worker, Male	15.4	470	0.033	0.28	0.04
Sedentary Worker, Female	12.6	407	0.031	0.30	0.05
15 Year-Old Male	14.0	439	0.032	0.29	0.05
15 Year-Old Female	10.9	397	0.027	0.35	0.06
10 Year-Old	10.6	293	0.036	0.26	0.04
5 Year-Old	6.1	198	0.031	0.30	0.05
1 Year-Old	3.6	97.1	0.037	0.25	0.04
3 Month-Old	2.0	65.8	0.030	0.31	0.05
HEC - Default	13.8	200	0.069	0.14	0.02
[a] These values are from the ICRP publication, Tables 8, 27, B.16a, B.16b and B.17 (ICRP, 1994). [b] These values are from the ICRP publication, Tables 1 and 5 (ICRP, 1994).					

2. EXAMPLE 2: CATEGORY 1 GAS, TRACHEOBRONCHIAL EFFECTS, HYPOTHETICAL CHEMICAL

The DAF for a Category 1 gas or vapor exhibiting effects in the TB region is based on the animal to human ratio of the V_e divided by the SA of the TB region for each species. The DAF is typically calculated using the following equation:

$$RGDR_{TB} = \frac{\left(\frac{V_e}{SA_{TB}}\right)_{animal}}{\left(\frac{V_e}{SA_{TB}}\right)_{human}} = \frac{\frac{0.14\ L/min}{22.5\ cm^2}}{\frac{13.8\ L/min}{3200\ cm^2}} = 1.4 \qquad \textbf{(Equation A-2)}^{48}$$

This example assumes that the hypothetical chemical has been tested on Wistar rats and therefore utilizes the EPA animal default values for that strain. The V_e value used is 0.14 L/min (0.20 m^3/day) and the default SA_{TB} is 22.5 cm^2 (USEPA, 1994). EPA's default human values are 13.8 L/min (20 m^3/day) for V_e and 3200 cm^2 for SA_{TB} (USEPA, 1994). The RGDR for the TB region ($RGDR_{TB}$) is calculated using these values for the rat and the human, as shown in Equation A-2. The example also assumes a NOAEL adjusted for continuous exposure ($NOAEL_{[ADJ]}$) of 0.16 mg/m^3 as the point of departure. The $NOAEL_{[HEC]}$ is the $NOAEL_{[ADJ]}$ multiplied by the $RGDR_{TB}$.

Table A-2 shows little variation across age and activity groups in the $NOAEL_{[HEC]}$. The variation from the default (less than a factor of 2) is less than the default value of 10 used for the uncertainty factor for intraspecies variability when deriving the RfC. Application of the normal procedure for

[48] This equation is the reduced, default version of Equation 4-19 of the *Inhalation Dosimetry Methodology*. Equation 4-19 is reduced to this form consistent with the derivation of the reduced form of the RGDR equation of extrathoracic effects described in section 4.3.6.1 and Appendix I of the *Inhalation Dosimetry Methodology*.

determining the RfC will accommodate the observed variation. In addition, RfCs and IURs are developed for chronic exposure and will generally involve an exposure for multiple years.

TABLE A-2
COMPARISON OF THE HEC-DEFAULT (EPA, 1994) WITH EXAMPLE $LOAEL_{[HEC]}$ VALUES FOR HUMANS OF DIFFERENT AGES AND ACTIVITY PATTERNS FOR THE TRACHEOBRONCHIAL REGION

	Total $V_{e\,(human)}$ (L/min)[a]	$SA_{TB\,(human)}$ (cm^2)[b]	$(V_e/SA_{TB})_{human}$ (L/min-cm^2)	$RGDR_{TB}$	$NOAEL_{[HEC]}$ (mg/m^3)
Outdoor Worker M	17.5	2660	0.0066	0.94	0.15
Sedentary Worker M	15.4	2660	0.0058	1.1	0.18
Sedentary Worker F	12.6	2640	0.0048	1.3	0.21
15 year M	14.0	2520	0.0056	1.1	0.18
15 year F	10.9	2250	0.0048	1.3	0.21
10 Year	10.6	1830	0.0058	1.1	0.18
5 Year	6.1	1340	0.0046	1.4	0.22
1 Year	3.6	857	0.0042	1.5	0.24
3 Months	2.0	712	0.0028	2.2	0.35
HEC-default	13.8	3200	0.0043	1.4	0.22

[a] These values are from the ICRP publication, Tables 8, 27, B.16a, B.16b and B.17 (ICRP, 1994).
[b] These values are from the ICRP publication, Tables 1 and 5 (ICRP, 1994).

3. EXAMPLE 3: CATEGORY 1 GAS, PULMONARY EFFECTS, HYPOTHETICAL CHEMICAL

The DAF for a Category 1 gas or vapor with an effect in the PU region is based on the animal to human ratio of the alveolar ventilation rate (Q-alv) divided by the SA of the PU region (SA_{PU}) for each species. The Q-alv is approximately equal to the V_e multiplied by 0.7. This adjustment accounts for the anatomic/physiologic deadspace in the PU region, making the Q-alv equivalent to the amount of inspired air available for gas exchange (West, 2000). The DAF for this region of the respiratory tract is typically calculated using the following equation:

$$RGDR_{PU} = \frac{\left(\frac{Q-alv}{SA_{PU}}\right)_{animal}}{\left(\frac{Q-alv}{SA_{PU}}\right)_{human}} = \frac{\frac{0.1\,L/min}{0.34\,m^2}}{\frac{9.7\,L/min}{54\,m^2}} = 1.6 \qquad \textbf{(Equation A-3)}^{49}$$

This example assumes that the hypothetical chemical has been tested on Wistar rats and therefore utilizes the EPA animal default values for that strain. The V_e valued used is 0.14 L/min (0.20 m^3/day), which when multiplied by 0.7, yields a Q-alv of 0.1 L/min. The example uses the EPA default rat SA_{PU} of 0.34 m^2 (USEPA, 1994). EPA's default human values are 13.8 L/min (20

[49] This equation is the reduced, default version of Equation 4-23 of the *Inhalation Dosimetry Methodology*. Equation 4-23 is reduced to this form consistent with the derivation of the reduced form of the RGDR equation of extrathoracic effects described in section 4.3.6.1 and Appendix I of the *Inhalation Dosimetry Methodology*.

m^3/day) for V_e (which yields a Q-alv of 9.7 L/min) and 54 m^2 for SA_{PU} (USEPA, 1994). The RGDR for the PU region ($RGDR_{PU}$) is calculated using these values for the rat and the human, as shown in Equation A-3. The example also assumes a $NOAEL_{[ADJ]}$ of 0.16 mg/m^3 as the point of departure. The $NOAEL_{[HEC]}$ is the $NOAEL_{[ADJ]}$ multiplied by the $RGDR_{PU}$.

Table A-3 below provides the Q-alv values for humans based on the daily time-budgeted V_e for different ages and activity levels from the ICRP publication (1994). SA data for the PU region in the ICRP publication are estimated using an allometric scaling model fitted to data from a morphometric analysis of SA_{PU} in a sample of seven children (ranging in age from 26 days to 5 years) and eight adults (Zeltner et al., 1987). ORD selected the Zeltner analysis for this example because these SA_{PU} data are based on empirical morphometric measurements of human lungs as opposed to scaled estimates determined from lung models (such as those done by Yu and Xu, 1987 or Yu and Yoon, 1991). In addition, the children and adult SA_{PU} values calculated in the Zeltner analysis are supported by several independent studies that measured SA_{PU} in children (Langston et al., 1984) or in adults using similar morphometric techniques (Crapo et al., 1982 & 1983; Stone et al., 1992; Mercer et al., 1994).

Table A-3 shows little variation in the resultant $NOAEL_{[HEC]}$ across the groups in this example. The default procedure produces the lowest $NOAEL_{[HEC]}$ value in Table A-3 and is, therefore, sufficient to cover all of these groups.

TABLE A-3

COMPARISON OF THE HEC-DEFAULT (EPA, 1994) WITH EXAMPLE $LOAEL_{[HEC]}$ VALUES FOR HUMANS OF DIFFERENT AGES AND ACTIVITY PATTERNS FOR THE PULMONARY REGION

	Total V_e (L/min)[a]	Q-$alv_{(human)}$ (L/min)[b]	$SA_{PU\ (human)}$ (m^2)	$(Q\text{-}alv/SA_{PU})_{human}$ (L/min-m^2)	$RGDR_{PU}$	$NOAEL_{HEC}$ (mg/m^3)
Outdoor Worker, Male	17.5	12	139	0.088	3.3	0.53
Sedentary Worker, Male	15.4	11	139	0.078	3.7	0.59
Sedentary Worker, Female	12.6	8.8	114	0.077	3.8	0.61
15 Year-Old Male	14.0	9.8	108	0.091	3.2	0.51
15 Year-Old Female	10.9	7.6	100	0.076	3.8	0.61
10 Year-Old	10.6	7.4	62.0	0.12	2.4	0.38
5 Year-Old	6.1	4.3	37.3	0.11	2.6	0.42
1 Year-Old	3.6	2.5	18.5	0.14	2.1	0.34
3 Month-Old	2.0	1.4	11.0	0.13	2.2	0.35
HEC-Default	13.8	9.7	54.0	0.18	1.6	0.26

[a] These values are from the ICRP publication, Tables 8, 27, B.16a, B.16b and B.17 (ICRP, 1994).
[b] These values are from Zeltner et al. (1987).

4. CATEGORY 3 GASES

The DAF for a Category 3 gas or vapor is based on the ratio of the animal blood:gas partition coefficient to the human blood:gas partition coefficient and is typically calculated using the following equation:

$$DAF = \frac{(H_{b/g})_{animal}}{(H_{b/g})_{human}} \qquad \textbf{(Equation A-4)}$$

The blood:gas partition coefficient is primarily determined by the solubility of the gas in an aqueous medium as well as the protein and lipid content of the blood. There is little reason to suspect that the blood:gas partition coefficient for a non-metabolized chemical will vary greatly across the human population. The limited data available indicate no difference in the blood:gas partition coefficient with age for methylene chloride in mice (Thomas et al., 1996), and for sevoflurane, isoflurane, and halothane in humans (Malviya and Lerman, 1990). Two studies examining the solubility of volatile anesthetics (isoflurane, enflurane, halothane, and methoxyflurane) in the blood and body tissues found higher blood:gas partition coefficients in adults compared with children (Lerman, et al., 1984 & 1986). Any variability in the blood:gas partition coefficient with age is expected to be less than the default value of 10 used for the uncertainty factor for intraspecies variability when deriving the RfC. Any variability in the blood:gas partition coefficient with age is also not expected to cause a large overestimate or underestimate in the calculated cancer risk.

Because of the limited data available, the *Inhalation Dosimetry Methodology* makes the science policy decision to use a value of one for the ratio of the partition coefficients when the animal to human ratio exceeds one or when the animal or human value is unknown. At this time, all chemicals on IRIS for which both human and animal data are available have an animal to human ratio of partition coefficient greater than 1.[50] Therefore, the default assumption of one is a conservative approach that is not likely to underestimate the chemical-specific DAF.

5. PARTICLE DEPOSITION ACROSS AGE GROUPS

The DAF for a particle causing an effect in the respiratory tract, the Regional Dose Deposition Ratio ($RDDR_r$), is based on the animal to human ratio of the V_e and the fractional deposition of the particle in that region (F_r), divided by the surface area of the region where the effect occurs (SA_r) (USEPA, 1994). Inherent in this derivation is the assumption that 100 percent of the deposited dose remains in the respiratory tract and any clearance mechanisms are not considered. The $RDDR_r$ is typically calculated using the following equation:

$$RDDR_r = \frac{\left(\frac{V_e}{SA_r} \times F_r\right)_{animal}}{\left(\frac{V_e}{SA_r} \times F_r\right)_{human}} \qquad \textbf{(Equation A-5)}$$

[50] While 1,4-dioxane has not yet been evaluated on IRIS, it provides an exception to this statement, in that the blood:gas partition coefficient is 2750 for mice, 1850 for rats, and 3650 for humans, yielding an animal to human ratio of 0.75 for mice and 0.51 for rats (Reitz et al., 1990).

The DAF for a particle causing an extra-respiratory (ER) effect, the $RDDR_{ER}$, is based on the animal to human ratio of the V_e and the total deposition of the particle in the entire respiratory tract (F_{total}), divided by body weight (BW) (USEPA, 1994). The $RDDR_{ER}$ assumes that 100 percent of the deposited dose in the entire respiratory tract is available for uptake into the systemic circulation. The following general equation can be used to estimate the $RDDR_{ER}$:

$$RDDR_{ER} = \frac{\left(\frac{V_e}{BW} \times F_{total}\right)_{animal}}{\left(\frac{V_e}{BW} \times F_{total}\right)_{human}} \qquad \textbf{(Equation A-6)}$$

The information on particle deposition in various age groups is quite limited. A discussion of the current state of the science can be found in the *Air Quality Criteria for Particulate Matter Volume II*, Section 6.2.3.2 (USEPA, 2004; hereafter, *PM Criteria Document*).

Experimental and modeling results are summarized in Table A-4. The results for experimental studies are mixed, some suggesting higher deposition in children and others finding no difference across age groups. Bennett and Zeman (1998) and Schiller-Scotland et al. (1994) found no difference between total deposition of particles in the respiratory tract of children (aged 7 to14 and 6 to12, respectively) and adults for 1 to 2 micrometer particles. Schiller-Scotland et al. did find two- to three-fold higher total particulate deposition in 6 to 12 year olds for particles of 2 to 3 micrometers in size. In addition, Bennett et al. (1997) found that deposition in the ETh region was 50 percent greater in children than adults. The *PM Criteria Document* concludes that "these...studies ...do not provide unequivocal evidence for significant differences in deposition between adults and children" (USEPA, 2004, page 6-29). The document notes, however, that children may have higher activity levels and higher associated minute ventilation per lung size, potentially causing a greater size-specific dose of particles to the lung.

Modeled results suggest a higher deposition of particles in the TB region of children when compared to adults, depending on the particle size (Xu and Yu (1986); Hofmann et al. (1989); Musante and Martonen (1999); Phalen and Oldham (2001); Asgharian et al. (2004); Jarabek et al. (2005); Ginsberg et al. (2005)). Mixed results again are found in modeling studies for total deposition and deposition in other respiratory regions. In general, where differences are observed in either experimental or modeled studies, variability in deposition between age groups has been reported to be most often in the range of 1- to 3-fold greater for children than for adults, but ranging from equivalency or less up to 7-fold greater.[51]

[51] A modeling analysis examining deposition fraction per unit area at various airway generations of the lung as a function of age for various particle sizes (ranging from 0.01 to 10 μm) reported comparisons between a 3-month old and 21-year old that ranged from equivalency up to a 14-fold difference in this metric for some specific airway generations (Asgharian et al., 2004).

TABLE A-4
PARTICLE DEPOSITION ACROSS AGE GROUPS

Study	Particle Size	Results
Experimental Studies		
Becquemin et al. (1991)	Various	Nasal deposition higher in adults (up to 1.8-fold higher at rest and up to 3.4-fold higher during exercise) than children – meaning that thoracic airways of children are less protected than those of adults.
Bennett et al. (1997)	4.5 µm	-ETh deposition of particles 50 percent greater in children (higher for younger ages). -No significant difference in total respiratory tract deposition.
Bennett and Zeman (1998)	1-2 µm	No difference between 7-14 year olds and adults in total deposition of particles in the respiratory tract.
Schiller-Scotland et al. (1994)	1-2 µm	No difference between 6-12 year olds and adults in total deposition of particles in the respiratory tract.
	2-3 µm	Two- to three-fold higher total deposition of particles in 6-12 year olds versus adults.
Modeled Studies		
Asgharian et al. (2004)	0.01-10 µm	-Up to 1.2-fold higher total deposition in 3 month olds compared to adults in the TB region. -Up to 1.5-fold higher total deposition in 8 year olds compared to adults in the alveolar region. Total deposition higher in adults than 3 and 23 month olds (up to 2-fold). -Estimates of deposition fraction per unit area at various airway generations of the lung and various particle sizes highest for 3 month olds compared to adults (up to 14-fold). Higher deposition also seen for 23 month olds (up to 5-fold) and 8 year olds (up to 3-fold) compared with adults. No difference in deposition in 14 year olds compared to adults.
Cheng et al. (1995)	0.0046-0.2 µm	Nasal casts of children's airways found increased deposition efficiency for ultrafine particles with decreasing age, suggesting that young children may receive a higher dose of ultrafine particles to the upper airways.
Ginsberg et al. (2005)	0.001-10 µm	-Higher deposition in 3 month olds compared with adults for coarse and fine particles in the upper TB (up to 2-fold) and PU (up to 4-fold) regions. -Higher deposition in adults in the lower TB region.
Hoffmann et al. (1989)	1-2 µm	-1.5- to 2-fold higher total deposition in the TB region for particles in resting 8 year olds versus adults. -40-50 percent lower total deposition of particles in 8 year olds under conditions of exercise.
Jarabek et al. (2005)	0.3-6 µm	-Retained mass in the TB region normalized to regional SA was compared across age groups. -Up to 2-fold lower deposition in 3 month olds compared to adults. -Up to 2-fold higher deposition in 3 year olds and 14 year olds compared to adults.
Musante and Martonen (1999)	0.25-5 µm	-Total deposition was generally higher in children (ages 7, 22, 48, and 98 months) than adults (e.g., total lung deposition in 48-month olds was 38 percent higher than adults for 1µm particles). -TB deposition monotonically decreased as a function of age (i.e., younger children had increased TB deposition). -PU deposition greatest in the 48 and 98-month children.
Musante and Martonen (2000)	2 µm	3-fold higher deposition of particles in the PU region for 7 month olds versus adults.
Oldham et al. (1997)	Various	Airway models of trachea and bronchial airways showed total deposition in children (ages 4 and 7) greater than adult (up to approximately 7-fold higher for 4 year olds compared to adults for 4.5 µm particles).
Phalen and Oldham (2001)	0.1-10 µm	-No difference in total deposition of particles in 2 year olds versus adults. -Somewhat higher (13-81 percent; depending on particle size) deposition of particles in the TB region. -Lower deposition of particles in the PU region.
Xu and Yu (1986)	Various	Increased total deposition (up to 1.5-fold higher) in children aged 6 months, 2 years, and 8 years compared with adults for particles of varying sizes.

6. CONCLUSIONS

The examples and discussions included in this appendix suggest that the *Inhalation Dosimetry Methodology's* default approaches for derivation of the HEC for Category 1 gases with effects in the ETh, TB, and PU regions and for Category 3 gases typically are sufficient to cover variation across human age- and activity-level groups. The process for deriving an RfC from the HEC includes applying an uncertainty factor (UF) to account for within-species variability, adding further protection. When deriving an IUR for a carcinogen, UFs are not used. However the procedures for estimating an IUR incorporate conservative assumptions that would likely accommodate the degree of variation observed in these examples.

Experimental and modeling results for particles suggest the potential for small differences in deposition of particles in the respiratory tract as a function of age. The assumption that 100 percent of the deposited dose is available for uptake into the systemic circulation (for remote acting toxicants), or for activity in the respiratory tract (for local toxicity) is likely to result in an overestimation of dose to the target tissue. Any small variation in deposition among age groups should be considered against the potential magnitude of such overestimation. These differences in calculated deposition are small relative to the default 10-fold UF that accounts for intra-species variability in the derivation of the RfC. In addition, RfCs and IURs are developed for chronic exposure and will generally involve an exposure for multiple years. No additional correction of the toxicity values for these age groups is needed when the RfC or IUR is used in a risk assessment. Calculations in these examples are based on empirical data from sources listed and referenced in ICRP Publication 66 (ICRP, 1994). While ORD selected the ICRP values as the best estimates for these examples, other published values for V_e and SA exist. The use of alternate values may change the $LOAEL_{[HEC]}$ calculated for the various populations and life stages and may show more or less variability in results across the age and activity groups. In addition, the examples for the TB and PU regions are based on a hypothetical chemical, since currently no RfCs for gases on IRIS are calculated based on animal studies showing health effects occurring in these regions of the respiratory system. Given the parameter values used in the default method for calculating the HEC, it is likely that the process would yield results sufficient to cover populations and life stages with varying activities and physiologic characteristics.

Note that the available data, albeit limited, generally support these conclusions. As recommended by the Reference Dose (RfD)/RfC Technical Panel (USEPA, 2002), EPA has been exploring issues involving dose to the young from inhalation exposures, both theoretically and experimentally as well as further considering the existing animal-to-human extrapolation procedures described in current methodologies (e.g., USEPA, 1994). This is especially important because of the significant developmental changes that occur in the lung from birth well into adolescence (Pinkerton and Joad, 2000). The review and updating of these methodologies will be based on the best available science.

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APPENDIX B

APPENDIX B

CHEMICALS ON IRIS WITH EXTRAPOLATED INHALATION UNIT RISKS

Table B-1 contains chemicals on the Environmental Protection Agency's (EPA's) Integrated Risk Information System (IRIS) with Inhalation Unit Risk (IUR) values calculated by extrapolation using the default ventilation rate and body weight from the oral Cancer Slope Factor (CSF). These chemicals cause tumors remote from the respiratory tract. Also listed is the year EPA verified the cancer assessment. The list was compiled in September 2008.

EPA recommends that extrapolated IURs should be used with risk Equations 6 and 11 in the main document without additional modification for calculation of cancer risk by the inhalation route of exposure. It is generally not appropriate to make adjustments based on ventilation rate and body weight using the intake equation, because the amount of the chemical that reaches the target site of the chemical through the inhalation pathway is not a simple function of the inhalation rate and body weight. Risk assessors should outline the uncertainties involved in using extrapolated IURs in the risk characterization section of the risk assessment.

TABLE B-1
CHEMICALS WITH EXTRAPOLATED INHALATION UNIT RISKS ON IRIS

Chemical	Year of Verification
Acrylamide[1]	1988
Aldrin	1987
Aramite	1991
Azobenzene	1988
Bromoform	1989
Chlordane	1997
Chloroform[1]	1987
DDT	1987
1,2-Dichloroethane	1986
Dieldrin	1987
1,2-Diphenylhydrazine	1986
Heptachlor	1987
Heptachlor epoxide	1987
Hexachlorobenzene	1989
Hexachlorobutadiene[1]	1986
Alpha-hexachlorocyclohexane	1986
Beta-hexachlorocyclohexane	1986
Technical-hexachlorocyclohexane	1986
Hexachlorodibenzo-p-dioxin mixture	1987
Hexachloroethane	1986
N-nitroso-di-n-butylamine	1986
N-nitrosodiethylamine	1986
N-nitrosodimethylamine	1986
N-nitrosopyrrolidine	1986
Polychlorinated biphenyls	1996
1,1,2,2-Tetrachloroethane	1986
1,1,1,2-Tetrachloroethane	1988
Toxaphene	1987
1,1,2-Trichloroethane	1986
2,4,6-Trichlorophenol	1989

[1] Note that this chemical's IUR is currently under review.

APPENDIX C

APPENDIX C

STSC's PROCESS FOR DERIVING ALTERNATIVE INHALATION TOXICITY VALUES

If Reference Concentration (RfC) and/or Inhalation Unit Risk (IUR) values for an inhaled contaminant are not available from the sources in the Environmental Protection Agency's (EPA's) Office of Solid Waste and Emergency Response (OSWER) hierarchy, risk assessors should first contact the National Center for Environmental Assessment's (NCEA's) Superfund Health Risk Technical Support Center (STSC) for guidance.[52] Risk assessors working on Superfund sites can contact STSC to determine whether a provisional peer-reviewed toxicity value (PPRTV) exists for a contaminant; if not, the risk assessor, in cooperation with the appropriate EPA Regional office may request that STSC develop a PPRTV document or that STSC develop an inhalation toxicity value as a "consult." The latter would be specific to the site in question only.

As a first choice, if human or whole animal studies exist providing a suitable No Observable Adverse Effect Level (NOAEL)/Lowest Observable Adverse Effect Level (LOAEL) or Point of Departure (POD) from a Benchmark Dose (BMD) analysis, this data normally will be used by STSC to develop an inhalation toxicity value. If, in addition, a suitable human inhalation physiologically based pharmacokinetic (PBPK) model exists that can be utilized to refine the dose metric to the target organ, then this information generally will be included in developing an inhalation toxicity value.

If no appropriate whole animal or human studies exist, but an appropriate peer reviewed human inhalation PBPK model exists that has been validated by experimental results, then STSC usually will attempt to derive an inhalation toxicity value from this model. If none exists, but a suitable PBPK animal inhalation models exists, STSC may attempt developing a human model and deriving an inhalation value.

PBPK modeling quantitatively describes the absorption/metabolism/distribution and elimination of the chemical from a point of entry (oral, inhalation, dermal) to the target organ(s). In some cases, an oral PBPK model can be extrapolated to the inhalation pathway, but care must be taken to consider direct pulmonary effects that may not be evident by oral dosing.

As a next approach, STSC typically will evaluate development of an inhalation toxicity value using a suitable surrogate chemical based on a quantitative structure-activity relationship (QSAR) model with structural selection criteria and solubility/toxicity considerations. STSC may evaluate possible surrogate chemicals based on several available structural models and provide a comparison. Selection of the appropriate surrogate may depend on the weight of evidence of these models.

[52] All contact with STSC should be performed by an EPA regional risk assessor. States and other entities should first contact their EPA regional risk assessor with questions on inhalation toxicity values. Regional risk assessors can then contact STSC on their behalf.

If STSC uses any of the methods for developing toxicity values other than from human or whole animal data, the value normally will be presented as a "screening" value with the caveat that it should not be used as a risk driver for a site without consultation with the STSC. The uncertainties associated with using toxicity values derived through PBPK modeling or QSAR, or with using a surrogate value should be described in the risk characterization portion of the risk assessment (see Section 9). Risk assessors are discouraged from performing simplistic route-to-route extrapolations from oral data using default assumptions about Inhalation Rate (IR) and body weight (BW).[53]

[53] If STSC indicates that no quantitative toxicity information for the inhalation route is available, the risk assessor should conduct a qualitative evaluation of this exposure route. The risk assessor should discuss in the uncertainty section of the risk assessment report the implications of not quantitatively assessing risks due to inhalation exposures to chemicals lacking inhalation toxicity data. See the section on Risk Characterization (Section 9) in the main text of this guidance for more information.

T-RACT AACC

$\frac{0.0023\ ug/m^3}{year} \times 70\ years = 0.161\ ug/m^3$

cumulative dose over 70 years at T-RACT AACC

$0.00414\ \frac{ug}{m^3} \times 16\ years = 0.066\ ug/m^3$

MAX EMISSION BASED ON MAX DAILY PRODUCTION LIMIT

Number of years until PRODUCTION LIMIT OF MINE is Reached

$0.00207\ \frac{ug}{m^3} \times 32\ years = 0.066\ ug/m^3$

EPA/630/P-03/001F
March 2005

Guidelines for Carcinogen Risk Assessment

Risk Assessment Forum
U.S. Environmental Protection Agency
Washington, DC

EX NO. 221
COPE
DATE 10-7-24
ASSOCIATED REPORTING & VIDEO

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1. INTRODUCTION

1.1. PURPOSE AND SCOPE OF THE GUIDELINES

These guidelines revise and replace the U.S. Environmental Protection Agency's (EPA's, or the Agency's) *Guidelines for Carcinogen Risk Assessment,* published in 51 FR 33992, September 24, 1986 (U.S. EPA, 1986a) and the 1999 interim final guidelines (U.S. EPA, 1999a; see U.S. EPA 2001b). They provide EPA staff with guidance for developing and using risk assessments. They also provide basic information to the public about the Agency's risk assessment methods.

These cancer guidelines are used with other risk assessment guidelines, such as the *Guidelines for Mutagenicity Risk Assessment* (U.S. EPA, 1986b) and the *Guidelines for Exposure Assessment* (U.S. EPA, 1992a). Consideration of other Agency guidance documents is also important in assessing cancer risks where procedures for evaluating specific target organ effects have been developed (e.g., assessment of thyroid follicular cell tumors, U.S. EPA, 1998a). All of EPA's guidelines should be consulted when conducting a risk assessment in order to ensure that information from studies on carcinogenesis and other health effects are considered together in the overall characterization of risk. This is particularly true in the case in which a precursor effect for a tumor is also a precursor or endpoint of other health effects or when there is a concern for a particular susceptible life-stage for which the Agency has developed guidance, for example, *Guidelines for Developmental Toxicity Risk Assessment* (U.S. EPA, 1991a). The developmental guidelines discuss hazards to children that may result from exposures during preconception and prenatal or postnatal development to sexual maturity. Similar guidelines exist for reproductive toxicant risk assessments (U.S. EPA, 1996a) and for neurotoxicity risk assessment (U.S. EPA, 1998b). The overall characterization of risk is conducted within the context of broader policies and guidance such as Executive Order 13045, "Protection of Children From Environmental Health Risks and Safety Risks"(Executive Order 13045, 1997) which is the primary directive to federal agencies and departments to identify and assess environmental health risks and safety risks that may disproportionately affect children.

The cancer guidelines encourage both consistency in the procedures that support scientific components of Agency decision making and flexibility to allow incorporation of innovations and contemporaneous scientific concepts. In balancing these goals, the Agency relies on established scientific peer review processes (U.S. EPA, 2000a; OMB 2004). The cancer guidelines incorporate basic principles and science policies based on evaluation of the currently available information. The Agency intends to revise these cancer guidelines when substantial changes are necessary. As more information about carcinogenesis develops, the need may arise to make appropriate changes in risk assessment guidance. In the interim, the Agency intends to issue special reports, after appropriate peer review, to supplement and update guidance on single topics (e.g., U.S. EPA, 1991b). One such guidance document, *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* ("Supplemental Guidance"), was developed in conjunction with these cancer guidelines (U.S. EPA., 2005). Because both the methodology and the data in the Supplemental Guidance (see Section 1.3.6) are expected to evolve more rapidly than the issues addressed in these cancer guidelines, the two were developed as separate documents. The Supplemental Guidance, however, as well as any other relevant (including subsequent) guidance documents, should be considered along with these cancer guidelines as risk assessments for carcinogens are generated. The use of supplemental guidance, such as the Supplemental Guidance for Assessing Cancer Susceptibility from Early-life Exposure to Carcinogens, has the advantage of allowing the Supplemental Guidance to be modified as more data become available. Thus, the consideration of new, peer-reviewed scientific understanding and data in an assessment can always be consistent with the purposes of these cancer guidelines.

These cancer guidelines are intended as guidance only. They do not establish any substantive "rules" under the Administrative Procedure Act or any other law and have no binding effect on EPA or any regulated entity, but instead represent a non-binding statement of policy. EPA believes that the cancer guidelines represent a sound and up-to-date approach to cancer risk assessment, and the cancer guidelines enhance the application of the best available science in EPA's risk assessments. However, EPA cancer risk assessments may be conducted differently than envisioned in the cancer guidelines for many reasons, including (but not limited to) new

information, new scientific understanding, or new science policy judgment. The science of risk assessment continues to develop rapidly, and specific components of the cancer guidelines may become outdated or may otherwise require modification in individual settings. Use of the cancer guidelines in future risk assessments will be based on decisions by EPA that the approaches are suitable and appropriate in the context of those particular risk assessments. These judgments will be tested through peer review, and risk assessments will be modified to use different approaches if appropriate.

1.2. ORGANIZATION AND APPLICATION OF THE CANCER GUIDELINES

1.2.1. Organization

Publications by the Office of Science and Technology (OSTP, 1985) and the National Research Council (NRC) (NRC, 1983, 1994) provide information and general principles about risk assessment. Risk assessment uses available scientific information on the properties of an agent[1] and its effects in biological systems to provide an evaluation of the potential for harm as a consequence of environmental exposure. The 1983 and 1994 NRC documents organize risk assessment information into four areas: hazard identification, dose-response assessment, exposure assessment, and risk characterization. This structure appears in these cancer guidelines, with additional emphasis placed on characterization of evidence and conclusions in each area of the assessment. In particular, the cancer guidelines adopt the approach of the NRC's 1994 report in adding a dimension of characterization to the hazard identification step: an evaluation of the conditions under which its expression is anticipated. Risk assessment questions addressed in these cancer guidelines are as follows.

- For hazard—Can the identified agent present a carcinogenic hazard to humans and, if so, under what circumstances?

- For dose response—At what levels of exposure might effects occur?

[1] The term "agent" refers generally to any chemical substance, mixture, or physical or biological entity being assessed, unless otherwise noted (See Section 1.2.2 for a note on radiation.).

- For exposure—What are the conditions of human exposure?

- For risk—What is the character of the risk? How well do data support conclusions about the nature and extent of the risk from various exposures?

The risk characterization process first summarizes findings on hazard, dose response, and exposure characterizations and then develops an integrative analysis of the whole risk case. It ends in the writing of a technical risk characterization. Other documents, such as summaries for the risk managers and the public, reflecting the key points of the risk characterization are usually written. A summary for managers is a presentation for those who may or may not be familiar with the scientific details of cancer assessment. It also provides information for other interested readers. The initial steps in the risk characterization process are to make building blocks in the form of characterizations of the assessments of hazard, dose response, and exposure. The individual assessments and characterizations are then integrated to arrive at risk estimates for exposure scenarios of interest. As part of the characterization process, explicit evaluations are made of the hazard and risk potential for susceptible lifestages, including children (U.S. EPA, 1995, 2000b).

The 1994 NRC document also explicitly called attention to the role of the risk assessment process in identifying scientific uncertainties that, if addressed, could serve to reduce their uncertainty in future iterations of the risk assessment. NRC recommended that when the Agency "reports estimates of risk to decisions-makers and the public, it should present not only point estimates of risk, but also the sources and magnitudes of uncertainty associated with these estimates" (p. 15). Thus, the identified uncertainties serve as a feedback loop to the research community and decisionmakers, specifying areas and types of information that would be particularly useful.

There are several reasons for individually characterizing the hazard, dose response, and exposure assessments. One is that they are often done by different people than those who do the integrative analyses. The second is that there is very often a lapse of time between the conduct of hazard and dose-response analyses and the conduct of exposure assessment and integrative

analysis. Thus, it is important to capture characterizations of assessments as the assessments are done to avoid the need to go back and reconstruct them. Finally, frequently a single hazard assessment is used by several programs for several different exposure scenarios. There may be one or several documents involved. "Integrative analysis" is a generic term; and many documents that have other titles may contain integrative analyses. In the following sections, the elements of these characterizations are discussed.

1.2.2. Application

The cancer guidelines apply within the framework of policies provided by applicable EPA statutes and do not alter such policies.

- The cancer guidelines cover the assessment of available data. They do not imply that one kind of data or another is prerequisite for regulatory action concerning any agent. It is important that, when evaluating and considering the use of any data, EPA analysts incorporate the basic standards of quality, as defined by the EPA Information Quality Guidelines (U.S. EPA, 2002a see Appendix B) and other Agency guidance on data quality such as the EPA Quality Manual for Environmental Programs (U.S. EPA, 2000e), as well as *OMB Guidelines for Ensuring and Maximizing the Quality, Utility, and Integrity of Information Disseminated by Federal Agencies* (OMB, 2002). It is very important that all analyses consider the basic standards of quality, including objectivity, utility, and integrity. A summary of the factors and considerations generally used by the Agency when evaluating and considering the use of scientific and technical information is contained in EPA's *A Summary of General Assessment Factors for Evaluating the Quality of Scientific and Technical Information* (U.S. EPA, 2003).

- Risk management applies directives in statutes, which may require consideration of potential risk or solely hazard or exposure potential, along with social, economic, technical, and other factors in decision making. Risk assessments may be used to support

decisions, but in order to maintain their integrity as decision-making tools, they are not influenced by consideration of the social or economic consequences of regulatory action.

The assessment of risk from radiation sources is informed by the continuing examination of human data by the National Academy of Sciences/NRC in its series of numbered reports: "Biological Effects of Ionizing Radiation." Although some of the general principles of these cancer guidelines may also apply to radiation risk assessments, some of the details of their risk assessment procedures may not, as they are most focused on other kinds of agents. Therefore, these cancer guidelines are not intended to provide the primary source of, or guidance for, the Agency's evaluation of the carcinogenic risks of radiation.

Not every EPA assessment has the same scope or depth, a factor recognized by the National Academy of Sciences (NRC, 1996). For example, EPA's Information Quality Guidelines (U.S. EPA, 2002a, see Appendix B) discuss influential information that "will have or does have a clear and substantial impact ... on important public policies or private sector decisions ... that should adhere to a rigorous standard of quality." It is often difficult to know *a priori* how the results of a risk assessment are likely to be used by the Agency. Some risk assessments may be used by Agency economists and policy analysts, and the necessary information for such analyses, as discussed in detail later in this document, should be included when practicable (U.S. EPA, 2002a). On the other hand, Agency staff often conduct screening-level assessments for priority setting or separate assessments of hazard or exposure for ranking purposes or to decide whether to invest resources in collecting data for a full assessment. Moreover, a given assessment of hazard and dose response may be used with more than one exposure assessment that may be conducted separately and at different times as the need arises in studying environmental problems related to various exposure media. The cancer guidelines apply to these various situations in appropriate detail, given the scope and depth of the particular assessment. For example, a screening assessment may be based almost entirely on structure-activity relationships (SARs) and default options, when other data are not readily available. When more data and resources are readily available, assessments can use a critical analysis of all of the available data as the starting point of the risk assessment. Under these conditions, default

options would only be used to address uncertainties or the absence of critical data. Default options are inferences based on general scientific knowledge of the phenomena in question and are also matters of policy concerning the appropriate way to bridge uncertainties that concern potential risk to human health.

These cancer guidelines do not suggest that all of the kinds of data covered here will need to be available or used for either assessment or decision making. The level of detail of an assessment is a matter of Agency management discretion regarding applicable decision-making needs. The Agency generally presumes that key cancer information (e.g., assessments contained in the Agency's Integrated risk Information System) is "influential information" as defined by the EPA Information Quality Guidelines and "highly influential" as defined by OMB's Information Quality Bulletin for Peer Review (OMB 2004).

1.3. KEY FEATURES OF THE CANCER GUIDELINES

1.3.1. Critical Analysis of Available Information as the Starting Point for Evaluation

As an increasing understanding of carcinogenesis is becoming available, these cancer guidelines adopt a view of default options that is consistent with EPA's mission to protect human health while adhering to the tenets of sound science. Rather than viewing default options as the starting point from which departures may be justified by new scientific information, these cancer guidelines view a critical analysis of all of the available information that is relevant to assessing the carcinogenic risk as the starting point from which a default option may be invoked if needed to address uncertainty or the absence of critical information. Preference is given to using information that has been peer reviewed, e.g., reported in peer-reviewed scientific journals. The primary goal of EPA actions is protection of human health; accordingly, as an Agency policy, risk assessment procedures, including default options that are used in the absence of scientific data to the contrary, should be health protective (U.S. EPA, 1999b).

Use of health protective risk assessment procedures as described in these cancer guidelines means that estimates, while uncertain, are more likely to overstate than understate hazard and/or risk. NRC (1994) reaffirmed the use of default options as "a reasonable way to cope with uncertainty about the choice of appropriate models or theory" (p. 104). NRC saw the

need to treat uncertainty in a predictable way that is "scientifically defensible, consistent with the agency's statutory mission, and responsive to the needs of decision-makers" (p. 86). The extent of health protection provided to the public ultimately depends upon what risk managers decide is the appropriate course of regulatory action. When risk assessments are performed using only one set of procedures, it may be difficult for risk managers to determine how much health protectiveness is built into a particular hazard determination or risk characterization. When there are alternative procedures having significant biological support, the Agency encourages assessments to be performed using these alternative procedures, if feasible, in order to shed light on the uncertainties in the assessment, recognizing that the Agency may decide to give greater weight to one set of procedures than another in a specific assessment or management decision.

Encouraging risk assessors to be receptive to new scientific information, NRC discussed the need for departures from default options when a "sufficient showing" is made. It called on EPA to articulate clearly its criteria for a departure so that decisions to depart from default options would be "scientifically credible and receive public acceptance" (p. 91). It was concerned that *ad hoc* departures would undercut the scientific credibility of a risk assessment. NRC envisioned that principles for choosing and departing from default options would balance several objectives, including "protecting the public health, ensuring scientific validity, minimizing serious errors in estimating risks, maximizing incentives for research, creating an orderly and predictable process, and fostering openness and trustworthiness" (p. 81).

Appendices N-1 and N-2 of NRC (1994) discussed two competing standards for choosing default options articulated by members of the committee. One suggested approach would evaluate a departure in terms of whether "it is scientifically plausible" and whether it "tends to protect public health in the face of scientific uncertainty" (p. 601). An alternative approach "emphasizes scientific plausibility with regard to the use of alternative models" (p. 631). Reaching no consensus on a single approach, NRC recognized that developing criteria for departures is an EPA policy matter.

The basis for invoking a default option depends on the circumstances. Generally, if a gap in basic understanding exists or if agent-specific information is missing, a default option may be used. If agent-specific information is present but critical analysis reveals inadequacies, a default

option may also be used. If critical analysis of agent-specific information is consistent with one or more biologically based models as well as with the default option, the alternative models and the default option are both carried through the assessment and characterized for the risk manager. In this case, the default model not only fits the data, but also serves as a benchmark for comparison with other analyses. This case also highlights the importance of extensive experimentation to support a conclusion about mode of action, including addressing the issue of whether alternative modes of action are also plausible. Section 2.4 provides a framework for critical analysis of mode of action information to address the extent to which the available information supports the hypothesized mode of action, whether alternative modes of action are also plausible, and whether there is confidence that the same inferences can be extended to populations and lifestages that are not represented among the experimental data.

Generally, cancer risk decisions strive to be "scientifically defensible, consistent with the agency's statutory mission, and responsive to the needs of decision-makers" (NRC, 1994). Scientific defensibility would be evaluated through use of EPA's Science Advisory Board, EPA's Office of Pesticide Programs' Scientific Advisory Panel, or other independent expert peer review panels to determine whether a consensus among scientific experts exists. Consistency with the Agency's statutory mission would consider whether the risk assessment overall supports EPA's mission to protect human health and safeguard the natural environment. Responsiveness to the needs of decisionmakers would take into account pragmatic considerations such as the nature of the decision; the required depth of analysis; the utility, time, and cost of generating new scientific data; and the time, personnel, and resources allotted to the risk assessment.

With a multitude of types of data, analyses, and risk assessments, as well as the diversity of needs of decisionmakers, it is neither possible nor desirable to specify step-by-step criteria for decisions to invoke a default option. A discussion of major default options appears in the Appendix. Screening-level assessments may more readily use default parameters, even worst-case assumptions, that would not be appropriate in a full-scale assessment. On the other hand, significant risk management decisions will often benefit from a more comprehensive assessment, including alternative risk models having significant biological support. To the extent practicable, such assessments should provide central estimates of potential risks in conjunction with lower

and upper bounds (e.g., confidence limits) and a clear statement of the uncertainty associated with these estimates.

In the absence of sufficient data or understanding to develop of a robust, biologically based model, an appropriate policy choice is to have a single preferred curve-fitting model for each type of data set. Many different curve-fitting models have been developed, and those that fit the observed data reasonably well may lead to several-fold differences in estimated risk at the lower end of the observed range. In addition, goodness-of-fit to the experimental observations is not by itself an effective means of discriminating among models that adequately fit the data (OSTP, 1985). To provide some measure of consistency across different carcinogen assessments, EPA uses a standard curve-fitting procedure for tumor incidence data. Assessments that include a different approach should provide an adequate justification and compare their results with those from the standard procedure. Application of models to data should be conducted in an open and transparent manner.

1.3.2. Mode of Action

The use of mode of action[2] in the assessment of potential carcinogens is a main focus of these cancer guidelines. This area of emphasis arose because of the significant scientific advances that have developed concerning the causes of cancer induction. Elucidation of a mode of action for a particular cancer response in animals or humans is a data-rich determination. Significant information should be developed to ensure that a scientifically justifiable mode of action underlies the process leading to cancer at a given site. In the absence of sufficiently, scientifically justifiable mode of action information, EPA generally takes public health-protective, default positions regarding the interpretation of toxicologic and epidemiologic data:

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[2] The term *"mode of action"* is defined as a sequence of key events and processes, starting with interaction of an agent with a cell, proceeding through operational and anatomical changes, and resulting in cancer formation. A *"key event"* is an empirically observable precursor step that is itself a necessary element of the mode of action or is a biologically based marker for such an element. Mode of action is contrasted with "*mechanism of action,*" which implies a more detailed understanding and description of events, often at the molecular level, than is meant by mode of action. The toxicokinetic processes that lead to formation or distribution of the active agent to the target tissue are considered in estimating dose but are not part of the mode of action as the term is used here. There are many examples of possible modes of carcinogenic action, such as mutagenicity, mitogenesis, inhibition of cell death, cytotoxicity with reparative cell proliferation, and immune suppression.

animal tumor findings are judged to be relevant to humans, and cancer risks are assumed to conform with low dose linearity.

Understanding of mode of action can be a key to identifying processes that may cause chemical exposures to differentially affect a particular population segment or lifestage. Some modes of action are anticipated to be mutagenic and are assessed with a linear approach. This is the mode of action of radiation and several other agents that are known carcinogens. Other modes of action may be modeled with either linear or nonlinear[3] approaches after a rigorous analysis of available data under the guidance provided in the framework for mode of action analysis (see Section 2.4.3).

1.3.3. Weight of Evidence Narrative

The cancer guidelines emphasize the importance of weighing all of the evidence in reaching conclusions about the human carcinogenic potential of agents. This is accomplished in a single integrative step after assessing all of the individual lines of evidence, which is in contrast to the step-wise approach in the 1986 cancer guidelines. Evidence considered includes tumor findings, or lack thereof, in humans and laboratory animals; an agent's chemical and physical properties; its structure-activity relationships (SARs) as compared with other carcinogenic agents; and studies addressing potential carcinogenic processes and mode(s) of action, either *in vivo* or *in vitro*. Data from epidemiologic studies are generally preferred for characterizing human cancer hazard and risk. However, all of the information discussed above could provide valuable insights into the possible mode(s) of action and likelihood of human cancer hazard and risk. The cancer guidelines recognize the growing sophistication of research methods,

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[3]The term "*nonlinear*" is used here in a narrower sense than its usual meaning in the field of mathematical modeling. In these cancer guidelines, the term "*nonlinear*" refers to threshold models (which show no response over a range of low doses that include zero) and some nonthreshold models (e.g., a quadractic model, which shows some response at all doses above zero). In these cancer guidelines, a nonlinear model is one whose slope is zero at (and perhaps above) a dose of zero. A *low-dose-linear* model is one whose slope is greater than zero at a dose of zero. A low-dose-linear model approximates a straight line only at very low doses; at higher doses near the observed data, a low-dose-linear model can display curvature. The term "*low-dose-linear*" is often abbreviated "linear," although a low-dose-linear model is not linear at all doses. Use of nonlinear approaches does not imply a biological threshold dose below which the response is zero. Estimating thresholds can be problematic; for example, a response that is not statistically significant can be consistent with a small risk that falls below an experiment's power of detection.

particularly in their ability to reveal the modes of action of carcinogenic agents at cellular and subcellular levels as well as toxicokinetic processes.

Weighing of the evidence includes addressing not only the likelihood of human carcinogenic effects of the agent but also the conditions under which such effects may be expressed, to the extent that these are revealed in the toxicological and other biologically important features of the agent.

The weight of evidence narrative to characterize hazard summarizes the results of the hazard assessment and provides a conclusion with regard to human carcinogenic potential. The narrative explains the kinds of evidence available and how they fit together in drawing conclusions, and it points out significant issues/strengths/limitations of the data and conclusions. Because the narrative also summarizes the mode of action information, it sets the stage for the discussion of the rationale underlying a recommended approach to dose-response assessment.

In order to provide some measure of clarity and consistency in an otherwise free-form, narrative characterization, standard descriptors are used as part of the hazard narrative to express the conclusion regarding the weight of evidence for carcinogenic hazard potential. There are five recommended standard hazard descriptors: "*Carcinogenic to Humans*," "*Likely to Be Carcinogenic to Humans*," "*Suggestive Evidence of Carcinogenic Potential*," "*Inadequate Information to Assess Carcinogenic Potential*," and "*Not Likely to Be Carcinogenic to Humans*." Each standard descriptor may be applicable to a wide variety of data sets and weights of evidence and is presented only in the context of a weight of evidence narrative. Furthermore, as described in Section 2.5 of these cancer guidelines, more than one conclusion may be reached for an agent.

1.3.4. Dose-response Assessment

Dose-response assessment evaluates potential risks to humans at particular exposure levels. The approach to dose-response assessment for a particular agent is based on the conclusion reached as to its potential mode(s) of action for each tumor type. Because an agent may induce multiple tumor types, the dose-response assessment includes an analysis of all tumor types, followed by an overall synthesis that includes a characterization of the risk estimates across tumor types, the strength of the mode of action information of each tumor type, and the

anticipated relevance of each tumor type to humans, including susceptible populations and lifestages (e.g., childhood).

Dose-response assessment for each tumor type is performed in two steps: assessment of observed data to derive a point of departure (POD),[4] followed by extrapolation to lower exposures to the extent that is necessary. Data from epidemiologic studies, of sufficient quality, are generally preferred for estimating risks. When animal studies are the basis of the analysis, the estimation of a human-equivalent dose should utilize toxicokinetic data to inform cross-species dose scaling if appropriate and if adequate data are available. Otherwise, default procedures should be applied. For oral dose, based on current science, an appropriate default option is to scale daily applied doses experienced for a lifetime in proportion to body weight raised to the 3/4 power (U.S. EPA, 1992b). For inhalation dose, based on current science, an appropriate default methodology estimates respiratory deposition of particles and gases and estimates internal doses of gases with different absorption characteristics. When toxicokinetic modeling (see Section 3.1.2) is used without toxicodynamic modeling (see Section 3.2.2), the dose-response assessment develops and supports an approach for addressing toxicodynamic equivalence, perhaps by retaining some of the cross-species scaling factor (see Section 3.1.3). Guidance is also provided for adjustment of dose from adults to children (see Section 4.3.1).

Response data on effects of the agent on carcinogenic processes are analyzed (nontumor data) in addition to data on tumor incidence. If appropriate, the analyses of data on tumor incidence and on precursor effects may be used in combination. To the extent the relationship between precursor effects and tumor incidence are known, precursor data may be used to estimate a dose-response function below the observable tumor data. Study of the dose-response function for effects believed to be part of the carcinogenic process influenced by the agent may also assist in evaluating the relationship of exposure and response in the range of observation and at exposure levels below the range of observation.

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[4] A "*point of departure*" (POD) marks the beginning of extrapolation to lower doses. The POD is an estimated dose (usually expressed in human-equivalent terms) near the lower end of the observed range, without significant extrapolation to lower doses.

The first step of dose-response assessment is evaluation within the range of observation. Approaches to analysis of the range of observation of epidemiologic studies are determined by the type of study and how dose and response are measured in the study. In the absence of adequate human data for dose-response analysis, animal data are generally used. If there are sufficient quantitative data and adequate understanding of the carcinogenic process, a biologically based model may be developed to relate dose and response data on an agent-specific basis. Otherwise, as a default procedure, a standard model can be used to curve-fit the data.

The POD for extrapolating the relationship to environmental exposure levels of interest, when the latter are outside the range of observed data, is generally the lower 95% confidence limit on the lowest dose level that can be supported for modeling by the data. SAB (1997) suggested that, "it may be appropriate to emphasize lower statistical bounds in screening analyses and in activities designed to develop an appropriate human exposure value, since such activities require accounting for various types of uncertainties and a lower bound on the central estimate is a scientifically-based approach accounting for the uncertainty in the true value of the ED_{10} [or central estimate]." However, the consensus of the SAB (1997) was that, "both point estimates and statistical bounds can be useful in different circumstances, and recommended that the Agency routinely calculate and present the point estimate of the ED_{10} [or central estimate] and the corresponding upper and lower 95% statistical bounds." For example, it may be appropriate to emphasize the central estimate in activities that involve formal uncertainty analysis that are required by OMB Circular A-4 (OMB, 2003) as well as ranking agents as to their carcinogenic hazard. Thus, risk assessors should calculate, to the extent practicable, and present the central estimate and the corresponding upper and lower statistical bounds (such as confidence limits) to inform decisionmakers.

The second step of dose-response assessment is extrapolation to lower dose levels, if needed. This extrapolation is based on extension of a biologically based model if supported by substantial data (see Section 3.3.2). Otherwise, default approaches can be applied that are consistent with current understanding of mode(s) of action of the agent, including approaches that assume linearity or nonlinearity of the dose-response relationship, or both. A default approach for linearity extends a straight line from the POD to zero dose/zero response (see

Section 3.3.3). The linear approach is used when: (1) there is an absence of sufficient information on modes of action or (2) the mode of action information indicates that the dose-response curve at low dose is or is expected to be linear. Where alternative approaches have significant biological support, and no scientific consensus favors a single approach, an assessment may present results using alternative approaches. A nonlinear approach can be used to develop a reference dose or a reference concentration (see Section 3.3.4).

1.3.5. Susceptible Populations and Lifestages

An important use of mode of action information is to identify susceptible populations and lifestages. It is rare to have epidemiologic studies or animal bioassays conducted in susceptible individuals. This information need can be filled by identifying the key events of the mode of action and then identifying risk factors, such as differences due to genetic polymorphisms, disease, altered organ function, lifestyle, and lifestage, that can augment these key events. To do this, the information about the key precursor events is reviewed to identify particular populations or lifestages that can be particularly susceptible to their occurrence (see Section 2.4.3.4). Any information suggesting quantitative differences between populations or lifestages is flagged for consideration in the dose-response assessment (see Section 3.5 and U.S. EPA 2002b).

1.3.6. Evaluating Risks from Childhood Exposures

NRC (1994) recommended that "EPA should assess risks to infants and children whenever it appears that their risks might be greater than those of adults." Executive Order 13045 (1997) requires that "each Federal Agency shall make it a high priority to identify and assess environmental health and safety risks that may disproportionately affect children, and shall ensure that their policies, programs, and standards address disproportionate risks that result from environmental health risks or safety risks." In assessing risks to children, EPA considers both effects manifest during childhood and early-life exposures that can contribute to effects at any time later in life.

These cancer guidelines view childhood as a sequence of lifestages rather than viewing children as a subpopulation, the distinction being that a subpopulation refers to a portion of the

population, whereas a lifestage is inclusive of the entire population. Exposures that are of concern extend from conception through adolescence and also include pre-conception exposures of both parents. These cancer guidelines use the term "childhood" in this more inclusive sense.

Rarely are there studies that directly evaluate risks following early-life exposure. Epidemiologic studies of early-life exposure to environmental agents are seldom available. Standard animal bioassays generally begin dosing after the animals are several weeks old, when many organ systems are mature. This could lead to an understatement of risk, because an accepted concept in the science of carcinogenesis is that young animals are usually more susceptible to the carcinogenic activity of a chemical than are mature animals (McConnell, 1992).

At this time, there is some evidence of higher cancer risks following early-life exposure. For radiation carcinogenesis, data indicate that risks for several forms of cancer are highest following childhood exposure (NRC, 1990; Miller, 1995; U.S. EPA, 1999c). These human results are supported by the few animal bioassays that include perinatal (prenatal or early postnatal) exposure. Perinatal exposure to some agents can induce higher incidences of the tumors seen in standard bioassays; some examples include vinyl chloride (Maltoni et al., 1981), diethylnitrosamine (Peto et al., 1984), benzidine, DDT, dieldrin, and safrole (Vesselinovitch et al., 1979). Moreover, perinatal exposure to some agents, including vinyl chloride (Maltoni et al., 1981) and saccharin (Cohen, 1995; Whysner and Williams, 1996), can induce different tumors that are not seen in standard bioassays. Surveys comparing perinatal carcinogenesis bioassays with standard bioassays for a limited number of chemicals (McConnell, 1992; U.S. EPA, 1996b) have concluded that

- the same tumor sites are usually observed following either perinatal or adult exposure, and

- perinatal exposure in conjunction with adult exposure usually increases the incidence of tumors or reduces the latent period before tumors are observed.

The risk attributable to early-life exposure often appears modest compared with the risk from lifetime exposure, but it can be about 10-fold higher than the risk from an exposure of similar duration occurring later in life (Ginsberg, 2003). Further research is warranted to investigate the extent to which these findings apply to specific agents, chemical classes, and modes of action or in general.

These empirical results are consistent with current understanding of the biological processes involved in carcinogenesis, which leads to a reasonable expectation that children can be more susceptible to many carcinogenic agents (Anderson et al., 2000; Birnbaum and Fenton, 2003; Ginsberg, 2003; Miller et al., 2002; Scheuplein et al., 2002). Some aspects potentially leading to childhood susceptibility are listed below.

- Differences in the capacity to metabolize and clear chemicals can result in larger or smaller internal doses of the active agent(s).

- More frequent cell division during development can result in enhanced expression of mutations due to the reduced time available for repair of DNA lesions (Slikker et al., 2004).

- Some embryonic cells, such as brain cells, lack key DNA repair enzymes.

- More frequent cell division during development can result in clonal expansion of cells with mutations from prior unrepaired DNA damage (Slikker et al., 2004).

- Some components of the immune system are not fully functional during development (Holladay and Smialowicz, 2000; Holsapple et al., 2003).

- Hormonal systems operate at different levels during different lifestages.

- Induction of developmental abnormalities can result in a predisposition to carcinogenic effects later in life (Anderson et al., 2000; Birnbaum and Fenton, 2003; Fenton and Davis, 2002).

To evaluate risks from early-life exposure, these cancer guidelines emphasize the role of toxicokinetic information to estimate levels of the active agent in children and toxicodynamic information to identify whether any key events of the mode of action are of increased concern early in life. Developmental toxicity studies can provide information on critical periods of exposure for particular targets of toxicity.

An approach to assessing risks from early-life exposure is presented in Figure 1-1. In the hazard assessment, when there are mode of action data, the assessment considers whether these data have special relevance during childhood, considering the various aspects of development listed above. Examples of such data include toxicokinetics that predict a sufficiently large internal dose in children or a mode of action where a key precursor event is more likely to occur during childhood. There is no recommended default to settle the question of whether tumors arising through a mode of action are relevant during childhood; and adequate understanding the mode of action implies that there are sufficient data (on either the specific agent or the general mode of action) to form a confident conclusion about relevance during childhood (see Section 2.4.3.4).

In the dose-response assessment, the potential for susceptibility during childhood warrants explicit consideration in each assessment. These cancer guidelines encourage developing separate risk estimates for children according to a tiered approach that considers what pertinent data are available (see Section 3.5). Childhood may be a susceptible period; moreover, exposures during childhood generally are not equivalent to exposures at other times and may be treated differently from exposures occurring later in life (see Section 3.5). In addition, adjustment of unit risk estimates may be warranted when used to estimate risks from childhood exposure (see Section 4.4).

At this time, several limitations preclude a full assessment of children's risk. There are no generally used testing protocols to identify potential environmental causes of cancers that are

unique to children, including several forms of childhood cancer and cancers that develop from parental exposures, and cases where developmental exposure may alter susceptibility to carcinogen exposure in the adult (Birnbaum and Fenton, 2003). Dose-response assessment is limited by an inability to observe how developmental exposure can modify incidence and latency and an inability to estimate the ultimate tumor response resulting from induced susceptibility to later carcinogen exposures.

To partially address the limitations identified above, EPA developed in conjunction with these cancer guidelines, *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* ("Supplemental Guidance"). The Supplemental Guidance addresses a number of issues pertaining to cancer risks associated with early-life exposures generally, but provides specific guidance on procedures for adjusting cancer potency estimates only for carcinogens acting through a mutagenic mode of action. This Supplemental Guidance recommends, for such chemicals when no chemical-specific data exist, a default approach using estimates from chronic studies (i.e., cancer slope factors) with appropriate modifications to address the potential for differential risk of early-lifestage exposure.

The Agency considered both the advantages and disadvantages to extending the recommended, age dependent adjustment factors for carcinogenic potency to carcinogenic agents for which the mode of action remains unknown. EPA decided to recommend these factors only for carcinogens acting through a mutagenic mode of action based on a combination of analysis of available data and long-standing science policy positions which govern the Agency's overall approach to carcinogen risk assessment. In general, the Agency prefers to rely on analyses of data, rather than general defaults. When data are available for a sensitive lifestage, they would be used directly to evaluate risks for that chemical and that lifestage on a case-by-case basis. In the case of nonmutagenic carcinogens, when the mode of action is unknown, the data were judged by EPA to be too limited and the modes of action too diverse to use this as a category for which a general default adjustment factor approach can be applied. In this situation, a linear low-dose extrapolation methodology (without further adjustment) is recommended. It is the Agency's long-standing science policy position that use of the linear low-dose extrapolation approach

provides adequate public health conservatism in the absence of chemical-specific data indicating differential early-life sensitivity or when the mode of action is not mutagenic.

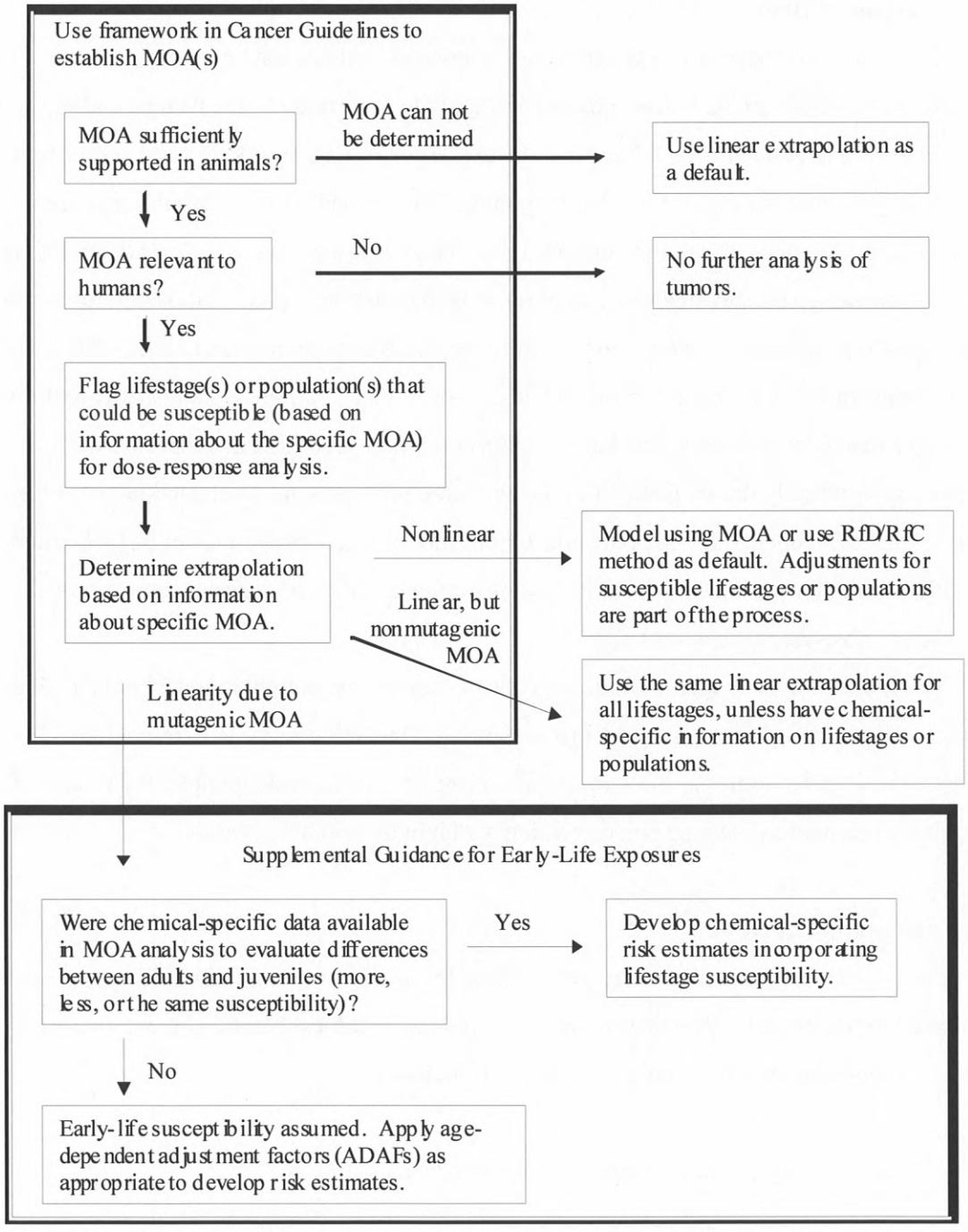
The Agency expects to produce additional supplemental guidance for other modes of action, as data from new research and toxicity testing indicate it is warranted. EPA intends to focus its research, and work collaboratively with its federal partners, to improve understanding of the implications of early life exposure to carcinogens. Development of guidance for estrogenic agents and chemicals acting through other processes resulting in endocrine disruption and subsequent carcinogenesis, for example, might be a reasonable priority in light of the human experience with diethylstilbesterol and the existing early life animal studies. It is worth noting that each mode of action for endocrine disruption will probably require separate analysis.

As the Agency examines additional carcinogenic agents, the age groupings may differ from those recommended for assessing cancer risks from early-life exposure to chemicals with a mutagenic mode of action. Puberty and its associated biological changes, for example, involve many biological processes that could lead to changes in sensitivity to the effects of some carcinogens, depending on their mode of action. The Agency is interested in identifying lifestages that may be particularly sensitive or refractory for carcinogenesis, and believes that the mode of action framework described in these cancer guidelines is an appropriate mechanism for elucidating these lifestages. For each additional mode of action evaluated, the various age groupings determined to be at differential risk may differ from those proposed in the Supplemental Guidance. For example, the age groupings selected for the age-dependent adjustments for carcinogens acting through a mutagenic mode of action were initially selected based on the available data, i.e., for the laboratory animal age range representative of birth to < 2 years in humans. More limited data and information on human biology were used to determine a science-informed policy regarding 2 to < 16 years. Data were not available to refine the latter age group. If more data become available regarding carcinogens with a mutagenic mode of action, consideration may be given to further refinement of these age groups.

1.3.7. Emphasis on Characterization

The cancer guidelines emphasize the importance of a clear and useful characterization narrative that summarizes the analyses of hazard, dose-response, and exposure assessment. These characterizations summarize the assessments to explain the extent and weight of evidence, major points of interpretation and rationale for their selection, strengths and weaknesses of the evidence and the analysis, and discuss alternative conclusions and uncertainties that deserve serious consideration (U.S. EPA, 2000b). They serve as starting materials for the overall risk characterization process that completes the risk assessment.

Figure 1-1. Flow chart for early-life risk assessment using mode of action framework.



2. HAZARD ASSESSMENT

2.1. OVERVIEW OF HAZARD ASSESSMENT AND CHARACTERIZATION

2.1.1. Analyses of Data

The purpose of hazard assessment is to review and evaluate data pertinent to two questions: (1) whether an agent may pose a carcinogenic hazard to human beings, and (2) under what circumstances an identified hazard may be expressed (NRC, 1994). Hazard assessment involves analyses of a variety of data that may range from observations of tumor responses to analysis of structure-activity relationships (SARs). The purpose of the assessment is not simply to assemble these separate evaluations; its purpose is to construct a total analysis examining what the biological data reveal as a whole about carcinogenic effects and mode of action of the agent, and their implications for human hazard and dose-response evaluation. Conclusions are drawn from weight-of-evidence evaluations based on the combined strength and coherence of inferences appropriately drawn from all of the available information. To the extent that data permit, hazard assessment addresses the question of mode of action of an agent as both an initial step in identifying human hazard potential and as a component in considering appropriate approaches to dose-response assessment.

The topics in this chapter include analysis of tumor data, both human and animal, and analysis of other key information about properties and effects that relate to carcinogenic potential. The chapter addresses how information can be used to evaluate potential modes of action. It also provides guidance on performing a weight of evidence evaluation.

2.1.2. Presentation of Results

Presentation of the results of hazard assessment should be informed by Agency guidance as discussed in Section 2.6. The results are presented in a technical hazard characterization that serves as a support to later risk characterization. It includes:

- a summary of the evaluations of hazard data,
- the rationales for its conclusions, and

- an explanation of the significant strengths or limitations of the conclusions.

Another presentation feature is the use of a weight of evidence narrative that includes both a conclusion about the weight of evidence of carcinogenic potential and a summary of the data on which the conclusion rests. This narrative is a brief summary that *in toto* replaces the alphanumerical classification system used in EPA's 1986 cancer guidelines (U.S. EPA, 1986a).

2.2. ANALYSIS OF TUMOR DATA

Evidence of carcinogenicity comes from finding tumor increases in humans or laboratory animals exposed to a given agent or from finding tumors following exposure to structural analogues to the compound under review. The significance of observed or anticipated tumor effects is evaluated in reference to all the other key data on the agent. This section contains guidance for analyzing human and animal studies to decide whether there is an association between exposure to an agent or a structural analogue and occurrence of tumors. Note that the use of the term "tumor" in these cancer guidelines is defined as malignant neoplasms or a combination of malignant and corresponding benign neoplasms.

Observation of only benign neoplasia may or may not have significance for evaluation under these cancer guidelines. Benign tumors that are not observed to progress to malignancy are assessed on a case-by-case basis. There is a range of possibilities for their overall significance. They may deserve attention because they are serious health problems even though they are not malignant; for instance, benign tumors may be a health risk because of their effect on the function of a target tissue such as the brain. They may be significant indicators of the need for further testing of an agent if they are observed in a short- term test protocol, or such an observation may add to the overall weight of evidence if the same agent causes malignancies in a long-term study. Knowledge of the mode of action associated with a benign tumor response may aid in the interpretation of other tumor responses associated with the same agent. In other cases, observation of a benign tumor response alone may have no significant health hazard implications when other sources of evidence show no suggestion of carcinogenicity.

2.2.1. Human Data

Human data may come from epidemiologic studies or case reports. (Clinical human studies, which involve intentional exposures to substances, may provide toxicokinetic data, but generally not data on carcinogenicity.) The most common sources of human data for cancer risk assessment are epidemiologic investigations. Epidemiology is the study of the distribution of disease in human populations and the factors that may influence that distribution. The goals of cancer epidemiology are to identify distribution of cancer risk and determine the extent to which the risk can be attributed causally to specific exposures to exogenous or endogenous factors (see Centers for Disease Control and Prevention [CDC, 2004]). Epidemiologic data are extremely valuable in risk assessment because they provide direct evidence on whether a substance is likely to produce cancer in humans, thereby avoiding issues such as: species-to-species inference, extrapolation to exposures relevant to people, effects of concomitant exposures due to lifestyles. Thus, epidemiologic studies typically evaluate agents under more relevant conditions. When human data of high quality and adequate statistical power are available, they are generally preferable over animal data and should be given greater weight in hazard characterization and dose-response assessment, although both can be used.

Null results from epidemiologic studies alone generally do not prove the absence of carcinogenic effects because such results can arise either from an agent being truly not carcinogenic or from other factors such as: inadequate statistical power, inadequate study design, imprecise estimates, or confounding factors. Moreover, null results from a well-designed and well-conducted epidemiologic study that contains usable exposure data can help to define upper limits for the estimated dose of concern for human exposure in cases where the overall weight of the evidence indicates that the agent is potentially carcinogenic in humans. Furthermore, data from a well designed and well conducted epidemiologic study that does not show positive results, in conjunction with compelling mechanistic information, can lend support to a conclusion that animal responses may not be predictive of a human cancer hazard.

Epidemiology can also complement experimental evidence in corroborating or clarifying the carcinogenic potential of the agent in question. For example, epidemiologic studies that show elevated cancer risk for tumor sites corresponding to those at which laboratory animals

experience increased tumor incidence can strengthen the weight of evidence of human carcinogenicity. Furthermore, biochemical or molecular epidemiology may help improve understanding of the mechanisms of human carcinogenesis.

2.2.1.1. *Assessment of Evidence of Carcinogenicity from Human Data*

All studies that are considered to be of acceptable quality, whether yielding positive or null results, or even suggesting protective carcinogenic effects, should be considered in assessing the totality of the human evidence. Conclusions about the overall evidence for carcinogenicity from available studies in humans should be summarized along with a discussion of uncertainties and gaps in knowledge. Conclusions regarding the strength of the evidence for positive or negative associations observed, as well as evidence supporting judgments of causality, should be clearly described. In assessing the human data within the overall weight of evidence, determination about the strength of the epidemiologic evidence should clearly identify the degree to which the observed associations may be explained by other factors, including bias or confounding.

Characteristics that are generally desirable in epidemiologic studies include (1) clear articulation of study objectives or hypothesis; (2) proper selection and characterization of comparison groups (exposed and unexposed groups or case and control groups); (3) adequate characterization of exposure; (4) sufficient length of follow-up for disease occurrence; (5) valid ascertainment of the causes of cancer morbidity and mortality; (6) proper consideration of bias and confounding factors; (7) adequate sample size to detect an effect; (8) clear, well-documented, and appropriate methodology for data collection and analysis; (9) adequate response rate and methodology for handling missing data; and (10) complete and clear documentation of results. No single criterion determines the overall adequacy of a study. Practical and resource constraints may limit the ability to address all of these characteristics in a study. The risk assessor is encouraged to consider how the limitations of the available studies might influence the conclusions. While positive biases may be due, for example, to a healthy worker effect, it is also important to consider negative biases, for example, workers who may leave the workforce due to illness caused either by high exposures to the agent or to effects of confounders such as smoking.

The following discussions highlight the major factors included in an analysis of epidemiologic studies.

2.2.1.2. *Types of Studies*

The major types of cancer epidemiologic study designs used for examining environmental causes of cancer are analytical studies and descriptive studies. Each study type has well-known strengths and weaknesses that affect interpretation of results, as summarized below (Lilienfeld and Lilienfeld, 1979; Mausner and Kramer, 1985; Kelsey et al., 1996; Rothman and Greenland, 1998).

Analytical epidemiologic studies, which include case-control and cohort designs, are generally relied on for identifying a causal association between human exposure and adverse health effects. In case-control studies, groups of individuals with (cases) and without (controls) a particular disease are identified and compared to determine differences in exposure. In cohort studies, a group of "exposed" and "nonexposed" individuals are identified and studied over time to determine differences in disease occurrence. Cohort studies can be performed either prospectively or retrospectively from historical records. The type of study chosen may depend on the hypothesis to be evaluated. For example, case-control studies may be more appropriate for rare cancers while cohort studies may be more appropriate for more commonly occurring cancers.

On the other hand, descriptive epidemiologic studies examine symptom or disease rates among populations in relation to personal characteristics such as age, gender, race, and temporal or environmental conditions. Descriptive studies are most frequently used to generate hypotheses about exposure factors, but subsequent analytical designs are necessary to infer causality. For example, cross-sectional designs might be used to compare the prevalence of cancer between areas near and far from a Superfund site. However, in studies where exposure and disease information applies only to the current conditions, it is not possible to infer that the exposure actually *caused* the disease. Therefore, these studies are used to identify patterns or trends in disease occurrence over time or in different geographical locations, but typical

limitations in the characterization of populations in these studies make it difficult to infer the causal agent or degree of exposure.

Case reports describe a particular effect in an individual or group of individuals who were exposed to a substance. These reports are often anecdotal or highly selective in nature and generally are of limited use for hazard assessment. Specifically, cancer causality can rarely be inferred from case reports alone. Investigative follow-up may or may not accompany such reports. For cancer, the most common types of case series are associated with occupational and childhood exposures. Case reports can be particularly valuable for identifying unique features, such as an association with an uncommon tumor (e.g., inhalation of vinyl chloride and hepatic angiosarcoma in workers or ingestion of diethylstilbestrol by mothers and clear-cell carcinoma of the vagina in offspring).

2.2.1.3. *Exposure Issues*.

For epidemiologic data to be useful in determining whether there is an association between health effects and exposure to an agent, there should be adequate characterization of exposure information. In general, greater weight should be given to studies with more precise and specific exposure estimates.

Questions to address about exposure are: What can one reliably conclude about the exposure parameters including (but not limited to) the level, duration, route, and frequency of exposure of individuals in one population as compared with another? How sensitive are study results to uncertainties in these parameters?

Actual exposure measurements are not available for many retrospective studies. Therefore, surrogates are often used to reconstruct exposure parameters. These may involve attributing exposures to job classifications in a workplace or to broader occupational or geographic groupings. Use of surrogates carries a potential for misclassification, i.e., individuals may be placed in an incorrect exposure group. Misclassification generally leads to reduced ability of a study to detect differences between study and referent populations.

When either current or historical monitoring data are available, the exposure evaluation includes consideration of the error bounds of the monitoring and analytic methods and whether

the data are from routine or accidental exposures. The potential for misclassification and for measurement errors is amenable to both qualitative and quantitative analysis. These are essential analyses for judging a study's results, because exposure estimation is the most critical part of a retrospective study.

2.2.1.4. *Biological Markers*.

Biological markers potentially offer excellent measures of exposure (Hulka and Margolin, 1992; Peto and Darby, 1994). In some cases, molecular or cellular effects (e.g., DNA or protein adducts, mutation, chromosomal aberrations, levels of thyroid-stimulating hormone) can be measured in blood, body fluids, cells, and tissues to serve as biomarkers of exposure in humans and animals (Callemen et al., 1978; Birner et al., 1990). As such, they can act as an internal surrogate measure of chemical dose, representing, as appropriate, either recent exposure (e.g., serum concentration) or accumulated exposure over some period (e.g., hemoglobin adducts). Validated markers of exposure such as alkylated hemoglobin from exposure to ethylene oxide (Van Sittert et al., 1985) or urinary arsenic (Enterline et al., 1987) can improve estimates of dose over the relevant time periods for the markers. Markers closely identified with effects promise to greatly increase the ability of studies to distinguish real effects from bias at low levels of relative risk between populations (Taylor et al., 1994; Biggs et al., 1993) and to resolve problems of confounding risk factors. However, when using molecular or cellular effects as biomarkers of exposure, since many of these changes are often not specific to just one type of exposure, it is important to be aware that changes may be due to exposures unrelated to the exposure of interest and attention must be paid to controlling for potential confounders.

Biochemical or molecular epidemiologic studies may use biological markers of effect as indicators of disease or its precursors. The application of techniques for measuring cellular and molecular alterations due to exposure to specific environmental agents may allow conclusions to be drawn about the mechanisms of carcinogenesis (see section 2.4 for more information on this topic).

2.2.1.5. *Confounding Factors*.

Control for potential confounding factors is an important consideration in the evaluation of the design and in the analysis of observational epidemiologic studies. A confounder is a variable that is related to both the health outcome of concern (cancer) and exposure. Common examples include age, socioeconomic status, smoking habits, and diet. For instance, if older people are more likely to be exposed to a given contaminant as well as more likely to have cancer because of their age, age is considered a confounder. Adjustment for potentially confounding factors (from a statistical as contrasted with an epidemiologic point of view) can occur either in the design of the study (e.g., individual or group matching on critical factors) or in the statistical analysis of the results (stratification or direct or indirect adjustment). Direct adjustment in the statistical analysis may not be possible owing to the presentation of the data or because needed information was not collected during the study. In this case, indirect comparisons may be possible. For example, in the absence of data on smoking status among individuals in the study population, an examination of the possible contribution of cigarette smoking to increased lung cancer risk may be based on information from other sources, such as the American Cancer Society's longitudinal studies (Hammand, 1966; Garfinkel and Silverberg, 1991). The effectiveness of adjustments contributes to the ability to draw inferences from a study.

Different studies involving exposure to an agent may have different confounding factors. If consistent increases in cancer risk are observed across a collection of studies with different confounding factors, the inference that the agent under investigation was the etiologic factor is strengthened.

There may also be instances where the agent of interest is a risk factor in conjunction with another agent. For instance, interaction as well as effect-measure modification are sometimes construed to be confounding, but they are different than confounding. Interaction is described as a situation in which two or more risk factors modify the effect of each other with regard to the occurrence of a given effect. This phenomenon is sometimes described as effect-measure modification or heterogeneity of effect (Szklo and Nieto, 2000). Effect-measure modification refers to variation in the magnitude of measure exposure effect across levels of another variable (Rothman and Greenland, 1998). The variable across which the effect measure varies and is

called an *effect modifier* (e.g., hepatitis virus B and aflatoxin in hepatic cancer). Interaction, on the other hand, means effect of the exposure on the outcome differs, depending on the presence of another variable (the effect modifier). When the effect of the exposure of interest is accentuated by another variable, it is said to be synergistic interaction. Synergistic interaction can be additive (e.g., hepatitis virus B and aflatoxin in hepatic cancer) or multiplicative (e.g., asbestos and smoking in lung cancer). If the effect of exposure is diminished or eliminated by another variable, it said to be antagonistic interaction (e.g., intake of vitamin E and lower occurrence of lung cancer).

2.2.1.6. ***Statistical Considerations.***

The analysis should apply appropriate statistical methods to ascertain whether the observed association between exposure and effects would be expected by chance. A description of the method or methods used should include the reasons for their selection. Statistical analyses of the bias, confounding, and interaction are part of addressing the significance of an association and the power of a study to detect an effect.

The analysis augments examination of the results for the whole population with exploration of the results for groups with comparatively greater exposure or time since first exposure. This may support identifying an association or establishing a dose-response trend. When studies show no association, such exploration may apply to determining an upper limit on potential human risk for consideration alongside results of animal tumor effects studies.

2.2.1.6.1. ***Likelihood of observing an effect.*** The power of a study – the likelihood of observing an effect if one exists – increases with sample size, i.e., the number of subjects studied from a population. (For example, a quadrupling of a background rate in the 1 per 10,000 range would require more subjects who have experienced greater or longer exposure or lengthier follow-up, than a doubling of a background rate in the 1 per 100 range.) If the size of the effect is expected to be very small at low doses, higher doses or longer durations of exposure may be needed to have an appreciable likelihood of observing an effect with a given sample size. Because of the often long latency period in cancer development, the likelihood of observing an effect also

depends on whether adequate time has elapsed since exposure began for effects to occur. Since the design of the study and the choice of analysis, as well as the design level of certainty in the results and the magnitude of response in an unexposed population also affect the likelihood of observing an effect, it is important to carefully interpret the absence of an observed effect. A unique feature that can be ascribed to the effects of a particular agent (such as a tumor type that is seen only rarely in the absence of the agent) can increase sensitivity by permitting separation of bias and confounding factors from real effects. Similarly, a biomarker particular to the agent can permit these distinctions. Statistical re-analyses of data, particularly an examination of different exposure indices, can give insight into potential exposure-response relationships. These are all factors to explore in statistical analysis of the data.

2.2.1.6.2. ***Sampling and other bias issues.*** When comparing cases and controls or exposed and non-exposed populations, it would be preferable for the two populations to differ only in exposure to the agent in question. Because this is seldom the case, it is important to identify sources of sampling and other potential biases inherent in a study design or data collection methods.

Bias is a systematic error. In epidemiologic studies, bias can occur in the selection of cases and controls or exposed and non-exposed populations, as well as the follow up of the groups, or the classification of disease or exposure. The size of the risks observed can be affected by noncomparability between populations of factors such as general health, diet, lifestyle, or geographic location; differences in the way case and control individuals recall past events; differences in data collection that result in unequal ascertainment of health effects in the populations; and unequal follow-up of individuals (Rothman and Greenland, 1998). Other factors worth consideration can be inherent in the available cohorts, e.g., use of occupational studies (the healthy worker effect), absence of one sex, or limitations in sample size for one or more ethnicities.

The mere presence of biases does not invalidate a study, but should be reflected in the judgment of its strengths or weaknesses. Acceptance of studies for assessment depends on identifying their sources of bias and the possible effects on study results.

2.2.1.6.3. ***Combining statistical evidence across studies.*** Meta-analysis is a means of integrating the results of multiple studies of similar health effects and risk factors. This technique is particularly useful when various studies yield varying degrees of risk or even conflicting associations (negative and positive). It is intended to introduce consistency and comprehensiveness into what otherwise might be a more subjective review of the literature. The value of such an analysis is dependent upon a systematic review of the literature that uses transparent criteria of inclusion and exclusion. In interpreting such analyses, it is important to consider the effects of differences in study quality, as well as the effect of publication bias. Meta-analysis may not be advantageous in some circumstances. These include when the relationship between exposure and disease is obvious from the individual studies; when there are only a few studies of the key health outcomes; when there is insufficient information from available studies related to disease, risk estimate, or exposure classification to insure comparability; or when there are substantial confounding or other biases that cannot be adjusted for in the analysis (Blair et al., 1995; Greenland, 1987; Peto, 1992).

2.2.1.7. ***Evidence for Causality***

Determining whether an observed association (risk) is causal rather than spurious involves consideration of a number of factors. Sir Bradford Hill (Hill, 1965) developed a set of guidelines for evaluating epidemiologic associations that can be used in conjunction with the discussion of causality such as the 2004 Surgeon General's report on smoking (CDC, 2004) and in other documents (e.g., Rothman and Greenland 1998; IPCS, 1999) . The critical assessment of epidemiologic evidence is conceptually based upon consideration of salient aspects of the evidence of associations so as to reach fundamental judgments as to the likely causal significance of the observed associations. In so doing, it is appropriate to draw from those aspects initially presented in Hill's classic monograph (Hill, 1965) and widely used by the scientific community in conducting such evidence-based reviews. A number of these aspects are judged to be particularly salient in evaluating the body of evidence available in this review, including the aspects described by Hill as strength, experiment, consistency, plausibility, and coherence. Other aspects identified by Hill, including temporality and biological gradient, are also relevant and

considered here (e.g., in characterizing lag structures and concentration-response relationships), but are more directly addressed in the design and analyses of the individual epidemiologic studies included in this assessment. As discussed below, these salient aspects are interrelated and considered throughout the evaluation of the epidemiologic evidence generally reflected in the integrative synthesis of the mode of action framework.

The general evaluation of the strength of the epidemiological evidence reflects consideration not only of the magnitude of reported effects estimates and their statistical significance, but also of the precision of the effects estimates and the robustness of the effects associations. Consideration of the robustness of the associations takes into account a number of factors, including in particular the impact of alternative models and model specifications and potential confounding factors, as well issues related to the consequences of measurement error. Consideration of the consistency of the effects associations involves looking across the results of studies conducted by different investigators in different places and times. Particular weight may be given, consistent with Hill's views, to the presence of "similar results reached in quite different ways, e.g., prospectively and retrospectively" (Hill, 1965). Looking beyond the epidemiological evidence, evaluation of the biological plausibility of the associations observed in epidemiologic studies reflects consideration of both exposure-related factors and toxicological evidence relevant to identification of potential modes of action (MOAs). Similarly, consideration of the coherence of health effects associations reported in the epidemiologic literature reflects broad consideration of information pertaining to the nature of the biological markers evaluated in toxicologic and epidemiologic studies.

In identifying these aspects as being particularly salient in this assessment, it is also important to recognize that no one aspect is either necessary or sufficient for drawing inferences of causality. As Hill (1965) emphasized:

> "None of my nine viewpoints can bring indisputable evidence for or against the cause-and-effect hypothesis and none can be required as *a sine qua non*. What they can do, with greater or less strength, is to help us to make up our minds on the fundamental question — is there any other way of explaining the set of facts

before us, is there any other answer equally, or more, likely than cause and effect?"

While these aspects frame considerations weighed in assessing the epidemiologic evidence, they do not lend themselves to being considered in terms of simple formulas or hard-and-fast rules of evidence leading to answers about causality (Hill, 1965). One, for example, cannot simply count up the numbers of studies reporting statistically significant results or statistically non-significant results for carcinogenesis and related MOAs and reach credible conclusions about the relative strength of the evidence and the likelihood of causality. Rather, these important considerations are taken into account throughout the assessment with a goal of producing an objective appraisal of the evidence (informed by peer and public comment and advice), which includes the weighing of alternative views on controversial issues. Thus, although these guidelines have become known as "causal criteria," it is important to note that they cannot be used as a strictly quantitative checklist. Rather, these "criteria" should be used to determine the strength of the evidence for concluding causality. In particular, the absence of one or more of the "criteria" does not automatically exclude a study from consideration (e.g., see discussion in CDC, 2004). The list below has been adapted from Hill's guidelines as an aid in judging causality.

(a) Consistency of the observed association. An inference of causality is strengthened when a pattern of elevated risks is observed across several independent studies. The reproducibility of findings constitutes one of the strongest arguments for causality. If there are discordant results among investigations, possible reasons such as differences in exposure, confounding factors, and the power of the study are considered.

(b) Strength of the observed association. The finding of large, precise risks increases confidence that the association is not likely due to chance, bias, or other factors. A modest risk, however, does not preclude a causal association and may reflect a lower level of exposure, an agent of lower potency, or a common disease with a high background level.

(c) Specificity of the observed association. As originally intended, this refers to increased inference of causality if one cause is associated with a single effect or disease (Hill, 1965). Based on our current understanding that many agents cause cancer at multiple sites, and

many cancers have multiple causes, this is now considered one of the weaker guidelines for causality. Thus, although the presence of specificity may support causality, its absence does not exclude it.

(d) Temporal relationship of the observed association. A causal interpretation is strengthened when exposure is known to precede development of the disease. Because a latent period of up to 20 years or longer is often associated with cancer development in adults, the study should consider whether exposures occurred sufficiently long ago to produce an effect at the time the cancer is assessed. This is among the strongest criteria for an inference of causality.

(e) Biological gradient (exposure-response relationship). A clear exposure-response relationship (e.g., increasing effects associated with greater exposure) strongly suggests cause and effect, especially when such relationships are also observed for duration of exposure (e.g., increasing effects observed following longer exposure times). There are many possible reasons that an epidemiologic study may fail to detect an exposure-response relationship. For example, an analysis that included decreasing exposures due to improved technology that is combined with higher prior exposure in an initial analysis can require a segmented analysis to apportion exposure. Other reasons for failure to detect a relationship may include a small range of exposures. Thus, the absence of an exposure-response relationship does not exclude a causal relationship.

(f) Biological plausibility. An inference of causality tends to be strengthened by consistency with data from experimental studies or other sources demonstrating plausible biological mechanisms. A lack of mechanistic data, however, is not a reason to reject causality.

(g) Coherence. An inference of causality may be strengthened by other lines of evidence that support a cause-and-effect interpretation of the association. Information is considered from animal bioassays, toxicokinetic studies, and short-term studies. The absence of other lines of evidence, however, is not a reason to reject causality.

(h) Experimental evidence (from human populations). Experimental evidence is seldom available from human populations and exists only when conditions of human exposure have occurred to create a "natural experiment" at different levels of exposure. Strong evidence

for causality can be provided when a change in exposure brings about a change in disease frequency, for example, the decrease in the risk of lung cancer that follows cessation of smoking.

(i) Analogy. SARs and information on the agent's structural analogues can provide insight into whether an association is causal. Similarly, information on mode of action for a chemical, as one of many structural analogues, can inform decisions regarding likely causality.

2.2.2. Animal Data

Various whole-animal test systems are currently used or are under development for evaluating potential carcinogenicity. Cancer studies involving chronic exposure for most of the lifespan of an animal are generally accepted for evaluation of tumor effects (Tomatis et al., 1989; Rall, 1991; Allen et al., 1988; but see Ames and Gold, 1990). Other studies of special design are useful for observing formation of preneoplastic lesions or tumors or investigating specific modes of action. Their applicability is determined on a case-by-case basis.

2.2.2.1. *Long-term Carcinogenicity Studies*

The objective of long-term carcinogenesis bioassays is to determine the potential carcinogenic hazard and dose-response relationships of the test agent. Carcinogenicity rodent studies are designed to examine the production of tumors as well as preneoplastic lesions and other indications of chronic toxicity that may provide evidence of treatment-related effects and insights into the way the test agent produces tumors. Current standardized carcinogenicity studies in rodents test at least 50 animals per sex per dose group in each of three treatment groups and in a concurrent control group, usually for 18 to 24 months, depending on the rodent species tested (OECD, 1981; U.S. EPA, 1998c). The high dose in long-term studies is generally selected to provide the maximum ability to detect treatment-related carcinogenic effects while not compromising the outcome of the study through excessive toxicity or inducing inappropriate toxicokinetics (e.g., overwhelming absorption or detoxification mechanisms). The purpose of two or more lower doses is to provide some information on the shape of the dose-response curve. Similar protocols have been and continue to be used by many laboratories worldwide.

All available studies of tumor effects in whole animals should be considered, at least preliminarily. The analysis should discard studies judged to be wholly inadequate in protocol, conduct, or results. Criteria for the technical adequacy of animal carcinogenicity studies have been published and should be used as guidance to judge the acceptability of individual studies (e.g., NTP, 1984; OSTP, 1985; Chhabra et al., 1990). As these criteria, in whole or in part, may be updated by the National Toxicology Program (NTP) and others, the analyst should consult the appropriate sources to determine both the current standards as well as those that were contemporaneous with the study. Care should be taken to include studies that provide some evidence bearing on carcinogenicity or that help interpret effects noted in other studies, even if these studies have some limitations of protocol or conduct. Such limited, but not wholly inadequate, studies can contribute as their deficiencies permit. The findings of long-term rodent bioassays should be interpreted in conjunction with results of prechronic studies along with toxicokinetic studies and other pertinent information, if available. Evaluation of tumor effects takes into consideration both biological and statistical significance of the findings (Haseman, 1984, 1985, 1990, 1995). The following sections highlight the major issues in the evaluation of long-term carcinogenicity studies.

2.2.2.1.1. ***Dosing issues***. Among the many criteria for technical adequacy of animal carcinogenicity studies is the appropriateness of dose selection. The selection of doses for chronic bioassays is based on scientific judgments and sound toxicologic principles. Dose selection should be made on the basis of relevant toxicologic information from prechronic, mechanistic, and toxicokinetic and mechanistic studies. A scientific rationale for dose selection should be clearly articulated (e.g., NTP, 1984; ILSI, 1997). How well the dose selection is made is evaluated after the completion of the bioassay.

Interpretation of carcinogenicity study results is profoundly affected by study exposure conditions, especially by inappropriate dose selection. This is particularly important in studies that do not show positive results for carcinogenicity, because failure to use a sufficiently high dose reduces the sensitivity of the studies. A lack of tumorigenic responses at exposure levels that cause significant impairment of animal survival may also not be acceptable. In addition,

overt toxicity or qualitatively altered toxicokinetics due to excessively high doses may result in tumor effects that are secondary to the toxicity rather than directly attributable to the agent.

With regard to the appropriateness of the high dose, an adequate high dose would generally be one that produces some toxic effects without unduly affecting mortality from effects other than cancer or producing significant adverse effects on the nutrition and health of the test animals (OECD, 1981; NRC, 1993a). If the test agent does not appear to cause any specific target organ toxicity or perturbation of physiological function, an adequate high dose can be specified in terms of a percentage reduction of body weight gain over the lifespan of the animals. The high dose would generally be considered inadequate if neither toxicity nor change in weight gain is observed. On the other hand, significant increases in mortality from effects other than cancer generally indicate that an adequate high dose has been exceeded.

Other signs of treatment-related toxicity associated with an excessive high dose may include (a) significant reduction of body weight gain (e.g., greater than 10%), (b) significant increases in abnormal behavioral and clinical signs, (c) significant changes in hematology or clinical chemistry, (d) saturation of absorption and detoxification mechanisms, or (e) marked changes in organ weight, morphology, and histopathology. It should be noted that practical upper limits have been established to avoid the use of excessively high doses in long-term carcinogenicity studies of environmental chemicals (e.g., 5% of the test substance in the feed for dietary studies or 1 g/kg body weight for oral gavage studies [OECD, 1981]).

For dietary studies, weight gain reductions should be evaluated as to whether there is a palatability problem or an issue with food efficiency; certainly, the latter is a toxic manifestation. In the case of inhalation studies with respirable particles, evidence of impairment of normal clearance of particles from the lung should be considered along with other signs of toxicity to the respiratory airways to determine whether the high exposure concentration has been appropriately selected (U.S. EPA, 2001a). For dermal studies, evidence of skin irritation may indicate that an adequate high dose has been reached (U.S. EPA, 1989).

In order to obtain the most relevant information from a long-term carcinogenicity study, it is important to maximize exposure conditions to the test material. At the same time, caution is appropriate in using excessive high-dose levels that would confound the interpretation of study

results to humans. The middle and lowest doses should be selected to characterize the shape of the dose-response curve as much as possible. It is important that the doses be adequately spaced so that the study can provide relevant dose-response data for assessing human hazard and risk. If the testing of potential carcinogenicity is being combined with an evaluation of noncancer chronic toxicity, the study should be designed to include one dose in addition to the control(s) that is not expected to elicit adverse effects.

There are several possible outcomes regarding the study interpretation of the significance and relevance of tumorigenic effects associated with exposure or dose levels below, at, or above an adequate high dose. The general guidance is given here; for each case, the information at hand should be evaluated and a rationale should be given for the position taken.

- *Adequately high dose*. If an adequately high dose has been used, tumor effects are judged positive or negative depending on the presence or absence of significant tumor incidence increases, respectively.

- *Excessively high dose*. If toxicity or mortality is excessive at the high dose, interpretation depends on whether or not tumors are found.

  - Studies that show tumor effects only at excessive doses may be compromised and may or may not carry weight, depending on the interpretation in the context of other study results and other lines of evidence. Results of such studies, however, are generally not considered suitable for dose-response extrapolation if it is determined that the mode(s) of action underlying the tumorigenic responses at high doses is not operative at lower doses.

  - Studies that show tumors at lower doses, even though the high dose is excessive and may be discounted, should be evaluated on their own merits.

- If a study does not show an increase in tumor incidence at a toxic high dose and appropriately spaced lower doses are used without such toxicity or tumors, the study is generally judged as negative for carcinogenicity.

- *Inadequately high dose*. Studies of inadequate sensitivity where an adequately high dose has not been reached may be used to bound the dose range where carcinogenic effects might be expected.

2.2.2.1.2. ***Statistical considerations***. The main aim of statistical evaluation is to determine whether exposure to the test agent is associated with an increase of tumor development. Statistical analysis of a long-term study should be performed for each tumor type separately. The incidence of benign and malignant lesions of the same cell type, usually within a single tissue or organ, are considered separately but may be combined when scientifically defensible (McConnell et al., 1986).

Trend tests and pairwise comparison tests are the recommended tests for determining whether chance, rather than a treatment-related effect, is a plausible explanation for an apparent increase in tumor incidence. A trend test such as the Cochran-Armitage test (Snedecor and Cochran, 1967) asks whether the results in all dose groups together increase as dose increases. A pairwise comparison test such as the Fisher exact test (Fisher, 1950) asks whether an incidence in one dose group is increased over that of the control group. By convention, for both tests a statistically significant comparison is one for which p is less than 0.05 that the increased incidence is due to chance. Significance in either kind of test is sufficient to reject the hypothesis that chance accounts for the result.

A statistically significant response may or may not be biologically significant and vice versa. The selection of a significance level is a policy choice based on a trade-off between the risks of false positives and false negatives. A result with a significance level of greater or less than 5% (the most common significance level) is examined to see if the result confirms other scientific information. When the assessment departs from a simple 5% level, this should be

highlighted in the risk characterization. A two-tailed test or a one-tailed test can be used. In either case a rationale is provided.

Statistical power can affect the likelihood that a statistically significant result could reasonably be expected. This is especially important in studies or dose groups with small sample sizes or low dose rates. Reporting the statistical power can be useful for comparing and reconciling positive and negative results from different studies.

Considerations of multiple comparisons should also be taken into account. Haseman (1983) analyzed typical animal bioassays that tested both sexes of two species and concluded that, because of multiple comparisons, a single tumor increase for a species-sex-site combination that is statistically significant at the 1% level for common tumors or 5% for rare tumors corresponds to a 7–8% significance level for the study as a whole. Therefore, animal bioassays presenting only one significant result that falls short of the 1% level for a common tumor should be treated with caution.

2.2.2.1.3. ***Concurrent and historical controls.*** The standard for determining statistical significance of tumor incidence comes from a comparison of tumors in dosed animals with those in concurrent control animals. Additional insights about both statistical and biological significance can come from an examination of historical control data (Tarone, 1982; Haseman, 1995). Historical control data can add to the analysis, particularly by enabling identification of uncommon tumor types or high spontaneous incidence of a tumor in a given animal strain. Identification of common or uncommon situations prompts further thought about the meaning of the response in the current study in context with other observations in animal studies and with other evidence about the carcinogenic potential of the agent. These other sources of information may reinforce or weaken the significance given to the response in the hazard assessment. Caution should be exercised in simply looking at the ranges of historical responses, because the range ignores differences in survival of animals among studies and is related to the number of studies in the database.

In analyzing results for uncommon tumors in a treated group that are not statistically significant in comparison with concurrent controls, the analyst may be informed by the

experience of historical controls to conclude that the result is in fact unlikely to be due to chance. However, caution should be used in interpreting results. In analyzing results for common tumors, a different set of considerations comes into play. Generally speaking, statistically significant increases in tumors should not be discounted simply because incidence rates in the treated groups are within the range of historical controls or because incidence rates in the concurrent controls are somewhat lower than average. Random assignment of animals to groups and proper statistical procedures provide assurance that statistically significant results are unlikely to be due to chance alone. However, caution should be used in interpreting results that are barely statistically significant or in which incidence rates in concurrent controls are unusually low in comparison with historical controls.

In cases where there may be reason to discount the biological relevance to humans of increases in common animal tumors, such considerations should be weighed on their own merits and clearly distinguished from statistical concerns.

When historical control data are used, the discussion should address several issues that affect comparability of historical and concurrent control data, such as genetic drift in the laboratory strains, differences in pathology examination at different times and in different laboratories (e.g., in criteria for evaluating lesions; variations in the techniques for the preparation or reading of tissue samples among laboratories), and comparability of animals from different suppliers. The most relevant historical data come from the same laboratory and the same supplier and are gathered within 2 or 3 years one way or the other of the study under review; other data should be used only with extreme caution.

2.2.2.1.4. ***Assessment of evidence of carcinogenicity from long-term animal studies***. In general, observation of tumors under different circumstances lends support to the significance of the findings for animal carcinogenicity. Significance is generally increased by the observation of more of the factors listed below. For a factor such as malignancy, the severity of the observed pathology can also affect the significance. The following observations add significance to the tumor findings:

- uncommon tumor types;
- tumors at multiple sites;
- tumors by more than one route of administration;
- tumors in multiple species, strains, or both sexes;
- progression of lesions from preneoplastic to benign to malignant;
- reduced latency of neoplastic lesions;
- metastases;
- unusual magnitude of tumor response;
- proportion of malignant tumors; and
- dose-related increases.

In these cancer guidelines, tumors observed in animals are generally assumed to indicate that an agent may produce tumors in humans. Mode of action may help inform this assumption on a chemical-specific basis. Moreover, the absence of tumors in well-conducted, long-term animal studies in at least two species provides reasonable assurance that an agent may not be a carcinogenic concern for humans.

2.2.2.1.5. ***Site concordance.*** Site concordance of tumor effects between animals and humans should be considered in each case. Thus far, there is evidence that growth control mechanisms at the level of the cell are homologous among mammals, but there is no evidence that these mechanisms are site concordant. Moreover, agents observed to produce tumors in both humans and animals have produced tumors either at the same site (e.g., vinyl chloride) or different sites (e.g., benzene) (NRC, 1994). Hence, site concordance is not always assumed between animals and humans. On the other hand, certain modes of action with consequences for particular tissue sites (e.g., disruption of thyroid function) may lead to an anticipation of site concordance.

2.2.2.2. *Perinatal Carcinogenicity Studies*

The objective of perinatal carcinogenesis studies is to determine the carcinogenic potential and dose-response relationships of the test agent in the developing organism. Some

investigators have hypothesized that the age of initial exposure to a chemical carcinogen may influence the carcinogenic response (Vesselinovitch et al., 1979; Rice, 1979; McConnell, 1992). Current standardized long-term carcinogenesis bioassays generally begin dosing animals at 6–8 weeks of age and continue dosing for the lifespan of the animal (18–24 months). This protocol has been modified in some cases to investigate the potential of the test agent to induce transplacental carcinogenesis or to investigate the potential differences following perinatal and adult exposures, but currently there is not a standardized protocol for testing agents for carcinogenic effects following prenatal or early postnatal exposure.

Several cancer bioassay studies have compared adult and perinatal exposures (see McConnell, 1992; U.S. EPA, 1996b). A review of these studies reveals that perinatal exposure rarely identifies carcinogens that are not found in standard animal bioassays. Exposure that is perinatal can increase the incidence of a given type of tumor. The increase may reflect an increased length of exposure and a higher dose for the developing organism relative to the adult or an increase in susceptibility in some cases. Additionally, exposure that is perinatal through adulthood sometimes reduces the latency period for tumors to develop in the growing organism (U.S. EPA, 1996b). EPA evaluates the usefulness of perinatal studies on an agent-by-agent basis (e.g., U.S. EPA, 1997a, b).

Perinatal study data analysis generally follows the principles discussed above for evaluating other long-term carcinogenicity studies. When differences in responses between perinatal animals and adult animals suggest an increased susceptibility of perinatal or postnatal animals, such as the ones below, a separate evaluation of the response should be prepared:

- a difference in dose-response relationship,
- the presence of different tumor types,
- an earlier onset of tumors, or
- an increase in the incidence of tumors.

2.2.2.3. *Other Studies*

Intermediate-term and acute dosing studies often use protocols that screen for carcinogenic or preneoplastic effects, sometimes in a single tissue. Some protocols involve the development of various proliferative lesions, such as foci of alteration in the liver (Goldsworthy et al., 1986). Others use tumor endpoints, such as the induction of lung adenomas in the sensitive strain A mouse (Maronpot et al., 1986) or tumor induction in initiation-promotion studies using various organs such as the bladder, intestine, liver, lung, mammary gland, and thyroid (Ito et al., 1992). In these tests, the selected tissue rather than the whole animal is, in a sense, the test system. Important information concerning the steps in the carcinogenic process and mode of action can be obtained from "start/stop" experiments. In these protocols, an agent is given for a period of time to induce particular lesions or effects and then stopped in order to evaluate the progression or reversibility of processes (Todd, 1986; Marsman and Popp, 1994).

Assays in genetically engineered rodents may provide insight into the chemical and gene interactions involved in carcinogenesis (Tennant et al., 1995). These mechanistically based approaches involve activated oncogenes that are introduced (transgenic) or tumor suppressor genes that are deleted (knocked out). If appropriate genes are selected, not only may these systems provide information on mechanisms, but the rodents typically show tumor development earlier than in the standard bioassay. Transgenic mutagenesis assays also represent a mechanistic approach for assessing the mutagenic properties of agents as well as developing quantitative linkages between exposure, internal dose, and mutation related to tumor induction (Morrison and Ashby, 1994; Sisk et al., 1994; Hayward et al., 1995).

The support that these studies give to a determination of carcinogenicity rests on their contribution to the consistency of other evidence about an agent. For instance, benzoyl peroxide has promoter activity on the skin, but the overall evidence may be less supportive (Kraus et al., 1995). These studies also may contribute information about mode of action. It is important to recognize the limitations of these experimental protocols, such as short duration, limited histology, lack of complete development of tumors, or experimental manipulation of the carcinogenic process, that may limit their contribution to the overall assessment. Generally, their results are appropriate as aids in the interpretation of other toxicological evidence (e.g., rodent

chronic bioassays), especially regarding potential modes of action. On the basis of currently available information, it is unlikely that any of these assays, which are conducted for 6 months with 15 animals per group, will replace all chronic bioassays for hazard identification (Spalding et al., 2000; Gulezian et al., 2000; ILSI, 2001).

2.2.3. Structural Analogue Data

For some chemical classes, there is significant available information, largely from rodent bioassays, on the carcinogenicity of analogues. Analogue effects are instructive in investigating carcinogenic potential of an agent as well as in identifying potential target organs, exposures associated with effects, and potential functional class effects or modes of action. All appropriate studies should be included and analyzed, whether indicative of a positive effect or not. Evaluation includes tests in various animal species, strains, and sexes; with different routes of administration; and at various doses, as data are available. Confidence in conclusions is a function of how similar the analogues are to the agent under review in structure, metabolism, and biological activity. It is important to consider this confidence to ensure a balanced position.

2.3. ANALYSIS OF OTHER KEY DATA

The physical, chemical, and structural properties of an agent, as well as data on endpoints that are thought to be critical elements of the carcinogenic process, provide valuable insights into the likelihood of human cancer risk. The following sections provide guidance for analyses of these data.

2.3.1. Physicochemical Properties

Physicochemical properties affect an agent's absorption, tissue distribution (bioavailability), biotransformation, and degradation in the body and are important determinants of hazard potential (and dose-response analysis). Properties that should be analyzed include, but are not limited to, molecular weight, size, and shape; valence state; physical state (gas, liquid, solid); water or lipid solubility, which can influence retention and tissue distribution; and potential for chemical degradation or stabilization in the body.

An agent's potential for chemical reaction with cellular components, particularly with DNA and proteins, is also important. The agent's molecular size and shape, electrophilicity, and charge distribution are considered in order to decide whether they would facilitate such reactions.

2.3.2. Structure-Activity Relationships (SARs)

SAR analyses and models can be used to predict molecular properties, surrogate biological endpoints, and carcinogenicity (see, e.g., Richard, 1998a, b; Richard and Williams, 2002; Contrera et al., 2003). Overall, these analyses provide valuable initial information on agents, they may strengthen or weaken concern, and they are part of the weight of evidence.

Currently, SAR analysis is most useful for chemicals and metabolites that are believed to initiate carcinogenesis through covalent interaction with DNA (i.e., DNA-reactive, mutagenic, electrophilic, or proelectrophilic chemicals) (Ashby and Tennant, 1991). For organic chemicals, the predictive capability of SAR analysis combined with other toxicity information has been demonstrated (Ashby and Tennant, 1994). The following parameters are useful in comparing an agent to its structural analogues and congeners that produce tumors and affect related biological processes such as receptor binding and activation, mutagenicity, and general toxicity (Woo and Arcos, 1989):

- nature and reactivity of the electrophilic moiety or moieties present;
- potential to form electrophilic reactive intermediate(s) through chemical, photochemical, or metabolic activation;
- contribution of the carrier molecule to which the electrophilic moiety(ies) is attached;
- physicochemical properties (e.g., physical state, solubility, octanol/water partition coefficient, half-life in aqueous solution);

- structural and substructural features (e.g., electronic, stearic, molecular geometric);

- metabolic pattern (e.g., metabolic pathways and activation and detoxification ratio); and

- possible exposure route(s) of the agent.

Suitable SAR analysis of non-DNA-reactive chemicals and of DNA-reactive chemicals that do not appear to bind covalently to DNA should be based on knowledge or postulation of the probable mode(s) of action of closely related carcinogenic structural analogues (e.g., receptor mediated, cytotoxicity related). Examination of the physicochemical and biochemical properties of the agent may then provide the rest of the information needed in order to make an assessment of the likelihood of the agent's activity by that mode of action.

2.3.3. Comparative Metabolism and Toxicokinetics

Studies of the absorption, distribution, biotransformation, and excretion of agents permit comparisons among species to assist in determining the implications of animal responses for human hazard assessment, supporting identification of active metabolites, identifying changes in distribution and metabolic pathway or pathways over a dose range, and making comparisons among different routes of exposure.

If extensive data are available (e.g., blood/tissue partition coefficients and pertinent physiological parameters of the species of interest), physiologically based toxicokinetic models can be constructed to assist in a determination of tissue dosimetry, species-to-species extrapolation of dose, and route-to-route extrapolation (Conolly and Andersen, 1991; see Section 3.1.2). If sufficient data are not available, it may be assumed as a default that toxicokinetic and metabolic processes are qualitatively comparable among species. Discussion of appropriate procedures for quantitative, interspecies comparisons appears in Chapter 3.

The *qualitative* question of whether an agent is absorbed by a particular route of exposure is important for weight of evidence classification, discussed in Section 2.5. Decisions about

whether route of exposure is a limiting factor on expression of any hazard, e.g., absorption does not occur by a specified route, are generally based on studies in which effects of the agent or its structural analogues have been observed by different routes, on physical-chemical properties, or on toxicokinetics studies.

Adequate metabolism and toxicokinetic data can be applied toward the following, as data permit. Confidence in conclusions is enhanced when *in vivo* data are available.

- *Identifying metabolites and reactive intermediates of metabolism and determining whether one or more of these intermediates is likely to be responsible for the observed effects*. Information on the reactive intermediates focuses on SAR analysis, analysis of potential modes of action, and estimation of internal dose in dose-response assessment (D'Souza et al., 1987; Krewski et al., 1987).

- *Identifying and comparing the relative activities of metabolic pathways in animals and in humans, and at different ages*. This analysis can provide insights for extrapolating results of animal studies to humans.

- *Describing anticipated distribution within the body and possibly identifying target organs*. Use of water solubility, molecular weight, and structure analysis can support qualitative inferences about anticipated distribution and excretion. In addition, describing whether the agent or metabolite of concern will be excreted rapidly or slowly or whether it will be stored in a particular tissue or tissues to be mobilized later can identify issues in comparing species and formulating dose-response assessment approaches.

- *Identifying changes in toxicokinetics and metabolic pathways with increases in dose*. These changes may result in important differences between high and low dose levels in disposition of the agent or generation of its active forms. These

studies play an important role in providing a rationale for dose selection in carcinogenicity studies.

- *Identifying and comparing metabolic process differences by age, sex, or other characteristic so that susceptible subpopulations can be recognized.* For example, metabolic capacity with respect to P450 enzymes in newborn children is extremely limited compared to that in adults, so that a carcinogenic metabolite formed through P450 activity will have limited effect in the young, whereas a carcinogenic agent deactivated through P450 activity will result in increased susceptibility of this lifestage (Cresteil, 1998). A variety of changes in toxicokinetics and physiology occur from the fetal stage to post-weaning to young child. Any of these changes may make a difference for risk (Renwick, 1998).

- *Determining bioavailability via different routes of exposure by analyzing uptake processes under various exposure conditions.* This analysis supports identification of hazards for untested routes. In addition, use of physicochemical data (e.g., octanol-water partition coefficient information) can support an inference about the likelihood of dermal absorption (Flynn, 1990).

Attempts should be made in all of these areas to clarify and describe as much as possible the variability to be expected because of differences in species, sex, age, and route of exposure. The analysis takes into account the presence of subpopulations of individuals who are particularly vulnerable to the effects of an agent because of toxicokinetic or metabolic differences (genetically or environmentally determined) (Bois et al., 1995) and is a special emphasis for assessment of risks to children.

2.3.4. Toxicological and Clinical Findings

Toxicological findings in experimental animals and clinical observations in humans are important resources for the cancer hazard assessment. Such findings provide information on

physiological effects and effects on enzymes, hormones, and other important macromolecules as well as on target organs for toxicity. For example, given that the cancer process represents defects in processes such as terminal differentiation, growth control, and cell death, developmental studies of agents may provide an understanding of the activity of an agent that carries over to cancer assessment. Toxicity studies in animals by different routes of administration support comparison of absorption and metabolism by those routes. Data on human variability in standard clinical tests may also provide insight into the range of human susceptibility and the common mechanisms of agents that affect the tested parameters.

2.3.5. Events Relevant to Mode of Carcinogenic Action

Knowledge of the biochemical and biological changes that precede tumor development (which include, but are not limited to, mutagenesis, increased cell proliferation, inhibition of programmed cell death, and receptor activation) may provide important insight for determining whether a cancer hazard exists and may help inform appropriate consideration of the dose-response relationship below the range of observable tumor response. Because cancer can result from a series of genetic alterations in the genes that control cell growth, division, and differentiation (Vogelstein et al., 1988; Hanahan and Weinberg, 2000; Kinzler and Vogelstein, 2002), the ability of an agent to affect genotype (and hence gene products) or gene expression is of obvious importance in evaluating its influence on the carcinogenic process. Initial and key questions to examine are: Does the agent (or its metabolite) interact directly with DNA, leading to mutations that bring about changes in gene products or gene expression? Does the agent bring about effects on gene expression via other nondirect DNA interaction processes?

Furthermore, carcinogenesis involves a complex series and interplay of events that alter the signals a cell receives from its extracellular environment, thereby promoting uncontrolled growth. Many, but not all, mutagens are carcinogens, and some, but not all, agents that induce cell proliferation lead to tumor development. Thus, understanding the range of key steps in the carcinogenic process upon which an agent might act is essential for evaluating its mode of action. Determination of carcinogens that are operating by a mutagenic mode of action, for example, entails evaluation of *in vivo* or *in vitro* short-term testing results for genetic endpoints, metabolic

profiles, physicochemical properties, and structure-activity relationship (SAR) analyses in a weight-of-evidence approach (Dearfield et al., 1991; U.S. EPA, 1986b; Waters et al., 1999). Key data for a mutagenic mode of action may be evidence that the carcinogen or a metabolite is DNA-reactive and/or has the ability to bind to DNA. Also, mutagenic carcinogens usually produce positive effects in multiple test systems for different genetic endpoints, particularly gene mutations and structural chromosome aberrations, and in tests performed *in vivo* which generally are supported by positive tests *in vitro*. Additionally, carcinogens may be identified as operating via a mutagenic mode of action if they have similar properties and SAR to mutagenic carcinogens. Endpoints that provide insight into an agent's ability to alter gene products and gene expression, together with other features of an agent's potential mode of carcinogenic action, are discussed below.

2.3.5.1. *Direct DNA-Reactive Effects*

It is well known that many carcinogens are electrophiles that interact with DNA, resulting in DNA adducts and breakage (referred to in these cancer guidelines as direct DNA effects). Usually during the process of DNA replication, these DNA lesions can be converted into and fixed as mutations and chromosomal alterations that then may initiate and otherwise contribute to the carcinogenic process (Shelby and Zeiger, 1990; Tinwell and Ashby, 1991; IARC, 1999). Thus, studies of mutations and other genetic lesions continue to inform the assessment of potential human cancer hazard and in the understanding of an agent's mode of carcinogenic action.

EPA has published testing guidelines for detecting the ability of an agent to damage DNA and produce mutations and chromosomal alterations (as discussed in Dearfield et al., 1991). Briefly, standard tests for gene mutations in bacteria and mammalian cells *in vitro* and *in vivo* and for structural chromosomal aberrations *in vitro* and *in vivo* are important examples of relevant methods. New molecular approaches, such as mouse mutations and cancer transgenic models, are providing a means to examine mutation at tissue sites where the tumor response is observed (Heddle and Swiger, 1996; Tennant et al., 1999). Additionally, continued improvements in fluorescent-based chromosome staining methods (fluorescent *in situ*

hybridization [FISH]) will allow the detection of specific chromosomal abnormalities in relevant target tissues (Tucker and Preston, 1998).

Endpoints indicative of DNA damage but not measures of mutation *per se*, such as DNA adducts or strand breakage, may be detected in relevant target tissues and thus contribute to evaluating an agent's mutagenic potential. Evidence of chemical-specific DNA adducts (e.g., reactions at oxygen sites in DNA bases or with ring nitrogens of guanine and adenine) provides information on a mutagen's ability to directly interact with DNA (La and Swenberg, 1996). Some planar molecules (e.g., 9-aminoacridine) intercalate between base pairs of DNA, which results in a physical distortion in DNA that may lead to mutations when DNA replicates. As discussed below, some carcinogens do not interact directly with DNA, but they can produce increases in endogenous levels of DNA adducts (e.g., 8-hydroxyguanine) by indirect mechanisms.

2.3.5.2. *Indirect DNA Effects or Other Effects on Genes/Gene Expression*

Although some carcinogens may result in an elevation of mutations or cytogenetic anomalies, as detected in standard assays, they may do so by indirect mechanisms. These effects may be brought about by chemical-cell interactions rather than by the chemical (or its metabolite) directly interacting with DNA. An increase in mutations might be due to cytotoxic exposures causing regenerative proliferation or to mitogenic influences (Cohen and Ellwein, 1990). Increased cell division may elevate mutation by clonal expansion of initiated cells or by increasing the number of genetic errors by rapid cell division and reduced time for DNA repair. Some agents might result in an elevation of mutations by interfering with the enzymes involved in DNA repair and recombination (Barrett and Lee, 1992). Damage to certain critical DNA repair genes or other genes (e.g., the p53 gene) may result in genomic instability, which predisposes cells to further genetic alterations and increases the probability of neoplastic progression (Harris and Hollstein, 1993; Levine et al., 1994; Rouse and Jackson, 2002). Likewise, DNA repair processes may be saturated at certain doses of a chemical, leading to an elevation of genetic alterations.

The initiation of programmed cell death (apoptosis) can potentially be blocked by an agent, thereby permitting replication of cells carrying genetic errors that would normally be removed from the proliferative pool. At certain doses an agent may also generate reactive oxygen species that produce oxidative damage to DNA and other macromolecules (Chang et al. 1988; Kehrer, 1993; Clayson et al., 1994). The role of cellular alterations that are attributable to oxidative damage in tumorigenesis (e.g., 8-hydroxyguanine) is currently unclear.

Several carcinogens have been shown to induce aneuploidy (the loss or gain of chromosomes) (Barrett, 1992; Gibson et al., 1995). Aneuploidy can result in the loss of heterozygosity or genomic instability (Cavenee et al., 1986; Fearon and Vogelstein, 1990). Agents that cause aneuploidy typically interfere with the normal process of chromosome segregation by interacting with non-DNA targets such as the proteins needed for chromosome segregation and chromosome movement. Whether this chromosome imbalance is the cause or the effect of tumorigenesis is not clear. Thus, it is important to understand if the agent induces aneuploidy as a key early event in the carcinogenic process.

It is possible for an agent to alter gene expression by transcriptional, translational, or post-translational modifications. For example, perturbation of DNA methylation patterns may cause effects that contribute to carcinogenesis (Jones, 1986; Holliday, 1987; Goodman and Counts, 1993; Chuang et al., 1996; Baylin and Bestor, 2002). Overexpression of genes by DNA amplification has been observed in certain tumors (Vainio et al., 1992). Mechanisms of altering gene expression may involve cellular reprogramming through hormonal or receptor-mediated mechanisms (Barrett, 1992; Ashby et al., 1994).

Both cell proliferation and programmed cell death can be part of the maintenance of homeostasis in many normal tissues, and alterations in the level or rate of either can be important elements of the carcinogenic process. The balance between the two can directly affect the survival and growth of initiated cells as well as preneoplastic and tumor cell populations (i.e., increase in cell proliferation or decrease in cell death) (Moolgavkar, 1986; Cohen and Ellwein, 1990, 1991; Cohen et al., 1991; Bellamy et al., 1995). Thus, measurements of these events can contribute to the weight of the evidence for cancer hazard prediction and to mode of action

understanding. In studies of proliferative effects, distinctions should be made between mitogenesis and regenerative proliferation (Cohen and Ellwein, 1990, 1991; Cohen et al., 1991).

In applying information from studies on cell proliferation and apoptosis to risk assessment, it is important to identify the tissues and target cells involved, to measure effects in both normal and neoplastic tissue, to distinguish between apoptosis and necrosis, and to determine the dose that affects these processes. Gap-junctional intercellular communication is believed to play a role in tissue and organ development and in the maintenance of a normal cellular phenotype within tissues. A growing body of evidence suggests that chemical interference with gap-junctional intercellular communication is a contributing factor in tumor development (Swierenga and Yamasaki, 1992; Yamasaki, 1995).

2.3.5.3. *Precursor Events and Biomarker Information*

Most testing schemes for mutagenicity and other short-term assays were designed for hazard identification purposes; thus, these assays are generally conducted using acute exposures. For data on "precursor steps" to be useful in informing the dose-response curve for tumor induction below the level of observation, it is often useful for data to come from *in vivo* studies and from studies where exposure is repeated or given over an extended period of time. Although consistency of results across different assays and animal models provides a stronger basis for drawing conclusions, it is desirable to have data on the precursor event in the same target organ, sex, animal strain, and species as the tumor data. In evaluating an agent's mode of action, it is usually not sufficient to determine that some event commences upon dosing. It is important to understand whether it is a necessary event that plays a key role in the process that leads to tumor development versus an effect of the cancer process itself or simply an associated event.

Various endpoints can serve as biological markers of effects in biological systems or samples. These may help identify doses at which elements of the carcinogenic process are operating; aid in interspecies extrapolations when data are available from both experimental animal and human cells; and under certain circumstances, provide insights into the possible shape of the dose-response curve below levels where tumor incidences are observed (e.g., Choy, 1993).

Genetic and other findings (such as changes in proto-oncogenes and tumor suppressor genes in preneoplastic and neoplastic tissue or, possibly, measures of endocrine disruption) can indicate the potential for disease and, as such, serve as biomarkers of effect. They, too, can be used in different ways.

- The spectrum of genetic changes in proliferative lesions and tumors following chemical administration to experimental animals can be determined and compared with that in spontaneous tumors in control animals, in animals exposed to other agents of varying structural and functional activities, and in persons exposed to the agent under study.

- Biomarkers of effect and/or precursors may help to identify subpopulations of individuals who may be at an elevated risk for a certain cancer or exposure to a certain agent, e.g., cytochrome P450 2D6/debrisoquine sensitivity for lung cancer (Caporaso et al., 1989) or inherited colon cancer syndromes (Kinzler et al., 1991; Peltomäki et al., 1993).

- As with biomarkers of exposure, it may be justified in some cases to use biomarkers of effect and/or precursors for dose-response assessment or to provide insight into the potential shape of the dose-response curve at doses below those at which tumors are induced experimentally.

In applying biomarker data to cancer assessment an assessment should consider:

- analytical methodology,
- routes of exposure,
- exposure to mixtures,
- time after exposure,
- sensitivity and specificity of biomarkers, and
- dose-response relationships.

2.3.5.4. *Judging Data*

Criteria that are generally applicable for judging the adequacy of mechanistically based data include:

- mechanistic relevance of the data to carcinogenicity,
- number of studies of each endpoint,
- consistency of results in different test systems and different species,
- similar dose-response relationships for tumor and mode of action-related effects,
- conduct of the tests in accordance with generally accepted protocols, and
- degree of consensus and general acceptance among scientists regarding interpretation of the significance and specificity of the tests.

Although important information can be gained from *in vitro* test systems, a higher level of confidence is generally given to data that are derived from *in vivo* systems, particularly those results that show a site concordance with the tumor data.

It is important to remember that when judging and considering the use of any data, the basic standard of quality, as defined by the EPA Information Quality Guidelines, should be satisfied.

2.4. MODE OF ACTION—GENERAL CONSIDERATIONS AND FRAMEWORK FOR ANALYSIS

2.4.1. General Considerations

The interaction between the biology of the organism and the chemical properties of the agent determine whether there is an adverse effect. Thus, mode of action analysis is based on physical, chemical, and biological information that helps to explain key events in an agent's influence on development of tumors. The entire range of information developed in the assessment is reviewed to arrive at a reasoned judgment. An agent may work by more than one mode of action, both at different sites and at the same tumor site. Thus the mode of action and human relevance cannot necessarily be generalized to other toxic endpoints or tissues or cell types without additional analyses (IPCS, 1999; Meek et al., 2003). At least some information

bearing on mode of action (e.g., SAR, screening tests for mutagenicity) is present for most agents undergoing assessment of carcinogenicity, even though certainty about exact molecular mechanisms may be rare.

Information for mode of action analysis generally includes tumor data in humans and animals and among structural analogues, as well as the other key data. The more complete the data package and the generic knowledge about a given mode of action, the more confidence one has and the more one can rely on assessment of available data rather than reverting to default options to address the absence of information on mode of action. Reasoned judgments are generally based on a data-rich source of chemical, chemical class, and tumor type-specific information. Many times there will be conflicting data and gaps in the information base; it is important to carefully evaluate these uncertainties before reaching any conclusion.

In making decisions about potential modes of action and the relevance of animal tumor findings to humans (Ashby et al., 1990; Ashby and Tennant, 1991; Tennant, 1993; IPCS 1999; Sonich-Mullin et al., 2001; Meek et al., 2003), very often the results of chronic animal studies may give important clues. Some of the important factors to review include:

- tumor types, for example, those responsive to endocrine influence or those produced by DNA-reactive carcinogens;

- number of studies and of tumor sites, sexes, and species affected or unaffected in those studies and if the data present a coherent story;

- similarity of metabolic activation and detoxification for a specific chemical between humans and tested species;

- influence of route of exposure on the spectrum of tumors and whether they occur at point of exposure or systemic sites;

- effect of high dose exposures on the target organ or systemic toxicity that may not reflect typical physiological conditions, for example, urinary chemical changes associated with stone formation, effects on immune surveillance;

- presence of proliferative lesions, for example, hepatic foci, or hyperplasia;

- effect of dose and time on the progression of lesions from preneoplastic to benign tumors, then to malignant;

- ratio of malignant to benign tumors as a function of dose and time;

- time of appearance of tumors after commencing exposure;

- development of tumors that invade locally or systemically, or lead to death;

- tumors at organ sites with high or low background historical incidence in laboratory animals;

- biomarkers in tumor cells, both induced and spontaneous, for example, DNA or protein adducts, mutation spectra, chromosome changes, oncogene activation; and/or

- shape of the dose-response curve in the range of tumor observation, for example, linear versus nonlinear.

Some of the myriad ways in which information from chronic animal studies influences mode of action judgments include, but are not limited to, the following:

- multisite and multispecies tumor effects that are often associated with mutagenic agents;

- tumors restricted to one sex or species suggesting an influence restricted to gender, strain, or species;

- late onset of tumors that are primarily benign, are at sites with a high historical background incidence, or show reversal of lesions on cessation of exposure suggesting a growth-promoting mode of action;

- the possibility that an agent acting differently in different tissues; or

- the possibility that has more than one mode of action in a single tissue.

Simple knowledge of sites of tumor increase in rodent studies can give preliminary clues as to mode of action. Experience at the National Toxicology Program (NTP) indicates that substances that are DNA reactive and that produce gene mutations may be unique in producing tumors in certain anatomical sites, whereas tumors at other sites may arise from both mutagenic or nonmutagenic influences (Ashby and Tennant, 1991; Huff et al., 1991).

The types of data and their influence on judgments regarding mode of action are expected to evolve, both as science advances and as the risk assessment community gains more experience with these analyses. This section contains a framework for evaluating hypothesized mode(s) of action. This framework has similarities to and differences with the concepts presented in other MOA frameworks (e.g., IPCS, 1999; Sonich-Mullin et al., 2001; Meek et al., 2003). Differences are often due to the context of the use for the framework. For example, the Meek et al. (2003) presents a stand-alone document for addressing mode of action issues; thus, it recommends that conclusions concerning MOA be rendered separately. In these cancer guidelines, however, they are incorporated into the context of all of the data regarding weight of the evidence for carcinogenicity.

2.4.2. Evaluating an Hypothesized Mode of Action

2.4.2.1. *Peer Review*

In reaching conclusions, the question of "general acceptance" of a mode of action should be tested as part of the independent peer review that EPA obtains for its assessment and conclusions. In some cases the mode of action may already have been established by development of a large body of research information and characterization of the phenomenon over time. In some cases there will have been development of an Agency policy (e.g., mode of action involving alpha-2u-globulin in the male rat [U.S. EPA, 1991b]) or a series of previous assessments in which both the mode of action and its applicability to particular cases has been explored. If so, the assessment and its peer review can focus on the evidence that a particular agent acts in this mode. The peer review should also evaluate the strengths and weaknesses of competing modes of action.

In other cases, the mode of action may not have previously been the subject of an Agency document. If so, the data to support both the mode of action and the associated activity of the agent should undergo EPA assessment and subsequent peer review.

2.4.2.2. *Use of the Framework*

The framework supports a full analysis of mode of action information, but it can also be used as a screen to decide whether sufficient information is available to evaluate or whether the data gaps are too substantial to justify further analysis. Mode of action conclusions are used to address the question of human relevance of animal tumor responses, to address differences in anticipated response among humans, such as between children and adults or men and women; and as the basis of decisions about the anticipated shape of the dose-response relationship. Guidance on the latter appears in Section 3.

This framework is intended to provide an analytical approach for evaluating the mode of action. It is neither a checklist nor a list of required criteria. As the type and amount of information will depend on the mode of action postulated, scientific judgment is important to determine if the weight of evidence is sufficient.

2.4.3. Framework for Evaluating Each Hypothesized Carcinogenic Mode of Action

This framework is intended to be an analytic tool for judging whether available data support a mode of carcinogenic action hypothesized for an agent. It is based upon considerations for causality in epidemiologic investigations originally articulated by Hill (1965) but later modified by others and extended to experimental studies. The original Hill criteria were applied to epidemiologic data, whereas this framework is applied to a much wider assortment of experimental data, so it retains the basic principles of Hill but is much modified in content.

The modified Hill criteria can be useful for organizing thinking about aspects of causation, and they are consistent with the scientific method of developing hypotheses and testing those hypotheses experimentally. During analysis by EPA, and as guidance for peer review, a key question is whether the data to support a mode of action meet the standards generally applied in experimental biology regarding inference of causation.

All pertinent studies are reviewed in analyzing a mode of action, and an overall weighing of evidence is performed, laying out the strengths, weaknesses, and uncertainties of the case as well as potential alternative positions and rationales. Identifying data gaps and research needs is also part of the assessment.

To evaluate whether an hypothesized mode of action is operative, an analysis starts with an outline of the scientific findings regarding the hypothesized key events leading to cancer, and then weighing information to determine whether there is a causal relationship between these events and cancer formation, i.e., that the effects are critical for induction of tumors. It is not generally expected that the complete sequence will be known at the molecular level. Instead, empirical observations made at different levels of biological organization—biochemical, cellular, physiological, tissue, organ, and system—are analyzed.

Several important points should be considered when working with the framework:

- The topics listed for analysis should *not* be regarded as a checklist of necessary "proofs." The judgment of whether an hypothesized mode of action is supported by available data takes account of the analysis as a whole.

- The framework provides a structure for organizing the facts upon which conclusions as to mode of action rest. The purpose of using the framework is to make analysis transparent and to allow the reader to understand the facts and reasoning behind a conclusion.

- The framework does not dictate an answer. The weight of evidence that is sufficient to support a decision about a mode of action may be less or more, depending on the purpose of the analysis, for example, screening, research needs identification, or full risk assessment. To make the reasoning transparent, the purpose of the analysis should be made apparent to the reader.

- Toxicokinetic studies may contribute to mode of action analysis by contributing to identifying the active form(s) of an agent that is central to the mode of action. Apart from contributing in this way, toxicokinetics studies may reveal effects of saturation of metabolic processes. These may not be considered key events in a mode of action, but they are given separate consideration in assessing dose metrics and potential nonlinearity of the dose-response relationship.

- Generally, "sufficient" support is a matter of scientific judgment in the context of the requirements of the decisionmaker or in the context of science policy guidance regarding a certain mode of action.

- Even when an hypothesized mode of action is supported for a described response in a specific tissue, it may not explain other tumor responses observed, which should get separate consideration in hazard and dose-response assessment.

For each tumor site being evaluated, the mode of action analysis should begin with a description of the relevant data and key events that may be associated with an hypothesized mode of action and its sequence of key events (see Section 2.4.3.1). This can be followed by a

discussion of various aspects of the experimental support for hypothesized mode(s) of action in animals and humans (see Section 2.4.3.2). The possibility of other modes of action also should be considered and discussed (see Section 2.4.3.3); if there is evidence for more than one mode of action, each should receive a separate analysis. Conclusions about each hypothesized mode of action should address whether the mode of action is supported in animals and is relevant to humans and which populations or lifestages can be particularly susceptible (see Section 2.4.3.4). In a risk assessment document, the analysis of an hypothesized mode of action can be presented before or with the characterization of an agent's potential hazard to humans.

2.4.3.1. *Description of the Hypothesized Mode of Action*

Summary description of the hypothesized mode of action. For each tumor site, the mode of action analysis begins with a description of the hypothesized mode of action and its sequence of key events. If there is evidence for more than one mode of action, each receives a separate analysis.

Identification of key events. In order to judge how well data support involvement of a key event in carcinogenic processes, the experimental definition of the event or events should be clear and reproducible. To support an association, experiments should define and measure an event consistently.

- Can a list of events be identified that are key to the carcinogenic process?

- Are the events well defined?

Pertinent observations may include, but are not limited to, receptor-ligand changes, cytotoxicity, cell cycle effects, increased cell growth, organ weight differences, histological changes, hormone or other protein perturbations, or DNA and chromosome effects.

2.4.3.2. *Discussion of the Experimental Support for the Hypothesized Mode of Action*

The experimental support for the hypothesized mode of action should be discussed from several viewpoints patterned after the Hill criteria (see Section 2.2.1.7). For illustration, the explanation of each topic includes typical questions to be addressed to the available empirical data and experimental observations anticipated to be pertinent. The latter will vary from case to case. For a particular mode of action, certain observations may be established as essential in practice or policy, for example, measures of thyroid hormone levels in supporting thyroid hormone elevation as a key event in carcinogenesis.

Strength, consistency, specificity of association. A statistically significant association between events and a tumor response observed in well-conducted studies is generally supportive of causation. Consistent observations in a number of such studies with differing experimental designs increase that support, because different designs may reduce unknown biases. Studies showing "recovery," i.e, absence or reduction of carcinogenicity when the event is blocked or diminished, are particularly useful tests of the association. Specificity of the association, without evidence of other modes of action, strengthens a causal conclusion. A lack of strength, consistency, and specificity of association weakens the causal conclusions for a particular mode of action.

- What is the level of statistical and biological significance for each event and for cancer?

- Do independent studies and different experimental hypothesis-testing approaches produce the same associations?

- Does the agent produce effects other than those hypothesized?

- Is the key event associated with precursor lesions?

Pertinent observations include tumor response associated with events (site of action logically relates to event[s]), precursor lesions associated with events, initiation-promotion studies, and stop/recovery studies.

Dose-response concordance. If a key event and tumor endpoints increase with dose such that the key events forecast the appearance of tumors at a later time or higher dose, a causal association can be strengthened. Dose-response associations of the key event with other precursor events can add further strength. Difficulty arises when an event is not causal but accompanies the process generally. For example, if tumors and the hypothesized precursor both increase with dose, the two responses will be correlated regardless of whether a causal relationship exists. This is similar to the issue of confounding in epidemiologic studies. Dose-response studies coupled with mechanistic studies can assist in clarifying these relationships.

- What are the correlations among doses producing events and cancer?

Pertinent observations include, but are not limited to, 2-year bioassay observation of lesions correlated with observations of hormone changes and the same lesions in shorter term studies or in interim sacrifice.

Temporal relationship. If an event is shown to be causally linked to tumorigenesis, it will precede tumor appearance. An event may also be observed contemporaneously or after tumor appearance; these observations may add to the strength of association but not to the temporal association.

- What is the ordering of events that underlie the carcinogenic process?

- Is this ordering consistent among independent studies?

Pertinent observations include studies of varying duration observing the temporal sequence of events and development of tumors.

Biological plausibility and coherence. It is important that the hypothesized mode of action and the events that are part of it be based on contemporaneous understanding of the biology of cancer to be accepted. If the body of information under scrutiny is consistent with other examples (including structurally related agents) for which the hypothesized mode of action is accepted, the case is strengthened. Because some modes of action can be anticipated to evoke effects other than cancer, the available toxicity database on noncancer effects, for example, reproductive effects of certain hormonal disturbances, can contribute to this evaluation.

- Is the mode of action consistent with what is known about carcinogenesis in general and for the case specifically?

- Are carcinogenic effects and events consistent across structural analogues?

- Is the database on the agent internally consistent in supporting the purported mode of action, including relevant noncancer toxicities?

Pertinent observations include the scientific basis for considering an hypothesized mode of action generally, given the contemporaneous state of knowledge of carcinogenic processes; previous examples of data sets showing the mode of action; data sets on analogues; and coherence of data in this case from cancer and noncancer toxicity studies.

2.4.3.3. *Consideration of the Possibility of Other Modes of Action*

The possible involvement of more than one mode of action at the tumor site should be considered. Pertinent observations that are not consistent with the hypothesized mode of action can suggest the possibility of other modes of action. Some pertinent observations can be consistent with more than one mode of action. Furthermore, different modes of action can operate in different dose ranges; for example, an agent can act predominantly through cytotoxicity at high doses and through mutagenicity at lower doses where cytotoxicity may not occur.

If there is evidence for more than one mode of action, each should receive a separate analysis. There may be an uneven level of experimental support for the different modes of action. Sometimes this can reflect disproportionate resources spent on investigating one particular mode of action and not the validity or relative importance of the other possible modes of action. Ultimately, however, the information on all of the modes of action should be integrated to better understand how and when each mode acts, and which mode(s) may be of interest for exposure levels relevant to human exposures of interest.

2.4.3.4. *Conclusions About the Hypothesized Mode of Action*

Conclusions about the hypothesized mode of action should address the issues listed below. For those agents for which the mode of action is considered useful for the risk assessment, the weight of the evidence concerning mode of action in animals as well as its relevance for humans would be incorporated into the weight of evidence narrative (Section 2.5).

(a) Is the hypothesized mode of action sufficiently supported in the test animals? Associations observed between key events and tumors may or may not support an inference of causation. The conclusion that the agent causes one or more key events that results in tumors is strengthened as more aspects of causation are satisfied and weakened as fewer are satisfied. Consistent results in different experiments that test the hypothesized mode of action build support for that mode of action. Replicating results in a similar experiment does not generally meaningfully strengthen the original evidence, and discordant results generally weaken that support. Experimental challenge to the hypothesized mode of action, where interrupting the sequence of key events suppresses the tumor response or enhancement of key events increases the tumor response, creates very strong support for the mode of action.

(b) Is the hypothesized mode of action relevant to humans? If an hypothesized mode of action is sufficiently supported in the test animals, the sequence of key precursor events should be reviewed to identify critical similarities and differences between the test animals and humans. The question of concordance can be complicated by cross-species differences in toxicokinetics or

toxicodynamics. For example, the active agent can be formed through different metabolic pathways in animals and humans. Any information suggesting quantitative differences between animals and humans is flagged for consideration in the dose-response assessment. This includes the potential for different internal doses of the active agent or for differential occurrence of a key precursor event.

"Relevance" of a potential mode of action is considered in the context of characterization of hazard, not level of risk. Anticipated levels of human exposure are not used to determine whether the hypothesized mode of action is relevant to humans. Exposure information is integrated into the overall risk characterization.

The question of relevance considers all populations and lifestages. It is possible that the conditions under which a mode of action operates exist primarily in a particular population or lifestage, for example, in those with a pre-existing hormonal imbalance. Other populations or lifestages may not be analogous to the test animals, in which case the question of relevance would be decided by inference.

Special attention should be paid to whether tumors can arise from childhood exposure, considering various aspects of development during these lifestages. Because the studies that support a mode of action are typically conducted in mature animals, conclusions about relevance during childhood generally rely on inference. There is currently no standard Agency position regarding the issue of whether tumors arising through the hypothesized mode of action are relevant during childhood; understanding the mode of action implies that there are sufficient data (on either the specific agent or the general mode of action) to form a confident conclusion about relevance during childhood.

(c) Which populations or lifestages can be particularly susceptible to the hypothesized mode of action? If an hypothesized mode of action is judged relevant to humans, information about the key precursor event(s) is reviewed to identify populations or lifestages that might reasonably expected to be particularly susceptible to their occurrence. Although agent-specific data would provide the strongest indication of susceptibility, this review may also rely on general knowledge about the precursor events and characteristics of individuals susceptible to these

events. Any information suggesting quantitative differences between populations or lifestages should be flagged for consideration in the dose-response assessment (see Section 3.5). This includes the potential for a higher internal dose of the active agent or for an increased occurrence of a key precursor event. Quantitative differences may result in separate risk estimates for susceptible populations or lifestages.

The possibility that childhood is a susceptible period for exposure should be explicitly addressed. Generic understanding of the mode of action can be used to gauge childhood susceptibility, and this determination can be refined through analysis of agent-specific data.

2.4.4 Evolution with Experience

Several groups have proposed or incorporated mode of action into their risk assessments (see, e.g., U.S. EPA , 1991b; Sonich-Mullin et al., 2001; Meek et al., 2003). As the frameworks and mandates under which these evaluations were produced differ, the specific procedures described in and conclusions drawn may also differ. Nevertheless, the number of case studies from all venues remains limited. More experience with differing modes of action are expected to highlight and illustrate the strengths and limitations of the general framework proposed in these cancer guidelines. Moreover, additional toxicological techniques may expand or change scientific judgments regarding which information is useful for mode of action determinations. As warranted, additional guidance may be proposed as experience is gained and/or as toxicological knowledge advances.

2.5. WEIGHT OF EVIDENCE NARRATIVE

The *weight of evidence narrative* is a short summary (one to two pages) that explains an agent's human carcinogenic potential and the conditions that characterize its expression. It should be sufficiently complete to be able to stand alone, highlighting the key issues and decisions that were the basis for the evaluation of the agent's potential hazard. It should be sufficiently clear and transparent to be useful to risk managers and non-expert readers. It may be useful to summarize all of the significant components and conclusions in the first paragraph of the narrative and to explain complex issues in more depth in the rest of the narrative.

The weight of the evidence should be presented as a narrative laying out the complexity of information that is essential to understanding the hazard and its dependence on the quality, quantity, and type(s) of data available, as well as the circumstances of exposure or the traits of an exposed population that may be required for expression of cancer. For example, the narrative can clearly state to what extent the determination was based on data from human exposure, from animal experiments, from some combination of the two, or from other data. Similarly, information on mode of action can specify to what extent the data are from *in vivo* or *in vitro* exposures or based on similarities to other chemicals. The extent to which an agent's mode of action occurs only on reaching a minimum dose or a minimum duration should also be presented. A hazard might also be expressed disproportionately in individuals possessing a specific gene; such characterizations may follow from a better understanding of the human genome. Furthermore, route of exposure should be used to qualify a hazard if, for example, an agent is not absorbed by some routes. Similarly, a hazard can be attributable to exposures during a susceptible lifestage on the basis of our understanding of human development.

The weight of evidence-of-evidence narrative should highlight:

- the quality and quantity of the data;
- all key decisions and the basis for these major decisions; and
- any data, analyses, or assumptions that are unusual for or new to EPA.

To capture this complexity, a weight of evidence narrative generally includes

- conclusions about human carcinogenic potential (choice of descriptor(s), described below),

- a summary of the key evidence supporting these conclusions (for each descriptor used), including information on the type(s) of data (human and/or animal, *in vivo* and/or *in vitro*) used to support the conclusion(s),

- available information on the epidemiologic or experimental conditions that characterize expression of carcinogenicity (e.g., if carcinogenicity is possible only by one exposure route or only above a certain human exposure level),

- a summary of potential modes of action and how they reinforce the conclusions,

- indications of any susceptible populations or lifestages, when available, and

- a summary of the key default options invoked when the available information is inconclusive.

To provide some measure of clarity and consistency in an otherwise free-form narrative, the weight of evidence descriptors are included in the first sentence of the narrative. Choosing a descriptor is a matter of judgment and cannot be reduced to a formula. Each descriptor may be applicable to a wide variety of potential data sets and weights of evidence. These descriptors and narratives are intended to permit sufficient flexibility to accommodate new scientific understanding and new testing methods as they are developed and accepted by the scientific community and the public. Descriptors represent points along a continuum of evidence; consequently, there are gradations and borderline cases that are clarified by the full narrative. Descriptors, as well as an introductory paragraph, are a short summary of the complete narrative that preserves the complexity that is an essential part of the hazard characterization. **Users of these cancer guidelines and of the risk assessments that result from the use of these cancer guidelines should consider the entire range of information included in the narrative rather than focusing simply on the descriptor.**

In borderline cases, the narrative explains the case for choosing one descriptor and discusses the arguments for considering but not choosing another. For example, between "suggestive" and "likely" or between "suggestive" and "inadequate," the explanation clearly communicates the information needed to consider appropriately the agent's carcinogenic potential in subsequent decisions.

Multiple descriptors can be used for a single agent, for example, when carcinogenesis is dose- or route-dependent. For example, if an agent causes point-of-contact tumors by one exposure route but adequate testing is negative by another route, then the agent could be described as likely to be carcinogenic by the first route but not likely to be carcinogenic by the second. Another example is when the mode of action is sufficiently understood to conclude that a key event in tumor development would not occur below a certain dose range. In this case, the agent could be described as likely to be carcinogenic above a certain dose range but not likely to be carcinogenic below that range.

Descriptors can be selected for an agent that has not been tested in a cancer bioassay if sufficient other information, e.g., toxicokinetic and mode of action information, is available to make a strong, convincing, and logical case through scientific inference. For example, if an agent is one of a well-defined class of agents that are understood to operate through a common mode of action and if that agent has the same mode of action, then in the narrative the untested agent would have the same descriptor as the class. Another example is when an untested agent's effects are understood to be caused by a human metabolite, in which case in the narrative the untested agent could have the same descriptor as the metabolite. As new testing methods are developed and used, assessments may increasingly be based on inferences from toxicokinetic and mode of action information in the absence of tumor studies in animals or humans.

When a well-studied agent produces tumors only at a point of initial contact, the descriptor generally applies only to the exposure route producing tumors unless the mode of action is relevant to other routes. The rationale for this conclusion would be explained in the narrative.

When tumors occur at a site other than the point of initial contact, the descriptor generally applies to all exposure routes that have not been adequately tested at sufficient doses. An

exception occurs when there is convincing information, e.g., toxicokinetic data that absorption does not occur by another route.

When the response differs qualitatively as well as quantitatively with dose, this information should be part of the characterization of the hazard. In some cases reaching a certain dose range can be a precondition for effects to occur, as when cancer is secondary to another toxic effect that appears only above a certain dose. In other cases exposure duration can be a precondition for hazard if effects occur only after exposure is sustained for a certain duration. These considerations differ from the issues of relative absorption or potency at different dose levels because they may represent a discontinuity in a dose-response function.

When multiple bioassays are inconclusive, mode of action data are likely to hold the key to resolution of the more appropriate descriptor. When bioassays are few, further bioassays to replicate a study's results or to investigate the potential for effects in another sex, strain, or species may be useful.

When there are few pertinent data, the descriptor makes a statement about the database, for example, "Inadequate Information to Assess Carcinogenic Potential," or a database that provides "Suggestive Evidence of Carcinogenic Potential." With more information, the descriptor expresses a conclusion about the agent's carcinogenic potential to humans. If the conclusion is positive, the agent could be described as "Likely to Be Carcinogenic to Humans" or, with strong evidence, "Carcinogenic to Humans." If the conclusion is negative, the agent could be described as "Not Likely to Be Carcinogenic to Humans."

Although the term "likely" can have a probabilistic connotation in other contexts, its use as a weight of evidence descriptor does not correspond to a quantifiable probability of whether the chemical is carcinogenic. This is because the data that support cancer assessments generally are not suitable for numerical calculations of the probability that an agent is a carcinogen. Other health agencies have expressed a comparable weight of evidence using terms such as "Reasonably Anticipated to Be a Human Carcinogen" (NTP) or "Probably Carcinogenic to Humans" (International Agency for Research on Cancer).

The following descriptors can be used as an introduction to the weight of evidence narrative. The examples presented in the discussion of the descriptors are illustrative. The

examples are neither a checklist nor a limitation for the descriptor. The complete weight of evidence narrative, rather than the descriptor alone, provides the conclusions and the basis for them.

"Carcinogenic to Humans"

This descriptor indicates strong evidence of human carcinogenicity. It covers different combinations of evidence.

- This descriptor is appropriate when there is convincing epidemiologic evidence of a causal association between human exposure and cancer.

- Exceptionally, this descriptor may be equally appropriate with a lesser weight of epidemiologic evidence that is strengthened by other lines of evidence. It can be used when all of the following conditions are met: (a) there is strong evidence of an association between human exposure and either cancer or the key precursor events of the agent's mode of action but not enough for a causal association, and (b) there is extensive evidence of carcinogenicity in animals, and (c) the mode(s) of carcinogenic action and associated key precursor events have been identified in animals, and (d) there is strong evidence that the key precursor events that precede the cancer response in animals are anticipated to occur in humans and progress to tumors, based on available biological information. In this case, the narrative includes a summary of both the experimental and epidemiologic information on mode of action and also an indication of the relative weight that each source of information carries, e.g., based on human information, based on limited human and extensive animal experiments.

"Likely to Be Carcinogenic to Humans"

This descriptor is appropriate when the weight of the evidence is adequate to demonstrate carcinogenic potential to humans but does not reach the weight of evidence for the descriptor

"Carcinogenic to Humans." Adequate evidence consistent with this descriptor covers a broad spectrum. As stated previously, the use of the term "likely" as a weight of evidence descriptor does not correspond to a quantifiable probability. The examples below are meant to represent the broad range of data combinations that are covered by this descriptor; they are illustrative and provide neither a checklist nor a limitation for the data that might support use of this descriptor. Moreover, additional information, e.g., on mode of action, might change the choice of descriptor for the illustrated examples. Supporting data for this descriptor may include:

- an agent demonstrating a plausible (but not definitively causal) association between human exposure and cancer, in most cases with some supporting biological, experimental evidence, though not necessarily carcinogenicity data from animal experiments;

- an agent that has tested positive in animal experiments in more than one species, sex, strain, site, or exposure route, with or without evidence of carcinogenicity in humans;

- a positive tumor study that raises additional biological concerns beyond that of a statistically significant result, for example, a high degree of malignancy, or an early age at onset;

- a rare animal tumor response in a single experiment that is assumed to be relevant to humans; or

- a positive tumor study that is strengthened by other lines of evidence, for example, either plausible (but not definitively causal) association between human exposure and cancer or evidence that the agent or an important metabolite causes events generally known to be associated with tumor formation (such as DNA reactivity or effects on cell growth control) likely to be related to the tumor response in this case.

"Suggestive Evidence of Carcinogenic Potential"

This descriptor of the database is appropriate when the weight of evidence is suggestive of carcinogenicity; a concern for potential carcinogenic effects in humans is raised, but the data are judged not sufficient for a stronger conclusion. This descriptor covers a spectrum of evidence associated with varying levels of concern for carcinogenicity, ranging from a positive cancer result in the only study on an agent to a single positive cancer result in an extensive database that includes negative studies in other species. Depending on the extent of the database, additional studies may or may not provide further insights. Some examples include:

- a small, and possibly not statistically significant, increase in tumor incidence observed in a single animal or human study that does not reach the weight of evidence for the descriptor "Likely to Be Carcinogenic to Humans." The study generally would not be contradicted by other studies of equal quality in the same population group or experimental system (see discussions of *conflicting evidence* and *differing results*, below);

- a small increase in a tumor with a high background rate in that sex and strain, when there is some but insufficient evidence that the observed tumors may be due to intrinsic factors that cause background tumors and not due to the agent being assessed. (When there is a high background rate of a specific tumor in animals of a particular sex and strain, then there may be biological factors operating independently of the agent being assessed that could be responsible for the development of the observed tumors.) In this case, the reasons for determining that the tumors are not due to the agent are explained;

- evidence of a positive response in a study whose power, design, or conduct limits the ability to draw a confident conclusion (but does not make the study fatally

flawed), but where the carcinogenic potential is strengthened by other lines of evidence (such as structure-activity relationships); or

- a statistically significant increase at one dose only, but no significant response at the other doses and no overall trend.

"Inadequate Information to Assess Carcinogenic Potential"

This descriptor of the database is appropriate when available data are judged inadequate for applying one of the other descriptors. Additional studies generally would be expected to provide further insights. Some examples include:

- little or no pertinent information;

- conflicting evidence, that is, some studies provide evidence of carcinogenicity but other studies of equal quality in the same sex and strain are negative. *Differing results*, that is, positive results in some studies and negative results in one or more different experimental systems, do not constitute *conflicting evidence,* as the term is used here. Depending on the overall weight of evidence, differing results can be considered either suggestive evidence or likely evidence; or

- negative results that are not sufficiently robust for the descriptor, "Not Likely to Be Carcinogenic to Humans."

"Not Likely to Be Carcinogenic to Humans"

This descriptor is appropriate when the available data are considered robust for deciding that there is no basis for human hazard concern. In some instances, there can be positive results in experimental animals when there is strong, consistent evidence that each mode of action in experimental animals does not operate in humans. In other cases, there can be convincing

evidence in both humans and animals that the agent is not carcinogenic. The judgment may be based on data such as:

- animal evidence that demonstrates lack of carcinogenic effect in both sexes in well-designed and well-conducted studies in at least two appropriate animal species (in the absence of other animal or human data suggesting a potential for cancer effects),
- convincing and extensive experimental evidence showing that the only carcinogenic effects observed in animals are not relevant to humans,
- convincing evidence that carcinogenic effects are not likely by a particular exposure route (see Section 2.3), or
- convincing evidence that carcinogenic effects are not likely below a defined dose range.

A descriptor of "not likely" applies only to the circumstances supported by the data. For example, an agent may be "Not Likely to Be Carcinogenic" by one route but not necessarily by another. In those cases that have positive animal experiment(s) but the results are judged to be not relevant to humans, the narrative discusses why the results are not relevant.

Multiple Descriptors

More than one descriptor can be used when an agent's effects differ by dose or exposure route. For example, an agent may be "Carcinogenic to Humans" by one exposure route but "Not Likely to Be Carcinogenic" by a route by which it is not absorbed. Also, an agent could be "Likely to Be Carcinogenic" above a specified dose but "Not Likely to Be Carcinogenic" below that dose because a key event in tumor formation does not occur below that dose.

2.6. HAZARD CHARACTERIZATION

The *hazard characterization* contains the hazard information needed for a full risk characterization (U.S. EPA, 2000b). It presents the results of the hazard assessment and explains how the weight of evidence conclusion was reached. The hazard characterization summarizes, in plain language, conclusions about the agent's potential effects, whether they can be expected to depend qualitatively on the circumstances of exposure, and if anyone can be expected to be especially susceptible. It discusses the extent to which these conclusions are supported by data or are the result of default options invoked because the data are inconclusive. It explains how complex cases with differing results in different studies were resolved. The hazard characterization highlights the major issues addressed in the hazard assessment and discusses alternative interpretations of the data and the degree to which they are supportable scientifically and are consistent with EPA guidelines.

When the conclusion is supported by mode of action information, the hazard characterization also provides a clear summary of the mode of action conclusions (see Section 2.4.3.4), including the completeness of the data, the strengths and limitations of the inferences made, the potential for other modes of action, and the implications of the mode of action for selecting viable approaches to the dose-response assessment. The hazard characterization also discusses the extent to which mode of action information is available to address the potential for disproportionate risks in specific populations or lifestages or the potential for enhanced risks on the basis of interactions with other agents or stressors, if anticipated.

Topics that can be addressed in a hazard characterization include:

- summary of the results of the hazard assessment;

- identification of any likely susceptible populations and lifestages, especially attending to children, infants, and fetuses;

- conclusions about the agent's mode of action, and implications for selecting approaches to the dose-response assessment;

- identification of the available lines of evidence (e.g., animal bioassays, epidemiologic studies, toxicokinetic information, mode of action studies, and information about structural analogues or metabolites), highlighting data quality and coherence of results from different lines of evidence; and
- strengths and limitations of the hazard assessment, highlighting significant issues in interpreting the data, alternative interpretations that are considered equally plausible, critical data gaps, and default options invoked when the available information is inconclusive.

3. DOSE-RESPONSE ASSESSMENT

Dose-response assessment estimates potential risks to humans at exposure levels of interest. Dose-response assessments are useful in many applications: estimating risk at different exposure levels, estimating the risk reduction for different decision options, estimating the risk remaining after an action is taken, providing the risk information needed for benefit-cost analyses of different decision options, comparing risks across different agents or health effects, and setting research priorities. The purpose of the assessment should consider the quality of the data available, which will vary from case to case.

A dose-response analysis is generally developed from each study that reports quantitative data on dose and response. Alternative measures of dose are available for analyzing human and animal studies (see Section 3.1). A two-step approach distinguishes analysis of the dose-response data from inferences made about lower doses. The first step is an analysis of dose and response in the range of observation of the experimental or epidemiologic studies (see Section 3.2). Modeling is encouraged to incorporate a wide range of experimental data into the dose-response assessment (see Sections 3.1.2, 3.2.1, 3.2.2, 3.2.3). The modeling yields a point of departure (POD) near the lower end of the observed range, without significant extrapolation to lower doses (see Sections 3.2.4, 3.2.5). The second step is extrapolation to lower doses (see Section 3.3). The extrapolation approach considers what is known about the agent's mode of action (see Section 3.3.1). Both linear and nonlinear approaches are available (see Sections 3.3.3, 3.3.4). When multiple estimates can be developed, the strengths and weaknesses of each are presented. In some cases, they may be combined in a way that best represents human cancer risk (see Section 3.3.5). Special consideration is given to describing dose-response differences attributable to different human exposure scenarios (see Section 3.4) and to susceptible populations and lifestages (see Section 3.5). It is important to discuss significant uncertainties encountered in the analysis (see Section 3.6) and to characterize other important aspects of the dose-response assessment (see Section 3.7).

The scope, depth, and use of a dose-response assessment vary in different circumstances. Although the quality of dose-response data is not necessarily related to the weight of evidence

descriptor, dose-response assessments are generally completed for agents considered "Carcinogenic to Humans" and "Likely to Be Carcinogenic to Humans." When there is suggestive evidence, the Agency generally would not attempt a dose-response assessment, as the nature of the data generally would not support one; however, when the evidence includes a well-conducted study, quantitative analyses may be useful for some purposes, for example, providing a sense of the magnitude and uncertainty of potential risks, ranking potential hazards, or setting research priorities. In each case, the rationale for the quantitative analysis is explained, considering the uncertainty in the data and the suggestive nature of the weight of evidence. These analyses generally would not be considered Agency consensus estimates. Dose-response assessments are generally not done when there is inadequate evidence, although calculating a bounding estimate from an epidemiologic or experimental study that does not show positive results can indicate the study's level of sensitivity and capacity to detect risk levels of concern.

Cancer is a collection of several diseases that develop through cell and tissue changes over time. Dose-response assessment procedures based on tumor incidence have seldom taken into account the effects of key precursor events within the whole biological process due to lack of empirical data and understanding about these events. In this discussion, response data include measures of key precursor events considered integral to the carcinogenic process in addition to tumor incidence. These responses may include changes in DNA, chromosomes, or other key macromolecules; effects on growth signal transduction, including induction of hormonal changes; or physiological or toxic effects that include proliferative events diagnosed as precancerous but not pathology that is judged to be cancer. Analysis of such responses may be done along with that of tumor incidence to enhance the tumor dose-response analysis. If dose-response analysis of nontumor key events is more informative about the carcinogenic process for an agent, it can be used in lieu of, or in conjunction with, tumor incidence analysis for the overall dose-response assessment.

As understanding of mode of action improves and new types of data become available, dose-response assessment will continue to evolve. These cancer guidelines encourage the development and application of new methods that improve dose-response assessment by reflecting new scientific understanding and new sources of information.

3.1. ANALYSIS OF DOSE

For each effect observed, dose-response assessment should begin by determining an appropriate *dose metric*. Several dose metrics have been used, e.g., delivered dose, body burden, and area under the curve, and others may be appropriate depending on the data and mode of action.

Selection of an appropriate dose metric considers what data are available and what is known about the agent's mode of action at the target site, and uncertainties involved in estimation and application of alternative metrics. The dose metric specifies:

- the agent measured, preferably the active agent (administered agent or a metabolite);
- proximity to the target site (exposure concentration, potential dose, internal dose, or delivered dose,[5] reflecting increasing proximity); and

- the time component of the effective dose (cumulative dose, average dose, peak dose, or body burden).

Analyses can be based on estimates of animal dose metrics or human dose metrics. The assessment should describe the approach used to select a dose metric and the reasons for this approach. The final analysis, however, should determine a human equivalent dose metric. This facilitates comparing results from different datasets and effects by using human equivalent dose/concentrations as common metrics. When appropriate, it may be necessary to convert dose metrics across exposure routes. When route-to-route extrapolations are made, the underlying data, algorithms, and assumptions are clearly described.

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[5] *Exposure* is contact of an agent with the outer boundary of an organism. *Exposure concentration* is the concentration of a chemical in its transport or carrier medium at the point of contact. *Dose* is the amount of a substance available for interaction with metabolic processes or biologically significant receptors after crossing the outer boundary of an organism. *Potential dose* is the amount ingested, inhaled, or applied to the skin. *Applied dose* is the amount of a substance presented to an absorption barrier and available for absorption (although not necessarily having yet crossed the outer boundary of the organism). *Absorbed dose* is the amount crossing a specific absorption barrier (e.g., the exchange boundaries of skin, lung, and digestive tract) through uptake processes. *Internal dose* is a more general term, used without respect to specific absorption barriers or exchange boundaries. *Delivered dose* is the amount of the chemical available for interaction by any particular organ or cell (U.S. EPA, 1992a).

Timing of exposure can also be important. When there is a susceptible lifestage, doses during the susceptible period are not equivalent to doses at other times, and they would be analyzed separately.

3.1.1. Standardizing Different Experimental Exposure Regimens

Complex exposure or dosing regimens are often present in experimental and epidemiologic studies. The resulting internal dose depends on many variables, including concentration, duration, frequency of administration, and duration of recovery periods between administrations. Internal dose also depends on variables that are intrinsic to the exposed individual, such as lifestage and rates of metabolism and clearance. To facilitate comparing results from different study designs and to make inferences about human exposures, a summary estimate of the dose metric, whether the administered dose or inhalation exposure concentration or an internal metric, may be derived for a complex exposure regimen.

Toxicokinetic modeling is the preferred approach for estimating dose metrics from exposure. Toxicokinetic models generally describe the relationship between exposure and measures of internal dose over time. More complex models can reflect sources of intrinsic variation, such as polymorphisms in metabolism and clearance rates. When a robust model is not available, or when the purpose of the assessment does not warrant developing a model, simpler approaches may be used.

For chronic exposure studies, the cumulative exposure or dose administered often is expressed as an average over the duration of the study, as one consistent dose metric. This approach implies that a higher dose administered over a short duration is equivalent to a commensurately lower dose administered over a longer duration. Uncertainty usually increases as the duration becomes shorter relative to the averaging duration or the intermittent doses become more intense than the averaged dose. Moreover, doses during any specific susceptible or refractory period would not be equivalent to doses at other times. For these reasons, cumulative exposure or potential dose may be replaced by a more appropriate dose metric when indicated by the data.

For mode of action studies, the dose metric should be calculated over a duration that reflects the time to occurrence of the key precursor effects. Mode of action studies are often of limited duration, as the precursors can be observed after less-than-chronic exposures. When the experimental exposure regimen is specified on a weekly basis (for example, 4 hours a day, 5 days a week), the daily exposure may be averaged over the week, where appropriate.

Doses in studies at the cellular or molecular level can be difficult to relate to organ- or organism-level dose metrics. Toxicokinetic modeling can sometimes be used to relate doses at the cellular or molecular level to doses or exposures at higher levels of organization.

3.1.2. Toxicokinetic Data and Modeling

In the absence of chemical-specific data, physiologically based toxicokinetic modeling is potentially the most comprehensive way to account for biological processes that determine internal dose. Physiologically based models commonly describe blood flow between physiological compartments and simulate the relationship between applied dose and internal dose. Toxicokinetic models generally need data on absorption, distribution, metabolism, and elimination of the administered agent and its metabolites.

Additionally, in the case of inhalation exposures, models can explicitly characterize the geometry of the respiratory tract and the airflow through it, as well as the interaction of this airflow with the entrained particles or fibers and gases (Kimbell et al., 2001; Subramaniam et al., 2003). Because of large interspecies differences in airway morphometry such models can be particularly useful in interspecies extrapolations. When employed, however, the potential for large inter-individual differences in airway morphometry, are considered to ensure that the models provide information representative of human populations.

Toxicokinetic models can improve dose-response assessment by revealing and describing nonlinear relationships between applied and internal dose. Nonlinearity observed in a dose-response curve often can be attributed to toxicokinetics (Hoel et al., 1983; Gaylor et al., 1994), involving, for example, saturation or induction of enzymatic processes at high doses. In some cases, toxicokinetic processes tend to become linear at sufficiently low doses (Hattis, 1990).

A discussion of confidence should accompany the presentation of model results and include consideration of model validation and sensitivity analysis, stressing the predictive performance of the model and whether the model is sufficient to support decision-making. Quantitative uncertainty analysis is important for evaluating the performance of a model, whether the model is based primarily on default assumptions or chemical-specific data. The uncertainty analysis covers questions of *model uncertainty* (e.g., Is the model based on the appropriate biology and how does that affect estimates of dose metrics?) and *parameter uncertainty* (e.g., Do the data support unbiased and stable estimates of the model parameters?). When a delivered dose measure is used in animal-to-human extrapolation, the assessment discusses the confidence of the target tissue and its toxicodynamics being the same in both species (see Section 3.6). Toxicokinetic modeling results may be presented alone as the preferred method of estimating human equivalent exposures or doses, or these results may be presented in parallel with default procedures (see Section 3.1.3), depending on the confidence in the modeling.

3.1.3. Cross-species Scaling Procedures

Standard cross-species scaling procedures are available when the data are not sufficient to support a toxicokinetic model or when the purpose of the assessment does not warrant developing one. The aim is to define exposure levels for humans and animals that are expected to produce the same degree of effect (U.S. EPA, 1992b), taking into account differences in scale between test animals and humans, such as size and lifespan.

3.1.3.1. Oral Exposures

For oral exposures, administered doses should be scaled from animals to humans on the basis of equivalence of $mg/kg^{3/4}$-d (milligrams of the agent normalized by the 3/4 power of body weight per day) (U.S. EPA, 1992b). The 3/4 power is consistent with current science, including empirical data that allow comparison of potencies in humans and animals, and it is also supported by analysis of the allometric variation of key physiological parameters across mammalian species. It is generally more appropriate at low doses, where sources of nonlinearity such as saturation of enzyme activity are less likely to occur. This scaling is intended as an

unbiased estimate rather than a conservative one. Equating exposure concentrations in food or water is an alternative version of the same approach, because daily intakes of food or water are approximately proportional to the 3/4 power of body weight.

The aim of these cross-species scaling procedures is to estimate administered doses in animals and humans that result in equal lifetime risks. It is useful to recognize two components of this equivalence: *toxicokinetic equivalence*, which determines administered doses in animals and humans that yield equal tissue doses, and *toxicodynamic equivalence*, which determines tissue doses in animals and humans that yield equal lifetime risks (U.S. EPA, 1992b). Toxicokinetic modeling (see Section 3.1.2) addresses factors associated with toxicokinetic equivalence, and toxicodynamic modeling (see Section 3.2.2) addresses factors associated with toxicodynamic equivalence. When toxicokinetic modeling is used without toxicodynamic modeling, the dose-response assessment develops and supports an approach for addressing toxicodynamic equivalence, perhaps by retaining some of the cross-species scaling factor (e.g., using the square root of the cross-species scaling factor or using a factor of 3 to cover toxicodynamic differences between animals and humans, as is currently done in deriving inhalation reference concentrations [U.S. EPA, 1994]).

When assessing risks from childhood exposure, the $mg/kg^{3/4}$-d scaling factor does not use the child's body weight (U.S. EPA, 1992b). This reflects several uncertainties in extrapolating risks to children:

- The data supporting the $mg/kg^{3/4}$-d scaling factor were derived for differences across species and may not apply as well to differently sized individuals of the same species or to different lifestages.

- In addition to metabolic differences, there are also important toxicodynamic differences; for example, children have faster rates of cell division than do adults, so scaling across different lifestages and species simultaneously may be particularly uncertain.

3.1.3.2. Inhalation Exposures

For inhalation exposures experimental exposure concentrations are replaced with human equivalent concentrations calculated using EPA's methods for deriving inhalation reference concentrations (U.S. EPA, 1994), which give preference to the use of toxicokinetic modeling. When toxicokinetic models are unavailable, default dosimetry models are employed to extrapolate from experimental exposure concentrations to human equivalent concentrations. When toxicokinetic modeling or dosimetry modeling is used without toxicodynamic modeling, the dose-response assessment develops and supports an approach for addressing toxicodynamic equivalence.

The default dosimetry models typically involve the use of species-specific physiologic and anatomic factors relevant to the form of the agent (e.g., particle or gas) and categorized with regard to whether the response occurs either locally (i.e., within the respiratory tract) or remotely. For example, current default models (U.S. EPA, 1994) use parameters such as:

- inhalation rate and surface area of the affected part of the respiratory tract for gases eliciting the response locally,
- blood:gas partition coefficients for remote acting gases,
- fractional deposition with inhalation rate and surface area of the affected part of the respiratory tract for particles eliciting the response locally, and
- fractional deposition with inhalation rate and body weight for particles eliciting the response remotely.

The current default values for some parameters used in the default models (e.g., breathing rate and respiratory tract surface area) are based on data from adults (U.S. EPA, 1994). The human respiratory system passes through several distinct stages of maturation and growth during the first several years of life and into adolescence (Pinkerton and Joad, 2000), during which

characteristics important to disposition of inhaled toxicants may vary. Children and adults breathing the same concentration of an agent may receive different doses to the body or lungs (U.S. EPA, 2002b). Consequently, it may be appropriate to evaluate the default models by considering physiologic and anatomic factors representative of early lifestages, for example through the substitution of child-specific parameters (U.S. EPA, 2002b). Such evaluation uses the default model and dosimetric adjustment in use at the time of the assessment coupled with the best understanding of child-specific parameters at that time (e.g., drawn from the scientific literature). This analysis is undertaken with caution: (1) because of the correlations between activity level, breathing rate, respiratory tract dimensions, and body weight and (2) to avoid the possibility of mismatching the type of agent (gas or particle) and its site of response (within the respiratory tract or remote from the respiratory tract) with the relevant dosimetry factors in use at the time of the assessment. Analyses of children's inhalation dosimetry are also considered when using model structures beyond the default models (e.g., physiologically based toxicokinetic models).

When using dosimetry modeling, the comparison of human-equivalent concentrations for different lifestages (e.g., for an adult and a child) can indicate whether it is important to carry both concentrations forward in the dose-response assessment or whether a verbal characterization of any findings will suffice.

3.1.4. Route Extrapolation

In certain situations, an assessment based on studies of one exposure route may be applied to another exposure route. Route-to-route extrapolation has both qualitative and quantitative aspects. For the qualitative aspect, the assessor should weigh the degree to which positive results by one exposure route support a judgment that similar results would be expected by another route. In general, confidence in making such a judgment is strengthened when tumors are observed at a site distant from the portal of entry and when absorption is similar through both routes. In the absence of contrary data, a qualitative default option can be used: if the agent is absorbed through an exposure route to give an internal dose, it may be carcinogenic by that route.

When a qualitative extrapolation can be supported, quantitative extrapolation may still be problematic due to the absence of adequate data. The differences in biological processes among routes of exposure (oral, inhalation, dermal) can be great because of, for example, first-pass effects and different results from different exposure patterns. There is no generally applicable method for accounting for these differences in uptake processes in a quantitative route-to-route extrapolation of dose-response data in the absence of good data on the agent of interest. Therefore, route-to-route extrapolation of dose data relies on a case-by-case analysis of available data. When good data on the agent itself are limited, an extrapolation analysis can be based on expectations from physical and chemical properties of the agent, properties and route-specific data on structurally analogous compounds, or *in vitro* or *in vivo* uptake data on the agent.

Route-to-route uptake models may be applied if model parameters are suitable for the compound of interest. Such models are currently considered interim methods; further model development and validation is awaiting the development of more extensive data. For screening or hazard ranking, route-to-route extrapolation may be based on assumed quantitative comparability as a default, as long as it is reasonable to assume absorption by compared routes. When route-to-route extrapolation is used, the assessor's degree of confidence in both the qualitative and quantitative extrapolation is discussed in the assessment and highlighted in the dose-response characterization.

Toxicokinetic modeling can be used to compare results of studies by different exposure routes. Results can also be compared on the basis of internal dose for effects distant from the point of contact.

Route extrapolation can be used to understand how internal dose and subsequent effects depend on exposure route. If testing by different exposure routes is available, the observation of similar or dissimilar internal doses can be important in determining whether and what conclusions can be made concerning the dose-response function(s) for different routes of exposure.

3.2. ANALYSIS IN THE RANGE OF OBSERVATION

The principle underlying these cancer guidelines is to use approaches that include as much information as possible. Quantitative information about key precursor events can be used to develop a toxicodynamic model. Alternatively, such information can be fitted by empirical models to extend the dose-response analysis of tumor incidence to lower doses and response levels. The analysis in the range of observation is used to establish a POD near the lower end of the observed range (see Section 3.3).

3.2.1. Epidemiologic Studies

Ideally, epidemiologic data would be used to select the dose-response function for human exposures. Because epidemiologic data are usually limited and many models may fit the data (Samet et al.,1998), other factors may influence model choice. For epidemiologic studies, including those with grouped data, analysis by linear models in the range of observation is generally appropriate unless the fit is poor. The relatively small exposure range observed in many epidemiologic studies, for example, makes it difficult to discern the shape of the exposure- or dose-response curve. Exposure misclassification and errors in exposure estimation also obscure the shape of the dose-response curve. When these errors are unsystematic or random, the result is frequently to bias the risk estimates toward zero. When a linear model fits poorly, more flexible models that allow for low-dose linearity, for example, a linear-quadratic model or a Hill model (Murrell et al., 1998), are often considered next.

Analysis of epidemiologic studies depends on the type of study and quality of the data, particularly the availability of quantitative measures of exposure. The objective is to develop a dose-response curve that estimates the incidence of cancer attributable to the dose (as estimated from the exposure) to the agent. In some cases, e.g., tobacco smoke or occupational exposures, the data are in the range of the exposures of interest. In other cases, as with data from animal experiments, information from the observable range is extrapolated to exposures of interest.

Analysis of effects raises additional issues:

- Many studies collect information from death certificates, which leads to estimates of mortality rather than incidence. Because survival rates vary for different cancers, the analysis may be improved by adjusting mortality figures to reflect the relationship between incidence and mortality.

- Epidemiologic studies, by their nature, are limited in the extent to which they can control for effects due to exposures from other agents. In some cases, the agent can have discernible interactive effects with another agent, making it possible to estimate the contribution of each agent as a risk factor for the effects of the other. For example, competing risks in a study population can limit the observed occurrence of cancer, while additive effects may lead to an increase occurrence of cancer. In the case of rates not already so adjusted, the analysis can be improved by correcting for competing or additive risks that are not similar in exposed and comparison groups.

- Comparison groups that are not free from exposure to the agent can bias the risk estimates toward zero. The analysis can be improved by considering background exposures in the exposed and comparison groups.

- The latent period for most cancers implies that exposures immediately preceding the detection of a tumor would be less likely to have contributed to its development and, therefore, may count less in the analysis. Study subjects who were first exposed near the end of the study may not have had adequate time since exposure for cancer to develop; therefore, analysis of their data may be similar to analysis of data for those who were not exposed. However, for carcinogens that act on multiple stages of the carcinogenic process, especially the later stages, all periods of exposure. including recent exposures, may be important.

Some study designs can yield only a partial characterization of the overall hazard and therefore risk as, for example, in studies that: (1) investigate only one effect (typical of many

case-control studies), (2) include only one population segment (e.g., male workers or workers of one socioeconomic class), or (3) include only one lifestage (e.g., childhood leukemia following maternal exposure to contaminated drinking water). To obtain a more complete characterization that includes risks of other cancers, estimates from these studies can be supplemented with estimates from other studies that investigated other cancers, population segments, or lifestages (see Section 3.5).

When several studies are available for dose-response analysis, *meta-analysis* can provide a systematic approach to weighing positive studies and those studies that do not show positive results, and calculating an overall risk estimate with greater precision. Issues considered include the comparability of studies, heterogeneity across studies, and the potential for a single large study to dominate the analysis. Confidence in a meta-analysis is increased when it considers study quality, including definition of the study population and comparison group, measurement of exposure, potential for exposure misclassification, adequacy of follow-up period, and analysis of confounders (see Section 2.2.1.3).

3.2.2. Toxicodynamic ("Biologically Based") Modeling

Toxicodynamic modeling can be used when there are sufficient data to ascertain the mode of action (see Section 2.4) and quantitatively support model parameters that represent rates and other quantities associated with the key precursor events of the mode of action. Toxicodynamic modeling is potentially the most comprehensive way to account for the biological processes involved in a response. Such models seek to reflect the sequence of key precursor events that lead to cancer. Toxicodynamic models can contribute to dose-response assessment by revealing and describing nonlinear relationships between internal dose and cancer response. Such models may provide a useful approach for analysis in the range of observation, provided the purpose of the assessment justifies the effort involved.

If a new model is developed for a specific agent, extensive data on the agent are important for identifying the form of the model, estimating its parameters, and building confidence in its results. Conformance to the observed tumor incidence data alone does not establish a model's validity, as a model can be designed with a sufficiently large number of parameters so as to fit

any given dataset. Peer review, including both an examination of the scientific basis supporting the model and an independent evaluation of the model's performance, is an essential part of evaluating the new model.

If a standard model already exists for the agent's mode of action, the model can be adapted for the agent by using agent-specific data to estimate the model's parameters. An example is the two-stage clonal expansion model developed by Moolgavkar and Knudson (1981) and Chen and Farland (1991). These models continue to be improved as more information becomes available.

It is possible for different models to provide equivalent fits to the observed data but to diverge substantially in their projections at lower doses. When model parameters are estimated from tumor incidence data, it is often the case that different combinations of parameter estimates can yield similar results in the observed range. For this reason, critical parameters (e.g., mutation rates and cell birth and death rates) are estimated from laboratory studies and not by curve-fitting to tumor incidence data (Portier, 1987). This approach reduces model uncertainty (see Section 3.6) and ensures that the model does not give answers that are biologically unrealistic. This approach also provides a robustness of results, where the results are not likely to change substantially if fitted to slightly different data.

Toxicodynamic modeling can provide insight into the relationship between tumors and key precursor events. For example, a model that includes cell proliferation can be used to explore the extent to which small increases in the cell proliferation rate can lead to large lifetime tumor incidences (Gaylor and Zheng, 1996). In this way, toxicodynamic modeling can be used to select and characterize an appropriate precursor response level (see Section 3.2.2, 3.2.5).

3.2.3. Empirical Modeling ("Curve Fitting")

When a toxicodynamic model is not available or when the purpose of the assessment does not warrant developing such a model, empirical modeling (sometimes called "curve fitting") should be used in the range of observation. A model can be fitted to data on either tumor incidence or a key precursor event. Goodness-of-fit to the experimental observations is not by itself an effective means of discriminating among models that adequately fit the data (OSTP,

1985). Many different curve-fitting models have been developed, and those that fit the observed data reasonably well may lead to several-fold differences in estimated risk at the lower end of the observed range. Another problem occurs when a multitude of alternatives are presented without sufficient context to make a reasoned judgment about the alternatives. This form of model uncertainty reflects primarily the availability of different computer models and not biological information about the agent being assessed or about carcinogenesis in general. In cases where curve-fitting models are used because the data are not adequate to support a toxicodynamic model, there generally would be no biological basis to choose among alternative curve-fitting models. However, in situations where there are alternative models with significant biological support, the decisionmaker can be informed by the presentation of these alternatives along with their strengths and uncertainties.

Quantitative data on precursors can be used in conjunction with, or in lieu of, data on tumor incidence to extend the dose-response curve to lower doses. Caution is used with rates of molecular events such as mutation or cell proliferation or signal transduction. Such rates can be difficult to relate to cell or tissue changes overall. The timing of observations of these phenomena, as well as the cell type involved, is linked to other precursor events to ensure that the measurement is truly a key event (Section 2.4).

For incidence data on either tumors or a precursor, an established empirical procedure is used to provide objectivity and consistency among assessments. The procedure models incidence, corrected for background, as an increasing function of dose. The models are sufficiently flexible in the observed range to fit linear and nonlinear datasets. Additional judgments and perhaps alternative analyses are used when the procedure fails to yield reliable results. For example, when a model's fit is poor, the highest dose is often omitted in cases where it is judged that the highest dose reflects competing toxicity that is more relevant at high doses than at lower doses. Another example is when there are large differences in survival across dose groups; here, models that includes time-to-tumor or time-to-event information may be useful.

For continuous data on key precursor effects, empirical models can be chosen on the basis of the structure of the data. The rationale for the choice of model, the alternatives

considered and rejected, and a discussion of model uncertainty are included in the dose-response characterization.

3.2.4. Point of Departure (POD)

For each tumor response, a POD from the observed data should be estimated to mark the beginning of extrapolation to lower doses. The POD is an estimated dose (expressed in human-equivalent terms) near the lower end of the observed range without significant extrapolation to lower doses.

The POD is used as the starting point for subsequent extrapolations and analyses. For linear extrapolation, the POD is used to calculate a *slope factor* (see Section 3.3.3), and for nonlinear extrapolation the POD is used in the calculation of a *reference dose* or *reference concentration* (see Section 3.3.4). In a risk characterization, the POD is part of the determination of a *margin of exposure* (see Section 5.4). With appropriate adjustments, it can also be used as the basis for *hazard rankings* that compare different agents or health effects.

The lowest POD is used that is adequately supported by the data. If the POD is above some data points, it can fail to reflect the shape of the dose-response curve at the lowest doses and can introduce bias into subsequent extrapolations (see Figure 3-1). On the other hand, if the POD is far below all observed data points, it can introduce model uncertainty and parameter uncertainty (see Section 3.6) that increase with the distance between the data and the POD. Use of a POD at the lowest level supported by the data seeks to balance these considerations. It uses information from the model(s) a small distance below the observed range rather than discarding this information and using extrapolation procedures in a range where the model(s) can provide some useful information. Statistical tests involving the ratio of the central estimate and its lower bound (i.e., ED_{xx}/LED_{xx}) can be useful for evaluating how well the data support a model's estimates at a particular response level. (Note that the ability to model at a particular response level is not the same as the study's ability to identify an increase at that response level as statistically significant.)

The POD for extrapolating the relationship to environmental exposure levels of interest, when the latter are outside the range of observed data, is generally the lower 95% confidence

limit on the lowest dose level that can be supported for modeling by the data. SAB (1997) suggested that, "it may be appropriate to emphasize lower statistical bounds in screening analyses and in activities designed to develop an appropriate human exposure value, since such activities require accounting for various types of uncertainties and a lower bound on the central estimate is a scientifically-based approach accounting for the uncertainty in the true value of the ED_{10} [or central estimate]." However, the consensus of the SAB (1997) was that, "both point estimates and statistical bounds can be useful in different circumstances, and recommended that the Agency routinely calculate and present the point estimate of the ED_{10} [or central estimate] and the corresponding upper and lower 95% statistical bounds." For example, it may be appropriate to emphasize the central estimate in activities that involve formal uncertainty analysis that are required by OMB Circular A-4 (OMB, 2003) as well as ranking agents as to their carcinogenic hazard. Thus, risk assessors should calculate, to the extent practicable, and present the central estimate and the corresponding upper and lower statistical bounds (such as confidence limits) to inform decisionmakers.

When tumor data are used, a POD is obtained from the modeled tumor incidences. Conventional cancer bioassays, with approximately 50 animals per group, generally can support modeling down to an increased incidence of 1–10%; epidemiologic studies, with larger sample sizes, below 1%. Various models commonly used for carcinogens yield similar estimates of the POD at response levels as low as 1% (Krewski and Van Ryzin, 1981; Gaylor et al., 1994). Consequently, response levels at or below 10% can often be used as the POD. As a modeling convention, the lower bound on the doses associated with standard response levels of 1, 5, and 10% can be analyzed, presented, and considered. For making comparisons at doses within the observed range, the ED_{10} and LED_{10} are also reported and can be used, with appropriate adjustments, in hazard rankings that compare different agents or health effects (U.S. EPA, 2002c). A *no-observed-adverse-effect level* (NOAEL) generally is not used for assessing the potential for carcinogenic response when one or more models can be fitted to the data.

When good quality precursor data are available and are clearly tied to the mode of action of the compound of interest, models that include both tumors and their precursors may be advantageous for deriving a POD. Such models can provide insight into quantitative

relationships between tumors and precursors (see Section 3.2.2), possibly suggesting the precursor response level that is associated with a particular tumor response level. The goal is to use precursor data to extend the observed range below what can be observed in tumor studies. EPA is continuing to examine this issue and anticipates that findings and conclusions may result in supplemental guidance to these cancer guidelines. If the precursor data are drawn from small samples or if the quantitative relationship between tumors and precursors is not well defined, then the tumor data will provide a more reliable POD. Precursor effects may or may not be biologically adverse in themselves; the intent is to consider not only tumors but also damage that can lead to subsequent tumor development by the agent. Analysis of continuous data may differ from discrete data; Murrell et al. (1998) discuss alternative approaches to deriving a POD from continuous data.

3.2.5. Characterizing the POD: The POD Narrative

As a single-point summary of a single dose-response curve, the POD alone does not convey all the critical information present in the data from which it is derived. To convey a measure of uncertainty, the POD should be presented as a central estimate with upper and lower bounds. A POD narrative summarizes other important features of the database and the POD that are important to account for in low-dose extrapolations or other analyses.

(a) Nature of the response. Is the POD based on tumors or a precursor? If on tumors, does the POD measure incidence or mortality? Is it a lifetime measure or was the study terminated early? The relationships between precursors and tumors, incidence and mortality, and lifetime and early-termination results vary from case to case. Modeling can provide quantitative insight into these relationships, for example, linking a change in a precursor response to a tumor incidence (see Section 3.2.2). This can aid in evaluating the significance of the response at the POD and adjusting different PODs to make them comparable.

(b) Level of the response. What level of response is associated with the POD, for example, 1% cancer risk, 10% cancer risk, or 10% change in a precursor measure?

(c) Nature of the study population. Is the POD based on humans or animals? How large is the effective sample size? Is the study group representative of the general population, of healthy adult workers, or of a susceptible group? Are both sexes represented? Did exposure occur during a susceptible lifestage?

(d) Slope of the dose-response curve at the POD. How does response change as dose is reduced below the POD? A steep slope indicates that risk decreases rapidly as dose decreases. On the other hand, a steep slope also indicates that errors in an exposure assessment can lead to large errors in estimating risk. Both aspects of the slope are important. The slope also indicates whether dose-response curves for different effects are likely to cross below the POD. For example, in the ED_{01} study where 2-acetylaminofluorene caused bladder carcinomas and liver carcinomas in mice (Littlefield et al., 1980), the dose-response curves for these tumors cross between 10% and 1% response (see Figure 3-2). This crossing, which can be inferred from the slopes of the curves at a 10% response, shows how considering the slope can lead to better inferences about the predominant effects expected at lower doses. Mode of action data can also be useful; quantitative information about key precursor events can be used to describe how risk decreases as dose decreases below the POD.

(e) Relationship of the POD with other cancers. How does the POD for this cancer relate to PODs for other cancers observed in the database? For example, a POD based on male workers would not reflect the implications of mammary tumors in female rats or mice.

(f) Extent of the overall cancer database. Have potential cancer responses been adequately studied (e.g., were all tissues examined), or is the database limited to particular effects, population segments, or lifestages? Do the mode of action data suggest a potential for cancers not observed in the database (e.g., disruption of particular endocrine pathways leading to related cancers)?

3.2.6. Relative Potency Factors

Relative potency factors (of which toxicity equivalence factors are a special case) can be used for a well-defined class of agents that operate through a common mode of action for the same toxic endpoint. A complete dose-response assessment is conducted for one well-studied member of the class that serves as the *index chemical* for the class. The other members of the class are tied to the index chemical by relative potency factors that are based on characteristics such as relative toxicological outcomes, relative metabolic rates, relative absorption rates, quantitative SARs, or receptor binding characteristics (U.S. EPA, 2000c). Examples of this approach are the *toxicity equivalence factors* for dioxin-like compounds and the relative potency factors for some carcinogenic polycyclic aromatic hydrocarbons. Whenever practicable, toxicity equivalence factors should be validated and accompanied by quantitative uncertainty analysis.

3.3. EXTRAPOLATION TO LOWER DOSES

The purpose of low-dose extrapolation is to provide as much information as possible about risk in the range of doses below the observed data. The most versatile forms of low-dose extrapolation are dose-response models that characterize risk as a probability over a range of environmental exposure levels. These risk probabilities allow estimates of the risk reduction under different decision options and estimates of the risk remaining after an action is taken and provide the risk information needed for benefit-cost analyses of different decision options.

When a dose-response model is not developed for lower doses, another form of low-dose extrapolation is a safety assessment that characterizes the safety of one lower dose, with no explicit characterization of risks above or below that dose. Although this type of extrapolation may be adequate for evaluation of some decision options, it may not be adequate for other purposes (e.g., benefit-cost analyses) that require a quantitative characterization of risks across a range of doses. At this time, safety assessment is the default approach for tumors that arise through a nonlinear mode of action; however, EPA continues to explore methods for quantifying dose-response relationships over a range of environmental exposure levels for tumors that arise through a nonlinear mode of action (U.S. EPA, 2002c). EPA program offices that need this more

explicit dose-response information may develop and apply methods that are informed by the methods described in these cancer guidelines.

3.3.1. Choosing an Extrapolation Approach

The approach for extrapolation below the observed data considers the understanding of the agent's mode of action at each tumor site (see Section 2.4). Mode of action information can suggest the likely shape of the dose-response curve at lower doses. The extent of inter-individual variation is also considered, with greater variation spreading the response over a wider range of doses.

Linear extrapolation should be used when there are MOA data to indicate that the dose-response curve is expected to have a linear component below the POD. Agents that are generally considered to be linear in this region include:

- agents that are DNA-reactive and have direct mutagenic activity, or

- agents for which human exposures or body burdens are high and near doses associated with key precursor events in the carcinogenic process, so that background exposures to this and other agents operating through a common mode of action are in the increasing, approximately linear, portion of the dose-response curve.

When the weight of evidence evaluation of all available data are insufficient to establish the mode of action for a tumor site and when scientifically plausible based on the available data, linear extrapolation is used as a default approach, because linear extrapolation generally is considered to be a health-protective approach. Nonlinear approaches generally should not be used in cases where the mode of action has not been ascertained. Where alternative approaches with significant biological support are available for the same tumor response and no scientific consensus favors a single approach, an assessment may present results based on more than one approach.

A *nonlinear approach* should be selected when there are sufficient data to ascertain the mode of action and conclude that it is not linear at low doses and the agent does not demonstrate mutagenic or other activity consistent with linearity at low doses. Special attention is important when the data support a nonlinear mode of action but there is also a suggestion of mutagenicity. Depending on the strength of the suggestion of mutagenicity, the assessment may justify a conclusion that mutagenicity is not operative at low doses and focus on a nonlinear approach, or alternatively, the assessment may use both linear and nonlinear approaches.

Both linear and nonlinear approaches may be used when there are multiple modes of action. If there are multiple tumor sites, one with a linear and another with a nonlinear mode of action, then the corresponding approach is used at each site. If there are multiple modes of action at a single tumor site, one linear and another nonlinear, then both approaches are used to decouple and consider the respective contributions of each mode of action in different dose ranges. For example, an agent can act predominantly through cytotoxicity at high doses and through mutagenicity at lower doses where cytotoxicity does not occur. Modeling to a low response level can be useful for estimating the response at doses where the high-dose mode of action would be less important.

3.3.2. Extrapolation Using a Toxicodynamic Model

The preferred approach is to develop a toxicodynamic model of the agent's mode of action and use that model for extrapolation to lower doses (see Section 3.2.2). The extent of extrapolation is governed by an analysis of *model uncertainty*, where alternative models that fit similarly in the observed range can diverge below that range (see Section 3.6). Substantial divergence is likely when model parameters are estimated from tumor incidence data, so that different combinations of parameter estimates yield similar fits in the observed range but have different implications at lower doses. An analysis of model uncertainty can be used to determine the range where extrapolation using the toxicodynamic model is supported and where further extrapolation would be based on either a linear or a nonlinear default, as appropriate (see Sections 3.3.3, 3.3.4).

3.3.3. Extrapolation Using a Low-dose, Linear Model

Linear extrapolation should be used in two distinct circumstances: (1) when there are data to indicate that the dose-response curve has a linear component below the POD, or (2) as a default for a tumor site where the mode of action is not established (see Section 3.3.1). For linear extrapolation, a line should be drawn from the POD to the origin, corrected for background. This implies a proportional (linear) relationship between risk and dose at low doses. (Note that the dose-response curve generally is not linear at higher doses.)

The slope of this line, known as the *slope factor*, is an upper-bound estimate of risk per increment of dose that can be used to estimate risk probabilities for different exposure levels. The slope factor is equal to $0.01/LED_{01}$ if the LED_{01} is used as the POD.

Unit risk estimates express the slope in terms of μg/L drinking water or $\mu g/m^3$ or ppm air. In general, the drinking water unit risk is derived by converting a slope factor from units of mg/kg-d to units of μg/L, whereas an inhalation unit risk is developed directly from a dose-response analysis using equivalent human concentrations already expressed in units of $\mu g/m^3$. Unit risk estimates often assume a standard intake rate (L/day drinking water or m^3/day air) and body weight (kg), which may need to be reconciled with the exposure factors for the population of interest in an exposure assessment (see Section 4.4). Alternatively, when the slope factor for inhalation is in units of ppm, it may sometimes be termed the inhalation unit risk. Although unit risks have not been calculated in the past for dermal exposures, both exposures that are absorbed into the systemic circulation and those that remain in contact with the skin are also important.

Risk-specific doses are derived from the slope factor or unit risk to estimate the dose associated with a specific risk level, for example, a one-in-a-million increased lifetime risk.

3.3.4. Nonlinear Extrapolation to Lower Doses

A nonlinear extrapolation method can be used for cases with sufficient data to ascertain the mode of action and to conclude that it is not linear at low doses but with not enough data to support a toxicodynamic model that may be either nonlinear or linear at low doses. Nonlinear extrapolation having a significant biological support may be presented in addition to a linear approach when the available data and a weight of evidence evaluation support a nonlinear

approach, but the data are not strong enough to ascertain the mode of action applying the Agency's mode of action framework. If the mode of action and other information can support chemical-specific modeling at low doses, it is preferable to default procedures.

For cases where the tumors arise through a nonlinear mode of action, an oral *reference dose* or an inhalation *reference concentration*, or both, should be developed in accordance with EPA's established practice for developing such values, taking into consideration the factors summarized in the characterization of the POD (see Section 3.2.5). This approach expands the past focus of such reference values (previously reserved for effects other than cancer) to include carcinogenic effects determined to have a nonlinear mode of action. As with other health effects of concern, it is important to put cancer in perspective with the overall health impact of an exposure by comparing reference value calculations for cancer with those for other health effects.

For effects other than cancer, reference values have been described as being based on the assumption of biological thresholds. The Agency's more current guidelines for these effects (U.S. EPA, 1996a, 1998b), however, do not use this assumption, citing the difficulty of empirically distinguishing a true threshold from a dose-response curve that is nonlinear at low doses.

Economic and policy analysts need to know how the probability of cancer varies at exposures above the reference value and whether, and to what extent, there are health benefits from reducing exposures below the reference value. The risk assessment community is working to develop better methods to provide more useful information to economic and policy analysts.

3.3.5. Comparing and Combining Multiple Extrapolations

When multiple estimates can be developed, all datasets should be considered and a judgment made about how best to represent the human cancer risk. Some options for presenting results include:

- adding risk estimates derived from different tumor sites (NRC, 1994),

- combining data from different datasets in a joint analysis (Putzrath and Ginevan, 1991; Stiteler et al., 1993; Vater et al., 1993),

- combining responses that operate through a common mode of action,

- representing the overall response in each experiment by counting animals with any tumor showing a statistically significant increase,

- presenting a range of results from multiple datasets (in this case, the dose-response assessment includes guidance on how to choose an appropriate value from the range),

- choosing a single dataset if it can be justified as most representative of the overall response in humans, or

- a combination of these options.

Cross-comparison of estimates from human and animal studies can provide a valuable risk perspective.

- Calculating an animal-derived slope factor and using it to estimate the risk expected in a human study can provide information with which to evaluate the human study design, for example, adequacy of exposure level and sample size.

- Calculating an upper-bound slope factor from a human study that does not show positive results but that has good exposure information, and comparing it to an animal-derived slope factor can indicate whether the animal and humans studies are consistent.

3.4. EXTRAPOLATION TO DIFFERENT HUMAN EXPOSURE SCENARIOS

As described in the previous cancer guidelines, special problems arise when the human exposure situation of concern suggests exposure regimens, e.g., route and dosing schedule, that are substantially different from those used in the relevant animal studies. Unless there is evidence to the contrary in a particular case, the cumulative dose received over a lifetime, expressed as average daily exposure prorated over a lifetime, is recommended as an appropriate measure of exposure to a carcinogen. That is, the assumption is made that a high dose of a carcinogen received over a short period of time is equivalent to a corresponding low dose spread over a lifetime. This approach becomes more problematical as the exposures in question become more intense but less frequent, especially when there is evidence that the agent has shown dose-rate effects (U.S. EPA 1986a).

Accordingly, *for lifetime human exposure scenarios* that involve intermittent or varying levels of exposure, the prevailing practice has been to assess exposure by calculating a *lifetime average daily exposure or dose* (U.S. EPA, 1992a).

For less-than-lifetime human exposure scenarios, too, the lifetime average daily exposure or dose has often been used. The use of these lifetime average exposure metrics was adopted with low-dose linear cancer assessments in mind. The lifetime averaging implies that less-than-lifetime exposure is associated with a linearly proportional reduction of the lifetime risk, regardless of when exposures occur. Such averaging may be problematic in some situations. This can be illustrated using both the multistage model and the two-stage clonal expansion model that predict that short-duration risks are not necessarily proportional to exposure duration and can depend on the nature of the carcinogen and the timing of exposure (Goddard et al., 1995; Murdoch et al., 1992). These examples indicate some circumstances in which use of a lifetime average daily dose (LADD) would underestimate cancer risk by two- to fivefold, and others in which it might overestimate risk (Murdoch et al., 1992). Thus, averaging over the duration of a lifestage or a critical window of exposure may be appropriate. As methodological research focuses on new approaches for estimating risks from less-than-lifetime exposures, methods and defaults can be expected to change.

This highlights the importance for each dose-response assessment to critically evaluate all information pertaining to less-than-lifetime exposure. For example, detailed stop-exposure studies can provide information about the relationship between exposure duration, precursor effects, potential for reversibility, and tumor development. Toxicokinetic modeling can investigate differences in internal dose between short-term and long-term exposure or between intermittent and constant exposure. Persistence in the body can be useful in explaining long-term effects resulting from shorter-term exposures.

For nonlinear cancer analyses, it may be appropriate to assess exposure by calculating a *daily dose* that is averaged over the exposure duration for the study (see Section 3.1.1). For example, when the analysis is based on precursor effects that result from less than a lifetime exposure, that exposure period may be used. This reflects an expectation that the precursor effects on which the analysis is based can result from less-than-lifetime exposure, bringing consistency to the methods used for dose-response assessment and exposure assessment in such cases. The dose-response assessment can provide a recommendation to exposure assessors about the averaging time that is appropriate to the mode of action and to the exposure duration of the scenario.

3.5. EXTRAPOLATION TO SUSCEPTIBLE POPULATIONS AND LIFESTAGES

The dose-response assessment strives to derive separate estimates for susceptible populations and lifestages so that these risks can be explicitly characterized. For a susceptible population, higher risks can be expected from exposures anytime during life, but this applies to only a portion of the general population (e.g., those bearing a particular genetic susceptibility). In contrast, for a susceptible lifestage, higher risks can be expected from exposures during only a portion of a lifetime, but everyone in the population may pass through those lifestages. Effects of exposures during a susceptible period are not equivalent to effects of exposures at other times; consequently, it is useful to estimate the risk attributable to exposures during each period.

Depending on the data available, a tiered approach should be used to address susceptible populations and lifestages.

- When there is an epidemiologic study or an animal bioassay that reports quantitative results for susceptible individuals, the data should be analyzed to provide a separate risk estimate for those who are susceptible. If susceptibility pertains to a lifestage, it is useful to characterize the portion of the lifetime risk that can be attributed to the susceptible lifestage.

- When there are data on some risk-related parameters that allow comparison of the general population and susceptible individuals, the data should be analyzed with an eye toward adjusting the general population estimate for susceptible individuals. This analysis can range from toxicokinetic modeling that uses parameter values representative of susceptible individuals to more simply adjusting a general population estimate to reflect differences in important rate-governing parameters. Care is taken to not make parameter adjustments in isolation, as the appropriate adjustment can depend on the interactions of several parameters; for example, the ratio of metabolic activation and clearance rates can be more appropriate than the activation rate alone (U.S. EPA, 1992b).
- In the absence of such agent-specific data, there is some general information to indicate that childhood can be a susceptible lifestage for exposure to some carcinogens (U.S. EPA, 2005); this warrants explicit consideration in each assessment. The potential for susceptibility from early-life exposure is expected to vary among specific agents and chemical classes. In addition, the concern that the dose-averaging generally used for assessing less-than-lifetime exposure is more likely to understate than overstate risk (see Section 3.4) contributes to the suggestion that alternative approaches be considered for assessing risks from less-than-lifetime exposure that occurs during childhood. Accompanying these cancer guidelines is the Supplemental Guidance that the Agency will use to assess risks from early-life exposure to potential carcinogens (U.S. EPA, 2005). The Supplemental Guidance may be updated to reflect new data and new understanding that may become available in the future.

3.6. UNCERTAINTY

The NRC (1983, 1994, 1996, 2002) has repeatedly advised that proper characterization of uncertainty is essential in risk assessment. An assessment that omits or underestimates uncertainty can leave decisionmakers with a false sense of confidence in estimates of risk. On the other hand, a high level of uncertainty does not imply that a risk assessment or a risk management action should be delayed (NRC, 2002). Uncertainty in dose-response assessment can be classified as either *model uncertainty* or *parameter uncertainty*. A related concept, *human variation*, is discussed below. Assessments should discuss the significant uncertainties encountered in the analysis, distinguishing, if possible, between model uncertainty, parameter uncertainty, and human variation. Origins of these uncertainties can span a range, from a single causal thread supported by sparse data, to abundant information that presents multiple possible conclusions or that does not coalesce. As described in Section 2.6 and in Section 5.1, all contributing features should be noted.

Model uncertainty refers to a lack of knowledge needed to determine which is the correct scientific theory on which to base a model. In risk assessment, model uncertainty is reflected in alternative choices for model structure, dose metrics, and extrapolation approaches. Other sources of model uncertainty concern whether surrogate data are appropriate, for example, using data on adults to make inferences about children. The full extent of model uncertainty usually cannot be quantified; a partial characterization can be obtained by comparing the results of alternative models. Model uncertainty is expressed through comparison of separate analyses from each model, coupled with a subjective probability statement, where feasible and appropriate, of the likelihood that each model might be correct (NRC, 1994).

Some aspects of model uncertainty that should be addressed in an assessment include the use of animal models as a surrogate for humans, the influence of cross-species differences in metabolism and physiology, the use of effects observed at high doses as an indicator of the potential for effects at lower doses, the effect of using linear or nonlinear extrapolation to estimate risks, the use of using small samples and subgroups to make inferences about entire human populations or subpopulations with differential susceptibilities, and the use of

experimental exposure regimens to make inferences about different human exposure scenarios (NRC, 2002).

Toxicokinetic and toxicodynamic models are generally premised on *site concordance* across species, modeling, for example, the relationship between administered dose and liver tissue concentrations to predict increased incidences of liver cancer. This relationship, which can be observed in animals, is typically only inferred for humans. There are, however, numerous examples of an agent causing different cancers in different species. The assessment should discuss the relevant data that bear on this form of model uncertainty.

Parameter uncertainty refers to a lack of knowledge about the values of a model's parameters. This leads to a distribution of values for each parameter. Common sources of parameter uncertainty include random measurement errors, systematic measurement errors, use of surrogate data instead of direct measurements, misclassification of exposure status, random sampling errors, and use of an unrepresentative sample. Most types of parameter uncertainty can be quantified by statistical analysis.

Human variation refers to person-to-person differences in biological susceptibility or in exposure. Although both human variation and uncertainty can be characterized as ranges or distributions, they are fundamentally different concepts. Uncertainty can be reduced by further research that supports a model or improves a parameter estimate, but human variation is a reality that can be better characterized, but not reduced, by further research. Fields other than risk assessment use "variation" or "variability" to mean dispersion about a central value, including measurement errors and other random errors that risk assessors address as uncertainty.

Probabilistic risk assessment, informed by expert judgment, has been used in exposure assessment to estimate human variation and uncertainty in lifetime average daily exposure concentration or dose. Probabilistic methods can be used in this exposure assessment application because the pertinent variables (for example, concentration, intake rate, exposure duration, and body weight) have been identified, their distributions can be observed, and the formula for combining the variables to estimate the lifetime average daily dose is well defined (see U.S. EPA, 1992a). Similarly, probabilistic methods can be applied in dose-response assessment when there is an understanding of the important parameters and their relationships, such as

identification of the key determinants of human variation (for example, metabolic polymorphisms, hormone levels, and cell replication rates), observation of the distributions of these variables, and valid models for combining these variables. With appropriate data and expert judgment, formal approaches to probabilistic risk assessment can be applied to provide insight into the overall extent and dominant sources of human variation and uncertainty. In doing this, it is important to note that analyses that omit or underestimate some principal sources of variation or uncertainty could provide a misleadingly narrow description of the true extent of variation and uncertainty and give decisionmakers a false sense of confidence in estimates of risk. Specification of joint probability distributions is appropriate when variables are not independent of each other. In each case, the assessment should carefully consider the questions of uncertainty and human variation and discuss the extent to which there are data to address them.

Probabilistic risk assessment has also been used in dose-response assessment to determine and distinguish the degree of uncertainty and variability in toxicokinetic and toxicodynamic modeling. Although this field is less advanced that probabilistic exposure assessment, progress is being made and these cancer guidelines are flexible enough to accommodate continuing advances in these approaches.

Advances in uncertainty analysis are expected as the field develops. The cancer guidelines are intended to be flexible enough to incorporate additional approaches for characterizing uncertainty that have less commonly been used by regulatory agencies. In all scientific and engineering fields, data and research limitations often limit the application of established methods. A dearth of data is a particular problem when quantifying the *probability distribution* of model outputs. In many of these scientific and engineering disciplines, researchers have used rigorous expert elicitation methods to overcome the lack of peer-reviewed methods and data. Although expert elicitation has not been widely used in environmental risk assessment, several studies have applied this methodology as a tool for understanding quantitative risk. For example, expert elicitation has been used in chemical risk assessment and its associated uncertainty (e.g., Richmond, 1981; Renn, 1999; Florig et al., 2001; Morgan et al., 2001; Willis et al., 2004), components of risk assessment such as hazard assessment and dose-response

evaluation (e.g., Hawkins and Graham 1988; Jelovsek et al., 1990; Evans et al., 1994; IEc, 2004; U.S. EPA 2004) and exposure assessment (e.g., Whitfield and Wallsten, 1989; Hawkins and Evans, 1989; Winkler et al., 1995; Stiber et al., 1999; Walker et al., 2001, 2003; Van Der Fels-Klerx et al., 2002), and for evaluating other types of risks (e.g., North and Merkhofer, 1976; Fos and McLin, 1990). These cancer guidelines are flexible enough to accommodate the use of expert elicitation to characterize cancer risks, as a complement to the methods presented in the cancer guidelines. According to NRC (NRC, 2002), the rigorous use of expert elicitation for the analyses of risks is considered to be quality science.

3.7. DOSE-RESPONSE CHARACTERIZATION

A *dose-response characterization* extracts the dose-response information needed in a full risk characterization (U.S. EPA, 2000b), including:

- presentation of the recommended estimates (slope factors, reference doses, reference concentrations) and alternatives with significant biological support,
- a summary of the data supporting these estimates,
- a summary and explanation of the modeling approaches used,
- a description of any special features such as the development and consolidation of multiple estimates as detailed in Section 3.3.5,
- the POD narrative (see Section 3.2.5),
- a summary of the key defaults invoked,
- identification of susceptible populations or lifestages and quantification of their differential susceptibility, and

- a discussion of the strengths and limitations of the dose-response assessment, highlighting significant issues in developing risk estimates, alternative approaches considered equally plausible, and how these issues were resolved.

All estimates should be accompanied by the weight of evidence descriptor and its narrative (see Section 2.5) to convey a sense of the qualitative uncertainty about whether the agent may or may not be carcinogenic.

Slope factors generally represent an upper bound on the average risk in a population or the risk for a randomly selected individual but not the risk for a highly susceptible individual or group. Some individuals face a higher risk and some face a lower risk. The use of upper bounds generally is considered to be a health-protective approach for covering the risk to susceptible individuals, although the calculation of upper bounds is not based on susceptibility data. Similarly, exposure during some lifestages can contribute more or less to the total lifetime risk than do similar exposures at other times. The dose-response assessment characterizes, to the extent possible, the extent of these variations.

Depending on the supporting data and modeling approach, a slope factor can have a mix of traits that tend to either estimate, overestimate, or underestimate risk.

Some examples of traits that tend to overestimate risk include the following.

- The slope factor is derived from data on a highly susceptible animal strain.

- Linear extrapolation is used as a default and extends over several orders of magnitude.

- The largest of several slope factors is chosen.

Some examples of traits that tend to underestimate risk include the following.

- Several tumor types were observed, but the slope factor is based on a subset of them.

- The study design does not include exposure during a susceptible lifestage, for example, perinatal exposure.

- The study population is of less-than-average susceptibility, for example, healthy adult workers.

- There is random exposure misclassification or random exposure measurement error in the study from which the slope factor is derived.

Some examples of traits that inherently neither overestimate nor underestimate risk include the following.

- The slope factor is derived from data in humans or in an animal strain that responds like humans.

- Linear extrapolation is appropriate for the agent's mode of action.

- Environmental exposures are close to the observed data.

- Several slope factors for the same tumor are averaged or a slope factor is derived from pooled data from several studies.

- The slope factor is derived from the only suitable study.

Figure 3-1. Compatibility of alternative points of departure with observed and modeled tumor incidences

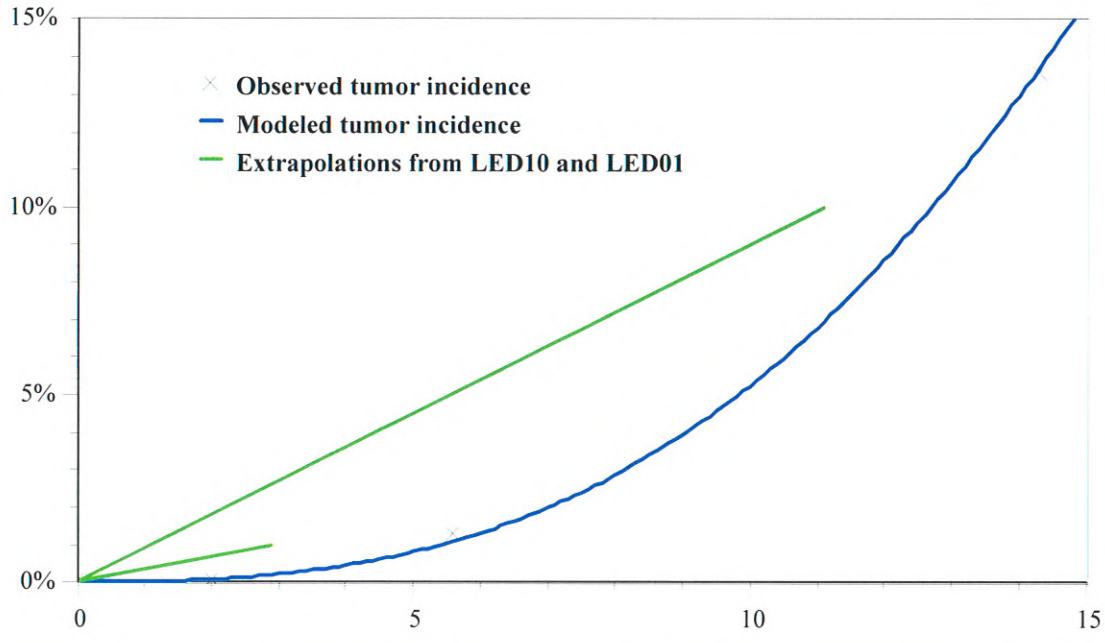
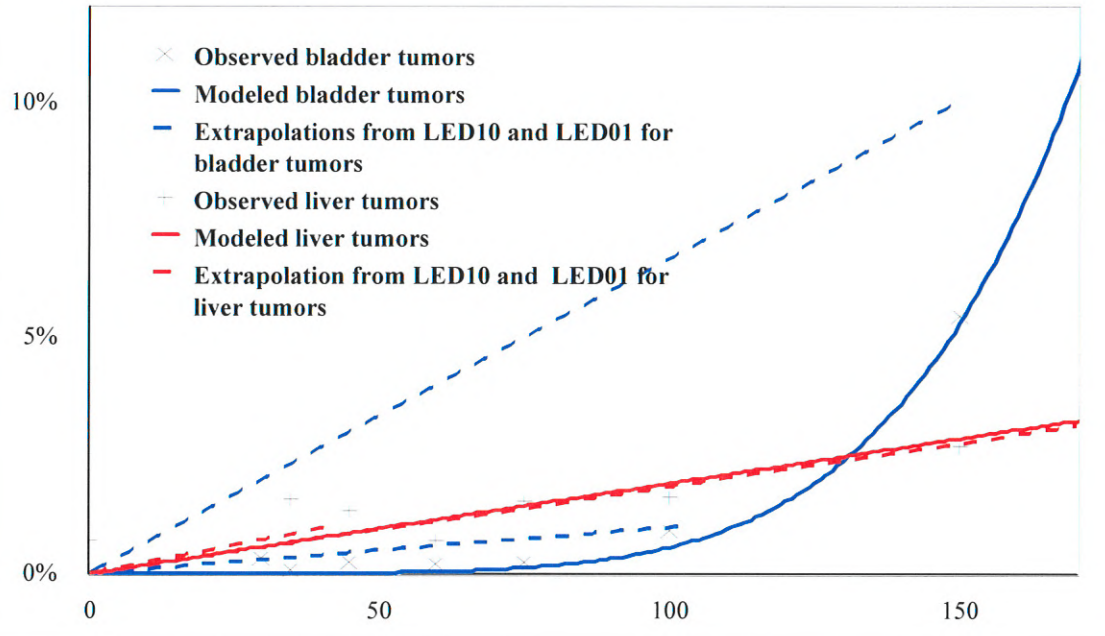


Figure 3-2. Crossing--between 10% and 1%--of dose-response curves for bladder carcinomas and liver carcinomas induced by 2-AAF



4. EXPOSURE ASSESSMENT

Exposure assessment is the determination (qualitative and quantitative) of the magnitude, frequency, and duration of exposure and internal dose (U.S. EPA, 1992a). This section provides a brief overview of exposure assessment principles, with an emphasis on issues related to carcinogenic risk assessment. The information presented here should be used in conjunction with other guidance documents, including *Guidelines for Exposure Assessment* (U.S. EPA, 1992a), *Science Policy Council Handbook: Risk Characterization* (U.S. EPA, 2000b), *Exposure Factors Handbook* (U.S. EPA, 1997c), the 1997 *Policy for Use of Probabilistic Analysis in Risk Assessments* (U.S. EPA, 1997d), and the 1997 *Guiding Principles for Monte Carlo Analysis* (U.S. EPA, 1997e). In addition, program-specific guidelines for exposure assessment should be consulted.

Exposure assessment generally consists of four major steps: defining the assessment questions, selecting or developing the conceptual and mathematical models, collecting data or selecting and evaluating available data, and exposure characterization. Each of these steps is briefly described below.

4.1. DEFINING THE ASSESSMENT QUESTIONS

In providing a clear and unambiguous statement of the purpose and scope of the exposure assessment (U.S. EPA, 1997e), consider the following.

- The management objectives of the assessment will determine whether deterministic screening level analyses are adequate or whether full probabilistic exposure characterization is needed.

- Identify and include all important sources (e.g., pesticide applications), pathways (e.g., food or water), and routes (e.g., ingestion, inhalation, and dermal) of exposure in the assessment. If a particular source, pathway, or route is omitted, a clear and transparent explanation should be provided.

- Separate analyses should be conducted for each definable subgroup within the population of interest. In particular, subpopulations or lifestages that are believed to be highly exposed or susceptible to a particular health effect should be studied. These include people with certain diseases or genetic susceptibilities and others whose behavior or physiology may lead to higher exposure or susceptibility. Consider the following examples:

  — Physiological differences between men and women (e.g., body weight and inhalation rate) may lead to important differences in exposures. See, for example, the discussion in *Exposure Factors Handbook* (U.S. EPA, 1997c, Appendix 1A).

  — Pregnant and lactating women may have exposures that differ from the general population (e.g., slightly higher water consumption) (U.S. EPA, 1997c). Further, exposure to pregnant women may result in exposure to the developing fetus (NRC, 1993b).

  — Children consume more food per body weight than do adults while consuming fewer types of foods, i.e., have a more limited diet (ILSI, 1992; NRC, 1993b; U.S. EPA, 1997c). In addition, children engage in crawling and mouthing (i.e., putting hands and objects in the mouth) behaviors, which can increase their exposures.

  — The elderly and disabled may have important differences in their exposures due to a more sedentary lifestyle (U.S. EPA, 1997c). In addition, the health status of this group may affect their susceptibility to the detrimental effects of exposure.

For further guidance, see *Guidelines for Exposure Assessment* (U.S. EPA, 1992a, § 3).

4.2. SELECTING OR DEVELOPING THE CONCEPTUAL AND MATHEMATICAL MODELS

Carcinogen risk assessment models have generally been based on the premise that risk is proportional to cumulative lifetime dose. For lifetime human exposure scenarios, therefore, the exposure metric used for carcinogenic risk assessment has been the lifetime average daily dose (LADD) or, in the case of inhalation exposure, the lifetime average exposure concentration. These metrics are typically used in conjunction with the corresponding slope factor to calculate individual excess cancer risk. The LADD is typically an estimate of the daily intake of a carcinogenic agent throughout the entire life of an individual, while the lifetime average exposure concentration is the corresponding estimate of average exposure concentration for the carcinogenic agent over the entire life of an individual. Depending on the objectives of the assessment, the LADD or lifetime average exposure concentration may be calculated deterministically (using point estimates for each factor to derive a point estimate of the exposure) or stochastically (using probability distributions to represent each factor and such techniques as Monte Carlo analysis to derive a distribution of the LADD) (U.S. EPA, 1997e). Stochastic analyses may help to identify certain population segments or lifestages that are highly exposed and may need to be assessed as a special subgroup. For further guidance, see *Guidelines for Exposure Assessment* (U.S. EPA, 1992a, § 5.3.5.2). As methodological research focuses on new approaches for estimating risks from less-than-lifetime exposures, methods and defaults can be expected to change.

There may be cases where the mode of action indicates that dose rates are important in the carcinogenic process. In these cases, short-term, less-than-lifetime exposure estimates may be more appropriate than the LADD for risk assessment. This may be the case when a nonlinear dose-response approach is used (see Section 3.3.4).

4.3. COLLECTING DATA OR SELECTING AND EVALUATING AVAILABLE DATA

After the assessment questions have been defined and the conceptual and mathematical models have been developed, it is important to compile and evaluate existing data or, if necessary, to collect new data. Depending on the exposure scenario under consideration, data on

a wide variety of exposure factors may be needed. EPA's *Exposure Factors Handbook* (U.S. EPA, 1997c) contains a large compilation of exposure data, with some analysis and recommendations. Some of these data are organized by age groups to assist with assessing such subgroups as children. See, for example, *Exposure Factors Handbook* (U.S. EPA, 1997c, Volume 1, Chapter 3). When using these existing data, it is important to evaluate the quality of the data and the extent to which the data are representative of the population under consideration. EPA's (U.S. EPA, 2000d) and OMB's (OMB 2002) guidance on information quality, as well as program-specific guidances can provide further assistance for evaluating existing data.

When existing data fail to provide an adequate surrogate for the needs of a particular assessment, it is important to collect new data. Such data collection efforts should be guided by the references listed above (e.g., *Guidance for Data Quality Assessment* and program-specific guidance). Once again, subpopulations or lifestages of concern are an important consideration in any data collection effort.

4.3.1. Adjusting Unit Risks for Highly Exposed Populations and Lifestages

Unit risk estimates that have been developed in the dose-response assessment often assumed standard adult intake rates. When an exposure assessment focuses on a population or lifestage with differential exposure, good exposure assessment practice would replace the standard intake rates with values representative of the exposed population. Small changes in exposure assessments can be approximated by using linearly proportional adjustments of exposure parameters, but a more accurate integrative analysis may require an analysis stratified by exposure duration (see Section 5.1) .

> *For example*, to adjust the drinking water unit risk for an active population that drinks 4 L/day (instead of 2 L/day), multiply the unit risk by 2.

Because children drink more water relative to their body weight than do adults (U.S. EPA, 2002d), adjustments to unit risk estimates are warranted whenever they are applied in an assessment of childhood exposure.

> *For example*, to adjust the drinking water unit risk for a 9-kg infant who drinks 1 L/day (instead of a 70-kg adult who drinks 2 L/day), multiply the unit risk by [(1 L/day) / (9 kg)] / [(2 L/day) / (70 kg)] = 3.9.

Inhalation dosimetry is employed to derive the human equivalent exposure concentrations on which inhalation unit risks, and reference concentrations, are based (U.S. EPA, 1994). As described previously (see Sections 3.1.2, 3.1.3), different dosimetry methods may be employed depending on the availability of relevant data and chemical-specific characteristics of the pollutant. Consideration of lifestage-particular physiological characteristics in the dosimetry analysis may result in a refinement to the human equivalent concentration (HEC) to insure relevance in risk assessment across lifestages, or might conceivably conclude with multiple HECs, and corresponding inhalation unit risk values (e.g., separate for childhood and adulthood).

The dose-response assessment discusses the key sources of uncertainty in estimating dosimetry, including any related to lifestage. Review of this discussion and of the dosimetric analysis performed in deriving the HEC and resultant unit risk will assist in the appropriate application of inhalation unit risk values to exposure across lifestages.

4.4. EXPOSURE CHARACTERIZATION

The exposure characterization is a technical characterization that presents the assessment results and supports the risk characterization. It provides a statement of the purpose, scope, and approach used in the assessment, identifying the exposure scenarios and population subgroups covered. It provides estimates of the magnitude, frequency, duration, and distribution of exposures among members of the exposed population as the data permit. It identifies and compares the contribution of different sources, pathways, and routes of exposure. In particular, a

qualitative discussion of the strengths and limitations (uncertainties) of the data and models are presented.

The discussion of uncertainties is a critical component of the exposure characterization. Uncertainties can arise out of problems with the conceptual and mathematical models. Uncertainties can also arise from poor data quality and data that are not quite representative of the population or scenario of interest. Consider the following examples of uncertainties.

- National data (i.e., data collected to represent the entire U.S. population) may not be representative of exposures occurring within a regional or local population.

- Use of short-term data to infer chronic, lifetime exposures should be done with caution. Use of short-term data to estimate long-term exposures has the tendency to underestimate the number of people exposed while overestimating the exposure levels experienced by those in the upper end (i.e., above the 90th percentile) of the exposure distribution. For further guidance, refer to *Guidelines for Exposure Assessment* (U.S. EPA, 1992a, § 5.3.1).

- Children's behavior, including their more limited diet, may lead to relatively high but intermittent exposures. This pattern of exposure, "one that gradually declines over the developmental period and which remains relatively constant thereafter" is not accounted for in the LADD model (ILSI, 1992). Further, the physiological characteristics of children may lead to important differences in exposure. Some of these differences can be accounted for in the LADD model. For further guidance, see *Guidelines for Exposure Assessment* (U.S. EPA, 1992a, § 5.3.5.2).

Overall, the exposure characterization should provide a full description of the sources, pathways, and routes of exposure. The characterization also should include a full description of the populations assessed. In particular, highly exposed or susceptible subpopulation or lifestage should be discussed. For further guidance on the exposure characterization, consult *Guidelines*

for Exposure Assessment (U.S. EPA, 1992a), the *Policy and Guidance for Risk Characterization* (U.S. EPA, 2000b,1995) and EPA's *Rule Writer's Guide to Executive Order 13045* (especially Attachment C: Technical Support for Risk Assessors—Suggestions for Characterizing Risks to Children [U.S. EPA, 1998d]).

5. RISK CHARACTERIZATION

5.1. PURPOSE

EPA has developed general guidance on risk characterization for use in its risk assessment activities. The core of EPA's risk characterization policy (U.S. EPA, 2000b, 1995) includes the following.

> Each risk assessment prepared in support of decision making at EPA should include a risk characterization that follows the principles and reflects the values outlined in this policy. A risk characterization should be prepared in a manner that is clear, transparent, reasonable, and consistent with other risk characterizations of similar scope prepared across programs in the Agency. Further, discussion of risk in all EPA reports, presentations, decision packages, and other documents should be substantively consistent with the risk characterization. The nature of the risk characterization will depend upon the information available, the regulatory application of the risk information, and the resources (including time) available. In all cases, however, the assessment should identify and discuss all the major issues associated with determining the nature and extent of the risk and provide commentary on any constraints limiting fuller exposition.

Risk characterization should be carried out in accordance with the EPA (U.S. EPA, 2002a) and OMB (2002) information quality guidelines. EPA's risk characterization handbook (U.S. EPA, 2000b) provides detailed guidance to Agency staff. The discussion below does not attempt to duplicate this material, but it summarizes its applicability to carcinogen risk assessment.

The risk characterization includes a summary for the risk manager in a nontechnical discussion that minimizes the use of technical terms. It is an appraisal of the science that informs the risk manager in public health decisions, as do other decision-making analyses of economic,

social, or technology issues. It also serves the needs of other interested readers. The summary is an information resource for preparing risk communication information, but being somewhat more technical than desired for communication with the general public, is not itself the usual vehicle for communication with every audience.

The risk characterization also brings together the assessments of hazard, dose response, and exposure to make risk estimates for the exposure scenarios of interest. This analysis that follows the summary is generally much more extensive. It typically will identify exposure scenarios of interest in decision making and present risk analyses associated with them. Some of the analyses may concern scenarios in several media; others may examine, for example, only drinking water risks. As these cancer guidelines allow different hazard characterizations and different potencies for specified conditions, e.g., exposure level, route of exposure, or lifestage, some of the integrative analyses may need to be stratified to accommodate the appropriate combinations of parameters across relevant exposure durations.

In constructing high end estimates of risk, the assessor should bear in mind that the high-end risk is a plausible estimate of the risk for those persons at the upper end of the risk distribution (U.S. EPA, 1992a). The intent of this approach is to convey an estimate of risk in the upper range of the distribution, but to avoid estimates that are beyond the true distribution. Overly conservative assumptions, when combined, can lead to unrealistic estimates of risk. This means that when constructing estimates from a series of factors (e.g., emissions, exposure, and unit risk estimates) not all factors should be set to values that maximize exposure, dose, or effect, since this will almost always lead to an estimate that is above the 99th-percentile confidence level and may be of limited use to decisionmakers. This is particularly problematic when using unbounded lognormal factor distributions.

While it is an appropriate aim to assure protection of health and the environment in the face of scientific uncertainty, common sense, reasonable applications of assumptions and policy, and transparency are essential to avoid unrealistically high estimates. It is also important to inform risk managers of the final distribution of risk estimates (U.S. EPA, 2000b; 1995). Otherwise, risk management decisions may be made on varying levels of conservatism, leading

to misplaced risk priorities and potentially higher overall risks. (Nichols and Zeckhauser,1986; Zeckhauser and Viscusi,1990).

The risk characterization presents an integrated and balanced picture of the analysis of the hazard, dose-response, and exposure. The risk analyst should provide summaries of the evidence and results and describe the quality of available data and the degree of confidence to be placed in the risk estimates. Important features include the constraints of available data and the state of knowledge, significant scientific issues, and significant science and science policy choices that were made when alternative interpretations of data exist (U.S. EPA, 1995, 2000b). Choices made about using data or default options in the assessment are explicitly discussed in the course of analysis, and if a choice is a significant issue, it is highlighted in the summary. In situations where there are alternative approaches for a risk assessment that have significant biological support, the decisionmaker can be informed by the presentation of these alternatives along with their strengths and uncertainties.

5.2. APPLICATION

Risk characterization is a necessary part of generating any Agency report on risk, whether the report is preliminary — to support allocation of resources toward further study — or comprehensive — to support regulatory decisions. In the former case, the detail and sophistication of the characterization are appropriately small in scale; in the latter case, appropriately extensive. Even if a document covers only parts of a risk assessment (hazard and dose-response analyses, for instance), the results of these are characterized.

Risk assessment is an iterative process that grows in depth and scope in stages from screening for priority making to preliminary estimation to fuller examination in support of complex regulatory decision making. Default options may be used at any stage, but they are predominant at screening stages and are used less as more data are gathered and incorporated at later stages. Various provisions in EPA-administered statutes require decisions based on differing findings for which differing degrees of analysis are appropriate. There are close to 30 provisions within the major statutes that require decisions based on risk, hazard, or exposure assessment. For example, Agency review of pre-manufacture notices under Section 5 of the Toxic Substances

Control Act relies on screening analyses, whereas requirements for industry testing under Section 4 of that Act rely on preliminary analyses of risk or simply of exposure. In comparison, air quality criteria under the Clean Air Act rest on a rich data collection and are required by statute to undergo periodic reassessment. There are provisions that require ranking of hazards of numerous pollutants — which may be addressed through a screening level of analysis — and other provisions for which a full assessment of risk is more appropriate.

Given this range in the scope and depth of analyses, not all risk characterizations can or should be equal in coverage or depth. The risk assessor should carefully decide which issues in a particular assessment are important to present, choosing those that are noteworthy in their impact on results. For example, health effect assessments typically rely on animal data because human data are rarely available. The objective of characterization of the use of animal data is not to recount generic issues about interpreting and using animal data; Agency guidance documents cover these issues. Rather, the objective is to highlight any significant issues that arose within the particular assessment being characterized and inform the reader about significant uncertainties that affect conclusions.

5.3. PRESENTATION OF THE RISK CHARACTERIZATION SUMMARY

The presentation is a nontechnical discussion of important conclusions, issues, and uncertainties that uses the hazard, dose response, exposure, and integrative analyses for technical support. The primary technical supports within the risk assessment are the hazard characterization, dose-response characterization, and exposure characterization described in these cancer guidelines. The risk characterization is derived from these. The presentation should fulfill the aims outlined in the purpose section above.

5.4. CONTENT OF THE RISK CHARACTERIZATION SUMMARY

Specific guidance on hazard, dose-response, and exposure characterization appears in previous sections. Overall, the risk characterization routinely includes the following, capturing the important items covered in hazard, dose response, and exposure characterization:

- primary conclusions about hazard, dose response, and exposure, including alternatives with significant biological support;

- nature of key supporting information and analytic methods;

- risk estimates and their attendant uncertainties, including key uses of default options when data are missing or uncertain.

  — With linear extrapolations, risk below the POD is typically approximated by multiplying the slope factor by an estimate of exposure, i.e., Risk = Slope Factor x Exposure. For exposure levels above the POD, the dose-response model is used instead of this approximation.

  — With nonlinear extrapolations, the method of risk assessment depends on the procedure used. If a nonlinear dose-response function has been determined, it can be used with the expected exposure to estimate a risk. If an RfD or RfC was calculated, the hazard can be expressed as a *hazard quotient* (HQ), defined as the ratio of an exposure estimate over the reference dose (RfD) or reference concentration (RfC), i.e., HQ = Exposure / (RfD or RfC). From the hazard quotient, it can generally be inferred whether the nonlinear mode of action is relevant at the environmental exposure level in question;

- statement of the extent of extrapolation of risk estimates from observed data to exposure levels of interest and its implications for certainty or uncertainty in quantifying risk. The extent of extrapolation can be expressed as a *margin of exposure* (MOE), defined as the ratio of the POD over an exposure estimate (MOE = POD / Exposure);

- significant strengths and limitations of the data and analyses, including any major peer review issues;

- appropriate comparison with similar EPA risk analyses or common risks with which people may be familiar; and

- comparison with all appropriate assessments of the same problem by others.

It is often difficult to know *a priori* when or how different results of a cancer risk assessment are likely to be used by Agency economists, policy analysts, and decisionmakers, so it is important that the resulting characterizations include the necessary information for these analyses to the extent practicable. OMB and EPA guidelines for benefit-cost analysis require expected or central estimates of risk and information on the uncertainty of the estimate when it is possible or practicable. The extent of the uncertainty information needed for analysis depends, in part, on the scale of the policy being considered, with formal quantitative analysis of uncertainty being required in some cases.[6] OMB Circular A-4 (OMB, 2003) emphasizes that agencies "should try to provide some estimate of the probability distribution of regulatory benefits and costs." These OMB guidelines note, "Whenever it is possible to characterize quantitatively the probability distribution, some estimates of expected value ... must be provided in addition to ranges, variances, specified low-end and high-end percentile estimates, and other characteristics of the distribution." The risk characterization should therefore include, where practicable, expected or central estimates of risk, as well as upper and lower bounds, e.g., confidence limits, based on the POD, if not a full characterization of uncertainty of the risk. As discussed in EPA's *Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by the Environmental Protection Agency* (Appendix B), statutory mandates, such as the Safe Drinking Water Act, the Food Quality Protection Act, and the Clean

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6 Specifically, OMB guidelines state: "For rules that exceed the $1 billion annual [economic effects] threshold, a formal quantitative analysis of uncertainty is required. For rules with annual benefits and/or costs in the range from 100 million to $1 billion, you should seek to use more rigorous approaches with higher consequence rules" (OMB, 2003, page 158)

Air Act, call for the Agency to generate specific kinds of risk information, and thus these updated cancer assessment guidelines should be read in conjunction with the Agency's statutory mandates regarding risk assessment.

APPENDIX A: MAJOR DEFAULT OPTIONS

This discussion covers the major default options commonly employed when data are missing or sufficiently uncertain in a cancer risk assessment, as adopted in these cancer guidelines. These options are predominantly inferences that help use the data observed under empirical conditions in order to estimate events and outcomes under environmental conditions. Several inferential issues arise when effects seen in a subpopulation of humans or animals are used to infer potential effects in the population of environmentally exposed humans. Several more inferential issues arise in extrapolating the exposure-effect relationship observed empirically to lower-exposure environmental conditions. The following issues cover the major default areas.

- Is the presence or absence of effects observed in a human population predictive of effects in another exposed human population?
- Is the presence or absence of effects observed in an animal population predictive of effects in exposed humans?
- How do metabolic pathways relate across species and among different age groups and between sexes in humans?
- How do toxicokinetic processes relate across species and among different age groups and between sexes in humans?
- What is the relationship between the observed dose-response relationship to the relationship at lower doses?

Is the Presence or Absence of Effects Observed in a Human Population Predictive of Effects in Another Exposed Human Population?

When cancer effects in exposed humans are attributed to exposure to an agent, the default option is that the resulting data are predictive of cancer in any other exposed human population. Most studies investigating cancer outcomes in humans from exposure to agents are often studies of occupationally exposed humans. By sex, age, and general health, workers may not be representative of the general population exposed environmentally to the same agents. In such studies there is no opportunity to observe subpopulations who are likely to be under represented, such as fetuses, infants and children, women, or people in poor health, who may respond differently from healthy workers. Therefore, it is understood that this option could still underestimate the response of certain human subpopulations (NRC, 1993b, 1994).

When cancer effects are not found in an exposed human population, this information by itself is not generally sufficient to conclude that the agent poses no carcinogenic hazard to this or other populations of potentially exposed humans, including susceptible subpopulations or lifestages. This is because epidemiologic studies often have low power to detect and attribute responses and typically evaluate cancer potential in a restricted population (e.g., by age, healthy workers). The topic of susceptibility and variation is addressed further in the discussion below of quantitative default options about dose-response relationships. Well-conducted studies that fail to detect a statistically significant positive association, however, may have value and should be judged on their merits, including population size, duration of the study, the quality of the exposure characterization and measures of outcome, and the magnitude and duration of the exposure.

There is not yet enough knowledge to form a basis for any generally applicable qualitative or quantitative inference to compensate for the gap in knowledge concerning other populations. In these cancer guidelines, this problem is left to analysis in individual cases, to be attended to with further general guidance as future research and information allow. When information on a susceptible subpopulation or lifestage exists, it will be used. For example, an agent such as diethylstilbestrol (DES) causes a rare form of vaginal cancer (clear-cell adenocarcinoma) (Herbst

et al., 1971) in about 1 per 1000 of adult women whose mothers were exposed during pregnancy (Hatch et al., 1998).

Is the Presence or Absence of Effects Observed in an Animal Population Predictive of Effects in Exposed Humans? *The default option is that positive effects in animal cancer studies indicate that the agent under study can have carcinogenic potential in humans.* Thus, if no adequate human or mode of action data are present, positive effects in animal cancer studies are a basis for assessing the carcinogenic hazard to humans. This option is a public health-protective policy, and it is both appropriate and necessary, given that we do not test for carcinogenicity in humans. The option is supported by the fact that nearly all of the agents known to cause cancer in humans are carcinogenic in animals in tests that have adequate protocols (IARC, 1994; Tomatis et al., 1989; Huff, 1994). Moreover, almost one-third of human carcinogens were identified subsequent to animal testing (Huff, 1993). Further support is provided by research on the molecular biology of cancer processes, which has shown that the mechanisms of control of cell growth and differentiation are remarkably homologous among species and highly conserved in evolution. Nevertheless, the same research tools that have enabled recognition of the nature and commonality of cancer processes at the molecular level also have the power to reveal differences and instances in which animal responses are not relevant to humans (Lijinsky, 1993; U.S. EPA, 1991b). Under these cancer guidelines, available mode of action information is studied for its implications in both hazard and dose-response assessment and its ability to obviate default options.

There may be instances in which the use of an animal model would identify a hazard in animals that is not truly a hazard in humans (e.g., the alpha-2u-globulin association with renal neoplasia in male rats [U.S. EPA, 1991b]). The extent to which animal studies may yield false positive indications for humans is a matter of scientific debate. To demonstrate that a response in animals is not relevant to any human situation, adequate data to assess the relevancy issue are important.

In general, while effects seen at the highest dose tested are assumed to be appropriate for assessment, it is necessary that the experimental conditions be scrutinized. Animal studies

are conducted at high doses in order to provide statistical power, the highest dose being one that is minimally toxic (maximum tolerated dose or MTD). Consequently, the question often arises of whether a carcinogenic effect at the highest dose may be a consequence of cell killing with compensatory cell replication or of general physiological disruption rather than inherent carcinogenicity of the tested agent. There is little doubt that this may happen in some cases, but skepticism exists among some scientists that it is a pervasive problem (Ames and Gold, 1990; Melnick et al., 1993; Barrett, 1993). If adequate data demonstrate that the effects are solely the result of excessive toxicity rather than carcinogenicity of the tested agent *per se*, then the effects may be regarded as not appropriate to include in assessment of the potential for human carcinogenicity of the agent. This is a matter of expert judgment, with consideration given to all of the data available about the agent, including effects in other toxicity studies, structure-activity relationships, and effects on growth control and differentiation.

When cancer effects are not found in well-conducted animal cancer studies in two or more appropriate species and other information does not support the carcinogenic potential of the agent, these data provide a basis for concluding that the agent is not likely to possess human carcinogenic potential, in the absence of human data to the contrary. This default option about lack of cancer effects has limitations. It is recognized that animal studies (and epidemiologic studies as well) have very low power to detect cancer effects. Detection of a 10% tumor incidence is generally the limit of power with standard protocols for animal studies (with the exception of rare tumors that are virtually markers for a particular agent, e.g., angiosarcoma caused by vinyl chloride). In some situations, the tested animal species may not be predictive of effects in humans; for example, arsenic shows only minimal or no effect in animals, whereas it is clearly positive in humans. Therefore, it is important to consider other information as well; absence of mutagenic activity or absence of carcinogenic activity among structural analogues can increase the confidence that negative results in animal studies indicate a lack of human hazard.

Another limitation is that standard animal study protocols are not yet available for effectively studying perinatal effects. The potential for effects on the very young generally should be considered separately. Under existing Agency policy (U.S. EPA, 1997a, b), perinatal studies

accomplished by modification of existing adult bioassay protocols are important in special circumstances.

Target organ concordance is not a prerequisite for evaluating the implications of animal study results for humans. Target organs of carcinogenesis for agents that cause cancer in both animals and humans are most often concordant at one or more sites (Tomatis et al., 1989; Huff, 1994). However, concordance by site is not uniform. The mechanisms of control of cell growth and differentiation are concordant among species, but there are marked differences among species in the way control is managed in various tissues. For example, in humans, mutations of the tumor suppressor genes p53 and retinoblastoma are frequently observed genetic changes in tumors. These tumor-suppressor genes are also observed to be operating in some rodent tissues, but other growth control mechanisms predominate in other rodent tissues. Thus, an animal response may be due to changes in a control that are relevant to humans but appear in animals in a different way.

However, it is appropriate under these cancer guidelines to consider the influences of route of exposure, metabolism, and, particularly, some modes of action that may either support or not support target organ concordance between animals and humans. When data allow, these influences are considered in deciding whether agent-, species-, or organ-specific situations are appropriate to use in preference to this default assumption (NRC, 1994). In contrast, use of toxicokinetic modeling inherently assumes site concordance, as these models are used to estimate delivered dose to a particular tissue or organ in humans on the basis of the same tissue or organ from animal data.

The default is to include benign tumors observed in animal studies in the assessment of animal tumor incidence, if such tumors have the capacity to progress to the malignancies with which they are associated. This default is consistent with the approach of the National Toxicology Program and the International Agency for Research on Cancer and is more protective of public health than not including benign tumors in the assessment; benign and malignant tumors are treated as representative of related responses to the test agent (McConnell et al., 1986), which is scientifically appropriate. Nonetheless, in assessing findings from animal studies, a greater proportion of malignancy is weighed more heavily than is a response with a

greater proportion of benign tumors. Greater frequency of malignancy of a particular tumor type in comparison with other tumor responses observed in an animal study is also a factor to be considered in selecting the response to be used in dose-response assessment.

Benign tumors that are not observed to progress to malignancy are assessed on a case-by-case basis. There is a range of possibilities for the overall significance of benign tumors. They may deserve attention because they are serious health problems even though they are not malignant; for instance, benign tumors may be a health risk because of their effect on the function of a target tissue, such as the brain. They may be significant indicators of the need for further testing of an agent if they are observed in a short-term test protocol, or such an observation may add to the overall weight of evidence if the same agent causes malignancies in a long-term study. Knowledge of the mode of action associated with a benign tumor response may aid in the interpretation of other tumor responses associated with the same agent.

How Do Metabolic Pathways Relate Across Species and Among Different Age Groups and Between Sexes in Humans?

The default option is that there is a similarity of the basic pathways of metabolism and the occurrence of metabolites in tissues in regard to the species-to-species extrapolation of cancer hazard and risk. If comparative metabolism studies were to show no similarity between the tested species and humans and a metabolite(s) was the active form, there would be less support for an inference that the animal response(s) relates to humans. In other cases, parameters of metabolism may vary quantitatively between species; this becomes a factor in deciding on an appropriate human-equivalent dose based on animal studies, optimally in the context of a toxicokinetic model. Although the basic pathways are assumed to be the same among humans, the presence of polymorphisms in the general population and factors such as the maturation of the pathways in infants should be considered. The active form of an agent may be present to differing degrees, or it may be completely absent, which may result in greater or lesser risk for subpopulations.

How Do Toxicokinetic Processes Relate Across Species and Among Different Age Groups and Between Sexes in Humans?

A major issue is how to estimate human-equivalent doses in extrapolating from animal studies. *As a default for oral exposure, a human equivalent dose for adults is estimated from data on another species by an adjustment of animal applied oral dose by a scaling factor based on body weight to the 3/4 power. The same factor is used for children because it is slightly more protective than using children's body weight (see Section 3.1.3).* This adjustment factor is used because it represents scaling of metabolic rate across animals of different size. Because the factor adjusts for a parameter that can be improved on and brought into more sophisticated toxicokinetic modeling when such data become available, they are usually preferable to the default option.

For inhalation exposure, a human equivalent dose for adults is estimated by default methodologies that provide estimates of lung deposition and internal dose (U.S. EPA, 1994). The methodologies can be refined to more sophisticated forms with data on toxicokinetic and metabolic parameters of the specific agent. This default option, like the one for oral exposure, is selected in part because it lays a foundation for incorporating better data. The use of information to improve dose estimation from applied to internal to delivered dose is encouraged, including use of toxicokinetic modeling instead of any default, where data are available.

There are important differences between infants, adults, and older adults in the processes of absorption, distribution, and elimination; for example, infants tend to absorb metals through the gut more rapidly and more efficiently than do older children or adults (Calabrese, 1986). Renal elimination is also not as efficient in infants. Although these processes reach adult competency at about the time of weaning, they may have important implications, particularly when the dose-response relationship for an agent is considered to be nonlinear and there is an exposure scenario disproportionately affecting infants, because in these cases the magnitude of dose is more pertinent than the usual approach in linear extrapolation of averaging dose across a lifetime. Efficiency of intestinal absorption in older adults tends to be generally less overall for most chemicals. Another notable difference is that, post-weaning (about 1 year), children have a

higher metabolic rate than do adults (Renwick, 1998), and they may toxify or detoxify agents at a correspondingly higher rate.

For a route-to-route exposure extrapolation, *the default option is that an agent that causes internal tumors by one route of exposure will be carcinogenic by another route if it is absorbed by the second route to give an internal dose.* This is a qualitative option and is considered to be public-health protective. The rationale is that for internal tumors an internal dose is significant no matter what the route of exposure. Additionally, the metabolism of the agent will be qualitatively the same for an internal dose. The issue of quantitative extrapolation of the dose-response relationship from one route to another is addressed case by case. Quantitative extrapolation is complicated by considerations such as first-pass metabolism.

What Is the Correlation of the Observed Dose-Response Relationship to the Relationship at Lower Doses?

If sufficient data are available, a biologically based model for both the observed range and extrapolation below that range may be used. Although no standard biologically based models are in existence, an agent-specific model may be developed if extensive data exist in a particular case and the purpose of the assessment justifies the investment of the resources needed. *The default procedure for the observed range of data when a biologically based model is not used is to use a curve-fitting model for incidence data.*

In the absence of data supporting a biologically based model for extrapolation outside of the observed range, the choice of approach is based on the view of mode of action of the agent arrived at in the hazard assessment. If more than one approach (e.g., both a nonlinear and linear approach) are supported by the data, they should be used and presented to the decisionmaker.

A linear extrapolation approach is used when the mode of action information is supportive of linearity or mode of action is not understood. The linear approach is used when a view of the mode of action indicates a linear response, for example, when a conclusion is made that an agent directly causes alterations in DNA, a kind of interaction that not only theoretically requires one reaction but also is likely to be additive to ongoing, spontaneous gene mutation. Other kinds of activity may have linear implications, for example, linear rate-limiting steps

would also support a linear procedure. The linear approach is to draw a straight line between a point of departure from observed data, generally as a default, an LED chosen to be representative of the lower end of the observed range, and the origin (zero incremental dose, zero incremental response). This approach is generally considered to be public-health protective.

The linear default is thought to generally provide an upper-bound calculation of potential risk at low doses, for example, a 1/100,000 to 1/1,000,000 risk. This upper bound is thought to be public-health protective at low doses for the range of human variation, considering the typical Agency target range for risk management of 1/1,000,000 to 1/10,000, although it may not completely be so (Bois et al., 1995) if pre-existing disease or genetic constitution place a percentage of the population at greater risk from exposure to carcinogens. The question of what may be the actual variation in human susceptibility is one that was discussed in general in the NRC (1994) report, as well as the NRC report on pesticides in children and infants (NRC, 1993b). NRC has recommended research on the question, and EPA and other agencies are conducting such research. Given the current state of knowledge, EPA will assume that the linear default procedure adequately accounts for human variation unless there is case-specific information for a given agent or mode of action that indicates a particularly susceptible subpopulation or lifestage, in which case the special information will be used.

When adequate data on mode of action provide sufficient evidence to support a nonlinear mode of action for the general population and/or any subpopulations of concern, a different approach — a reference dose/reference concentration that assumes that nonlinearity – is used. The POD is again generally an BMDL when incidence data are modeled. A sufficient basis to support this nonlinear procedure is likely to include data on responses that are key events integral to the carcinogenic process. This means that the POD may be based on these precursor response data, for example, hormone levels or mitogenic effects rather than tumor incidence data.

When the mode of action information indicates that the dose-response function may be adequately described by both a linear and a nonlinear approach, then the results of both the linear and the nonlinear analyses are presented. An assessment may use both linear and nonlinear approaches if different responses are thought to result from different modes of action or a response appears to be very different at high and low doses due to influence of separate

modes of action. The results may be needed for assessment of combined risk from agents that have common modes of action.

Absent data to the contrary, the default assumption is that the cumulative dose received over a lifetime, expressed as a lifetime average daily dose or lifetime average daily exposure, is an appropriate measure of dose or exposure. This assumes that a high dose of such an agent received over a shorter period of time is equivalent to a low dose spread over a lifetime. This is thought to be a relatively public-health-protective option and has some empirical support (Monro, 1992). A counter example, i.e., effects of short-term, high exposure levels that result in subsequent cancer development, is treatment of cancer patients with certain chemotherapeutic agents. When sufficient information is available to support a different approach, it can be used. For example, short-term exposure estimates (several days to several months) may be more appropriate than the lifetime average daily dose. In these cases, both agent concentration and duration are likely to be important, because such effects may be reversible at cessation of very short-term exposures.

APPENDIX B: EPA's GUIDANCE FOR DATA QUALITY ASSESSMENT

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DEQ Position on the Arsenic Modeling Addendum To the Perpetua Resources Stibnite Gold Project Permit to Construct Application

(by Kevin Schilling, Stationary Source Air Modeling Supervisor)

1.0 Introduction

DEQ received an *Arsenic Modeling Addendum* from Air Science following discussions of concerns with existing Section 210 TAP analyses to support the Perpetua Resources Stibnite Gold Project (SGP) Permit to Construct application. This paper summarizes the process to this point, briefly describes the addendum, points out challenges working with the addendum within the context of existing sections of the application, and outlines potential paths forward.

2.0 Review of Permitting Project to this Point

2.1 First Two Comment Periods

In response to comments from the first public comment period and DEQ's further evaluation of TAP source applicability to Section 210 (and the exemption of NESHAP sources from analyses), a revised TAP emission inventory and air impact modeling analysis was performed. Results of these revisions and a new proposed Statement of Basis and draft permit were then put out for a second public comment period and public informational meeting.

Additional concerns of arsenic emissions and proper exclusion of NESHAP sources arose after the second public comment period in March 2021. In general, the issue was that certain TAP sources were excluded from the TAP increment compliance demonstration that should have been included. Of most importance was fugitive carcinogenic emissions from vehicle traffic on mining roads and other fugitive emission sources. Arsenic was the TAP driving the analyses.

2.2 Path Leading to Arsenic Modeling Addendum

Air Sciences (Perpetua's consultant) and Perpetua met with DEQ on June 17, 2021, to discuss potential options to achieve acceptable modeled impacts. Some of these "brainstorming ideas" discussed included: 1) demonstrate that T-RACT is used for arsenic sources, thereby increasing acceptable impacts by a factor of 10; 2) refine arsenic emission estimates for sources, and

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especially for road dust fugitive emission sources; 3) adjust averaging periods of modeled TAP impacts to reflect a longer period, as Acceptable Ambient Concentrations of Carcinogens are based on a 70-year exposure and the life of the mine is only 16 years; 4) perhaps propose permit operation/production limits based on multiple years (such as a 5-year rolling average); 5) define operational levels closer to what is actually anticipated. Ambient monitoring was mentioned as a means to increase the level of confidence if compliance is still not confidently demonstrated.

2.3 Arsenic Modeling Addendum Contents

On July 8, 2021, Air Sciences submitted an *Arsenic Modeling Addendum* for DEQ review. The addendum states the purpose is to address a public comment request that analyses be provided to assure compliance with Idaho Air Rules Section 161 regarding total project-wide arsenic emissions. The addendum also states that it "provides additional information requested by IDEQ to support its determination that the HAP/TAP emissions from the SGP comply with applicable regulations."

The addendum is based on operations as described in the SGP Refined Proposed Action – ModPRO2, which is the basis of a Supplemental Draft EIS currently in preparation by the Forest Service. ModPRO2 accounts for project improvements and refinements, with a smaller footprint of the mine.

The mine operational model used for the *Arsenic Modeling Addendum* is vastly different than that used in the original application. The original permit application provides a description of maximum operations of numerous emission sources that may occur at the facility, with an air quality assessment of emissions from those operations. ModPRO2 does not use this approach, but alternatively provides a best estimate of actual operations over the life of the mine. For example, the current DEQ Statement of Basis lists facility-wide arsenic emissions at 2.4 ton/year, but ModPRO2 lists emissions at 0.22 ton/year (as averaged over the 16 year life of the mine).

3.0 Why DEQ cannot Move Forward with Permit Issuance at this Point

DEQ is at the point in the permitting process where finishing touches are typically put on a permit or, at the most, slight adjustments are made to analyses or supporting data. Instead, with the concern over Section 210 analyses for arsenic we have an *Arsenic Modeling Addendum*

that, when combined with the existing application, looks like the confused mess of a "dog's breakfast."

First, how is the *Arsenic Modeling Addendum* to be used? Is it to replace the Section 210 analyses in the existing application (which DEQ asserts is incorrect), is it to supplement those analyses, or is it to merely respond to public concern about facility-wide arsenic impacts. Secondly, the addendum uses a substantially different approach from what is described in the application, Statement of Basis, and the draft PTC. Operational rates used for the inventory supporting the addendum lack substantiation and are radically different than those presented in other sections of the application. We're left wondering what should be disregarded in the application because of conflicting statements in the addendum. At this point, how does DEQ handle issues and concerns we may have on methods and data used in the addendum? How will permit limits be crafted to make claims in the addendum legally and practically enforceable, even to a minimally acceptable level? How does DEQ establish a timeline for permitting milestones at this point?

3.1 DEQ Permitting Process

Idaho Air Rules are very clear on the permit issuance process. As stated in Section 209, within 30 days after application submittal DEQ must determine whether the application is complete or "whether more information must be submitted . . ." Then, within 60 days DEQ must either approve or deny the permit. Once the application is complete, then the permitting decision is made based on that information submitted. These deadlines form a critical component of DEQ's performance measures designed to assure timely permitting.

Submission of new information, data, and analyses after the application has been declared complete constitutes an "out of scope" change, and a new permit application must be submitted. This is done for two important reasons: 1) the opportunity for public comment is based on the scope, data, and analyses provided in the original application; 2) entertaining substantial changes during the permit drafting phase requires substantial reworking by DEQ permitting staff, and keeping staff priorities on reworking a project is not fair to other permit applications recently submitted that may be complete. DEQ does periodically accept complementary information or minor corrections/clarifications after the completeness determination, as those do not substantially alter the underlying technical and regulatory basis of permit issuance. However, DEQ typically requires application withdraw and resubmittal for substantial changes that affect the emission inventory and especially when such changes require remodeling of air impacts.

3.3 Incomplete or Inadequate TAPs Compliance Demonstration

DEQ determined, after the March 2021 comment period, that TAP analyses used to demonstrate compliance with Idaho Air Rules Section 210 had again incorrectly excluded some TAP sources. It was assumed the *Arsenic Modeling Addendum* would address this issue. The addendum attempts to address arsenic, but does not provide any analyses of other TAPs for either modeling applicability or results from impact modeling.

3.4 Substantial change in Regulatory Approach

The *Arsenic Modeling Addendum* is a complete change in the regulatory approach used to demonstrate compliance with toxics. It abandons the Section 210 approach used in the application for an arsenic Section 161/210 hybrid analysis. The methods used in this unique analysis should be thoroughly vetted by DEQ well before a permit application is submitted. A month before permit issuance is not the time for developing a creative permitting approach with new emission inventory approaches, new modeling analyses, and challenges for crafting enforceable permit provisions/limits.

3.5 Inconsistency between NAAQS Inventory and Inventory used for Addendum

Emission inventories are estimated using emission source identification (including location and number of like sources), emission factors, emission control measures, operational levels, and operational schedules. Typically and most simply, permitting is done using maximum applicable factors, minimum control measures, and maximum operational levels and schedules. This makes for a relatively simple permit where claimed emissions and operations are easily made into verifiable permit conditions and minimal monitoring can assure compliance with the permit and, therefore, the underlying assumptions used in analyses.

The originally submitted application and previous revisions largely used maximum rates, with use of some operational scenarios where compliance with NAAQS was challenging by assuming maximum rates of all sources. The *Arsenic Modeling Addendum* uses an inventory that mostly uses the established emission factors and emission control measures; however, it accounts for temporally and spatially varying operational levels and schedules such that emissions are vastly less than those listed in other parts of the application. The addendum accounts for different operations and operational rates for each year of mine operation. Not only is there a question on whether the operational levels and schedules in the addendum can be translated into reasonably enforceable permit conditions/limits, but it is uncertain how other portions of the application and draft permit may be affected.

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5.7 Carcinogenic TAP Modeling Lifetime Exposure Adjustment

Maximum modeled concentrations for carcinogenic TAPs were adjusted to account for the life-of-mine production limits, which affects the lifetime exposure.

PRI evaluated the highest modeled annual carcinogenic TAP concentration from each of the 14 modeling scenarios for lifetime exposure as follows:

$$Lifetime\ exposure\ \left(\frac{\mu g}{m^3}\right) = \frac{Highest\ annual\ concentration\ \left(\frac{\mu g}{m^3}\right) \times 16\ (mine\ operation\ years)}{70\ (years, lifetime\ exposure)}$$

This equation assumes that the highest annual concentration from the 14 modeling scenarios is repeated for 16 years of mining operation. This was then averaged over 70 years to calculate the 70-year lifetime exposure.

PRI and Air Sciences contend that calculating lifetime exposure based on 16 years of mining operation is conservative. The annual emissions for carcinogenic TAP modeling are based on 135,000 tons/day (see Section 5.1 of this *Modeling Review Attachment*) and 365 days per year. Over 16 years, this equates to a potential mining production of 788.4 million tons:

$$\frac{135{,}000\ \left(\frac{tons}{day}\right) \times 365\ \left(\frac{days}{year}\right) \times 16\ years}{1{,}000{,}000\ \left(\frac{tons}{million\ ton}\right)} = 788.4\ million\ tons$$

The actual life-of-mine total production as described in the SGP *Refined Proposed Action* (*ModPRO2*) mine plan is only 402.86 million tons (Perpetua 2021), which is 51.1% of the potential life-of-mine production represented in the above equation and related emission evaluations.

5.8 Arsenic Compliance Demonstration for Modeling Scenarios W1-W4

To demonstrate compliance with the AACC for arsenic, PRI applied two additional operating limitations:

- The removal of Modeling Scenario W5 as a potential operating scenario
- Limiting the West End Pit's life-of-mine potential mining production to 50% of the total life-of-mine potential mining production of 788.4 million tons: 50% * 788.4 million tons = 394.2 million tons

PRI has determined that the West End Development Rock Storage Facility (DRSF) will not be constructed. This change eliminated Modeling Scenario W5 from the arsenic modeling evaluation. The remaining four West End Pit modeling scenarios (W1–W4) are evaluated using the 70-year lifetime exposure equation from Section 5.7 and adjusting for the proposed West End Pit life-of-mine production limit of 50% of the total production as follows:

$$LifeExpose_{Wi,j,n} = \left[\left(WEPExpose_{Wi,n}\right)(50\%) + \left(nonWEPExpose_{Sj,n}\right)(50\%)\right]\left[\frac{16\ year\ LOM}{70\ year\ exposure}\right]$$

where:

W*i*	=	West End Pit scenario, where *i* = 1 to 4.
S*j*	=	non West End Pit scenario, where *j* = B1, B2, H1, H2, H3, H4, Y1, Y2, and Y3.
n	=	specific receptor.
$LifeExpose_{Wi,j,n}$	=	lifetime exposure in µg/m^3 for West End Pit scenario *i*, non West End Pit scenario *j*, at receptor *n*.
$WEPExpose_{Wi,n}$	=	annual maximum impact in µg/m^3 for West End Pit scenario *i* at receptor *n*.
$nonWEPExpose_{Sj,n}$	=	annual maximum impact in µg/m^3 for non West End Pit scenario *j* at receptor *n*.
16 year LOM	=	maximum life-of-mine.
70 year exposure	=	Lifetime exposure used for development of AACCs in *Idaho Air Rules*.

The above equation was used to calculate the lifetime arsenic exposure from the West End Pit scenarios (W1–W4) on a receptor-by-receptor basis. Combining the concentrations from Modeling Scenarios W1–W4 with the highest concentration from the remaining non-West End Pit scenarios (B1, B2, H1, H2, H3, H4, Y1, Y2, or Y3) conservatively ensures that the maximum potential impacts from applicable sources are evaluated and remain below AACCs.

PRI contends that calculating lifetime arsenic exposure based on the proposed West End Pit life-of-mine production limit of 50% of the total production is conservative. The actual life-of-mine total production from the West End Pit as described in the ModPRO2 mine plan is only 198.26 million tons (Perpetua 2021), which is 50.3% of the proposed West End Pit life-of-mine production limit of 394.2 million tons.

6.0 Impact Results

TAP impact analysis results, as submitted in the *TAP Addendum* and as further assessed by DEQ, are discussed in this section. The effect of various operational refinements also reduced PM_{10} and $PM_{2.5}$ impacts, and this is discussed in Section 6.2.

6.1 TAP Impact Analyses Results

This section describes the revised TAP impact analyses and demonstrates that applicable TAP emissions resulting from operation of the SGP will not result in increased impacts that exceed AACs or AACCs.

6.1.1 Modeling Non-Carcinogenic TAPs

The non-carcinogenic TAPs subject to impact modeling requirements to demonstrate compliance with AACs of *Idaho Air Rules* Section 585 were modeled at the emission levels shown in Table 1 above. The maximum 24-hour modeled concentration for each of the 14 modeling scenarios demonstrates compliance with the applicable AAC, as summarized below in Table 5. PRI elected to include Scenario W5 in the modeling analysis for non-carcinogenic TAPs. Figure 1 illustrates the locations of the maximum impacts for each non-carcinogenic TAP.

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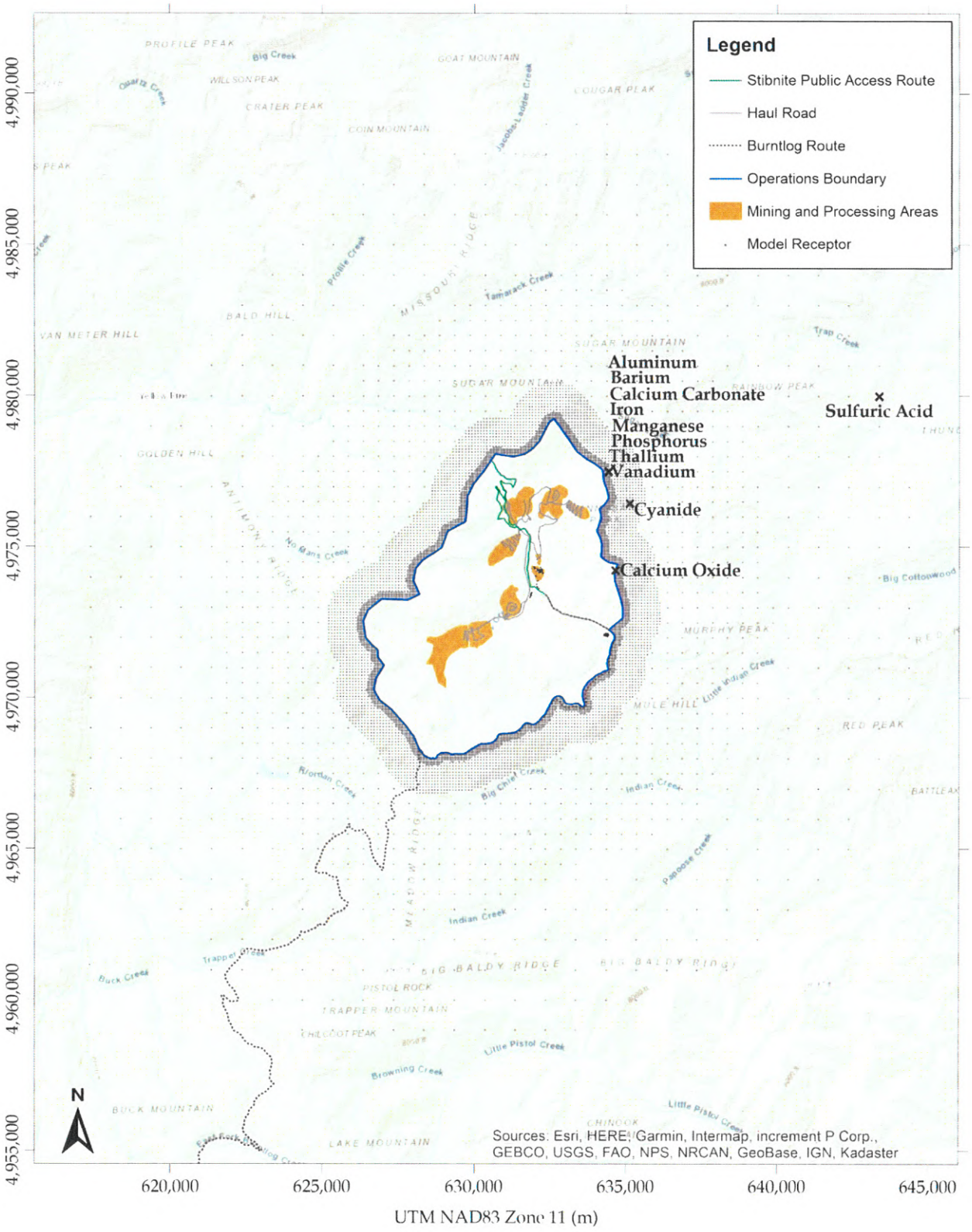
Table 5. RESULTS FOR TAPS IMPACT ANALYSES FOR NON-CARCINOGENIC TAPS.					
Toxic Air Pollutant	**Averaging Time**	**Maximum Modeled Concentration ($\mu g/m^3$)[a]**	**Model Scenario**	**AAC[b] ($\mu g/m^3$)**	**Percent of AAC**
Aluminum	24-hour	6.17	W5	500	1.23%
Barium	24-hour	0.07	W5	25	0.28%
Calcium carbonate	24-hour	1.22	W5	500	0.24%
Calcium oxide	24-hour	0.15	All	100	0.15%
Cyanide	24-hour	0.20	All	250	0.08%
Iron	24-hour	1.58	W5	50	3.16%
Manganese	24-hour	0.03	W5	250	0.01%
Phosphorus	24-hour	0.06	W5	5	1.20%
Sulfuric acid	24-hour	0.41	All	50	0.82%
Thallium	24-hour	0.001	W5	5	0.02%
Vanadium	24-hour	0.002	W5	2.5	0.08%

a. Micrograms per cubic meter.
b. Acceptable Ambient Concentration of a Non-carcinogenic TAP.

Figure 1. SGP NON-CARCINOGENIC MAXIMUM TAP IMPACT LOCATIONS.



6.1.2 Modeling Carcinogenic TAPs

The carcinogenic TAPs subject to impact modeling requirements to demonstrate compliance with AACCs of *Idaho Air Rules* Section 586 were modeled using an emission inventory that includes the T-RACT controls, long-term mining production limits, and other emission inventory refinements, as described in Section 4.0 and 5.0 of this *Modeling Review Attachment*.

The maximum modeled impact for each of the 14 modeling scenarios demonstrated compliance with the T-RACT AACC, as summarized below in Table 6. The SGP maximum concentrations were adjusted to account for the life-of-mine production limits, which affect the lifetime exposure, and to account for the elimination of Modeling Scenario W5. See Sections 5.7 and 5.8 of this *Modeling Review Attachment* for more detail. The locations of the maximum impacts for each carcinogenic TAP are presented in Figure 2. Arsenic concentrations are considerably lower in areas away from the location of maximum impact as shown in Figure 3.

Table 6. RESULTS FOR TAPS IMPACT ANALYSES FOR CARCINOGENIC TAPS.

Toxic Air Pollutant	Averaging Time	Maximum Modeled Lifetime Exposure Concentration ($\mu g/m^3$)[a,b]	Model Scenario	AACC[c] ($\mu g/m^3$)	T-RACT[d] AACC	Percent of T-RACT AACC
Arsenic	Annual	0.00095	W2	0.00023	0.0023	41.30%
Beryllium	Annual	0.00001	W1	0.0042	0.042	0.02%
Cadmium	Annual	0.000002	W1	0.00056	0.0056	0.04%
Formaldehyde	Annual	0.00007	W1	0.077	0.77	0.01%
Nickel	Annual	0.00001	W1	0.042	0.42	<0.01%

a. Micrograms per cubic meter.
b. The lifetime exposure concentrations are based on the proposed restrictions discussed in Sections 5.7 and 5.8 of this *Modeling Review Attachment.*
c. Acceptable Ambient Concentration of a Carcinogenic TAP.
d. Toxic Air Pollutant Reasonably Available Control Technology allows the AACCs to be increased by a factor of ten per *Idaho Air Rules* Section 210.12(b).

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BEFORE THE BOARD OF ENVIRONMENTAL QUALITY
STATE OF IDAHO

IN THE MATTER OF AIR QUALITY PERMIT TO CONSTRUCT P-2019.0047	)	Agency Case No. 0101-22-01
	)	OAH Case No. 23-245-01
NEZ PERCE TRIBE, IDAHO CONSERVATION LEAGUE, and SAVE THE SOUTH FORK SALMON	)	**EXPERT DECLARATION OF IAN H. VON LINDERN, P.E., Ph.D.**
Petitioners,	)	
v.	)	
IDAHO DEPARTMENT OF ENVIRONMENTAL QUALITY,	)	
Respondent,	)	
and	)	
PERPETUA RESOURCES IDAHO, INC.	)	
Intervenor-Respondent.	)	

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I, Ian H. von Lindern, P.E., Ph.D., hereby declare under penalty of perjury and pursuant to the law of the State of Idaho that the foregoing is true and correct:

QUALIFICATIONS

Name and Affiliation

1. My name is Ian von Lindern. I reside in Moscow, Idaho. I am a licensed Professional Engineer in Chemical Engineering in Idaho (License # 3044). I have practiced in the disciplines of Environmental Engineering and Risk Assessment in Idaho for the last 50 years. I was President and Principal Scientist for TerraGraphics Environmental Engineering with offices in Moscow, Kellogg, and Boise, Idaho for 30 years, retiring in 2016. TerraGraphics was the Idaho Department of Environmental Quality's (DEQ) prime consultant for the Bunker Hill Superfund Site (BHSF) and I was Project Manager and lead risk assessor for both the BHSF and the Coeur d'Alene Basin Superfund Sites from 1984 to 2014.

2. Since retiring from the consulting business, I co-founded the non-profit humanitarian organization TerraGraphics International Foundation (TIFO) and have continued to work in mining-related health and safety issues in low-income countries. TIFO's mission is to assist mining and mineral processing communities to operate as safely as practicable while maintaining essential economic activities. In that regard, we support scientifically sound and transparent analyses of the environmental and human health issues faced by mining communities, and the development of local solutions implemented within community socio-economic and cultural capabilities. Under my direction in the last ten years, TIFO has conducted and completed site characterization, risk assessment, and risk mitigation projects in

Russia, China, Peru, Dominican Republic, Senegal, Nigeria, Kyrgyzstan, Uzbekistan, and the Duck Valley Shoshone Paiute Reservation in Idaho and Nevada.

Education and Experience

3. I hold a B.S. degree in Chemical Engineering from Carnegie-Mellon University, Pittsburgh, Pennsylvania and Masters and Ph.D. degrees in Environmental Science and Engineering from Yale University, New Haven Connecticut, specializing in air pollution and public health. I have served on numerous advisory committees and the U.S. Environmental Protection Agency's (EPA) Science Advisory Board and Clean Air Science Advisory Committee on several occasions from 1975 to 2018, advising on topics relating to exposure and risk assessment in childhood heavy metal poisoning. During that tenure, I directed more than 30 major environmental health investigations at mining and smelting sites, both nationally and internationally. A current C.V. is attached.[1]

Relevant Projects and Assignments

4. I was the Regional Environmental Engineer for DEQ's predecessor agencies in both the Coeur d'Alene and Twin Falls offices. In that capacity, I processed air quality permits for the Agency for several years at the major mining and smelting operations in the State during the 1970s, and early 1980s, including the Bunker Hill Mining and Metallurgical Complex, the last U.S. operational antimony smelter at Big Creek, Idaho, and numerous mining operations in North and Central Idaho. I designed and directed the implementation of the Silver Valley Lead Health Study that investigated and provided emergency response to the childhood lead poisoning epidemic in the Coeur d'Alene mining district in the 1970-80s.

[1] Exhibit A.

5. I have particular experience with implementing EPA risk assessment guidance in Idaho. Beginning in 1984, DEQ's predecessor, Idaho Department of Health and Welfare-Division of Environment (IDHW-DOE) was the lead agency implementing the Risk Assessment and Cleanup Management Plan developed for the populated areas of the Bunker Hill Superfund Site (BHSS). The BHSS was the U.S. second largest Superfund site, and IDHW-DOE was among the first health/environmental agencies to implement the EPA Risk Assessment Guidance for Superfund (RAGS) in the late 1980s.

6. As Project Manager, I was responsible for developing and implementing the risk assessment/risk management protocols, and cleanup plan for the BHSS in collaboration with several State, federal, tribal, local governments, and industry. The project was monitored and collaboratively developed by several entities including EPA Regions VIII and X, the EPA National Center for Environmental Assessment (NCEA), EPA Headquarters, the Coeur d'Alene Tribe, the Panhandle Health District, and the States of Montana and Washington. I also served on a sub-committee of the EPA Science Advisory Board evaluating the consistency of heavy metals regulation across EPA Program Offices in the early 1990s.

7. Based on that experience, IDHW-DOE requested that I participate on the advisory committee regarding development of the toxic air pollutant (TAP) rules for the State. As a result, I had a diverse perspective in the development of the TAPS rules that afforded reasonable health protectiveness while relieving the regulators and industry of the burden of the risk assessment and risk management protocols evolving at the time. I continued as DEQ BHSS lead risk assessor until 2014.

8. In my most relevant recent experience, I am working with the international humanitarian organization Médecins Sans Frontières (MSF, or Doctors Without Borders) assisting the Kyrgyz Republic Ministry of Health in developing health protective strategies to reopen both mercury and antimony smelters in Batken, Kyrgyzstan. These facilities were among the largest mercury and antimony producers in the former Soviet Union and are essential to the regional economy.

9. TIFO is currently engaged with MSF, the U.S. Department of State, the Massachusetts College of Pharmacy and Health Sciences, and the Kyrgyz Ministry of Health in conducting risk assessment and risk mitigation activities in active and abandoned Kyrgyz antimony and mercury mining communities. Biological monitoring of the local populations indicates many children and reproductive aged women have arsenic and antimony blood and urine levels exceeding international norms. The principal source of metals contamination are mining-related fugitive dusts contaminating the community water, soil, air, and food sources.

10. I am the lead risk assessor for these projects and have produced several major reports in the last five years. The project is currently engaged in implementing medical, environmental, public health advocacy and educational interventions to reduce exposures and health risks. As such, I have considerable insight and experience with the issues associated with the proposed antimony-gold operation at Stibnite.

11. Over the past five years, I have monitored the development of the U.S. Forest Service Draft Environmental Impact Statement (DEIS) for the Stibnite Gold Project (SGP) and have reviewed and submitted comments regarding the several revisions of the Draft Permit to Construct (PTC) and associated support documents. As a result, I am familiar with the many

related issues, and particularly those related to contaminants of potential human health and environmental toxicity concerns.

ASSIGNMENT

12. My understanding is that the Board of Environmental Quality has remanded the PTC to the Hearing Officer for additional consideration of DEQ's analyses of ambient air arsenic and carcinogenic risk issues. The Petitioners in this case have requested that I provide an expert opinion regarding the Board of Environmental Quality conclusions and the Respondent's and Intervenor-Respondent's Declarations. I understand the purpose of my opinion is to assist the Hearing Officer regarding additional factual evidence on the ambient air concentration analysis performed by DEQ for the PTC analysis.

DOCUMENTS REVIEWED

13. For this assignment, I have reviewed the transcript of the May 1, 2024 special meeting of the Idaho Board of Environmental Quality in the matter of Air Quality Permit to Construct Issued to Perpetua Resources Idaho, Inc. (agency case number 11 0101-22-01)[2], the May 9, 2024 FINAL ORDER FROM THE BOARD, Case Docket No. 010-22-01 OAH Case No. 23-245-01 (Final Order in the Matter of Air Quality Permit to Construct P-2019.0045)[3], the subsequent May 23, 2024 Memorandum in Support of Joint Motion for Reconsideration and/or Clarification of Final Order,[4] the subsequent June 12, 2024, ORDER ON PETITIONS FOR RECONSIDERATION AND/OR CLARIFICATION OF FINAL ORDER[5], and the July 8, 2024 Scheduling Order.[6]

[2] TR 0156.
[3] REC 3695.
[4] REC 3731.
[5] REC 3835.
[6] REC 3867.

14. I have also reviewed the two DEQ Respondent Declarations and attached materials: EXPERT DECLARATION OF KEVIN SCHILLING and EXPERT DECLARATION OF NORKA E. PADEN, Ph.D., two Perpetua Intervenor-Respondent Declarations and attached materials: EXPERT DECLARATION OF KEVIN LEWIS and EXPERT DECLARATION OF THERESA LOPEZ, and the Petitioner Declaration and attached materials: DECLARATION OF WILL TIEDEMANN.

SUMMARY OF CONCLUSIONS

15. I have reviewed Idaho Board of Environmental Quality's Final Order and understand and agree with the Board's conclusions that:

a. DEQ Did Not Act Reasonably and in Accordance with Law When it Analyzed the Ambient Arsenic Air Concentrations for the SGP;

b. DEQ did not Act Reasonably in Using a Five-Year Rolling Average for T-RACT that was not Properly Supported by Permit Conditions;

c. There was Insufficient Evidence to Support the T-RACT Analysis Limiting the Non-West End Pit Production Limit; and

d. DEQ Did Not Act Reasonably and in Accordance with Law When it Applied the 16/70 Calculation to the Ambient Arsenic Air Concentration Analysis.

16. I have reviewed the transcript of the May 1, 2024 special meeting of the Idaho Board of Environmental Quality. I also concur with Vice Chair McMillan's testimony that:

> . . . DEQ has misinterpreted how the acceptable ambient concentration for carcinogens, the AACC, must be applied if it is to comply with our air quality rules.
>
> … DEQ's creation and application of a project-specific adjustment factor is not supported by Idaho's air quality rules.

> … the creation of a project-specific adjustment factor suggests that there is a significant ignorance about cancer, carcinogens, and carcinogenesis.
>
> … the short-sighted project-specific adjustment factor to the Stibnite Gold Project, DEQ created a misleading risk analysis that greatly underestimates the actual cancer risk.[7]

17. This report supports the Board of Environmental Quality's findings in the Final Order and concludes that:

a. DEQ's application of the 16/70 SGP Project-specific adjustment factor underestimates cancer risk and is inappropriate science and public health policy;

b. Ambient air arsenic concentrations and cancer risk are underestimated for the SGP by use of 5-year rolling average in the air quality modeling input factors;

c. Ambient air arsenic concentrations and cancer risk are underestimated for the SGP by improper application of the non-WEP emissions scenario;

d. The combined application the SGP 16/70, 5-year rolling average, and non-WEP Project-specific adjustment factors increase cancer risk and negate the health protectiveness of the TAPs rule; and

e. DEQ's SGP Project-specific adjustment factors represent a significant change in the regulation of carcinogenic risk in Idaho that increases both cancer risk and regulatory burden.

[7] TR 0159.

OPINIONS

A. DEQ's application of the 16/70 Project-specific adjustment factor is inappropriate science and public health policy.

18. DEQ has failed to properly implement Section 586 and T-RACT for the SGP PTC by introducing a 16/70 SGP Project-specific adjustment factor to allocate the full 70-year lifetime allowable cancer risk to the 16-year Life of Mine (LOM). The calculation averages the risk resulting from SGP emissions over the life of the receptor. This adjustment allows the SGP to emit as much as 70 years of allowable carcinogenic emissions in 16 years. This type of "adjustment factor," also known as risk amortization or cancer dose-averaging, undermines both the health protectiveness and the regulatory certainty of the TAPs rule. In the context of the existing TAPs rule, as applied the last 30 years, using the 16/70 Project-specific adjustment factor is an incorrect interpretation and represents unsound science and public health policy.

19. Specifically, DEQ misinterprets the purpose and function of the **maximum one-year annual average ambient air carcinogen concentration** in implementing the TAPs rule. It is important to review the development of the TAPs rule in understanding the strategy represented by this one-year annual standard. The Schilling Declaration asserts that the TAPs rule was developed nearly thirty years ago to accommodate DEQ's predecessor agency IDHW-DOE and the regulated communities' request to adopt rules that are: 1) are reasonably protective of public health, but still afford flexibility to facilities and projects; 2) are relatively easy to understand and implement; and 3) do not require excessive expenditure of time and resources by DEQ and the permittee during the permitting process.[8]

[8] Schilling Decl. ¶ 13.

20. I was invited by the IDHW-DOE Air Quality Bureau to engage in development of those rules at that time in an advisory committee role based on my previous experience outlined above. My recollection is that much of the IDHW-DOE's and regulated industries' initial experience with risk assessment analyses was in implementing Risk Assessment Guidance for Superfund at CERCLA sites.[9] Both IDHW-DOE and the regulated community were supportive of avoiding the onerous burden of incorporating similar risk assessment and risk management protocols into Idaho's TAPa rule. In short, after considerable effort, IDHW-DOE was successful in developing the Section 586[10] and T-RACT[11] rule with a strategy that simultaneously avoids requiring PTC applicants to submit risk assessment and risk management protocols, yet is protective of human health.

21. The resultant TAPs Section 586 and T-RACT rules are highly prescriptive. Strict adherence to the rules is requisite to simultaneously afford regulatory certainty and simplicity for the regulated community and provide health protectiveness to the public. The key aspects of the simple, yet protective, rules are: 1) the incremental nature of the rule relieves industry and DEQ of the burden of assessing multiple sources and exposures, and greatly simplifies the permitting process; and 2) a significant **margin of safety (MOS)** is provided to ensure surrounding communities are not subjected to industry-generated ambient air TAP concentrations exceeding health-based risk criteria.

22. The purpose and function of the MOS is to protect the community from those other sources and exposures, risk cofactors, and uncertainties that would otherwise be evaluated in comprehensive risk assessment and health impact analyses. The DEQ and the regulated

[9] Exhibit B. U.S. EPA, *The Risk Assessment Guidelines of 1986* (Aug. 1987).
[10] IDAPA 58.01.01.586.
[11] IDAPA 58.01.01.210.12.

community have successfully employed these TAPs rule in a productive and protective manner since the 1990s.

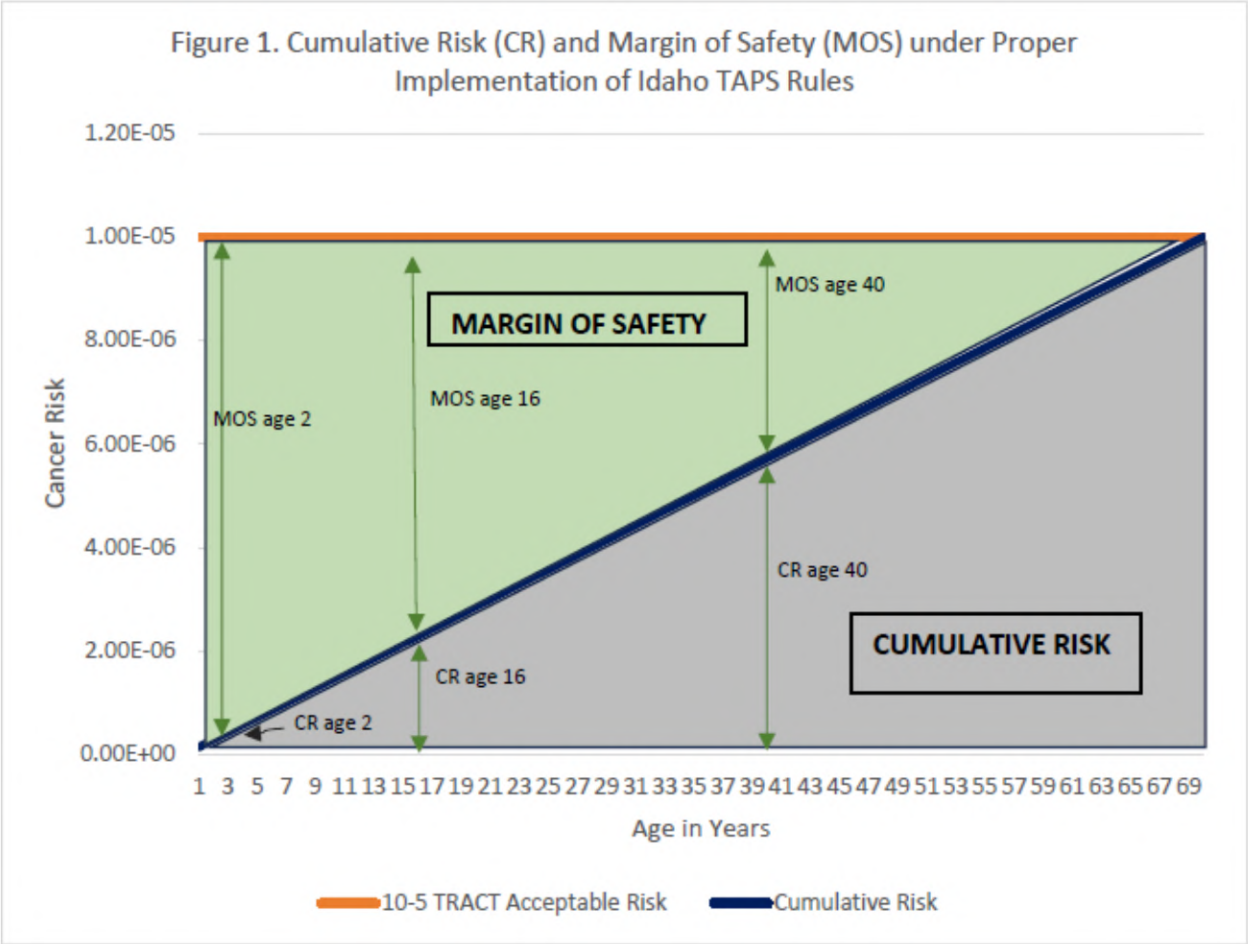
23. This prescriptive strategy specifically depends on protecting the public air space against the potential one-year annual maximum TAP emissions scenario throughout the life of the project. The one-year maximum emissions scenario is used to estimate **the maximum one-year annual average ambient air carcinogen concentration**. Ensuring that the maximum one-year annual ambient air carcinogen concentration does not exceed the acceptable ambient concentration for carcinogens (AACC) at the critical receptor location ensures that no receptor will be exposed to greater than the AACC by the incremental TAPs source for any year. The AACC is provided in Section 586 and is the ambient air concentration determined by dividing $1x10^{-5}$ lifetime risk by the Unit Risk Factor (URF). The URF is the lifetime cancer risk per 1.0 $\mu g/mg^3$ ambient air. Section 586 defines the AACC as an annual average.[12]

24. Ensuring that the criteria is achieved every year of the project guarantees the MOS will protect the individual receptors from other potential sources of the carcinogen that are not addressed in the incremental PTC analysis. Applying these criteria and MOS collectively to all individual sources assures that these health protections extend statewide.

25. Figure 1 illustrates the MOS and the cumulative lifetime risk at the critical receptor expected under the prescribed TAPS Section 586 maximum annual ambient concentration. The vertical axis is the carcinogenic risk. The horizontal axis represents the critical receptor's age commencing at the introduction of the incremental TAPs source. The

[12] *See* IDAPA 58.01.01.586 ("The AACC in this section are annual averages.").

maximum allowable lifetime risk is shown as the horizontal line at the top of the Figure ($1x10^{-5}$ T-RACT risk in this example).



26. If the TAPs rule is properly implemented, the cumulative incremental risk is shown by the diagonal line proceeding from birth to age 70 years (i.e., risk is allowed to accumulate at an annual rate of $(1x10^{-5})/70$ per year, or (AACC*URF/70) under T-RACT. The gray area below the diagonal line represents the portion of allowable lifetime risk accumulating from the incremental source. Risk increases proportional to the receptor age and the individual will have received the full allowable lifetime T-RACT exposure, and have a 10^{-5} carcinogenic risk burden at age 70-years.

27. The green area above the diagonal line represents the margin of safety (MOS) for the receptor to accommodate other contaminant exposures, risk cofactors, or uncertainties that might increase cancer risk from sources other than the incremental emissions regulated under TAPs Section 586 and T-RACT. Specifically, the large MOS safely accommodates those risk considerations that would otherwise be addressed in onerous risk and health assessment protocols. In this manner Idaho's TAPs compliance strategy purposefully, but safely, avoids requiring risk analyses.

28. The strategy also extends maximum protection to those population sub-groups most sensitive to carcinogenesis. Important life-stages of the receptor are indicated by the vertical lines at ages 0-2 years for infants and toddlers, ages 3-16 for children and adolescents, ages 17- 40 for reproductive-aged women and the fetus, and ages 41-70 years for older adults. This Idaho TAPs rule strategy affords minimal cumulative risk and maximal MOS protection during early life stages and pregnancy, acceptable risk levels during most of adulthood, with lesser protection at advanced ages when incremental cancer risk has limited effect on lifetime cumulative risk.

29. In the case of arsenic under the T-RACT criteria, the allowed annual rate of risk accumulation is a direct function of the .0023µg/m^3 T-RACT AACC multiplied by URL/70. As a result, contrary to Respondents' assertions, the AACC functions as an annual standard as historically applied in the TAPs rule. DEQ's and Perpetua's Declarations contend the Section 586 comparison of average annual ambient air arsenic concentration should utilize the average 70-year concentration, as opposed to basing health protectiveness on the worst-case **maximum one-year annual average ambient air carcinogen concentration** that is the foundation of the

MOS. Using the 70-year basis proposed by DEQ and Perpetua allows Perpetua to emit a lifetime of allowable emissions in 16 years, and undermines the health protectiveness of the rule and increases cancer risk.

30. The origin of DEQ's policy change can be found in the Lewis and Schilling Declarations. The initial Draft PTC offered by DEQ for public review exempted 99% of proposed allowable arsenic emissions from regulation and TAPs compliance because mining fugitive dust was not considered. Following subsequent public hearing testimony, DEQ required that Perpetua consider haul road dust arsenic emission under Section 586 TAPs rule.[13] As Schilling asserts, when subsequently required to consider the massive arsenic emissions, Perpetua informed DEQ that compliance with either the 10^{-6} AACC or the 10^{-5} T-RACT AACC limits were not achievable.[14] Any calculations or analyses to support these conclusions have never been disclosed.

31. According to Schilling, DEQ then suggested the ad hoc SGP 16/70 Project-specific adjustment factor, or dose-averaging approach, to avoid the annual one-year average constraints of the TAPs rule.

> Rather than revise the analytical approach to provide a less conservative assessment of impacts, I proposed that compliance with carcinogenic TAP increments could be based on cumulative cancer risk of the limited-duration project rather than the worst-case annual impact for a project of limited duration.[15]

32. The SGP 16/70 Project-specific Adjustment Factor was introduced in the TAPs Modeling Addendum, Section 4.3 AACC Adjustment for the Operational Life of the Mine.

[13] Lewis Decl. ¶ 18.
[14] Schilling Decl. ¶ 22.
[15] Schilling Decl. ¶ 22.

> [Perpetua] indicated the maximum life-of-mine will be 16 years. Life-time exposures to carcinogenic TAPs were refined by multiplying the maximum modeled annual impact by a ratio of 16/70.[16]

33. In defending this policy change, Schilling asserts that DEQ's position that the short-term factor of 10 applied to the allowable AACC when a project will have a duration of less than 5 years, shows that an adjustment in the exposure concentration is appropriate.[17] He further asserts that:

> . . . DEQ determined it would not be appropriate to subject individuals to a lifetime allowable cancer risk within a duration of less than 5 years. Therefore, the adjustment was capped at 10, rather than using a higher value or values calculated from exposure durations of 5 years of less (e.g., 70 years/5 years = 14 or 70 years/2 years = 35). These short-term projects were most commonly remediation and pilot-scale projects having a duration of up to several years.[18]

34. Schilling refers to IDHW-DOE's explicit 1992 interpretation,[19] also noted by Lopez,[20] that:

> For short term sources (usually less than five years in duration), such as remediation projects, a probability of greater than one in a million risk (over 70 years) will generally be acceptable to account for the decreased term of exposure. It is not acceptable however, for exposed individuals to receive a full 70-year exposure during the life of a short-term project. (Idaho DEQ 1992).[21]

35. In my opinion, nothing in the 1992 IDHW-DOE document suggests that an "adjustment factor" can be applied to any project with a life greater than 5 years, as the Schilling and Lopez Declarations imply is the modified DEQ policy. I am not aware of any quantitative

[16] REC 0698.
[17] Schilling Decl. ¶ 19.
[18] Schilling Decl. ¶ 19.
[19] Schilling Decl. ¶ 19.
[20] Lopez Decl., Memo. in Supp. of Decl. at 11.
[21] REC 3780.

"adjustment factor" connection between the 5-year project lifetime and the 70-year lifetime cancer risk basis. I believe that it is more accurate to describe the short-term factor of 10 as reflecting the order of magnitude increase in allowable risk from 10^{-6} to 10^{-5} criteria. This order-of-magnitude relief in allowable risk levels is commonly justified in cancer risk mitigation protocols throughout State and federal jurisdictions in various programs for various reasons, such as the Washington State protocols.[22]

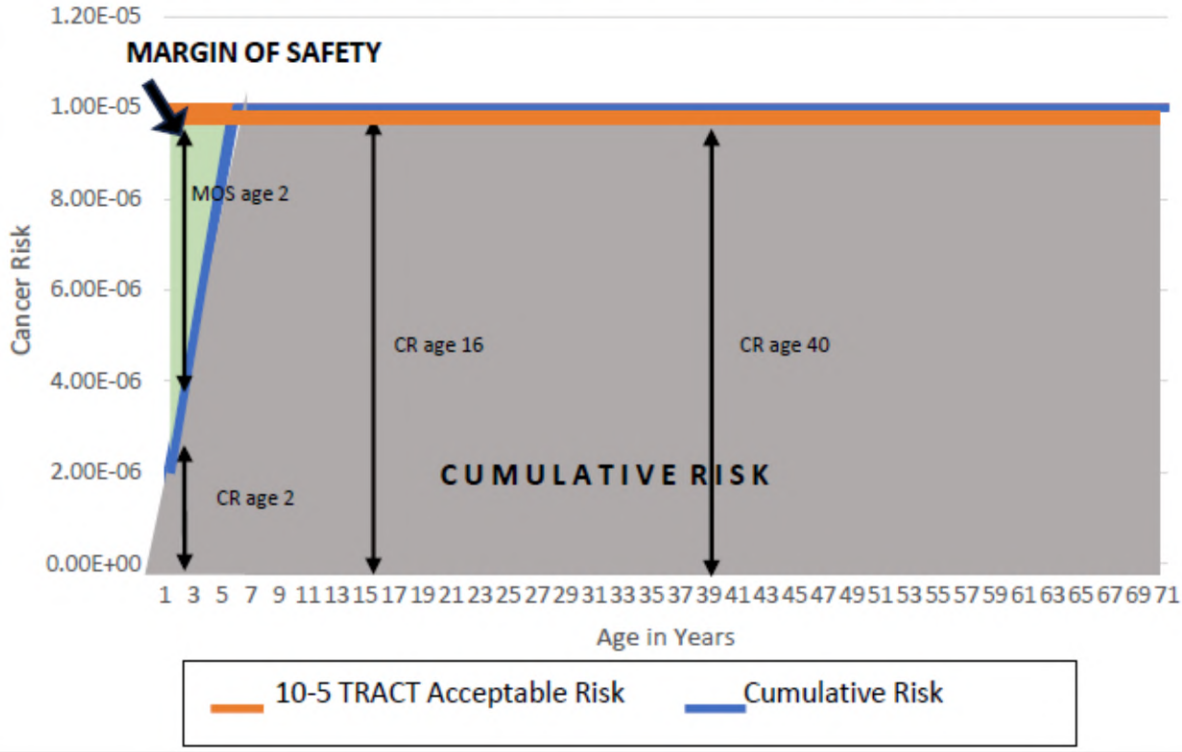
36. According to Schilling and Lopez, DEQ's modified policy implies that the SGP Project-specific adjustment factor can be applied to any carcinogenic source with a duration greater than five years. This shortsighted conclusion is incorrect, unprecedented, and not supported by EPA guidelines. The new policy is poor science and undermines the health protective strategy of regulating TAPs that has successfully been applied for the last thirty years.

37. Consider the extreme case of DEQ permitting a six-year (>5 yr.) life facility to emit sufficient carcinogens to expose individuals to the full 70-year lifetime acceptable risk in six years. The alleged allowable maximum annual ambient concentration would be 70/6 = 11.7 times the AACC, (or 117 times the AACC if T-RACT applied, (i.e. 1.17×10^{-4} cancer risk if applied for 70 years). DEQ's misinterpretation would allow emissions and consequent exposures of more than two orders of magnitude greater risk than the AACC (1.2×10^{-4} equivalent risk) for six years. At year 7 (or 10% of the receptor's assumed lifetime), the six-year-old child will have accumulated, and carry the lifetime burden, of a one-in-one hundred thousand cancer risk (10^{-5}). This risk burden will accompany the individual for the following six decades (> 90%) of the receptor's expected lifetime.

[22] Exhibit C. Washington State Department of Ecology, *Guidance Document First, Second, and Third Tier Review of Toxic Air Pollution Sources (Chapter 173-460 WAC)* (2010).

38. The effect of this dangerous scenario is illustrated in Figure 2. The MOS afforded this childhood receptor occurs briefly in the first six years of life. For the remainder of the receptor's lifetime, any additional arsenic exposure, from any source at any time, would immediately cause the cumulative lifetime exposure to exceed the unacceptable $>10^{-5}$ risk. The receptor would be challenged to avoid any additional arsenic exposures for the remainder of life.

Figure 2. Cumulative Risk (CR) and Margin of Safety (MOS) using the Project-specific (6/70) Adjustment Factor for a 6-year project



39. The ad hoc introduction of risk averaging by DEQ through a 6/70 adjustment factor, as depicted in Figure 2, would allow a six-year project to concentrate 70 years of emissions and lifetime cancer risk into both the 6-year life of the project and receptor child's first

six years of life. This scenario undermines the health protectiveness originally incorporated in Section 586, particularly with respect to neo-natal, pediatric, and adolescent cancers.

40. In justifying the use of the 16/70 Project-specific adjustment factor, the Respondents continually assert that the Unit Risk Factor (URF) is an average based on a 70-year lifetime. However, carcinogenic potency and cancer risk accumulation differ for various stages of life. The cancer dose varies based on contaminant intake and absorption rates and physiological factors such as body weight and organ development. Considering early life exposures, warrants additional examples of the inappropriateness of introducing the SGP 16/70 Project-specific adjustment factor. Pregnant women, the fetus, and pre-school children accumulate dose and risk at the highest rates and are especially vulnerable to disease due to age and developmental factors. Body weight, absorption, and hormonal considerations can make older children and adolescents more susceptible to childhood cancers.

41. DEQ's assertion that the SGP 16/70 Project-specific adjustment factor is health protective implies that it is permissible to subject these sensitive subpopulations to the equivalent $>10^{-4}$ risk levels from conceptus to school age because it will average out over the remainder of the child's life.

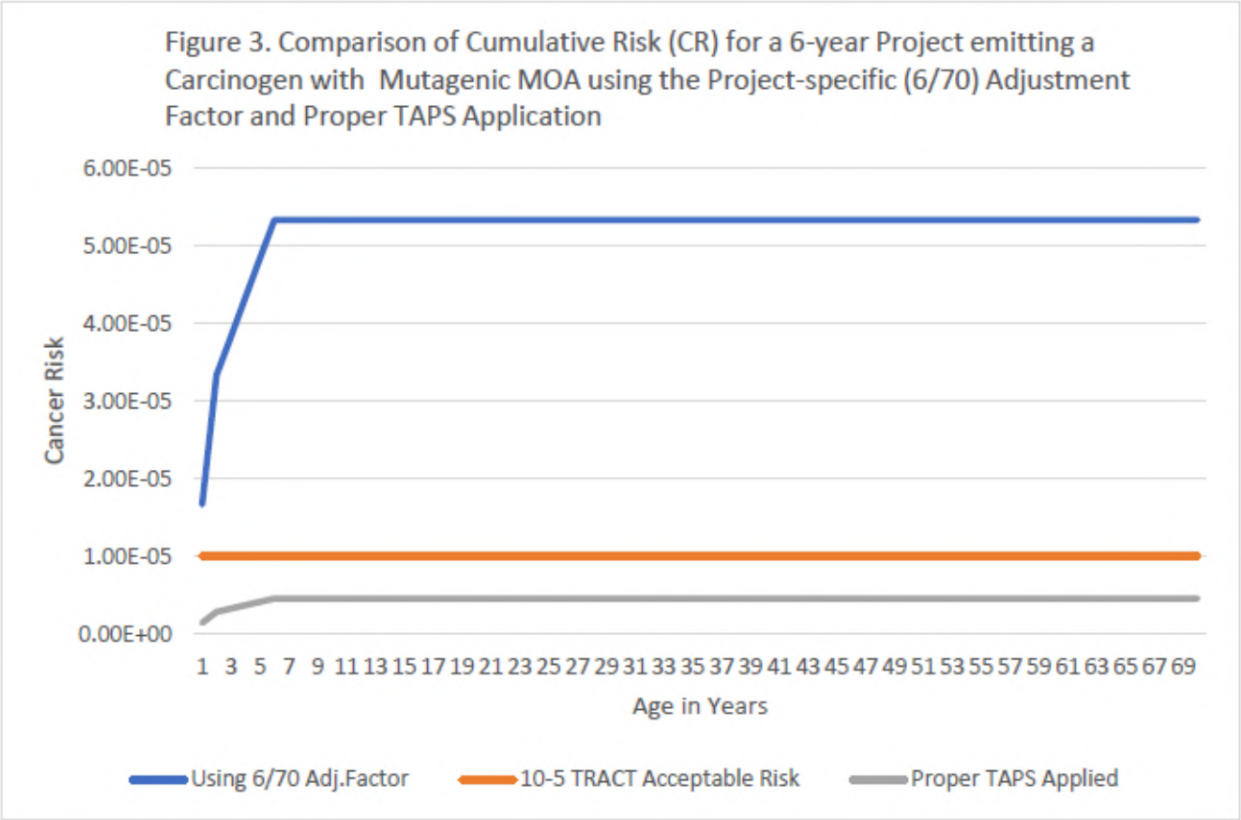
42. The SGP 16/70 Project-specific adjustment factor is a classic example of dose-averaging. The practice of averaging cancer risk over a receptor's lifetime progressively developed as an issue in the risk analyses applied to contaminated hazardous waste sites during the 1990s, and early 2000s. The EPA comprehensively considered the application of

dose-averaging or risk amortization in the Science Advisory Board (SAB) review *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens.*[23]

43. The excessive risk associated with early life-stage carcinogenic dose accumulation has long been recognized by most health authorities and specific protections were incorporated in EPA Risk Assessment Guidance for Superfund (RAGS) policy in 2009. The EPA recommends a quantitative adjustment of the toxicity value to account for early life susceptibility. This guidance recommends a 10-fold adjustment for exposures during the first 2 years of life; 3-fold adjustment for exposures from ages 2 to <16 years of age for carcinogens exhibiting mutagenic mode of action (MOA).[24]

44. Figure 3 shows lifetime cumulative risk were DEQ to apply the ad hoc 6/70 adjustment factor to a carcinogen exhibiting mutagenic MOA for the 6-year project life scenario (blue line). Applying the recommended age-specific adjustment factor shows that DEQs interpretation allowing dose-averaging over the 70-year lifetime would result in the allowable full lifetime exposure occurring by age 2 years, and the child's lifetime cumulative exposure will be $5.3x10^{-5}$ by age 6 (i.e., 53 times the one-in-one million criteria). These lifetime cumulative risks acquired by infants and toddlers, prior to adolescence far exceed EPA acceptable carcinogenic risk policy.

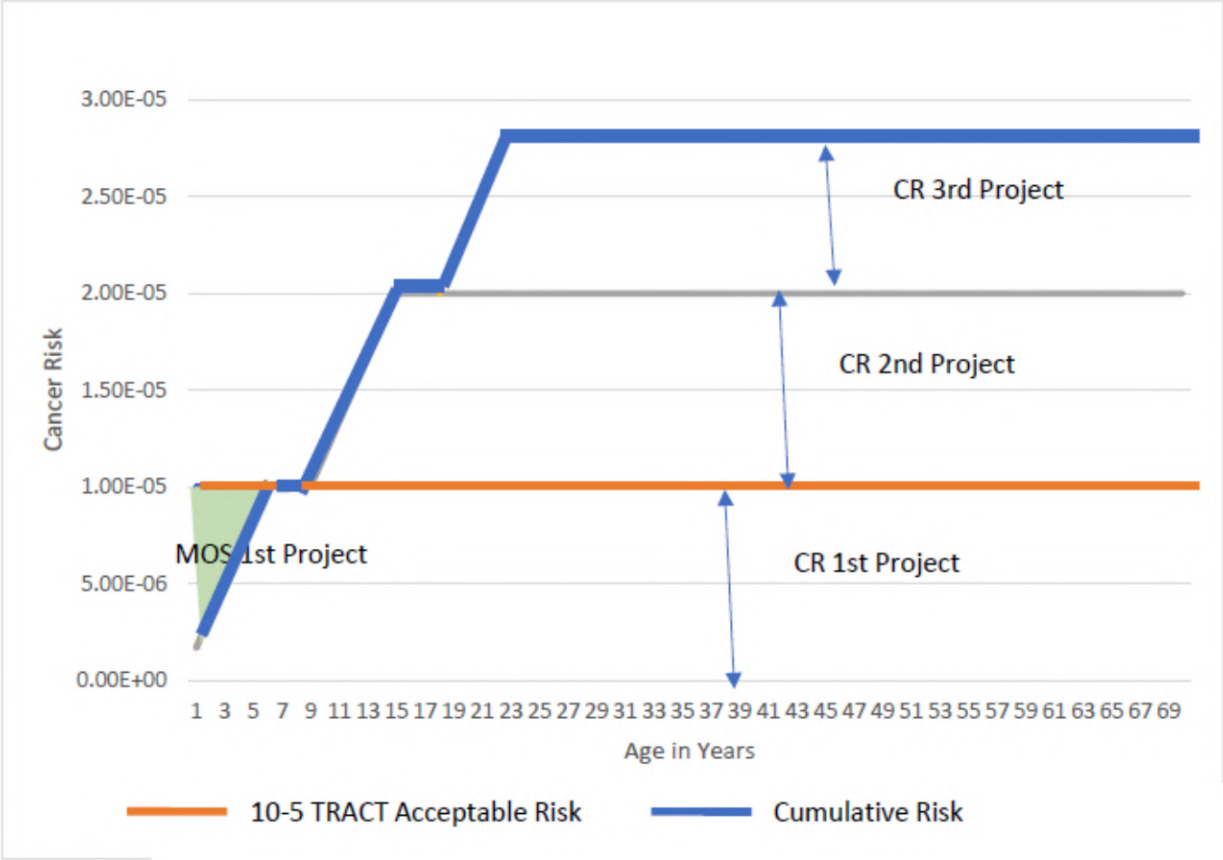
[23] Exhibit D. U.S. EPA, *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* (2005).
[24] Exhibit E. U.S. EPA, *Risk Assessment Guidance for Superfund. Vol. I: Human Health Evaluation Manual (Part F, Supplemental Guidance for Inhalation Risk Assessment* (Jan. 2009).



45. Conversely, proper application of the TAPs rule using the **maximum one-year annual average ambient air carcinogen concentration** is shown by the lower cumulative risk line (gray line). Proper implementation of the TAPs rule would result in 4.6×10^{-6} cumulative cancer risk at age six years, as shown in Figure 3. These results demonstrate that application of a 6/70 adjustment factor for a six-year facility increases a six-year-old child's cancer risk by 12 times over that were the TAPs rules applied under the past policy.

46. As another example, consider the case of two additional 6-year projects being implemented near the source represented in Figure 2 at years 9 and18 in this child's life. Figure 4 shows the child already exposed to the full lifetime allowable cancer $1x10^{-5}$ risk by age 6, will have double ($2x10^{-5}$) the acceptable risk level by adolescence, and will carry three times the allowable lifetime cumulative risk burden ($3x10^{-5}$) through the reproductive stage of life.

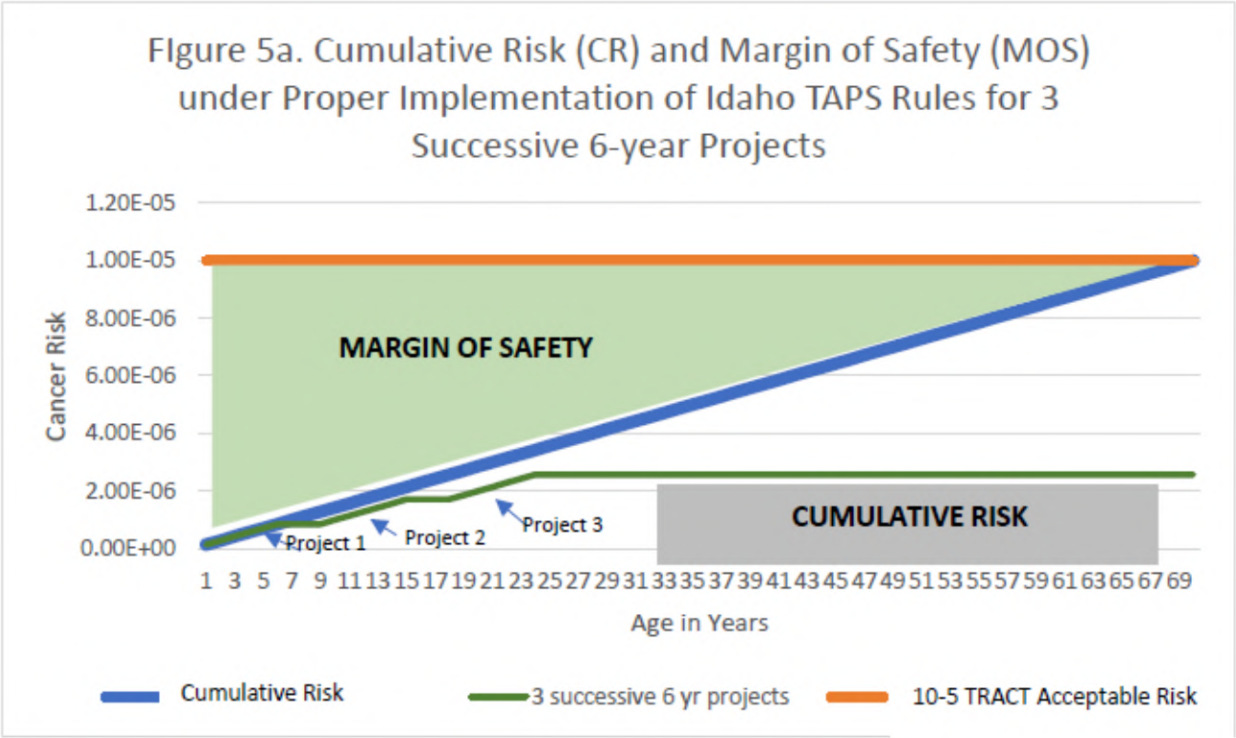
Figure 4. Cumulative Risk using the Project-specific (6/70) Adjustment Factors for 3 Successive 6-year Projects



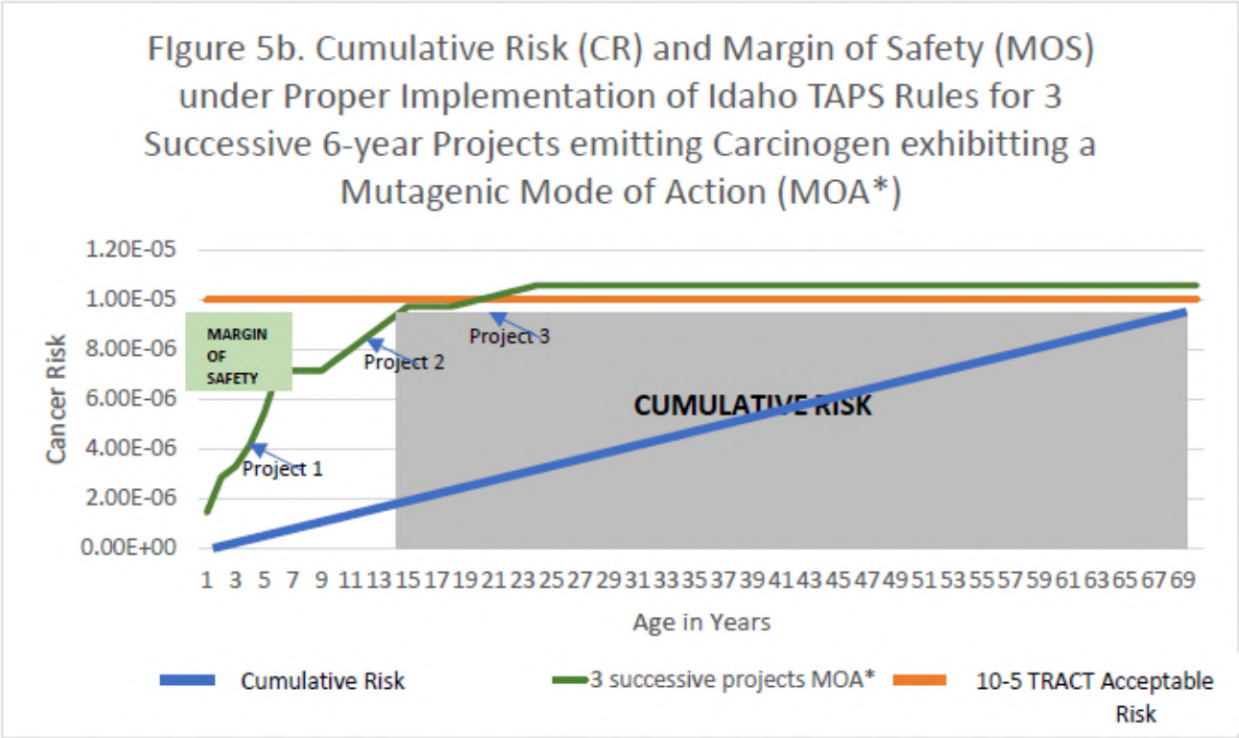
47. Consider the three sequential 6-year projects implemented under the new (6/16) adjustment factor emitting a carcinogen exhibiting mutagenic MOA. In this scenario, the three projects would increase individual cancer risk to >$1x10^{-5}$ lifetime allowable risk by age 2, to $5.3x10^{-5}$ for a 6-year-old child, $8.3x10^{-5}$ for a 16- year old adolescent, and $9.3x10^{-5}$ for a 24-year old adult. These are dangerous and unacceptable risks at vulnerable life stages.

48. Under Section 586, DEQ must consider these new projects incrementally. Thus, it would not account for the cumulative lifetime exposures associated with the earlier projects in a new source PTC application, and are not allowed to consider risk associated with those earlier projects. At Stibnite, for example, should SGP apply to open another pit at the mine, DEQ would be required to ignore the cumulative lifetime risk and cancer burden imposed by the proposed SGP 16-year LOM scenario.

49. Figures 5a and 5b demonstrate the same three sequential project scenarios under the proper implementation of the current TAPs rules using the **maximum one-year annual average ambient air carcinogen concentration** that incorporates the MOS to accommodate additional sources. Figure 5a shows the cumulative risk from all three projects for a carcinogen not exhibiting mutagenic MOA. In this case, a child growing up in the community would be protected from excess cancer risk through all life stages even though DEQ would not consider the earlier exposure in applying Section 586. The lifetime risk accrued by the individual is $2.6x10^{-6}$ as opposed to $3.0x10^{-5}$ in the earlier example. Allowing use of the 6/70 adjustment factor increases lifetime cancer risk by 12 times..



50. Figure 5b shows the cumulative risk for proper implementation of the current TAPs rule for three sequential 6-year projects emitting a carcinogen exhibiting mutagenic MOA. In this example, the MOS is successfully protective throughout childhood and adolescence, with the cumulative risk exceeding the 10^{-5} risk level at age 21. These examples illustrate the effectiveness of the MOS in accommodating additional sources and risk cofactors. The TAPs rule is health protective if properly implemented. Applying risk averaging through the use of the 16/70 Project-specific adjustment factors eliminates the MOS and substantially increases cancer risk, especially considering the incremental nature of the rule.



51. Figures 5a and 5b also demonstrate DEQ's shortsightedness in applying unprecedented cancer dose-averaging methods through the SGP 16/70 Project-specific adjustment factor. The inappropriate averaging is allegedly justified by ad hoc risk assessment calculations and risk management protocols that undermine both the simplicity and the health protectiveness of the TAPs rule. The MOS is compromised, the public is no longer secure, and the regulated industry is now obliged to include cancer risk and health impact assessments in TAPs PTC applications to support the assertions of health protectiveness.

52. There are no provisions in the Air Rules to allow manipulation of the required **maximum one-year annual average ambient air carcinogen concentration** or the **AACC,** or to submit risk calculations. The Respondents assert that because there are no specific prohibitions, using the SGP 16/70 Project-specific adjustment factor is permissible. DEQ did not

require any risk assessment justification during the PTC process, but only provided extremely limited risk analyses in post hoc declarations following the Special Board Hearing.[25]

53. In justifying the SGP Project-specific 16/70 adjustment factor, both the DEQ and Perpetua refer to the EPA Risk Assessment Guidance for Superfund (RAGS) risk assessment protocols eschewed by the agency for the last thirty years to support the ad hoc exposure averaging calculations. As noted in the Tiedeman Declaration, IDHW-DOE specifically avoided RAGS waste site remediation short-term risk protocols in developing the TAPS.[26]

54. The Board of DEQ Vice Chairman McMillan explicitly expressed concerns with this issue, indicating his belief that DEQ's creation and application of a Project-specific adjustment factor cannot be supported by Idaho's Air Rules and that DEQ has misinterpreted how the AACC must be applied if it is to comply with the those rules.

55. Vice Chairman McMillan further indicated that DEQ's application of what he called the "short-sighted" Project-specific adjustment factor to the Stibnite Gold Project created a misleading risk analysis that greatly underestimates the actual cancer risk. In his view:

> The Idaho rules are not ambiguous. There is an acceptable risk associated with the AACC standard. There is an acceptable risk associated with DEQ-approved T-RACT projects, and there is an acceptable risk associated with the short-term project that is five years or less. There are no other acceptable risks identified in Idaho's air quality rules.[27]

I agree with Dr. McMillan's statement.

[25] *See* Schilling Decl.; Paden Decl.; Lewis Decl.; Lopez Decl.
[26] Tiedemann Decl. ¶¶ 26-27.
[27] TR 0160.

B. Ambient air arsenic concentrations and cancer risk are underestimated for the SGP by using a 5-year rolling average in the air quality modeling input factors.

56. Another ad hoc SGP Project-specific adjustment factor DEQ applied to the exposure estimates (prior to implementing the 16/70 Project-specific adjustment factor) was a 5-year rolling average adjustment factor to the emissions rates used as input to the refined modeling. This disguised risk averaging technique results in the models predicting a five-year average ambient air carcinogen concentration rather than the **maximum one-year annual average ambient air carcinogen concentration** required under Section 586 and T-RACT, further undermining the health protectiveness of the TAPs rule.

57. The 5-year rolling average adjustment factor was introduced in the TAPS Modeling Addendum Section 4.2 -TAP Emission Averaging Period. In Section 4.2, DEQ asserts:

> Annual average emissions of carcinogenic TAPs are typically used in the dispersion model to estimate maximum annual impacts. PRI refined the analyses by using source-specific emission rates that are representative of a 5-year averaging period. This approach is appropriate because carcinogenic impacts are of concern from a long-term exposure basis.[28]

58. DEQ erroneously substitutes the 5-year rolling average emissions for the maximum one-year potential emissions required under Section 586 and T-RACT. Section 586 requires the prescribed maximum one-year annual average to be estimated by refined modeling of ambient concentrations based on maximum one-year potential emission rates, or PTE. The PTE should reflect the source configuration and operational scenario that would yield the maximum annual one-year ambient air arsenic concentration. This concentration is then

[28] REC 0698.

compared to the 10^{-6} AACC. If the 10^{-6} AACC is exceeded, the applicant may apply for 10-fold relief under TRACT.

59. DEQ has never disclosed this comparison. In response to public comments critical of DEQ for not calculating nor presenting the required AACC comparisons, DEQ provided the following rationale:

> The comparison offered, comparing maximum annual impacts to the T-RACT adjusted AACC, is irrelevant. Compliance with TAPs rules was demonstrated through a refined analysis, so there is no utility in focusing on results from a more conservative, less refined analysis.[29]

DEQ misinterprets the purpose the comparison and undermines the health protective strategy of the TAPS Rules as implemented in the past.

60. Instead, DEQ substituted the 5-year rolling average for the required maximum one-year emission rate. There is no provision in the TAPs rule for altering or adjusting the predicted maximum one-year annual average. This erroneous substitution significantly reduces the MOS inherent in proper allocation of the one-year maximum emission rates. To be health protective, the prescriptive Section 586 rule explicitly (not typically) requires predicting the **maximum one-year annual average contaminant concentration** using prescribed emissions estimates, and assuring that concentration is not exceeded during the life of the facility.

61. DEQ has never disclosed the required **maximum one-year ambient annual average arsenic concentration.** It is not possible from the available information provided by DEQ to determine how this 5-year rolling average compares to the maximum one-year emission rate that should have been used. I have estimated the underprediction by examining the ratio of

[29] REC 0693.

peak to mean 5-year rolling average emission rates presented in Figure 3 of Perpetua's TAP Addendum.[30] This figure shows estimated potential 5-year rolling average emissions for an alleged 16-year MODPRO2 operations plan. The estimated mean 5-year rolling average from this figure was calculated to be 0.132 lb/hr. Comparing this value to the maximum 0.232 lb/hr value suggests the peak to mean ratio for the alleged T-RACT PTE is approximately 1.8 (0.232 lb/hr / 0.132 lb/hr).

62. Because this Project-specific 5-year rolling average adjustment factor is inherently applied to the emissions input to the refined models, a 1.8 underprediction factor would translate directly to the estimated receptor point ambient air carcinogen estimates. As a result, the maximum one-year annual concentration in the model output is likely underpredicted by a factor of 1.8. The best estimate of the **maximum one-year annual ambient air arsenic concentration** for the modeled scenarios is 0.0125 $\mu g/m^3$ (1.8 x 0.00698 $\mu g/m^3$) for the WEP2.[31]

63. DEQ's application of the 5-year rolling average adjustment factor reduces the **maximum one-year annual ambient air arsenic concentration** and the associated cancer risk by 45%.

C. Ambient air arsenic concentrations and cancer risk are underestimated for the SGP by improper application of the non-WEP emissions scenarios.

64. A third SGP Project-specific adjustment, the non-WEP adjustment factor, was applied to model predicted ambient air concentrations. This is a second disguised dose-averaging step combining eight different 5-year rolling average scenarios, reducing the alleged WEP2

[30] Exhibit L. at 26.
[31] Exhibit L at PDF 224.

maximum annual average an additional 41%. DEQ averaged the maximum WEP2 scenario 5-year average arsenic concentration predicted by the model (i.e. 0.00698 μg/m^3) with the average of the seven model predicted non-WEP 5-year average concentrations (0.00134 μg/m^3). These alleged annual averages are actually an average of 5-year averages as these were predicted by the already diluted 5-year rolling average emissions input to the refined modeling. This non-WEP multi-averaging adjustment factor dilutes the ambient air carcinogenic concentration by an additional 41%, yielding the 0.00416 μg/m^3 alleged incremental annual ambient arsenic concentration. Paden and Lopez use this value to assert compliance with EPA cancer risk policies in subsequent risk calculations.[32]

65. DEQ and Perpetua assert this additional dose-averaging step is justified because no one scenario will apply throughout the 16-year LOM operation. In the context of properly applying the TAPs rule, the non-WEP adjustment factor is irrelevant. DEQ's obligation is to identify the emission scenario that produces the **maximum one-year annual average ambient air carcinogen concentration**. That value is the maximum WEP2 scenario, and would not consider non-WEP scenarios unless the non-WEP emissions sources were operating contemporaneously during the WEP2 emission maximum year. In that case, any non-WEP scenario operating in the same year as the WEP2 maximum configuration would add to, not dilute, the critical receptor maximum ambient air concentration.

66. DEQs applying the SGP Project-specific non-WEP adjustment factor effectively converts the 5-year alleged annual average value (0.00698 μg/m^3) to an arbitrary 0.00416 μg/m^3 16-year LOM average carcinogenic concentration. A variety of combinations of the different

[32] *See* Paden Decl. XXX; Lopez Decl. XXX.

modeling scenarios, based on alleged operations plans could have been combined to manipulate this multi-averaged hybrid LOM ambient air carcinogenic exposure estimate (e.g. 3-year rolling average and 70% non-WEP contribution).

67. The final effect of DEQ's application of an arbitrary multi-averaging non-WEP adjustment factor can be estimated by comparing the WEP2 and non-WEP average ambient air carcinogen estimates (i.e., (0.00698 $\mu g/m^3$ / 0.00416 $\mu g/m^3$), or by a factor of 1.7. Applying the non-WEP Project specific adjustment factor underpredicts the required **maximum one-year annual average ambient air carcinogen concentration** and associated cancer risk by an additional 41%.

D. The combined application of the SGP 16/70 Project-specific adjustment factor, the 5-year rolling average adjustment factor, and the non-WEP adjustment factor increase cancer risk and negate the health protectiveness of the TAPs rule.

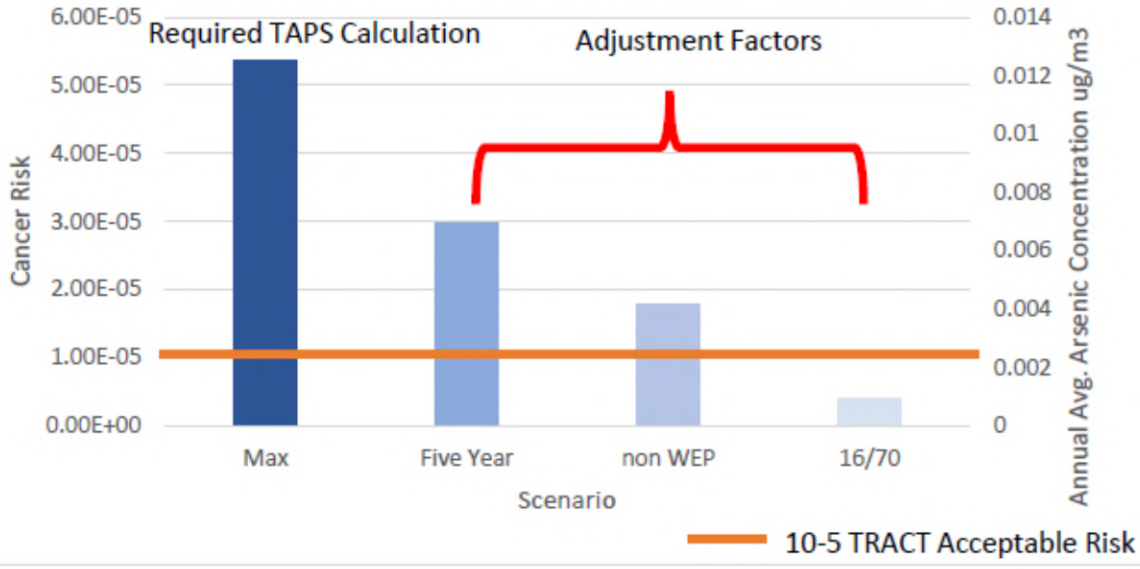
68. The conclusions in the DEQ Board's Final Order correctly identified the three Project-specific adjustment factors that undermine the health protectiveness of the TAPs rule for carcinogenic risk. The Board correctly concluded that application of these adjustment factors underestimates cancer risk. DEQ applied the: 1) 5-year rolling average; 2) non-WEP; and 3) SGP 16/70 LOM adjustment factors sequentially to the input and the output of the predictive air quality model. As a result, the dilution effects are multiplicative, rather than additive.

69. In summary, DEQ diluted the (0.0125 $\mu g/m^3$) maximum one-year annual average ambient air carcinogen concentration by 45% to 0.00698 $\mu g/m^3$ by applying the 5-year rolling average. DEQ further diluted 5-year average concentration by 41% to a value of 0.00416 $\mu g/m^3$ by applying the non-WEP adjustment factor, which is diluted an additional 78% to a value of 0.00095 $\mu g/m^3$ by applying the 16/70 SGP Project-specific adjustment factor. In total, DEQ

diluted the required **maximum one-year annual average ambient air carcinogen concentration** by 93%, or a factor of 13 times before calculating the corresponding cancer risk.

70. The risk levels associated with these exposures were similarly underpredicted as follows: the risk for estimated **maximum one-year annual average ambient air carcinogen concentration** of $5.3X10^{-5}$ was (1) diluted to $3x10^{-5}$ by applying the 5-year rolling average adjustment factor; (2) diluted to $1.8x10^{-5}$ by applying the non-WEP adjustment factor; and (3) to the alleged compliance $4x10^{-6}$ by applying the SGP 16/70 Project-specific adjustment factor. These results are shown in Figure 6. DEQs sequential application of the three SGP Project-specific adjustment factors underpredict cancer risk by 13 times, as these carcinogenic risk levels are employed in properly implementing the TAPs rule.

Figure 6. Effect of DEQs Application of the Project-specfic Adjustment Factors Compared to Required TAPS Calculation



71. These analyses confirm Vice-chairman McMillan's observation in the Special Hearing:

> The PTC proposes to allow 16 years higher daily carcinogen doses and disguises such doses using a non-rules-based mathematics.[33]

E. DEQ's SGP Project-specific adjustment factors represent a significant change in the regulation of carcinogenic risk in Idaho that increases both cancer risk and regulatory burden.

72. As DEQ admits,[34] cancer dose-averaging has seldom, if ever, been used in TAPs carcinogenic risk compliance evaluations for a stationary source under the Clean Air Act in Idaho. Although there is a history of using cancer dose-averaging in risk assessment and risk management protocols for short-term remediation projects at contaminated sites, applying it to the SGP PTC is unprecedented. In implementing the SGP 16/70 Project-specific adjustment factor, DEQ has deviated from the long-held prescribed TAPs rule protocol of guaranteeing the **maximum one-year annual average carcinogen concentration** will not exceed the AACC or T-RACT AACC for each year of the Project. This thirty-year health protective strategy has provided the public comfort that cancer risk exposures are within acceptable limits both near the source and Statewide.

73. Should application of risk averaging become precedent through acceptance of the SGP Project-specific adjustment factors, the conservative MOS inherent in the TAPs rule is significantly reduced. This major change in health protective strategy should simultaneously require PTC applications to include a comprehensive health risk assessment to consider other

[33] TR 0160.
[34] REC 1201.

potential sources otherwise inherently addressed in the MOS. Providing such evidence would be incumbent upon both the PTC applicants and DEQ.

74. These health and risk assessments would require new applicants to consider other past, present, and future sources that did, or may, expend significant portions of the critical receptor's lifetime allowable risk. A simple review of Washington State's required Health Impact Assessment (HIA) points out the numerous shortcomings in the ad hoc alleged risk analyses offered by the Respondents. The HIA requires specified emissions calculations, approved air dispersion modeling, AACC screening, risk assessment, hazard identification, exposure estimates considering other sources and exposure routes, dose-response criteria, non-carcinogenic risk characterization, uncertainty analysis, discussion of acceptability of risk, and a risk management analysis employing modified emission control strategies.[35]

75. DEQ has no history utilizing risk assessment to support TAPs rule applications, nor do the Idaho TAPs regulations offer any guidance for conducting health risk analyses. No comprehensive analyses, nor discussion related to risk and health assessment, are found in the Statement of Basis for the SGP PTC.[36] No comprehensive assessment of health and risk issues associated with application of the SGP Project-specific adjustment factors were required in Perpetua's application.

76. Additionally, from a regulatory standpoint, other Idaho air permit applicants may seek similar preferential relief. No facility plans for a 70-year life. The 70-year basis is an artifact of cancer risk analyses protocols, not a facility design criterion. Every facility ever to apply for a

[35] Exhibit C at 26.
[36] *See* REC 0410.

PTC that did not opt for short-term relief (less than 5 years) likely anticipated a project life of less than 70 years of operation. Will DEQ offer SGP-equivalent project-specific adjustment factor relief and require comprehensive Health Impact Analyses for 6/70, 10/70, 16/70, 20/70, 25/70, 30/70-year alleged project life, as Schilling Declaration suggests?[37] Will DEQ approve incremental emissions from a new source impacting the same critical receptor location that has already expended its lifetime allowable risk, as demonstrated in Figures 4 and 5, above? Will DEQ approve additional emissions from the same location after the original permit has exhausted the critical receptor lifetime allowable risk? Will DEQ require, and provide guidelines, for risk and health assessments to support the preferential relief?

77. These questions demonstrate the short-sightedness of DEQ's acquiescence to Perpetua in allowing dose-averaging concepts to be applied to the Section 586 TAPs rule. Proper application of the rule inherently precludes risk averaging to maintain health protectiveness, without requiring applicants to address the issues without guidance. The regulatory burden placed on future applicants by this modified policy is potentially immense.

78. Allowing Perpetua and the SGP to concentrate a lifetime of carcinogenic emissions and allowable risk in a shorter exposure period defined by the LOM introduces numerous issues and uncertainties that can appropriately be considered only in comprehensive risk assessment analyses.

79. There are numerous examples of inadequacies of the risk calculations offered by the Respondents. Among the more important are those related to the SGP Project-specific adjustment factors concentrating emissions and carcinogenic risk in childhood and adolescent

[37] *See* Schilling Decl. ¶ 19.

life stages. Environment Canada conducted an extensive review of the development and incorporation of life stage cumulative risk assessment, and particularly dose-averaging.[38]

80. This document provides an understandable and concise review of the several issues surrounding dose-averaging, and risk amortization in applying cumulative risk assessment to short-term exposure scenarios. The report also evaluates and describes how various U.S. and Canadian health agencies had implemented risk amortization policy in the preceding decade. Environment Canada's conclusions reflect earlier EPA's determinations that dose averaging generally underestimates risk for fetus, infant, toddler, school children and adolescents; can be appropriate for healthy adults; and overstates risk late in life.[39] Idaho's current TAPs rule MOS appropriately accommodates both these conclusions if properly implemented as illustrated in Figure 1, above.

81. Environment Canada's conclusion with regard to threshold carcinogens is most pertinent to consideration of the SGP 16/70 Project-specific adjustment factor. Environment Canada states:

> Without a sound basis for doing so (i.e. it cannot be a default assumption), **the human health risk assessor should not simply mathematically spread out a short-term dose over a long period and conclude that the short-term dose is toxicologically equivalent to a lower dose over the long period. In short, CSD recommends that the exposure be averaged over the total actual exposure period and compared with the appropriate TRV.** A scientific rationale is required to support any proposed amortization (dose averaging beyond actual exposure period) to ensure that short-term risks are not underestimated. This analysis needs to be done on a chemical-specific basis.[40] (emphasis added)

[38] Exhibit F. Environment Canada, *Interim Guidance on Human Health Risk Assessment for Short-Term Exposure to Carcinogens at Contaminated Sites* (2015).
[39] Exhibit F; Exhibit E.
[40] Exhibit F at 18.

82. TRV is the equivalent of the Idaho AACC. For the past 30 years Idaho has implemented the TAPs rule as Environment Canada recommends, providing a health-protective MOS that appropriately protects children, adolescents, and pregnancies. DEQ now proposes to endorse dose averaging through the three SGP Project-specific adjustment factors, increasing both cancer risk for these vulnerable populations and regulatory burden for PTC applicants.

83. Two examples of relevance to the SGP Project-specific adjustment factors demonstrate the inadequacy of the risk calculations offered by Paden and Lopez. A comprehensive HIA addressing arsenic at mining sites would address 1) Mode of Action (MOA); and 2) non-carcinogenic risk as these relate to critical life stages.

84. **MOA Considerations**: As the Lopez Declaration notes, arsenic is not considered a carcinogen exhibiting mutagenic MOA by the EPA at this time. Current EPA guidance does not specifically recommend applying the age-dependent adjustment factors to the arsenic inhalation URF. Current EPA policy requires life-stage adjustment for known mutagenic MOA carcinogens but leaves it to the risk assessment and risk managers' discretion whether to apply age-adjustments for carcinogens with unclear MOAs.[41] Some jurisdictions recommend applying age dependent adjustment factors to carcinogens for which the MOA is not definitive.[42] A comprehensive risk assessment would inform the risk management decision-makers that there is evidence suggesting arsenic, in combination with other co-stressors, has shown mutagenic

[41] Exhibit D.
[42] Exhibit G, California EPA, OEHHA, *Technical Support Document for Cancer Potency Factors: Methodologies for derivation, listing of available values, and adjustments to allow for early life stage exposures* (May 2009) at 3.

MOA.[43,44] A comprehensive risk assessment would inform the risk management decision-makers that there is evidence suggesting arsenic, in combination with other co-stressors, has shown mutagenic MOA.

85. **Non-carcinogenic Risk.** Environment Canada notes specific examples of non-carcinogenic arsenic health effects that can become the risk driver after applying age-specific exposure, absorption, and dose accumulation adjustments at contaminated sites where children may ingest, in addition to inhaling, arsenic laden dusts.[45]

86. Allocating a lifetime of allowable arsenic intake to children in 6 or 16 years, raises numerous non-carcinogenic concerns not mentioned in the Respondents' limited risk analyses.

87. The largest source of arsenic at the SGP are haul road fugitive dusts. Application of the SGP Project-specific adjustment factor allows the SGP to increase annual emission rates from haul roads by four to ten times more than that allowed under proper implementation of the TAPs rule.

88. This concentration of emissions in early childhood, not only increases ambient air arsenic concentrations, but more than quadruples the rate of arsenic laden dust deposition. It is well-known, in Idaho, nationally and internationally, that incidental ingestion of mining-related fugitive dusts is the major childhood exposure route for heavy metals in mining communities. Numerous DEQ risk assessments for abandoned mine sites in Idaho, including several at the

[43] Exhibit H, Environmental Health Perspectives, *Low-dose Arsenic: In Search of a Risk Threshold*, 122:5 (May 2014).
[44] Exhibit I. Speer, R.M., *et. al.*, *Arsenic and cancer: evidence and mechanisms*, Adv. Pharmacol. 96:151-202 (2023).
[45] Exhibit F at 18.

Bunker Hill and Coeur d'Alene Basin Superfund Site, have historically involved fugitive dusts from mining sites.[46, 47]

89. The EPA and DEQ Superfund regulators routinely apply age-dependent adjustment factors similar to those required for carcinogens that exhibit mutagenic MOAs.[48] There has been no consideration of non-carcinogenic risk for the SGP. Figures 3 and 5, above, demonstrate there is no need to assess other potential sources or non-carcinogenic risk if the TAPs rule is implemented properly using the **maximum one-year annual average carcinogen concentration**. Dust deposition would occur at rates anticipated under proper application of the TAPs rule. As a result, properly complying with the cancer risk criteria is also protective of non-carcinogenic risk.

90. The Paden and Lopez Declarations contain extremely limited risk calculations. Both Respondents use the inappropriately derived dose-averaged ambient concentration of 0.00095 $\mu g/m^3$ to calculate an alleged $4x10^{-6}$ cumulative cancer risk and assert compliance with EPA risk assessment policy. Both Respondents refer to the same EPA formulae found in Superfund guidance and simply compare the same long-term 70-year average value to the same range of alleged EPA allowable risk levels. Neither considers pertinent risk co-factors, vulnerable life stages, other potential sources, or a variety of other considerations inherent in the Idaho TAPs compliance strategy or MOS noted above. Neither mentions nor indicates understanding of the incremental nature of the TAPs Rule.

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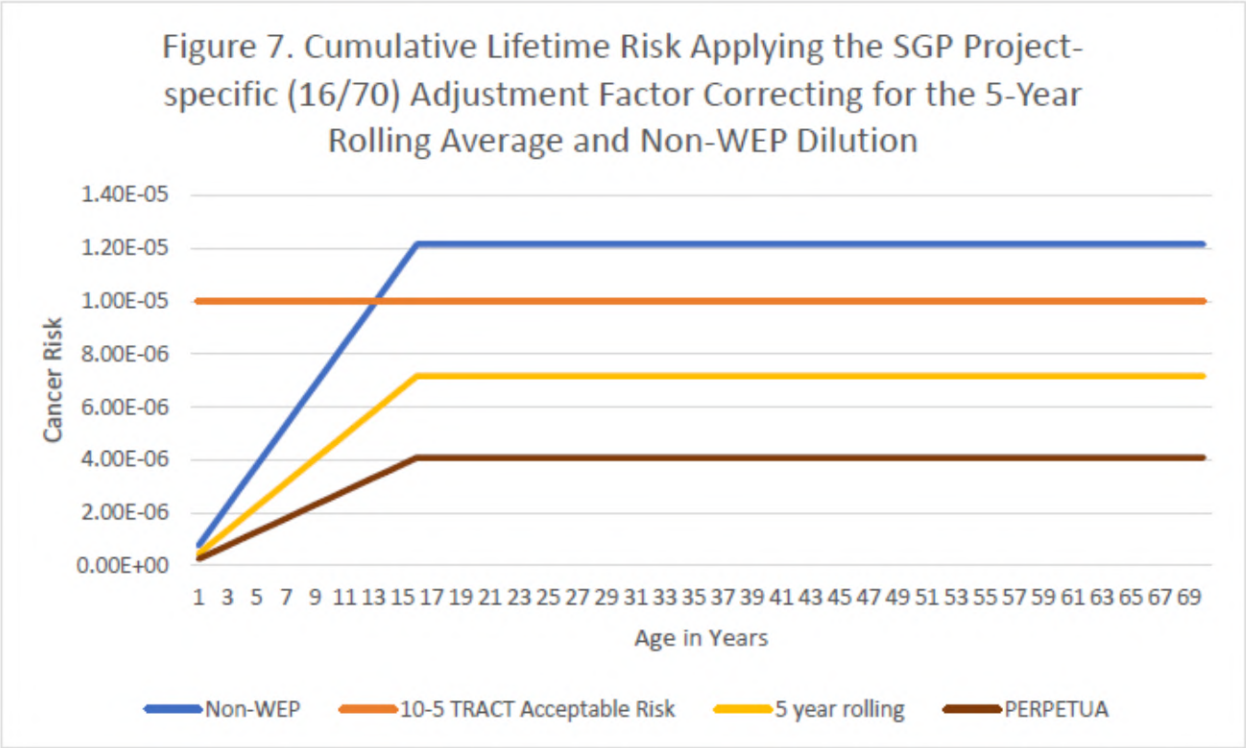
[46] Exhibit J. von Linder, I.H., *et. al.*, *Estimating Children's Soil/Dust Ingestion Rates through Retrospective Analyses of Blood Lead Biomonitoring from the Bunker Hill Superfund Site in Idaho*, Envtl. Health Perspectives, 124:9, 1462-1470 (2016).
[47] Exhibit K. U.S. EPA, *Estimation of Age-specific Soil and Dust Ingestion Rates for U.S. Children: Update to the Default Values for the Integrated Exposure Uptake Biokinetic Model for Lead in U.S. Children* (2021).
[48] Exhibit K.

91. Were the proper TAPs analysis conducted, the cumulative risk for long-term operations would be 5.1 $x10^{-5}$, as noted above. Figure 6, above, illustrated the sequential application of the three SGP Project-specific adjustment factors applied by DEQ (i.e., 5-year rolling average,, non-WEP sources, and 16/70 lifetime adjustment). The final 16/70 exposure dilution yields a cancer risk of $4.1x10^{-6}$. DEQ and the Respondents allege that 40% of the full lifetime allowable exposure is expended by the 16 years of SGP operations.

92. The $5.1x10^{-5}$ carcinogenic risk calculated for the SGP as TAPs requires does assume a 70-year basis. Figure 7 shows the application of the proper **maximum one-year annual average ambient air carcinogen concentration** (0.0125 $\mu g/m^3$) applied to the same 16-year LOM formulae used by the Respondents. After correcting for the 5-year rolling average and non-WEP adjustment factors disguised risk averaging steps, the cumulative risk after the16-year LOM is 1.2 x 10^{-5}.



93. This cumulative risk exceeds the allowable risk criteria by 20% using DEQ and Perpetua's calculation. Figure 7 also illustrates the effect of the serial application of SGP Project-specific 5-year rolling average and non-WEP Project-specific adjustment factors on cumulative cancer risk from the critical receptor viewpoint. Removing these dilution adjustments shows the individual receptor will experience a full lifetime allowable carcinogenic $1x10^{-5}$ equivalent exposure by year 13.

94. This opinion concludes that DEQs use of the ad hoc SGP Project-specific adjustment factors undermines the health protectiveness of the TAPs rule. The TAPs rule was specifically developed to avoid requiring risk assessment analyses by providing an inherent margin of safety (MOS). These SGP Project-specific adjustment factors facilitate cancer dose-averaging risk calculations that allow the SGP to significantly increase arsenic emissions

based on short-term Life of Mine (LOM) assumptions, but to nevertheless average the risk associated with those increased emission over 70-years.

95. This transfer of risk from the mine to the receptor's lifetime significantly reduces the MOS and negates the health protectiveness of the TAPs rule. The TAPs rule simply offers 10-fold increases in allowable risk, or emissions, for either 1) short-term projects of less than 5 years, or 2) T-RACT based relief based on available technology.

96. There is neither a provision, nor a need, for risk assessment if the TAPs Rules are properly implemented based on annual compliance with **maximum one-year annual average ambient air carcinogen concentration**. This application of the TAPs rule has served Idaho well for three decades. This policy change allowing risk averaging through the SGP Project-specific adjustment factors not only undermines the health protectiveness of the individual applicant source, but also the Statewide strategy that keeps all Idahoans safe with minimal regulatory burden.

DATED: October 4, 2024



Ian H. Von Lindern, P.E., Ph.D.

Exhibit A

Ian H. von Lindern, Ph.D., P.E.

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Education

Ph.D., Environmental Science and Engineering, Yale University, 1980
M.F.S., Biometeorology and Atmospheric Studies, Yale University, 1973
B.S., Chemical Engineering, Carnegie-Mellon University, 1971

Professional & Technical Certifications

Professional Engineer, Idaho # 3044 ChE (1975)

Professional Experience

Ian von Lindern is co-founder of TerraGraphics International Foundation (TIFO), a non-profit humanitarian environmental response organization. He served as Chief Executive Officer and Principal Scientist of TerraGraphics Environmental Engineering Inc. from 1984-2014. Under his direction, TerraGraphics developed into a one-hundred person multidisciplinary environmental firm, specializing in the design and management of complex projects including site characterization, risk assessment, hazardous waste remediation, engineering design, GIS and database, and remediation oversight. He has 46 years of national and international engineering and scientific experience that includes a variety of environmental assessments; studies in air, water, and soil pollution; toxic and hazardous materials investigations; remedial and cleanup plans; human health risk assessments; and application of statistical analysis techniques to multidisciplinary environmental problems. He has directed more than 40 major health/environmental projects including primary and secondary smelters, used battery processors, landfills, uranium mill tailings, and organic chemical waste sites in the U.S. He has designed and implemented international health risk assessment/remediation projects in countries with high levels of childhood morbidity and mortality including Russia, China, Peru, Bangladesh, Dominican Republic, Senegal, Nigeria, and Kyrgyzstan.

As a Principal Scientist at TIFO, Dr. von Lindern works with marginalized mining and recycling communities around the world to address pollution-related health and environmental issues. Projects are implemented at the local level acknowledging diverse ethnic, religious, socio-economic, and geographic backgrounds to protect future generations and maintain livelihoods in vulnerable communities. TIFO's mission focuses on building environmental health capacity in both the host countries and the next generation of US scientists by sponsoring and directing collaborative projects, pairing US and local professionals and students; and encouraging programmatic research publications summarizing project outcomes and lessons learned. Since 2010, TIFO has partnered with Médecins Sans Frontières (MSF, Doctors Without Borders) in implementing joint medical, public health and environmental responses. TIFO's recent projects are evolving into a global juxtaposition of simultaneously assisting indigenous and disadvantaged communities in both the US and poor/middle income countries responding to the exponential demand for gold and green-energy technologies in the US, central Asia and west Africa. These projects offer promise of reviving a specialty metals industry in the US and providing subsistence incomes for poor populations suffering from climate-related loss of traditional agricultural and pastoral support systems. Conversely, there is the potential for catastrophic health and environmental damages. US efforts involve rigorous technical analysis of sophisticated regulatory environmental impact and permit applications, conveying that to uninformed communities, and advocating for the highest levels of environmental responsibility. Responses in poor countries involve identifying and implementing protective measures achievable within the socio-economic, political and economic capacity of the community. International projects often involve developing practicable community, family, and individual worker level health interventions, as governments often lack the resources and capacity to effectively regulate industry in either the artisanal or formal sectors.

Dr. von Lindern has served as an EPA Science Advisory Board and Clean Air Scientific Advisory Committee (CASAC) Subcommittee Member on several occasions, including: EPA Criteria Assessment Committee for Lead in the Ambient Air (1975-1977), and subsequent CASAC NAAQS lead reviews (1982-1986, 2006-2008); Review Subcommittee Assessing the Use of the Biokinetic Model for Lead Absorption in Children at RCRA/CERCLA Sites (1988); Subcommittee Assessing the Consistency of Lead Health Regulations in U.S. EPA Programs (1992); SAB Review Subcommittee for Urban Soil Lead Abatement Demonstration Project (1993); the Ad Hoc All-Ages Lead Model (AALM) Review (2005-2007, 2019-2020); External Peer Review of EPA's Draft Report – Proposed Modeling Approaches for a Health-Based Benchmark for Lead in Drinking Water (2017).

Project Experience

Example Consulting Projects Directed by Dr. von Lindern

Bunker Hill Mining and Metallurgical Complex/Coeur d'Alene Basin Superfund Site, Idaho, 1974–2016

Dr. von Lindern has worked for the State of Idaho on various projects involving the Bunker Hill/Coeur d'Alene Basin Superfund Site for more than 40 years, both as the lead Risk Assessor and as TerraGraphics Project Manager for the State of Idaho CERCLA activities. In 1974, as an Environmental Engineer for the State of Idaho, he directed the field study of lead intoxication in children surrounding the Bunker Hill smelter. As the state oversight contractor for more than 20 years, his duties have included initial contact with local leaders, assisting IDEQ in Cooperative Agreement and PRP negotiations, legislative committee presentations, moderating Task Force meetings, reviewing PRP and EPA activities, and developing the risk management strategy and site-specific cleanup criteria. He has a number of peer-reviewed publications on the reduction of childhood blood lead levels and remedial activities at this site. He also represented the IDEQ at the National Academy of Sciences (NAS) review of this Project in Washington D.C. (Superfund and Mining Megasites Lessons Learned from the Coeur d'Alene River Basin, (NRC 2005)).

Washington State Department of Justice – Natural Resources Division Litigation Support and Expert Witness, Northeastern Washington State, December 2009– December 2012

Dr. von Lindern provided expert witness testimony and reports for numerous enforcement and civil environmental liability lawsuits and litigation at sites throughout the United States. He was Principal-in-Charge for a contract with the Washington State Attorney General Office, Natural Resources Division, regarding potential mining contamination in northeastern Washington state. He and other TerraGraphics personnel researched and visited numerous abandoned mine sites and collected samples to assess metal contamination. Dr. von Lindern provided his expert opinion to the client for litigation support.

Trail of the Coeur d'Alenes and Bayhorse Ghost Town Remediation and Idaho State Parks and Recreation (IDPR) Development

The Bayhorse Mine property is a well-known "ghost town" near Challis, Idaho with substantial historic value. After completion of an ASTM Phase I ESA and All Appropriate Inquiry standards, the IDPR was considering the site for development as a State of Idaho Park and wanted to ensure the site was suitable for such use. Dr. von Lindern led the team that completed the assessment of human health risk and water quality concerns for the purchase of the Bayhorse Mine property. After the assessment, IDPR successfully acquired the Bayhorse Mine properties for converting the "ghost town" and associated abandoned mine holdings into a cultural, historical, and adventure recreation park.

The Park design mimics innovative risk management strategies used at the Trail of the Coeur d'Alenes State Park in northern Idaho. Dr. von Lindern assisted IDEQ, IDPR, the U.S. EPA and other related agencies at both Parks by developing a risk management strategy that is protective of human health and the

environment, while allowing public access and preserving the historic and recreational value of the resource. The Park opened to the public in June 2009.

Example TIFO Humanitarian / Non-Profit Projects Directed by Dr. von Lindern

In 2005, the US National Academy of Sciences' exhaustive review of the BHSS cleanup effort determined the health response methodologies were sound and effective. Subsequently, Dr. von Lindern co-led the joint Research & Development initiative between TerraGraphics and the University of Idaho to apply environmental cleanup methodologies developed in Idaho mining districts to hazardous waste sites in low and middle-income countries. Humanitarian cleanups were undertaken in conjunction with local governments, universities, and NGOs in a variety of cultural, socio-economic and governmental venues in Russia, China, Dominican Republic, Senegal, and Nigeria. In 2012, he and Dr. Margrit von Braun sold the for-profit firm and founded TIFO as an independent non-profit organization to assist international communities in remediating hazardous waste sites. TIFO has conducted workshops and human health risk assessments in Kyrgyz Republic, Armenia, Slovenia, Bangladesh, and Mongolia in collaboration with local governments, universities, hospitals, and NGOs, including the international humanitarian organization Médecins Sans Frontières (MSF, Doctors Without Borders).

Lead Poisoning – Emergency Health Response, Haina, Dominican Republic 2007-2011.

The community of Paraiso del Dios bordered a former used lead acid battery recovery operation in the port city of Haina near Santo Domingo. In 1997, several hundred children were surveyed and found to have a mean blood lead level of 71 µg/dL (range: 9-234 µg/dL); twenty-eight percent (28%) of children required immediate medical treatment. Residents reported that several children suffered seizures during the factory's operational years and continue to exhibit learning disabilities. The factory closed in 2000 and a repository for waste materials was developed on-site. The site was then abandoned and was subject to extensive uncontrolled salvage activities. The concrete retaining wall was scavenged, releasing large amounts of buried waste into the community during rain events. The exposed wastes, exceeding 30% lead, were sold as scrap. Highly contaminated materials were recycled and used as building material and fill in the adjacent community. Children from the surrounding community accessed the industrial site on a daily basis, tracking soils from the site and exposing the rest of their families.

Dr. von Lindern designed and directed a sampling and risk assessment program in 2006-07, when the area was named one of the world's top ten most polluted sites. Extremely high lead concentrations were found on site and in adjacent residential lots. Contaminated wastes in the failed repository showed concentrations from 30% to 45% lead. Surface soil lead concentrations ranged from 4,000 to >300,000 mg/kg, orders of magnitude above the USEPA limit of 400 mg/kg. The project team then collaborated with the Ministries of Health and Environment to develop an intervention strategy recommending a blood lead monitoring and follow-up program, relocation of all high-level wastes to an off-site repository, an on-site repository for the low-level and mid-level soils, and dedication of the property as a public park with appropriate institutional controls to ensure sustainability. A blood lead monitoring program began in 2007 and found 80% of children >10 µg/dL, 24% >40 µg/dL, and 7% >70 µg/dL. In 2008, the Dominican Republic government commissioned a cleanup in which Dr. von Lindern provided technical assistance. More than 3000 cubic meters of hazardous wastes and 4000 cubic meters of contaminated soils were removed. The site was turned in to an "ecological park" with a dedication ceremony in 2010. The Ministry of Environment introduced the park as the first step in initiating a cleanup program for the entire country and dedicated an "ecological mural" to the Dominican environment and "heroes" of the cleanup effort.

Lead Poisoning – Emergency Health Response, Dakar, Senegal 2009-2011.

Thiaroye Sur Mer (TSM) was the site of Used Lead Acid Battery recovery since the 1970s. Multiple groups recovered lead from batteries to manufacture weights for local fishermen. Several thousand tons of discarded

battery sludge accumulated in the area over three decades. In 2007, dramatic increases in lead prices stimulated East Indian traders to purchase the lead oxide sludge. To minimize shipping costs, 200 local women were employed to sift out beach sand that had accumulated with the sludge. The process involved transporting, drying, sifting, and bagging the lead dust. Bags of lead product were stored in homes prior to sale. Many mothers brought their infants and toddlers with them to work. In 2007-08, 18 children died as a direct result of lead exposures. Mean blood lead levels in children were >100 μg/dL and individual levels were >350 μg/dL

Limited emergency remediation activities were undertaken in April and May of 2008. Three-hundred (300) tons of lead were removed from local homes. The World Health Organization (WHO) tested siblings of the deceased children and forty-one children were subsequently hospitalized and placed in temporary foster care. Massive flooding of the area during the rainy season delayed further action. After the flood subsided, TIFO collaborated with other partners to conduct extensive sampling and interviews of the TSM population. In collaboration with the Ministries of Health and Environment, Dr. von Lindern developed a health response and remediation strategy that was implemented in April 2009. The strategy included establishment of sentinel homes in the community where intensive interviews and sampling were conducted to determine the extent and severity of continuing exposures and to identify active lead exposure pathways. These homes and resident children were monitored to assess the effectiveness of the cleanup.

Lead Poisoning – Emergency Health Response, Zamfara and Niger State, Northern Nigeria, May 2010–Present

Beginning in 2010, Dr. von Lindern spent several months in northern Nigeria directing the characterization and remediation of the world's worst lead poisoning epidemic. The 2010-2013 epidemic in Zamfara, Nigeria was unprecedented in morbidity, mortality, and in the environmental health response. More than 400 young children died from acute lead poisoning associated with artisanal gold mining. Soil removal protocols developed at the U.S. Bunker Hill Superfund Site were adapted to local resources, labor practices, and cultural traditions. Dr. von Lindern and other TerraGraphics personnel worked cooperatively with local authorities, MSF, the Centers for Disease Control (CDC), the World Health Organization, the Blacksmith Institute, and government officials and villagers in remote areas to develop an emergency response and remove contaminated soils.

In 2011, TerraGraphics was recognized by the United Nations Environment Programme (UNEP) and Green Cross International with the Green Star Award, given to every two years in association with UN reviews of its environmental programs to recognize those who have made remarkable efforts to prevent, prepare for, and respond to environmental emergencies around the world. In 2012-13, remediation progressed from emergency response by international personnel to comprehensive cleanup implemented by the Nigerian government. TerraGraphics humanitarian successor, TIFO, partnered with MSF to provide guidance and assistance the Nigerian Federal, Zamfara State and local governments in the completion of the largest and most comprehensive cleanup implemented and funded by an African government. More than 27,000 m^3 of contaminated soils were removed from 820 residential areas and ore processing areas in eight villages, largely by hand labor, and disposed of in constructed landfills. Soil lead exposures decreased 97% for more than 17,000 villagers, allowing chelation treatment of 2349 children. Mean blood lead levels for children ≤5 years age declined from 173 μg/dL to <20 μg/dL over the four-year US $5M remedial program.

Subsequently, TIFO, MSF and other NGOs assisted local, state, and federal leadership in implementing long-term prevention and management programs in Zamfara State. In 2016, a second ASGM poisoning event killed 28 children in neighboring Niger State. The federal government requested TIFO assistance and mobilized trained technicians from Zamfara to lead the assessment and cleanup. Remediation was fully implemented with Nigerian funds, and Niger State assumed takeover of both medical and environmental operations and maintenance in 2018. This successful application was the impetus for the Nigerian Ministry of Mines and Steel/World Bank/MSF/TIFO sponsored Conference in Abuja in 2018, examining the legalization and support of ASGM as a mechanism to address poverty and population displacement in the Sahel, employing safer-mining initiatives.

Continued TIFO-Médecins Sans Frontières Collaborations: Bangladesh and Kyrgyzstan 2011-Present.

In 2014, following successful collaborations in west Africa, MSF and TIFO's partnered to assess and address pollutant-related hazards at formal and informal leather tanneries; small-scale plastic, aluminum, foundry, and textiles recycling operations; and artisanal family-scale scavenging and waste recovery and reuse operations in urban slums in Dhaka, Bangladesh. MSF has since been operating occupational health clinics employing environmental health/occupational remedies for several thousand workers and families.

Since 2016, TIFO and MSF have partnered with the Kyrgyz Ministry of Health (MOH) assessing the potential, and emergency response considerations, for seismic and climate-related catastrophic release of legacy mining and smelting hazardous wastes accumulated over 70 years of operations at the former Soviet Union's largest mercury and antimony factories. TIFO provided assistance with Staff Health and Safety planning and performing a Human Health Risk Assessment for women and children's health issues in the mercury/antimony/gold mining communities. In 2019, the joint TIFO/MSF/MOH team collected >500 soil, air, water and food samples to support health assessment and target blood, urine and hair surveys scheduled for summer 2020. These results will support establishing environmental/occupational health monitoring/intervention capacity in the local government, as Kyrgyz officials revitalize the Soviet-era mining operation to support the local economy and meet the growing demand for mercury in ASGM.

Gold and Strategic Minerals Development Impact Evaluations on Historic Tribal Lands, Intermountain West, USA, 2020 – Present.

TIFO's mission is to assist mining and mineral processing communities to operate as safely as practicable while maintaining essential economic activities. The unprecedented demand for gold and strategic metals has prompted several major exploration and mineral development proposals in western states. TIFO's international mission includes assessing and responding to health and environmental impacts of polluting activities on sovereign native and tribal lands within the US. In that regard TIFO supports scientifically-sound and transparent analyses of the environmental and human health issues faced by mining communities, and the development of solutions implemented within local socio-economic and cultural capabilities. Proposed gold, antimony, and cobalt mining in Idaho, Nevada and Washington States have the potential to adversely affect several reservations and aboriginal tribal lands. The Idaho Stibnite Gold Mine proposal, that claims it will meet 33% of the US antimony demand, is of interest because both the industry and the US regulatory arena have the capacity to implement best practices that are not available to poor communities throughout the world. Mining advocates allege these developments will be safe and secure, and are projecting unprecedented control levels for toxic contaminants. Conversely, the mining company consultants are arguing for relief from environmental regulatory requirements in these mining-friendly states. However, citizen-based interest groups and tribal authorities have limited capacity and resources to evaluate the complex environmental assessments and permit applications. Ironically, the Stibnite Gold Project is exploiting the same ores and metallurgical processes as the gold/antimony mining TIFO is assessing in Kyrgyzstan. As there are currently no smelters in the US that can process the antimony concentrates, the Idaho ores are currently projected to be exported to the same Chinese smelters processing the Kyrgyz ores. Through TIFO, Dr. von Lindern is providing independent review of these documents and submitting comments to the review agencies.

Regulatory Knowledge

Ian von Lindern has worked on projects regulated under Federal, State, local, and foreign regulations, including CERCLA, TSCA, CWA, CAA, NESHAPs, DOT, EPRCRA, SARA, NEPA, and RCRA in the U.S. He has provided litigation support and expert witness testimony in administrative and court proceedings. He has served on several U.S. government advisory panels, including the appointments pertinent to lead health and remediation as shown in the list below.

Special Appointments/Memberships/Affiliations

U.S. EPA Science Advisory Board. Peer Review. All Ages Lead Model (AALM). Washington, DC. October 16-20, 2019.

U.S. EPA External Peer Review. Draft Report, Proposed Modeling Approaches for a Health Based Benchmark for Lead in Drinking Water. Prepared for: U.S. Environmental Protection Agency, Office of Water, Washington, DC. June 27-28, 2017.

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U.S. EPA Science Advisory Board (CASAC). Review of the Integrated Science Assessment (ISA) for Lead in the Ambient Air. US EPA, Washington, D.C. 2012-2013

American University of Armenia, School of Public Health, Yerevan. Invited Professor, Graduate course Risk Assessment for Environmental Health Professionals for Master of Public Health (MPH) Students. 2012-present.

U.S. Centers for Disease Control and the Harvard University School of Public Health Initiative to address health effects of mining and smelting in the developing world. 2009-2013.

Affiliate Professor of Chemical Engineering, University of Idaho, Moscow, Idaho, 1981–2011

U.S. EPA Science Advisory Board. Review of the Lead National Ambient Air Quality Standard for Lead. U.S. EPA, Washington, DC. 2006-2008.

U.S. Clean Air Scientific Advisory Committee (CASAC). Review of the Air Quality Criteria Document for Lead. U.S. EPA, Washington, DC. 2010-2013, 2006-2007.

U.S. EPA Science Advisory Board. Review of EPA's Lead Renovation, Repair and Painting (LRRP) Activities. U.S. EPA, Washington, DC. 2007.

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U.S. EPA Science Advisory Board. Review Subcommittee for Urban Soil Lead Abatement Demonstration Project. U.S. EPA, Washington, DC, 1993-1995.

NIEHS Select Reviewer Grants Review Committee, Superfund/Hazardous Workers Training Program, NIEHS, RTP, NC. 1992.

Advisory Committee for Development of Lead Paint Abatement Guidelines for Public Housing in the United States, U.S. Dept of HUD, Washington, D.C., 1992.

U.S. EPA Science Advisory Board, Subcommittee Assessing the Consistency of Lead Health Regulations in U.S. EPA Programs, Special Report to the Administrator, Washington, D.C., 1992.

U.S. EPA Science Advisory Board, Review Subcommittee Assessing the Use of the Biokinetic Model for Lead Absorption in Children at RCRA/CERCLA sites. U.S. EPA, Washington DC, 1991.

Technical advisor and consultant to Latah County and North Central Health District Regional Solid Waste Advisory Committees, Moscow and Lewiston, ID. 1991.

Technical advisor to the National Alliance to End Lead Poisoning in Children, Washington, D.C. 1991-2001

NIEHS Select Reviewer Grants Review Committee, Superfund/Hazardous Workers Training Program, NIEHS, Research Triangle Park, NC, 1989-1993.

U.S. EPA Clean Air Scientific Advisory Committee (CASAC) Member, Subcommittee on Exposure Assessment Methodology, U.S. EPA, Washington D.C. 1988.

U.S. EPA Criteria Assessment Committee for Lead in the Ambient Air, RTP, NC. 1975-1986.

Additional Certifications/Training

PSMJ Conference for CEOs-2005

Ian H. von Lindern, Ph.D., P.E.

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Mining, Climate Change, and Conflict: Lessons from Nigeria and Kyrgyzstan. Society for Mining, Metallurgy, and Exploration, Southern California Chapter (virtual). 12 November 2020.

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Review of Existing Information and Identification of Data Gaps for Conducting Human Health Risk Assessments (HHRA) and Biomonitoring for Heavy Metal Exposures – Khaidarken, Batken Province, Kyrgyz Republic. Prepared for Kyrgyz Ministry of Health and Médecins Sans Frontières. April 2019.

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Presenter: Environmental Health and Risk Assessment: Workshop on MSF and Extractive Industries. Médecins sans Frontières, Geneva, Switzerland. 24-25 October 2018.

Instructor, Assessment and Remediation of Heavy Metal Contamination, Workshop on Extractive Industries, Médecins sans Frontières, Geneva, Switzerland, October 2018.

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The Life Cycle of Metals: Improving Health, Environment and Human Security, Symposium. University of Tokyo and Harvard University. Tokyo, Japan. October 2011.

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Comprehensive Health Response and Cleanup Strategy for the Rudnaya Pristan Site in Far East Russia. Prepared for the Far East Health Fund. Vladivostok, Primorye, Russia. November 2006.

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Exhibit B

United States
Environmental Protection
Agency

Office of Health and
Environmental Assessment
Washington DC 20460

EPA/600/8-87/045
August 1987

Research and Development

EPA

The Risk Assessment Guidelines of 1986

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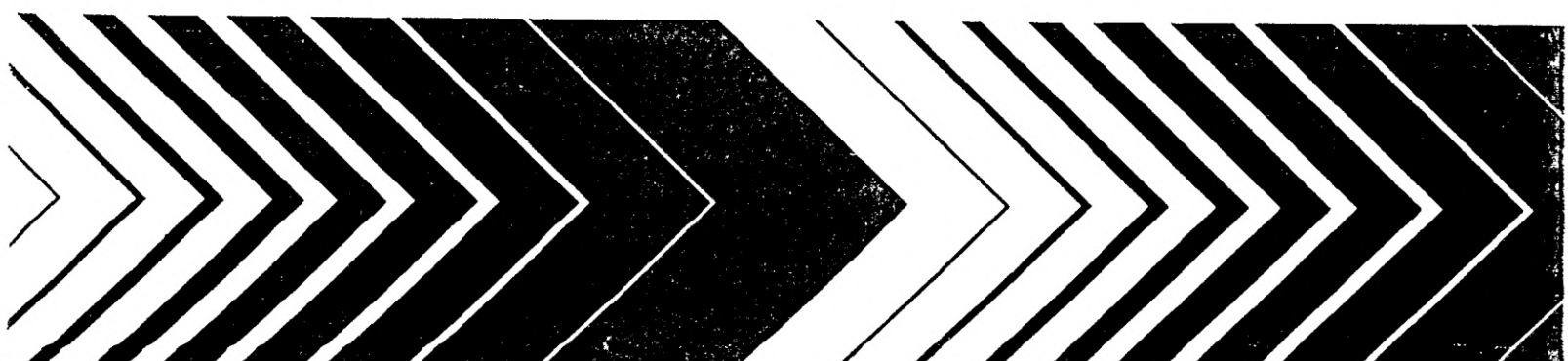

EPA/600/8-87/045
August 1987

THE RISK ASSESSMENT GUIDELINES OF 1986

U.S. Environmental Protection Agency
Washington, D.C.

TR 3350

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TR 3351

REC 6155

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TR 3352

REC 6156

PREFACE

On September 24, 1986, the U.S. Environmental Protection Agency (EPA) issued risk assessment guidelines relating to five areas: carcinogenicity, mutagenicity, chemical mixtures, suspect developmental toxicants, and estimating exposures (51 FR 33992-34054). The guidelines were developed to promote high technical quality and Agencywide consistency in the risk assessment process.

The guidelines were developed partly in response to a 1983 National Academy of Sciences publication entitled "Risk Assessment in the Federal Government: Managing the Process," which recommended that Federal regulatory agencies establish risk assessment guidelines. An EPA task force, convened by then Administrator William D. Ruckelshaus to study ways to improve the scientific foundation for Agency regulatory decisions, accepted the recommendation, and work on the guidelines began early in 1984.

The guidelines are products of a two-year Agency development and review process which included many scientists from the larger scientific community. They were developed as part of an interoffice guidelines development program under the auspices of the Office of Health and Environmental Assessment in the Agency's Office of Research and Development. The scientists involved were skilled in each topic, and early drafts were peer-reviewed by experts from academia, industry, public interest groups, and other governmental agencies. Subsequently, proposed guidelines were published in the *Federal Register*, reviewed by special panels of EPA's Science Advisory Board (SAB), and revised to take into account public and SAB comments. After final EPA review and Office of Management and Budget review, the guidelines were signed by EPA Administrator Lee M. Thomas on August 22, 1986, and published in the *Federal Register* on September 24, 1986.

Each of the five guidelines provides both technical information and science policy guidance relating to the conduct of EPA risk assessments and presentation of risk assessment information. The guidelines are sufficiently flexible to allow skilled scientists to make appropriate technical judgments on a case-by-case basis, giving full consideration to all relevant scientific information. The guidelines also stress that risk assessments should include a discussion of the strengths and weaknesses of each assessment by describing uncertainties, assumptions, and limitations, as well as the scientific basis and rationale for each assessment. They require risk assessors to inform Agency decisionmakers and the public about the assumptions used in and the implications of individual risk assessment conclusions, so that appropriate risk management decisions can be made and explained.

While these guidelines are published Agency documents, they should not be interpreted as static, but as the first step in the continuing process of identifying the best methods for assessing risk to environmental pollutants. Consequently, the risk assessment guidelines are constantly undergoing Agency scrutiny and will be revised in line with new methods and information, as appropriate.

This document presents the five guidelines as they originally appeared in the *Federal Register* but in a format that is easier to read.

TR 3353

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ABSTRACT

On September 24, 1986, the U.S. Environmental Protection Agency issued risk assessment guidelines relating to five areas: carcinogenicity, mutagenicity, chemical mixtures, suspect developmental toxicants, and estimating exposures (51 FR 33992-34054). The guidelines were developed to promote high technical quality and Agencywide consistency in the risk assessment process. This document presents the five guidelines as they originally appeared in the *Federal Register* but in a format that is easier to read.

TR 3354

51 FR 33992

GUIDELINES FOR CARCINOGEN RISK ASSESSMENT

SUMMARY: On September 24, 1986, the U.S. Environmental Protection Agency issued the following five guidelines for assessing the health risks of environmental pollutants.

Guidelines for Carcinogen Risk Assessment

Guidelines for Estimating Exposures

Guidelines for Mutagenicity Risk Assessment

Guidelines for the Health Assessment of Suspect Developmental Toxicants

Guidelines for the Health Risk Assessment of Chemical Mixtures

This section contains the Guidelines for Carcinogen Risk Assessment.

The Guidelines for Carcinogen Risk Assessment (hereafter "Guidelines") are intended to guide Agency evaluation of suspect carcinogens in line with the policies and procedures established in the statutes administered by the EPA. These Guidelines were developed as part of an interoffice guidelines development program under the auspices of the Office of Health and Environmental Assessment (OHEA) in the Agency's Office of Research and Development. They reflect Agency consideration of public and Science Advisory Board (SAB) comments on the Proposed Guidelines for Carcinogen Risk Assessment published November 23, 1984 (49 FR 46294).

This publication completes the first round of risk assessment guidelines development. These Guidelines will be revised, and new guidelines will be developed, as appropriate.

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SUPPLEMENTARY INFORMATION: In 1983, the National Academy of Sciences (NAS) published its book entitled *Risk Assessment in the Federal Government: Managing the Process*. In that book, the NAS recommended that Federal regulatory agencies establish "inference guidelines" to ensure consistency and technical quality in risk assessments and to ensure that the risk assessment process was maintained as a scientific effort separate from risk management. A task force within EPA accepted that recommendation and requested that Agency scientists begin to develop such guidelines.

General

The guidelines are products of a two-year Agencywide effort, which has included many scientists from the larger scientific community. These guidelines set forth principles and procedures to guide EPA scientists in the conduct of Agency risk assessments, and to inform Agency decision makers and the public about these procedures. In particular, the guidelines emphasize that risk assessments will be conducted on a case-by-case basis, giving full consideration to all relevant scientific information. This case-by-case approach means that Agency experts review the scientific information on each agent and use the most scientifically appropriate interpretation to assess risk. The guidelines also stress that this information will be fully presented in Agency risk assessment documents, and that Agency scientists will identify the strengths and weaknesses of each assessment by describing uncertainties, assumptions, and limitations, as well as the scientific basis and rationale for each assessment.

Finally, the guidelines are formulated in part to bridge gaps in risk assessment methodology and data. By identifying these gaps and the importance of the missing information to the risk assessment process, EPA wishes to encourage research and analysis that will lead to new risk assessment methods and data.

Guidelines for Carcinogen Risk Assessment

Work on the Guidelines for Carcinogen Risk Assessment began in January 1984. Draft guidelines were developed by Agency work groups composed of expert scientists from throughout the Agency. The drafts were peer-reviewed by expert scientists in the field of carcinogenesis from universities, environmental groups, industry, labor, and other governmental agencies. They were then proposed for public comment in the *FEDERAL REGISTER* (49 FR 46294). On November 9, 1984, the Administrator directed that Agency offices use the proposed guidelines in performing risk assessments until final guidelines become available.

TR 3355

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After the close of the public comment period, Agency staff prepared summaries of the comments, analyses of the major issues presented by the commentors, and proposed changes in the language of the guidelines to deal with the issues raised. These analyses were presented to review panels of the SAB on March 4 and April 22-23, 1985, and to the Executive Committee of the SAB on April 25-26, 1985. The SAB meetings were announced in the *FEDERAL REGISTER* as follows: February 12, 1985 (50 FR 5811) and April 4, 1985 (50 FR 13420 and 13421).

In a letter to the Administrator dated June 19, 1985, the Executive Committee generally concurred on all five of the guidelines, but recommended certain revisions, and requested that any revised guidelines be submitted to the appropriate SAB review panel chairman for review and concurrence on behalf of the Executive Committee. As described in the responses to comments (see Part B: Response to the Public and Science Advisory Board Comments), each guidelines document was revised, where appropriate, consistent with the SAB recommendations, and revised draft guidelines were submitted to the panel chairmen. Revised draft Guidelines for Carcinogen Risk Assessment were concurred on in a letter dated February 7, 1986. Copies of the letters are available at the Public Information Reference Unit, EPA Headquarters Library, as indicated elsewhere in this section.

Following this Preamble are two parts: Part A contains the Guidelines and Part B, the Response to the Public and Science Advisory Board Comments (a summary of the major public comments, SAB comments, and Agency responses to those comments).

The Agency is continuing to study the risk assessment issues raised in the guidelines and will revise these Guidelines in line with new information as appropriate.

References, supporting documents, and comments received on the proposed guidelines, as well as copies of the final guidelines, are available for inspection and copying at the Public Information Reference Unit (202-382-5926), EPA Headquarters Library, 401 M Street, S.W., Washington, DC, between the hours of 8:00 a.m. and 4:30 p.m.

I certify that these Guidelines are not major rules as defined by Executive Order 12291, because they are nonbinding policy statements and have no direct effect on the regulated community. Therefore, they will have no effect on costs or prices, and they will

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have no other significant adverse effects on the economy. These Guidelines were reviewed by the Office of Management and Budget under Executive Order 12291.

August 22, 1986

Lee M. Thomas,

Administrator

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Part A: Guidelines for Carcinogen Risk Assessment

I. Introduction

This is the first revision of the 1976 Interim Procedures and Guidelines for Health Risk Assessments of Suspected Carcinogens (U.S. EPA, 1976; Albert et al., 1977). The impetus for this revision is the need to incorporate into these Guidelines the concepts and approaches to carcinogen risk assessment that have been developed during the last ten years. The purpose of these Guidelines is to promote quality and consistency of carcinogen risk assessments within the EPA and to inform those outside the EPA about its approach to carcinogen risk assessment. These Guidelines emphasize the broad but essential aspects of risk assessment that are needed by experts in the various disciplines required (e.g., toxicology, pathology, pharmacology, and statistics) for carcinogen risk assessment. Guidance is given in general terms since the science of carcinogenesis is in a state of rapid advancement, and overly specific approaches may rapidly become obsolete.

These Guidelines describe the general framework to be followed in developing an analysis of carcinogenic risk and some salient principles to be used in evaluating the quality of data and in formulating judgments concerning the nature and magnitude of the cancer hazard from suspect carcinogens. It is the intent of these Guidelines to permit sufficient flexibility to accommodate new knowledge and new assessment methods as they emerge. It is also recognized that there is a need for new methodology that has not been addressed in this document in a number of areas, e.g., the characterization of uncertainty. As this knowledge and assessment methodology are developed, these Guidelines will be revised whenever appropriate.

A summary of the current state of knowledge in the field of carcinogenesis and a statement of broad scientific principles of carcinogen risk assessment, which was developed by the Office of Science and Technology Policy (OSTP, 1985), forms an important basis for these Guidelines; the format of these Guidelines is similar to that proposed by the National Research Council (NRC) of the National Academy of Sciences in a book entitled *Risk Assessment in the Federal Government: Managing the Process* (NRC, 1983).

These Guidelines are to be used within the policy framework already provided by applicable EPA statutes and do not alter such policies. These Guidelines provide general directions for analyzing and organizing available data. They do not imply that one kind of data or another is prerequisite for regulatory action to control, prohibit, or allow the use of a carcinogen.

Regulatory decision making involves two components: risk assessment and risk management. Risk assessment defines the adverse health consequences of exposure to toxic agents. The risk assessments will be carried out independently from considerations of the consequences of regulatory action. Risk management combines the risk assessment with the directives of regulatory legislation, together with socioeconomic, technical, political, and other considerations, to reach a decision as to whether or how much to control future exposure to the suspected toxic agents.

Risk assessment includes one or more of the following components: hazard identification, dose-response assessment, exposure assessment, and risk characterization (NRC, 1983).

Hazard identification is a qualitative risk assessment, dealing with the process of determining whether exposure to an agent has the potential to increase the incidence of cancer. For purposes of these Guidelines, both malignant and benign tumors are used in the evaluation of the carcinogenic hazard. The hazard identification component qualitatively answers the question of how likely an agent is to be a human carcinogen.

Traditionally, quantitative risk assessment has been used as an inclusive term to describe all or parts of dose-response assessment, exposure assessment, and risk characterization. Quantitative risk assessment can be a useful general term in some circumstances, but the more explicit terminology developed by the NRC (1983) is usually preferred. The dose-response assessment defines the relationship between the dose of an agent and the probability of induction of a carcinogenic effect. This component usually entails an extrapolation from the generally high doses administered to experimental animals or exposures noted in epidemiologic studies to the exposure levels expected from human contact with the agent in the environment; it also includes considerations of the validity of these extrapolations.

The exposure assessment identifies populations exposed to the agent, describes their composition and size, and presents the types, magnitudes, frequencies, and durations of exposure to the agent.

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In risk characterization, the results of the exposure assessment and the dose-response assessment are combined to estimate quantitatively the carcinogenic risk. As part of risk characterization, a summary of the strengths and weaknesses in the hazard identification, dose-response assessment, exposure assessment, and the public health risk estimates are presented. Major assumptions, scientific judgments, and, to the extent possible, estimates of the uncertainties embodied in the assessment are also presented, distinguishing clearly between fact, assumption, and science policy.

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The National Research Council (NRC, 1983) pointed out that there are many questions encountered in the risk assessment process that are unanswerable given current scientific knowledge. To bridge the uncertainty that exists in these areas where there is no scientific consensus, inferences must be made to ensure that progress continues in the assessment process. The OSTP (1985) reaffirmed this position, and generally left to the regulatory agencies the job of articulating these inferences. Accordingly, the Guidelines incorporate judgmental positions (science policies) based on evaluation of the presently available information and on the regulatory mission of the Agency. The Guidelines are consistent with the principles developed by the OSTP (1985), although in many instances are necessarily more specific.

II. Hazard Identification

A. Overview

The qualitative assessment or hazard identification part of risk assessment contains a review of the relevant biological and chemical information bearing on whether or not an agent may pose a carcinogenic hazard. Since chemical agents seldom occur in a pure state and are often transformed in the body, the review should include available information on contaminants, degradation products, and metabolites.

Studies are evaluated according to sound biological and statistical considerations and procedures. These have been described in several publications (Interagency Regulatory Liaison Group, 1979; OSTP, 1985; Peto et al., 1980; Mantel, 1980; Mantel and Haenszel, 1959; Interdisciplinary Panel on Carcinogenicity, 1984; National Center for Toxicological Research, 1981; National Toxicology Program, 1984; U.S. EPA, 1983a, 1983b, 1983c; Haseman, 1984). Results and conclusions concerning the agent, derived from different types of information, whether indicating positive or negative responses, are melded together into a weight-of-evidence determination. The strength of the evidence supporting a potential human carcinogenicity judgment is developed in a weight-of-evidence stratification scheme.

B. Elements of Hazard Identification

Hazard identification should include a review of the following information to the extent that it is available.

1. *Physical-Chemical Properties and Routes and Patterns of Exposure.* Parameters relevant to carcinogenesis, including physical state, physical-chemical properties, and exposure pathways in the environment should be described where possible.

2. *Structure-Activity Relationships.* This section should summarize relevant structure-activity correlations that support or argue against the prediction of potential carcinogenicity.

3. Meta*bolic and Pharmacokinetic Properties.* This section should summarize relevant metabolic information. Information such as whether the agent is direct-acting or requires conversion to a reactive carcinogenic (e.g., an electrophilic) species, metabolic pathways for such conversions, macromolecular interactions, and fate (e.g., transport, storage, and excretion), as well as species differences, should be discussed and critically evaluated. Pharmacokinetic properties determine the biologically effective dose and may be relevant to hazard identification and other components of risk assessment.

4. To*xicologic Effects.* Toxicologic effects other than carcinogenicity (e.g., suppression of the immune system, endocrine disturbances, organ damage) that are relevant to the evaluation of carcinogenicity should be summarized. Interactions with other chemicals or agents and with lifestyle factors should be discussed. Prechronic and chronic toxicity evaluations, as well as other test results, may yield information on target organ effects, pathophysiological reactions, and preneoplastic lesions that bear on the evaluation of carcinogenicity. Dose-response and time-to-response analyses of these reactions may also be helpful.

5. *Short-Term Tests.* Tests for point mutations, numerical and structural chromosome aberrations, DNA damage/repair, and *in vitro* transformation provide supportive evidence of carcinogenicity and may give information on potential carcinogenic mechanisms. A range of tests from each of the above end points helps to characterize an agent's response spectrum.

Short-term *in vivo* and *in vitro* tests that can give indication of initiation and promotion activity may also provide supportive evidence for carcinogenicity. Lack of positive results in short-term tests for genetic toxicity does not provide a basis for discounting positive results in long-term animal studies.

6. *Long-Term Animal Studies.* Criteria for the technical adequacy of animal carcinogenicity studies have been published (e.g., U.S. Food and Drug Administration, 1982; Interagency Regulatory Liaison Group, 1979; National Toxicology Program, 1984; OSTP, 1985; U.S. EPA, 1983a, 1983b, 1983c; Feron et al., 1980; Mantel, 1980) and should be used to judge the acceptability of individual studies. Transplacental and multigenerational carcinogenesis studies, in addition to more conventional long-term animal studies, can yield useful information about the carcinogenicity of agents.

It is recognized that chemicals that induce benign tumors frequently also induce malignant

tumors, and that benign tumors often progress to malignant tumors (Interdisciplinary Panel on Carcinogenicity, 1984). The incidence of benign and malignant tumors will be combined when scientifically defensible (OSTP, 1985; Principle 8). For example, the Agency will, in general, consider the combination of benign and malignant tumors to be scientifically defensible unless the benign tumors are not considered to have the potential to progress to the associated malignancies of the same histogenic origin. If an increased incidence of benign tumors is observed in the absence of malignant tumors, in most cases the evidence will be considered as limited evidence of carcinogenicity.

The weight of evidence that an agent is potentially carcinogenic for humans increases (1) with the increase in number of tissue sites affected by the agent; (2) with the increase in number of animal species, strains, sexes, and number of experiments and doses showing a carcinogenic response; (3) with the occurrence of clear-cut dose-response relationships as well as a high level of statistical significance of the increased tumor incidence in treated compared to control groups; (4) when there is a dose-related shortening of the time-to-tumor occurrence or time to death with tumor; and (5) when there is a dose-related increase in the proportion of tumors that are malignant.

Long-term animal studies at or near the maximum tolerated dose level (MTD) are used to ensure an adequate power for the detection of carcinogenic

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activity (NTP, 1984; IARC, 1982). Negative long-term animal studies at exposure levels above the MTD may not be acceptable if animal survival is so impaired that the sensitivity of the study is significantly reduced below that of a conventional chronic animal study at the MTD. The OSTP (1985; Principle 4) has stated that,

> The carcinogenic effects of agents may be influenced by non-physiological responses (such as extensive organ damage, radical disruption of hormonal function, saturation of metabolic pathways, formation of stones in the urinary tract, saturation of DNA repair with a functional loss of the system) induced in the model systems. Testing regimes inducing these responses should be evaluated for their relevance to the human response to an agent and evidence from such a study, whether positive or negative, must be carefully reviewed.

Positive studies at levels above the MTD should be carefully reviewed to ensure that the responses are not due to factors which do not operate at exposure levels below the MTD. Evidence indicating that high exposures alter tumor responses by indirect mechanisms that may be unrelated to effects at lower exposures should be dealt with on an individual basis. As noted by the OSTP (1985), "Normal metabolic activation of carcinogens may possibly also be altered and carcinogenic potential reduced as a consequence [of high-dose testing]."

Carcinogenic responses under conditions of the experiment should be reviewed carefully as they relate to the relevance of the evidence to human carcinogenic risks (e.g., the occurrence of bladder tumors in the presence of bladder stones and implantation site sarcomas). Interpretation of animal studies is aided by the review of target organ toxicity and other effects (e.g., changes in the immune and endocrine systems) that may be noted in prechronic or other toxicological studies. Time and dose-related changes in the incidence of preneoplastic lesions may also be helpful in interpreting animal studies.

Agents that are positive in long-term animal experiments and also show evidence of promoting or cocarcinogenic activity in specialized tests should be considered as complete carcinogens unless there is evidence to the contrary because it is, at present, difficult to determine whether an agent is only a promoting or cocarcinogenic agent. Agents that show positive results in special tests for initiation, promotion, or cocarcinogenicity and no indication of tumor response in well-conducted and well-designed long-term animal studies should be dealt with on an individual basis.

To evaluate carcinogenicity, the primary comparison is tumor response in dosed animals as compared with that in contemporary matched control animals. Historical control data are often valuable, however, and could be used along with concurrent control data in the evaluation of carcinogenic responses (Haseman et al., 1984). For the evaluation of rare tumors, even small tumor responses may be significant compared to historical data. The review of tumor data at sites with high spontaneous background requires special consideration (OSTP, 1985; Principle 9). For instance, a response that is significant with respect to the experimental control group may become questionable if the historical control data indicate that the experimental control group had an unusually low background incidence (NTP, 1984).

For a number of reasons, there are widely diverging scientific views (OSTP, 1985; Ward et al., 1979a, b; Tomatis, 1977; Nutrition Foundation, 1983) about the validity of mouse liver tumors as an indication of potential carcinogenicity in humans when such tumors occur in strains with high spontaneous background incidence and when they constitute the only tumor response to an agent. These Guidelines take the position that when the only tumor response is in the mouse liver and when other conditions for a classification of "sufficient" evidence in animal studies are met (e.g., replicate studies, malignancy; see section IV), the data should be considered as "sufficient" evidence of carcinogenicity. It is understood that this classification could be changed on a case-by-case basis to "limited," if warranted, when factors such as the following, are observed: an increased incidence

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of tumors only in the highest dose group and/or only at the end of the study; no substantial dose-related increase in the proportion of tumors that are malignant; the occurrence of tumors that are predominantly benign; no dose-related shortening of the time to the appearance of tumors; negative or inconclusive results from a spectrum of short-term tests for mutagenic activity; the occurrence of excess tumors only in a single sex.

Data from all long-term animal studies are to be considered in the evaluation of carcinogenicity. A positive carcinogenic response in one species/strain/sex is not generally negated by negative results in other species/strain/sex. Replicate negative studies that are essentially identical in all other respects to a positive study may indicate that the positive results are spurious.

Evidence for carcinogenic action should be based on the observation of statistically significant tumor responses in specific organs or tissues. Appropriate statistical analysis should be performed on data from long-term studies to help determine whether the effects are treatment-related or possibly due to chance. These should at least include a statistical test for trend, including appropriate correction for differences in survival. The weight to be given to the level of statistical significance (the p-value) and to other available pieces of information is a matter of overall scientific judgment. A statistically significant excess of tumors of all types in the aggregate, in the absence of a statistically significant increase of any individual tumor type, should be regarded as minimal evidence of carcinogenic action unless there are persuasive reasons to the contrary.

7. Human Studies. Epidemiologic studies provide unique information about the response of humans who have been exposed to suspect carcinogens. Descriptive epidemiologic studies are useful in generating hypotheses and providing supporting data, but can rarely be used to make a causal inference. Analytical epidemiologic studies of the case-control or cohort variety, on the other hand, are especially useful in assessing risks to exposed humans.

Criteria for the adequacy of epidemiologic studies are well recognized. They include factors such as the proper selection and characterization of exposed and control groups, the adequacy of duration and quality of follow-up, the proper identification and characterization of confounding factors and bias, the appropriate consideration of latency effects, the valid ascertainment of the causes of morbidity and death, and the ability to detect specific effects. Where it can be calculated, the statistical power to detect an appropriate outcome should be included in the assessment.

The strength of the epidemiologic evidence for carcinogenicity depends, among other things, on the type of analysis and on the magnitude and specificity of the response. The weight of evidence increases rapidly with the number of adequate studies that show comparable results on populations exposed to the same agent under different conditions.

It should be recognized that epidemiologic studies are inherently capable of detecting only comparatively large increases in the relative risk of

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cancer. Negative results from such studies cannot prove the absence of carcinogenic action; however, negative results from a well-designed and well-conducted epidemiologic study that contains usable exposure data can serve to define upper limits of risk; these are useful if animal evidence indicates that the agent is potentially carcinogenic in humans.

C. Weight of Evidence

Evidence of possible carcinogenicity in humans comes primarily from two sources: long-term animal tests and epidemiologic investigations. Results from these studies are supplemented with available information from short-term tests, pharmacokinetic studies, comparative metabolism studies, structure-activity relationships, and other relevant toxicologic studies. The question of how likely an agent is to be a human carcinogen should be answered in the framework of a weight-of-evidence judgment. Judgments about the weight of evidence involve considerations of the quality and adequacy of the data and the kinds and consistency of responses induced by a suspect carcinogen. There are three major steps to characterizing the weight of evidence for carcinogenicity in humans: (1) characterization of the evidence from human studies and from animal studies individually, (2) combination of the characterizations of these two types of data into an indication of the overall weight of evidence for human carcinogenicity, and (3) evaluation of all supporting information to determine if the overall weight of evidence should be modified.

EPA has developed a system for stratifying the weight of evidence (see section IV). This classification is not meant to be applied rigidly or mechanically. At various points in the above discussion, EPA has emphasized the need for an overall, balanced judgment of the totality of the available evidence. Particularly for well-studied substances, the scientific data base will have a complexity that cannot be captured by any classification scheme. Therefore, the hazard identification section should include a narrative summary of the strengths and weaknesses of the evidence as well as its categorization in the EPA scheme.

The EPA classification system is, in general, an adaptation of the International Agency for Research on Cancer (IARC, 1982) approach for classifying the

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weight of evidence for human data and animal data. The EPA classification system for the characterization of the overall weight of evidence for carcinogenicity (animal, human, and other supportive data) includes: Group A -- Carcinogenic to Humans; Group B -- Probably Carcinogenic to Humans; Group C -- Possibly Carcinogenic to Humans; Group D -- Not Classifiable as to Human Carcinogenicity; and Group E -- Evidence of Non-Carcinogenicity for Humans.

The following modifications of the IARC approach have been made for classifying human and animal studies.

For human studies:

(1) The observation of a statistically significant association between an agent and life-threatening benign tumors in humans is included in the evaluation of risks to humans.

(2) A "no data available" classification is added.

(3) A "no evidence of carcinogenicity" classification is added. This classificaton indicates that no association was found between exposure and increased risk of cancer in well-conducted, well-designed, independent analytical epidemiologic studies.

For animal studies:

(1) An increased incidence of combined benign and malignant tumors will be considered to provide sufficient evidence of carcinogenicity if the other criteria defining the "sufficient" classification of evidence are met (e.g., replicate studies, malignancy; see section IV). Benign and malignant tumors will be combined when scientifically defensible.

(2) An increased incidence of benign tumors alone generally constitutes "limited" evidence of carcinogenicity.

(3) An increased incidence of neoplasms that occur with high spontaneous background incidence (e.g., mouse liver tumors and rat pituitary tumors in certain strains) generally constitutes "sufficient" evidence of carcinogenicity, but may be changed to "limited" when warranted by the specific information available on the agent.

(4) A "no data available" classification has been added.

(5) A "no evidence of carcinogenicity" classification is also added. This operational classification would include substances for which there is no increased incidence of neoplasms in at least two well-designed and well-conducted animal studies of adequate power and dose in different species.

D. Guidance for Dose-Response Assessment

The qualitative evidence for carcinogenesis should be discussed for purposes of guiding the dose-response assessment. The guidance should be given in terms of the appropriateness and limitations of specific studies as well as pharmacokinetic considerations that should be factored into the dose-response assessment. The appropriate method of extrapolation should be factored in when the experimental route of exposure differs from that occurring in humans.

Agents that are judged to be in the EPA weight-of-evidence stratification Groups A and B would be regarded as suitable for quantitative risk assessments. Agents that are judged to be in Group C will generally be regarded as suitable for quantitative risk assessment, but judgments in this regard may be made on a case-by-case basis. Agents that are judged to be in Groups D and E would not have quantitative risk assessments.

E. Summary and Conclusion

The summary should present all of the key findings in all of the sections of the qualitative assessment and the interpretive rationale that forms the basis for the conclusion. Assumptions, uncertainties in the evidence, and other factors that may affect the relevance of the evidence to humans should be discussed. The conclusion should present both the weight-of-evidence ranking and a description that brings out the more subtle aspects of the evidence that may not be evident from the ranking alone.

III. Dose-Response Assessment, Exposure Assessment, and Risk Characterization

After data concerning the carcinogenic properties of a substance have been collected, evaluated, and categorized, it is frequently desirable to estimate the likely range of excess cancer risk associated with given levels and conditions of human exposure. The first step of the analysis needed to make such estimations is the development of the likely relationship between dose and response (cancer incidence) in the region of human exposure. This information on dose-response relationships is coupled with information on the nature and magnitude of human exposure to yield an estimate of human risk. The risk-characterization step also includes an interpretation of these estimates in light of the biological, statistical, and exposure assumptions and uncertainties that have arisen throughout the process of assessing risk.

The elements of dose-response assessment are described in section III.A. Guidance on human exposure assessment is provided in another EPA

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document (U.S. EPA, 1986); however, section III.B. of these Guidelines includes a brief description of the specific type of exposure information that is useful for carcinogen risk assessment. Finally, in section III.C. on risk characterization, there is a description of the manner in which risk estimates should be presented so as to be most informative.

It should be emphasized that calculation of quantitative estimates of cancer risk does not

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require that an agent be carcinogenic in humans. The likelihood that an agent is a human carcinogen is a function of the weight of evidence, as this has been described in the hazard identification section of these Guidelines. It is nevertheless important to present quantitative estimates, appropriately qualified and interpreted, in those circumstances in which there is a reasonable possibility, based on human and animal data, that the agent is carcinogenic in humans.

It should be emphasized in every quantitative risk estimation that the results are uncertain. Uncertainties due to experimental and epidemiologic variability as well as uncertainty in the exposure assessment can be important. There are major uncertainties in extrapolating both from animals to humans and from high to low doses. There are important species differences in uptake, metabolism, and organ distribution of carcinogens, as well as species and strain differences in target-site susceptibility. Human populations are variable with respect to genetic constitution, diet, occupational and home environment, activity patterns, and other cultural factors. Risk estimates should be presented together with the associated hazard assessment (section III.C.3.) to ensure that there is an appreciation of the weight of evidence for carcinogenicity that underlies the quantitative risk estimates.

A. Dose-Response Assessment

1. *Selection of Data.* As indicated in section II.D., guidance needs to be given by the individuals doing the qualitative assessment (toxicologists, pathologists, pharmacologists, etc.) to those doing the quantitative assessment as to the appropriate data to be used in the dose-response assessment. This is determined by the quality of the data, its relevance to human modes of exposure, and other technical details.

If available, estimates based on adequate human epidemiologic data are preferred over estimates based on animal data. If adequate exposure data exist in a well-designed and well-conducted negative epidemiologic study, it may be possible to obtain an upper-bound estimate of risk from that study. Animal-based estimates, if available, also should be presented.

In the absence of appropriate human studies, data from a species that responds most like humans should be used, if information to this effect exists. Where, for a given agent, several studies are available, which may involve different animal species, strains, and sexes at several doses and by different routes of exposure, the following approach to selecting the data sets is used: (1) The tumor incidence data are separated according to organ site and tumor type. (2) All biologically and statistically acceptable data sets are presented. (3) The range of the risk estimates is presented with due regard to biological relevance (particularly in the case of animal studies) and appropriateness of route of exposure. (4) Because it is possible that human sensitivity is as high as the most sensitive responding animal species, in the absence of evidence to the contrary, the biologically acceptable data set from long-term animal studies showing the greatest sensitivity should generally be given the greatest emphasis, again with due regard to biological and statistical considerations.

When the exposure route in the species from which the dose-response information is obtained differs from the route occurring in environmental exposures, the considerations used in making the route-to-route extrapolation must be carefully described. All assumptions should be presented along with a discussion of the uncertainties in the extrapolation. Whatever procedure is adopted in a given case, it must be consistent with the existing metabolic and pharmacokinetic information on the chemical (e.g., absorption efficiency via the gut and lung, target organ doses, and changes in placental transport throughout gestation for transplacental carcinogens).

Where two or more significantly elevated tumor sites or types are observed in the same study, extrapolations may be conducted on selected sites or types. These selections will be made on biological grounds. To obtain a total estimate of carcinogenic risk, animals with one or more tumor sites or types showing significantly elevated tumor incidence should be pooled and used for extrapolation. The pooled estimates will generally be used in preference to risk estimates based on single sites or types. Quantitative risk extrapolations will generally not be done on the basis of totals that include tumor sites without statistically significant elevations.

Benign tumors should generally be combined with malignant tumors for risk estimates unless the benign tumors are not considered to have the potential to progress to the associated malignancies of the same histogenic origin. The contribution of the benign tumors, however, to the total risk should be indicated.

2. *Choice of Mathematical Extrapolation Model.* Since risks at low exposure levels cannot be measured directly either by animal experiments or by epidemiologic studies, a number of mathematical models have been developed to extrapolate from high to low dose. Different extrapolation models, however, may fit the observed data reasonably well but may lead to large differences in the projected risk at low doses.

As was pointed out by OSTP (1985; Principle 26),

> No single mathematical procedure is recognized as the most appropriate for low-dose extrapolation in carcinogenesis. When relevant biological evidence on mechanism of action exists (e.g., pharmacokinetics, target organ dose), the models or procedures

employed should be consistent with the evidence. When data and information are limited, however, and when much uncertainty exists regarding the mechanism of carcinogenic action, models or procedures which incorporate low-dose linearity are preferred when compatible with the limited information.

At present, mechanisms of the carcinogenesis process are largely unknown and data are generally limited. If a carcinogenic agent acts by accelerating the same carcinogenic process that leads to the background occurrence of cancer, the added effect of the carcinogen at low doses is expected to be virtually linear (Crump et al., 1976).

The Agency will review each assessment as to the evidence on carcinogenesis mechanisms and other biological or statistical evidence that indicates the suitability of a particular extrapolation model. Goodness-of-fit to the experimental observations is not an effective means of discriminating among models (OSTP, 1985). A rationale will be included to justify the use of the chosen model. In the absence of adequate information to the contrary, the linearized multistage procedure will be employed. Where appropriate, the results of using various extrapolation models may be useful for comparison with the linearized multistage procedure. When longitudinal data on tumor development are available, time-to-tumor models may be used.

It should be emphasized that the linearized multistage procedure leads to

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a plausible upper limit to the risk that is consistent with some proposed mechanisms of carcinogenesis. Such an estimate, however, does not necessarily give a realistic prediction of the risk. The true value of the risk is unknown, and may be as low as zero. The range of risks, defined by the upper limit given by the chosen model and the lower limit which may be as low as zero, should be explicitly stated. An established procedure does not yet exist for making "most likely" or "best" estimates of risk within the range of uncertainty defined by the upper and lower limit estimates. If data and procedures become available, the Agency will also provide "most likely" or "best" estimates of risk. This will be most feasible when human data are available and when exposures are in the dose range of the data.

In certain cases, the linearized multistage procedure cannot be used with the observed data as, for example, when the data are nonmonotonic or flatten out at high doses. In these cases, it may be necessary to make adjustments to achieve low-dose linearity.

When pharmacokinetic or metabolism data are available, or when other substantial evidence on the mechanistic aspects of the carcinogenesis process exists, a low-dose extrapolation model other than the linearized multistage procedure might be considered more appropriate on biological grounds. When a different model is chosen, the risk assessment should clearly discuss the nature and weight of evidence that led to the choice. Considerable uncertainty will remain concerning response at low doses; therefore, in most cases an upper-limit risk estimate using the linearized multistage procedure should also be presented.

3. *Equivalent Exposure Units Among Species.* Low-dose risk estimates derived from laboratory animal data extrapolated to humans are complicated by a variety of factors that differ among species and potentially affect the response to carcinogens. Included among these factors are differences between humans and experimental test animals with respect to life span, body size, genetic variability, population homogeneity, existence of concurrent disease, pharmacokinetic effects such as metabolism and excretion patterns, and the exposure regimen.

The usual approach for making interspecies comparisons has been to use standardized scaling factors. Commonly employed standardized dosage scales include mg per kg body weight per day, ppm in the diet or water, mg per m^2 body surface area per day, and mg per kg body weight per lifetime. In the absence of comparative toxicological, physiological, metabolic, and pharmacokinetic data for a given suspect carcinogen, the Agency takes the position that the extrapolation on the basis of surface area is considered to be appropriate because certain pharmacological effects commonly scale according to surface area (Dedrick, 1973; Freireich et al., 1966; Pinkel, 1958).

B. Exposure Assessment

In order to obtain a quantitative estimate of the risk, the results of the dose-response assessment must be combined with an estimate of the exposures to which the populations of interest are likely to be subject. While the reader is referred to the Guidelines for Estimating Exposures (U.S. EPA, 1986) for specific details, it is important to convey an appreciation of the impact of the strengths and weaknesses of exposure assessment on the overall cancer risk assessment process.

At present there is no single approach to exposure assessment that is appropriate for all cases. On a case-by-case basis, appropriate methods are selected to match the data on hand and the level of sophistication required. The assumptions, approximations, and uncertainties need to be clearly stated because, in some instances, these will have a major effect on the risk assessment.

In general, the magnitude, duration, and frequency of exposure provide fundamental information for estimating the concentration of the carcinogen to which the organism is exposed. These data are generated from monitoring information, modeling results, and/or reasoned estimates. An appropriate treatment of exposure should consider

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the potential for exposure via ingestion, inhalation, and dermal penetration from relevant sources of exposures including multiple avenues of intake from the same source.

Special problems arise when the human exposure situation of concern suggests exposure regimens, e.g., route and dosing schedule that are substantially different from those used in the relevant animal studies. Unless there is evidence to the contrary in a particular case, the cumulative dose received over a lifetime, expressed as average daily exposure prorated over a lifetime, is recommended as an appropriate measure of exposure to a carcinogen. That is, the assumption is made that a high dose of a carcinogen received over a short period of time is equivalent to a corresponding low dose spread over a lifetime. This approach becomes more problematical as the exposures in question become more intense but less frequent, especially when there is evidence that the agent has shown dose-rate effects.

An attempt should be made to assess the level of uncertainty associated with the exposure assessment which is to be used in a cancer risk assessment. This measure of uncertainty should be included in the risk characterization (section III.C.) in order to provide the decision-maker with a clear understanding of the impact of this uncertainty on any final quantitative risk estimate. Subpopulations with heightened susceptibility (either because of exposure or predisposition) should, when possible, be identified.

C. Risk Characterization

Risk characterization is composed of two parts. One is a presentation of the numerical estimates of risk; the other is a framework to help judge the significance of the risk. Risk characterization includes the exposure assessment and dose-response assessment; these are used in the estimation of carcinogenic risk. It may also consist of a unit-risk estimate which can be combined elsewhere with the exposure assessment for the purposes of estimating cancer risk.

Hazard identification and dose-response assessment are covered in sections II. and III.A., and a detailed discussion of exposure assessment is contained in EPA's Guidelines for Estimating Exposures (U.S. EPA, 1986). This section deals with the numerical risk estimates and the approach to summarizing risk characterization.

1. *Options for Numerical Risk Estimates.* Depending on the needs of the individual program offices, numerical estimates can be presented in one or more of the following three ways.

a. Unit Risk -- Under an assumption of low-dose linearity, the unit cancer risk is the excess lifetime risk due to a continuous constant lifetime exposure of one unit of carcinogen concentration. Typical exposure units include ppm or ppb in food or water, mg/kg/day by ingestion, or ppm or $\mu g/m^3$ in air.

b. Dose Corresponding to a Given Level of Risk -- This approach can be useful, particularly when using nonlinear extrapolation models where the unit risk would differ at different dose levels.

c. Individual and Population Risks -- Risks may be characterized either in terms of the excess individual lifetime risks, the excess number of cancers

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produced per year in the exposed population, or both.

Irrespective of the options chosen, the degree of precision and accuracy in the numerical risk estimates currently do not permit more than one significant figure to be presented.

2. *Concurrent Exposure.* In characterizing the risk due to concurrent exposure to several carcinogens, the risks are combined on the basis of additivity unless there is specific information to the contrary. Interactions of cocarcinogens, promoters, and inititators with known carcinogens should be considered on a case-by-case basis.

3. *Summary of Risk Characterization.* Whichever method of presentation is chosen, it is critical that the numerical estimates not be allowed to stand alone, separated from the various assumptions and uncertainties upon which they are based. The risk characterization should contain a discussion and interpretation of the numerical estimates that affords the risk manager some insight into the degree to which the quantitative estimates are likely to reflect the true magnitude of human risk, which generally cannot be known with the degree of quantitative accuracy reflected in the numerical estimates. The final risk estimate will be generally rounded to one significant figure and will be coupled with the EPA classification of the qualitative weight of evidence. For example, a lifetime individual risk of 2×10^{-4} resulting from exposure to a "probable human carcinogen" (Group B2) should be designated as 2×10^{-4} [B2] . This bracketed designation of the qualitative weight of evidence should be included with all numerical risk estimates (i.e., unit risks, which are risks at a specified concentration or concentrations corresponding to a given risk). Agency statements, such as *FEDERAL REGISTER* notices, briefings, and action memoranda, frequently include numerical estimates of carcinogenic risk. It is recommended that whenever these numerical estimates are used, the qualitative weight-of-evidence classification should also be included.

The section on risk characterization should summarize the hazard identification, dose-response assessment, exposure assessment, and the public health risk estimates. Major assumptions, scientific judgments, and, to the extent possible, estimates of

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the uncertainties embodied in the assessment are presented.

IV. EPA Classification System for Categorizing Weight of Evidence for Carcinogenicity from Human and Animal Studies (Adapted from IARC)

A. Assessment of Weight of Evidence for Carcinogenicity from Studies in Humans

Evidence of carcinogenicity from human studies comes from three main sources:

1. Case reports of individual cancer patients who were exposed to the agent(s).
2. Descriptive epidemiologic studies in which the incidence of cancer in human populations was found to vary in space or time with exposure to the agent(s).
3. Analytical epidemiologic (case-control and cohort) studies in which individual exposure to the agent(s) was found to be associated with an increased risk of cancer.

Three criteria must be met before a causal association can be inferred between exposure and cancer in humans:

1. There is no identified bias that could explain the association.
2. The possibility of confounding has been considered and ruled out as explaining the association.
3. The association is unlikely to be due to chance.

In general, although a single study may be indicative of a cause-effect relationship, confidence in inferring a causal association is increased when several independent studies are concordant in showing the association, when the association is strong, when there is a dose-response relationship, or when a reduction in exposure is followed by a reduction in the incidence of cancer.

The weight of evidence for carcinogenicity[1] from studies in humans is classified as:

1. Sufficient evidence of carcinogenicity, which indicates that there is a causal relationship between the agent and human cancer.
2. Limited evidence of carcinogenicity, which indicates that a causal interpretation is credible, but that alternative explanations, such as chance, bias, or confounding, could not adequately be excluded.
3. Inadequate evidence, which indicates that one of two conditions prevailed: (a) there were few pertinent data, or (b) the available studies, while showing evidence of association, did not exclude chance, bias, or confounding, and therefore a causal interpretation is not credible.
4. No data, which indicates that data are not available.
5. No evidence, which indicates that no association was found between exposure and an increased risk of cancer in well-designed and well-conducted independent analytical epidemiologic studies.

B. Assessment of Weight of Evidence for Carcinogenicity from Studies in Experimental Animals

These assessments are classified into five groups:

1. Sufficient evidence[2] of carcinogenicity, which indicates that there is an increased incidence of malignant tumors or combined malignant and benign tumors:[3] (a) in multiple species or strains; or (b) in multiple experiments (e.g., with different routes of administration or using different dose levels); or (c) to an unusual degree in a single experiment with regard to high incidence, unusual site or type of tumor, or early age at onset.

Additional evidence may be provided by data on dose-response effects, as well as information from short-term tests or on chemical structure.

2. Limited evidence of carcinogenicity, which means that the data suggest a carcinogenic effect but are limited because: (a) the studies involve a single species, strain, or experiment and do not meet criteria for sufficient evidence (see section IV. B.1.c); (b) the experiments are restricted by inadequate dosage levels, inadequate duration of exposure to the agent, inadequate period of follow-up, poor survival, too few animals, or inadequate reporting; or (c) an increase in the incidence of benign tumors only.
3. Inadequate evidence, which indicates that because of major qualitative or quantitative limitations, the studies cannot be interpreted as showing either the presence or absence of a carcinogenic effect.
4. No data, which indicates that data are not available.
5. No evidence, which indicates that there is no increased incidence of neoplasms in at least two well-designed

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and well-conducted animal studies in different species.

The classifications "sufficient evidence" and "limited evidence" refer only to the weight of the experimental evidence that these agents are carcinogenic and not to the potency of their carcinogenic action.

[1] For purposes of public health protection, agents associated with life-threatening benign tumors in humans are included in the evaluation.

[2] An increased incidence of neoplasms that occur with high spontaneous background incidence (e.g., mouse liver tumors and rat pituitary tumors in certain strains) generally constitutes "sufficient" evidence of carcinogenicity, but may be changed to "limited" when warranted by the specific information available on the agent.

[3] Benign and malignant tumors will be combined unless the benign tumors are not considered to have the potential to progress to the associated malignancies of the same histogenic origin.

C. Categorization of Overall Weight of Evidence for Human Carcinogenicity

The overall scheme for categorization of the weight of evidence of carcinogenicity of a chemical for humans uses a three-step process. (1) The weight of evidence in human studies or animal studies is summarized; (2) these lines of information are combined to yield a tentative assignment to a category (see Table 1); and (3) all relevant supportive information is evaluated to see if the designation of the overall weight of evidence needs to be modified. Relevant factors to be included along with the tumor information from human and animal studies include structure-activity relationships; short-term test findings; results of appropriate physiological, biochemical, and toxicological observations; and comparative metabolism and pharmacokinetic studies. The nature of these findings may cause one to adjust the overall categorization of the weight of evidence.

The agents are categorized into five groups as follows:

Group A -- Human Carcinogen

This group is used only when there is sufficient evidence from epidemiologic studies to support a causal association between exposure to the agents and cancer.

Group B -- Probable Human Carcinogen

This group includes agents for which the weight of evidence of human carcinogenicity based on epidemiologic studies is "limited" and also includes agents for which the weight of evidence of carcinogenicity based on animal studies is "sufficient." The group is divided into two subgroups. Usually, Group B1 is reserved for agents for which there is limited evidence of carcinogenicity from epidemiologic studies. It is reasonable, for practical purposes, to regard an agent for which there is "sufficient" evidence of carcinogenicity in animals as if it presented a carcinogenic risk to humans. Therefore, agents for which there is "sufficient" evidence from animal studies and for which there is "inadequate evidence" or "no data" from epidemiologic studies would usually be categorized under Group B2.

Group C -- Possible Human Carcinogen

This group is used for agents with limited evidence of carcinogenicity in animals in the absence of human data. It includes a wide variety of evidence, e.g., (a) a malignant tumor response in a single well-conducted experiment that does not meet conditions for sufficient evidence, (b) tumor responses of marginal statistical significance in studies having inadequate design or reporting, (c) benign but not malignant tumors with an agent showing no response in a variety of short-term tests for mutagenicity, and (d) responses of marginal statistical significance in a tissue known to have a high or variable background rate.

Group D -- Not Classifiable as to Human Carcinogenicity

This group is generally used for agents with inadequate human and animal evidence of carcinogenicity or for which no data are available.

Group E -- Evidence of Non-Carcinogenicity for Humans

This group is used for agents that show no evidence for carcinogenicity in at least two adequate animal tests in different species or in both adequate epidemiologic and animal studies.

The designation of an agent as being in Group E is based on the available evidence and should not be interpreted as a definitive conclusion that the agent will not be a carcinogen under any circumstances.

V. References

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TABLE 1.--ILLUSTRATIVE CATEGORIZATION OF EVIDENCE BASED ON ANIMAL AND HUMAN DATA[1]

Human evidence	Animal evidence				
	Sufficient	Limited	Inadequate	No data	No evidence
Sufficient	A	A	A	A	A
Limited	B1	B1	B1	B1	B1
Inadequate	B2	C	D	D	D
No data	B2	C	D	D	E
No evidence	B2	C	D	D	E

1 The above assignments are presented for illustrative purposes. There may be nuances in the classification of both animal and human data indicating that different categorizations than those given in the table should be assigned. Furthermore, these assignments are tentative and may be modified by ancillary evidence. In this regard all relevant information should be evaluated to determine if the designation of the overall weight of evidence needs to be modified. Relevant factors to be included along with the tumor data from human and animal studies include structure-activity relationships, short-term test findings, results of appropriate physiological, biochemical, and toxicological observations, and comparative metabolism and pharmacokinetic studies. The nature of these findings may cause an adjustment of the overall categorization of the weight of evidence.

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Part B: Response to Public and Science Advisory Board Comments

I. Introduction

This section summarizes the major issues raised during both the public comment period on the Proposed Guidelines for Carcinogen Risk Assessment published on November 23, 1984 (49 FR 46294), and also during the April 22-23, 1985, meeting of the Carcinogen Risk Assessment Guidelines Panel of the Science Advisory Board (SAB).

In order to respond to these issues the Agency modified the proposed guidelines in two stages. First, changes resulting from consideration of the public comments were made in a draft sent to the SAB review panel prior to their April meeting. Secondly, the guidelines were further modified in response to the panel's recommendations.

The Agency received 62 sets of comments during the public comment period, including 28 from corporations, 9 from professional or trade associations, and 4 from academic institutions. In general, the comments were favorable. The commentors welcomed the update of the 1976 guidelines and felt that the proposed guidelines of

1985 reflected some of the progress that has occurred in understanding the mechanisms of carcinogenesis. Many commentors, however, felt that additional changes were warranted.

The SAB concluded that the guidelines are "reasonably complete in their conceptual framework and are sound in their overall interpretation of the scientific issues" (Report by the SAB Carcinogenicity Guidelines Review Group, June 19, 1985). The SAB suggested various editorial changes and raised some issues regarding the content of the proposed guidelines, which are discussed below. Based on these recommendations, the Agency has modified the draft guidelines.

II. Office of Science and Technology Policy Report on Chemical Carcinogens

Many commentors requested that the final guidelines not be issued until after publication of the report of the Office of Technology and Science Policy (OSTP) on chemical carcinogens. They further requested that this report be incorporated into the final Guidelines for Carcinogen Risk Assessment.

The final OSTP report was published in 1985 (50 FR 10372). In its deliberations, the Agency reviewed the final OSTP report and feels that the Agency's guidelines are consistent with the principles established by the OSTP. In its review, the SAB agreed that the Agency guidelines are generally consistent with the OSTP report. To emphasize this consistency, the OSTP principles have been incorporated into the guidelines when controversial issues are discussed.

III. Inference Guidelines

Many commentors felt that the proposed guidelines did not provide a sufficient distinction between scientific fact and policy decisions. Others felt that EPA should not attempt to propose firm guidelines in the absence of scientific consensus. The SAB report also indicated the need to "distinguish recommendations based on scientific evidence from those based on science policy decisions."

The Agency agrees with the recommendation that policy, judgmental, or inferential decisions should be clearly identified. In its revision of the proposed guidelines, the Agency has included phrases (e.g., "the Agency takes the position that") to more clearly distinguish policy decisions.

The Agency also recognizes the need to establish procedures for action on important issues in the absence of complete scientific knowledge or consensus. This need was acknowledged in both the National Academy of Sciences book entitled *Risk Management in the Federal Government: Managing the Process* and the OSTP report on chemical carcinogens. As the NAS report states, "Risk assessment is an analytic process that is firmly based on scientific considerations, but it also requires judgments to be made when the available information is incomplete. These judgments inevitably draw on both scientific and policy considerations."

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The judgments of the Agency have been based on current available scientific information and on the combined experience of Agency experts. These judgments, and the resulting guidance, rely on inference; however, the positions taken in these inference guidelines are felt to be reasonable and scientifically defensible. While all of the guidance is, to some degree, based on inference, the guidelines have attempted to distinguish those issues that depended more on judgment. In these cases, the Agency has stated a position but has also retained flexibility to accommodate new data or specific circumstances that demonstrate that the proposed position is inaccurate. The Agency recognizes that scientific opinion will be divided on these issues.

Knowledge about carcinogens and carcinogenesis is progressing at a rapid rate. While these guidelines are considered a best effort at the present time, the Agency has attempted to incorporate flexibility into the current guidelines and also recommends that the guidelines be revised as often as warranted by advances in the field.

IV. Evaluation of Benign Tumors

Several commentors discussed the appropriate interpretation of an increased incidence of benign tumors alone or with an increased incidence of malignant tumors as part of the evaluation of the carcinogenicity of an agent. Some comments were supportive of the position in the proposed guidelines, i.e., under certain circumstances, the incidence of benign and malignant tumors would be combined, and an increased incidence of benign tumors alone would be considered an indication, albeit limited, of carcinogenic potential. Other commentors raised concerns about the criteria that would be used to decide which tumors should be combined. Only a few commentors felt that benign tumors should never be considered in evaluating carcinogenic potential.

The Agency believes that current information supports the use of benign tumors. The guidelines have been modified to incorporate the language of the OSTP report, i.e., benign tumors will be combined with malignant tumors when scientifically defensible. This position allows flexibility in evaluating the data base for each agent. The guidelines have also been modified to indicate that, whenever benign and malignant tumors have been combined, and the agent is considered a candidate for quantitative risk extrapolation, the contribution of benign tumors to the estimation of risk will be indicated.

V. *Transplacental and Multigenerational Animal Bioassays*

As one of its two proposals for additions to the guidelines, the SAB recommended a discussion of transplacental and multigenerational animal bioassays for carcinogenicity.

The Agency agrees that such data, when available, can provide useful information in the evaluation of a chemical's potential carcinogenicity and has stated this in the final guidelines. The Agency has also revised the guidelines to indicate that such studies may provide additional information on the metabolic and pharmacokinetic properties of the chemical. More guidance on the specific use of these studies will be considered in future revisions of these guidelines.

VI. Maximum Tolerated Dose

The proposed guidelines discussed the implications of using a maximum tolerated dose (MTD) in bioassays for carcinogenicity. Many commentors requested that EPA define MTD. The tone of the comments suggested that the commentors were concerned about the uses and interpretations of high-dose testing.

The Agency recognizes that controversy currently surrounds these issues. The appropriate text from the OSTP report has been incorporated into the final guidelines which suggests that the consequences of high-dose testing be evaluated on a case-by-case basis.

VII. Mouse Liver Tumors

A large number of commentors expressed opinions about the assessment of bioassays in which the only increase in tumor incidence was liver tumors in the mouse. Many felt that mouse liver tumors were afforded too much credence, especially given existing information that indicates that they might arise by a different mechanism, e.g., tissue damage followed by regeneration. Others felt that mouse liver tumors were but one case of a high background incidence of one particular type of tumor and that all such tumors should be treated in the same fashion.

The Agency has reviewed these comments and the OSTP principle regarding this issue. The OSTP report does not reach conclusions as to the treatment of tumors with a high spontaneous background rate, but states, as is now included in the text of the guidelines, that these data require special consideration. Although questions have been raised regarding the validity of mouse liver tumors in general, the Agency feels that mouse liver tumors cannot be ignored as an indicator of carcinogenicity. Thus, the position in the proposed guidelines has not been changed: an increased incidence of only mouse liver tumors will be regarded as "sufficient" evidence of carcinogenicity if all other criteria, e.g., replication and malignancy, are met with the understanding that this classification could be changed to "limited" if warranted. The factors that may cause this re-evaluation are indicated in the guidelines.

VIII. Weight-of Evidence Catagories

The Agency was praised by both the public and the SAB for incorporating a weight-of-evidence scheme into its evaluation of carcinogenic risk. Certain specific aspects of the scheme, however, were criticized.

1. Several commentors noted that while the text of the proposed guidelines clearly states that EPA will use all available data in its categorization of the weight of the evidence that a chemical is a carcinogen, the classification system in Part A, section IV did not indicate the manner in which EPA will use information other than data from humans and long-term animal studies in assigning a weight-of-evidence classification.

The Agency has added a discussion to Part A, section IV.C. dealing with the characterization of overall evidence for human carcinogenicity. This discussion clarifies EPA's use of supportive information to adjust, as warranted, the designation that would have been made solely on the basis of human and long-term animal studies.

2. The Agency agrees with the SAB and those commentors who felt that a simple classification of the weight of evidence, e.g., a single letter or even a descriptive title, is inadequate to describe fully the weight of evidence for each individual chemical. The final guidelines propose that a paragraph summarizing the data should accompany the numerical estimate and weight-of-evidence classification whenever possible.

3. Several commentors objected to the descriptive title E (No Evidence of Carcinogenicity for Humans) because they felt the title would be confusing to people inexperienced with the classification system. The title for Group E, No Evidence of Carcinogenicity for Humans, was thought by these commentors to suggest the absence of data. This group, however, is intended to be reserved for agents for which there exists credible data demonstrating that the agent is not carcinogenic.

Based on these comments and further discussion, the Agency has changed the

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title of Group E to "Evidence of Non-Carcinogenicity for Humans."

4. Several commentors felt that the title for Group C, Possible Human Carcinogen, was not sufficiently distinctive from Group B, Probable Human Carcinogen. Other commentors felt that those agents that minimally qualified for Group C would lack sufficient data for such a label.

The Agency recognizes that Group C covers a range of chemicals and has considered whether to subdivide Group C. The consensus of the Agency's

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Carcinogen Risk Assessment Committee, however, is that the current groups, which are based on the IARC categories, are a reasonable stratification and should be retained at present. The structure of the groups will be reconsidered when the guidelines are reviewed in the future. The Agency also feels that the descriptive title it originally selected best conveys the meaning of the classification within the context of EPA's past and current activities.

5. Some commentors indicated a concern about the distinction between B1 and B2 on the basis of epidemiologic evidence only. This issue has been under discussion in the Agency and may be revised in future versions of the guidelines.

6. Comments were also received about the possibility of keeping the groups for animal and human data separate without reaching a combined classification. The Agency feels that a combined classification is useful; thus, the combined classification was retained in the final guidelines.

The SAB suggested that a table be added to Part A, section IV to indicate the manner in which human and animal data would be combined to obtain an overall weight-of-evidence category. The Agency realizes that a table that would present all permutations of potentially available data would be complex and possibly impossible to construct since numerous combinations of ancillary data (e.g., genetic toxicity, pharmacokinetics) could be used to raise or lower the weight-of-evidence classification. Nevertheless, the Agency decided to include a table to illustrate the most probable weight-of-evidence classification that would be assigned on the basis of standard animal and human data without consideration of the ancillary data. While it is hoped that this table will clarify the weight-of-evidence classifications, it is also important to recognize that an agent may be assigned to a final categorization different from the category which would appear appropriate from the table and still conform to the guidelines.

IX. Quantitative Estimates of Risk

The method for quantitative estimates of carcinogenic risk in the proposed guidelines received substantial comments from the public. Five issues were discussed by the Agency and have resulted in modifications of the guidelines.

1. The major criticism was the perception that EPA would use only one method for the extrapolation of carcinogenic risk and would, therefore, obtain one estimate of risk. Even commentors who concur with the procedure usually followed by EPA felt that some indication of the uncertainty of the risk estimate should be included with the risk estimate.

The Agency feels that the proposed guidelines were not intended to suggest that EPA would perform quantitative risk estimates in a rote or mechanical fashion. As indicated by the OSTP report and paraphrased in the proposed guidelines, no single mathematical procedure has been determined to be the most appropriate method for risk extrapolation. The final guidelines quote rather than paraphrase the OSTP principle. The guidelines have been revised to stress the importance of considering all available data in the risk assessment and now state, "The Agency will review each assessment as to the evidence on carcinogenic mechanisms and other biological or statistical evidence that indicates the suitability of a particular extrapolation model." Two issues are emphasized: First, the text now indicates the potential for pharmacokinetic information to contribute to the assessment of carcinogenic risk. Second, the final guidelines state that time-to-tumor risk extrapolation models may be used when longitudinal data on tumor development are available.

2. A number of commentors noted that the proposed guidelines did not indicate how the uncertainties of risk characterization would be presented. The Agency has revised the proposed guidelines to indicate that major assumptions, scientific judgments, and, to the extent possible, estimates of the uncertainties embodied in the risk assessment will be presented along with the estimation of risk.

3. The proposed guidelines stated that the appropriateness of quantifying risks for chemicals in Group C (Possible Human Carcinogen), specifically those agents that were on the boundary of Groups C and D (Not Classifiable as to Human Carcinogenicity), would be judged on a case-by-case basis. Some commentors felt that quantitative risk assessment should not be performed on any agent in Group C.

Group C includes a wide range of agents, including some for which there are positive results in one species in one good bioassay. Thus, the Agency feels that many agents in Group C will be suitable for quantitative risk assessment, but that judgments in this regard will be made on a case-by-case basis.

4. A few commentors felt that EPA intended to perform quantitative risk estimates on aggregate tumor incidence. While EPA will consider an increase in total aggregate tumors as suggestive of potential carcinogenicity, EPA does not generally intend to make quantitative estimates of carcinogenic risk based on total aggregate tumor incidence.

5. The proposed choice of body surface area as an interspecies scaling factor was criticized by several commentors who felt that body weight was also appropriate and that both methods should be used. The OSTP report recognizes that both scaling factors are in common use. The Agency feels that the choice of the body surface area scaling factor can be

justified from the data on effects of drugs in various species. Thus, EPA will continue to use this scaling factor unless data on a specific agent suggest that a different scaling factor is justified. The uncertainty engendered by choice of scaling factor will be included in the summary of uncertainties associated with the assessment of risk mentioned in point 1, above.

In the second of its two proposals for additions to the proposed guidelines, the SAB suggested that a sensitivity analysis be included in EPA's quantitative estimate of a chemical's carcinogenic potency. The Agency agrees that an analysis of the assumptions and uncertainties inherent in an assessment of carcinogenic risk must be accurately portrayed. Sections of the final guidelines that deal with this issue have been strengthened to reflect the concerns of the SAB and the Agency. In particular, the last paragraph of the guidelines states that "major assumptions, scientific judgments, and, to the extent possible, estimates of the uncertainties embodied in the assessment" should be presented in the summary characterizing the risk. Since the assumptions and uncertainties will vary for each assessment, the Agency feels that a formal requirement for a particular type of sensitivity analysis would be less useful than a case-by-case evaluation of the particular assumptions and uncertainties most significant for a particular risk assessment.

REC 6175

51 FR 34006

GUIDELINES FOR MUTAGENICITY RISK ASSESSMENT

SUMMARY: On September 24, 1986, the U.S. Environmental Protection Agency issued the following five guidelines for assessing the health risks of environmental pollutants.

Guidelines for Carcinogen Risk Assessment

Guidelines for Estimating Exposures

Guidelines for Mutagenicity Risk Assessment

Guidelines for the Health Assessment of Suspect Developmental Toxicants

Guidelines for the Health Risk Assessment of Chemical Mixtures

This section contains the Guidelines for Mutagenicity Risk Assessment.

The Guidelines for Mutagenicity Risk Assessment (hereafter "Guidelines") are intended to guide Agency analysis of mutagenicity data in line with the policies and procedures established in the statutes administered by the EPA. These Guidelines were developed as part of an interoffice guidelines development program under the auspices of the Office of Health and Environmental Assessment (OHEA) in the Agency's Office of Research and Development. They reflect Agency consideration of public and Science Advisory Board (SAB) comments on the Proposed Guidelines for Mutagenicity Risk Assessment published November 23, 1984 (49 FR 46314).

This publication completes the first round of risk assessment guidelines development. These Guidelines will be revised, and new guidelines will be developed, as appropriate.

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SUPPLEMENTARY INFORMATION: In 1983, the National Academy of Sciences (NAS) published its book entitled *Risk Assessment in the Federal Government: Managing the Process.* In that book, the NAS recommended that Federal regulatory agencies establish "inference guidelines" to ensure consistency and technical quality in risk assessments and to ensure that the risk assessment process was maintained as a scientific effort separate from risk management. A task force within EPA accepted that recommendation and requested that Agency scientists begin to develop such guidelines.

General

The guidelines are products of a two-year Agencywide effort, which has included many scientists from the larger scientific community. These guidelines set forth principles and procedures to guide EPA scientists in the conduct of Agency risk assessments, and to inform Agency decision makers and the public about these procedures. In particular, the guidelines emphasize that risk assessments will be conducted on a case-by-case basis, giving full consideration to all relevant scientific information. This case-by-case approach means that Agency experts review the scientific information on each agent and use the most scientifically appropriate interpretation to assess risk. The guidelines also stress that this information will be fully presented in Agency risk assessment documents, and that Agency scientists will identify the strengths and weaknesses of each assessment by describing uncertainties, assumptions, and limitations, as well as the scientific basis and rationale for each assessment.

Finally, the guidelines are formulated in part to bridge gaps in risk assessment methodology and data. By identifying these gaps and the importance of the missing information to the risk assessment process, EPA wishes to encourage research and analysis that will lead to new risk assessment methods and data.

Guidelines for Mutagenicity Risk Assessment

Work on the Guidelines for Mutagenicity Risk Assessment began in January 1984. Draft guidelines were developed by Agency work groups composed of expert scientists from throughout the Agency. The drafts were peer-reviewed by expert scientists in the field of genetic toxicology from universities, environmental groups, industry, labor, and other governmental agencies. They were then proposed for public comment in the *FEDERAL REGISTER* (49 FR 46314). On November 9, 1984, the Administrator directed that Agency offices use the proposed guidelines in performing risk assessments until final guidelines become available.

TR 2072
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After the close of the public comment period, Agency staff prepared summaries of the comments, analyses of the major issues presented by the commentors, and preliminary Agency responses to those comments. These analyses were presented to review panels of the SAB on March 4 and April 22-23, 1985, and to the Executive Committee of the SAB on April 25-26, 1985. The SAB meetings were announced in the *FEDERAL REGISTER* as follows: February 12, 1985 (50 FR 5811) and April 4, 1985 (50 FR 13420 and 13421).

In a letter to the Administrator dated June 19, 1985, the Executive Committee generally concurred on all five of the guidelines, but recommended certain revisions, and requested that any revised guidelines be submitted to the appropriate SAB review panel chairman for review and concurrence on behalf of the Executive Committee. As described in the responses to comments (see Part B: Response to the Public and Science Advisory Board Comments), each guidelines document was revised, where appropriate, consistent with the SAB recommendations, and revised draft guidelines were submitted to the panel chairmen. Revised draft Guidelines for Mutagenicity Risk Assessment were concurred on in a letter dated September 24, 1985. Copies of the letters are available at the Public Information Reference Unit, EPA Headquarters Library, as indicated elsewhere in this section.

Following this Preamble are two parts: Part A contains the Guidelines and Part B, the Response to the Public and Science Advisory Board Comments (a summary of the major public comments, SAB comments, and Agency responses to those comments).

The Agency is continuing to study the risk assessment issues raised in the guidelines and will revise these Guidelines in line with new information as appropriate.

References, supporting documents, and comments received on the proposed guidelines, as well as copies of the final guidelines, are available for inspection and copying at the Public Information Reference Unit (202-382-5926), EPA Headquarters Library, 401 M Street, S.W., Washington, DC, between the hours of 8:00 a.m. and 4:30 p.m.

I certify that these Guidelines are not major rules as defined by Executive Order 12291, because they are nonbinding policy statements and have no direct effect on the regulated community. Therefore, they will have no effect on costs or prices, and they will have no other significant adverse effects on the economy. These Guidelines were reviewed by the Office of Management

[51 FR 34007]

and Budget under Executive Order 12291.

August 22, 1986

Lee M. Thomas,

Administrator

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Part B: Response to Public and Science Advisory Board Comments

Part A: Guidelines for Mutagenicity Risk Assessment

I. Introduction

This section describes the procedures that the U.S. Environmental Protection Agency will follow in evaluating the potential genetic risk associated with human exposure to chemicals. The central purpose of the health risk assessment is to provide a judgment concerning the weight of evidence that an agent is a potential human mutagen, capable of inducing transmitted genetic changes, and, if so, to provide a judgment on how great an impact this agent is likely to have on public health. Regulatory decision making involves two components: risk assessment and risk management. Risk assessment estimates the potential adverse health consequences of exposure to toxic chemicals; risk management combines the risk assessment with the directives of the enabling regulatory legislation--together with socioeconomic, technical, political, and other considerations--to reach a decision as to whether or how much to control future exposure to the chemicals. The issue of risk management will not be dealt with in these Guidelines.

Risk assessment is comprised of the following components: hazard identification, dose-response assessment, exposure assessment, and risk characterization (1). Hazard identification is the qualitative risk assessment, dealing with the inherent toxicity of a chemical substance. The qualitative mutagenicity assessment answers the question of how likely an agent is to be a human mutagen. The three remaining components

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comprise quantitative risk assessment, which provides a numerical estimate of the public health consequences of exposure to an agent. The quantitative mutagenicity risk assessment deals with the question of how much mutational damage is likely to be produced by exposure to a given agent under particular exposure scenarios.

In a dose-response assessment, the relationship between the dose of a chemical and the probability of induction of an adverse effect is defined. The component generally entails an extrapolation from the high doses administered to experimental animals or noted in some epidemiologic studies to the low exposure levels expected from human contact with the chemical in the environment.

The exposure assessment identifies populations exposed to toxic chemicals, describes their composition and size, and presents the types, magnitudes, frequencies, and durations of exposure to the chemicals. This component is developed independently of the other components of the mutagenicity assessment and is addressed in separate Agency guidelines (2).

In risk characterization, the outputs of the exposure assessment and the dose-response assessment are combined to estimate quantitatively the mutation risk, which is expressed as either estimated increase of genetic disease per generation or per lifetime, or the fractional increase in the assumed background mutation rate of humans. In each step of the assessment, the strengths and weaknesses of the major assumptions need to be presented, and the nature and magnitude of uncertainties need to be characterized.

The procedures set forth in these Guidelines will ensure consistency in the Agency's scientific risk assessments for mutagenic effects. The necessity for a consistent approach to the evaluation of mutagenic risk from chemical substances arises from the authority conferred upon the Agency by a number of statutes to regulate potential mutagens. As appropriate, these Guidelines will apply to statutes administered by the Agency, including the Federal Insecticide, Fungicide, and Rodenticide Act; the Toxic Substances Control Act; the Clean Air Act; the Federal Water Pollution Control Act; the Safe Drinking Water Act; the Resource Conservation and Recovery Act; and the Comprehensive Environmental Response, Compensation, and Liability Act. Because each statute is administered by separate offices, a consistent Agency-wide approach for performing risk assessments is desirable.

The mutagenicity risk assessments prepared pursuant to these Guidelines will be utilized with the requirements and constraints of the applicable statutes to arrive at regulatory decisions concerning mutagenicity. The standards of the applicable statutes and regulations may dictate that additional considerations (e.g., the economic and social benefits associated with use of the chemical substance) will come into play in reaching appropriate regulatory decisions.

The Agency has not attempted to provide in the Guidelines a detailed discussion of the mechanisms of mutagenicity or of the various test systems that are currently in use to detect mutagenic potential. Background information on mutagenesis and mutagenicity test systems is available in "Identifying and Estimating the Genetic Impact of Chemical Mutagens", National Academy of Sciences (NAS) Committee on Chemical Environmental Mutagens (3), as well as in other recent publications (4, 5).

The Agency is concerned with the risk associated with both germ-cell mutations and somatic-cell mutations. Mutations carried in germ cells may be inherited by future generations and may contribute to genetic disease, whereas mutations occurring in somatic cells may be implicated in the etiology of several disease states, including cancer. These Guidelines, however, are only concerned with genetic damage as it relates to germ-cell mutations. The use of mutagenicity test results in the assessment of carcinogenic risk is described in the Guidelines for Carcinogen Risk Assessment (6).

As a result of the progress in the control of infectious diseases, increases in average human life span, and better procedures for identifying genetic disorders, a considerable heritable genetic disease burden has been recognized in the human population. It is estimated that at least 10% of all human disease is related to specific genetic abnormalities, such as abnormal composition, arrangement, or dosage of genes and chromosomes (3, 7, 8). Such genetic abnormalities can lead to structural or functional health impairments. These conditions may be expressed in *utero*; at the time of birth; or during infancy, childhood, adolescence, or adult life; they may be chronic or acute in nature. As a result, they often have a severe impact upon the affected individuals and their families in terms of physical and mental

[51 FR 34008]

suffering and economic losses, and upon society in general, which often becomes responsible for institutional care of severely affected individuals. Some examples of genetic disorders are Down and Klinefelter syndromes, cystic fibrosis, hemophilia, sickle-cell anemia, and achondroplastic dwarfism. Other commonly recognized conditions that are likely to have a genetic component include hypercholesterolemia, hypertension, pyloric stenosis, glaucoma, allergies, several types of cancer, and mental retardation. These disorders are only a few of the thousands that are at least partially genetically determined (9).

TR 3374

Estimation of the fraction of human genetic disorders that result from new mutations is difficult, although in certain specific cases insights are available (10). It is clear that recurring mutation is important in determining the incidence of certain genetic disorders, such as some chromosomal aberration syndromes (e.g., Down syndrome) and rare dominant and X-linked recessive diseases (e.g., achondroplasia and hemophilia A). For other single-factor disorders (e.g., sickle-cell anemia) and certain multifactorial disorders (e.g., pyloric stenosis), the contribution of new mutations to disease frequency is probably small. However, it is generally recognized that most newly-arising mutations that are phenotypically expressed are in some ways deleterious to the organism receiving them (3, 7, 8). Adverse effects may be manifested at the biochemical, cellular, or physiological levels of organization. Although mutations are the building blocks for further evolutionary change of species, it is believed that increases in the mutation rate could lead to an increased frequency of expressed genetic disorders in the first and subsequent generations.

Life in our technological society results in exposure to many natural and synthetic chemicals. Some have been shown to have mutagenic activity in mammalian and submammalian test systems, and thus may have the potential to increase genetic damage in the human population. Chemicals exhibiting mutagenic activity in various test systems have been found distributed among foods, tobacco, drugs, food additives, cosmetics, industrial compounds, pesticides, and consumer products. The extent to which exposure to natural and synthetic environmental agents may have increased the frequency of genetic disorders in the present human population and contributed to the mutational "load" that will be transmitted to future generations is unknown at this time. However, for the reasons cited above, it seems prudent to limit exposures to potential human mutagens.

A. Concepts Relating to Heritable Mutagenic Risk

These Guidelines are concerned with chemical substances or mixtures of substances that can induce alterations in the genome of either somatic or germinal cells. The mutagenicity of physical agents (e.g., radiation) is not addressed here. There are several mutagenic end points of concern to the Agency. These include point mutations (i.e., submicroscopic changes in the base sequence of DNA) and structural or numerical chromosome aberrations. Structural aberrations include deficiencies, duplications, insertions, inversions, and translocations, whereas numerical aberrations are gains or losses of whole chromosomes (e.g., trisomy, monosomy) or sets of chromosomes (haploidy, polyploidy).

Certain mutagens, such as alkylating agents, can directly induce alterations in the DNA. Mutagenic effects may also come about through mechanisms other than chemical alterations of DNA. Among these are interference with normal DNA synthesis (as caused by some metal mutagens), interference with DNA repair, abnormal DNA methylation, abnormal nuclear division processes, or lesions in non-DNA targets (e.g., protamine, tubulin).

Evidence that an agent induces heritable mutations in human beings could be derived from epidemiologic data indicating a strong association between chemical exposure and heritable effects. It is difficult to obtain such data because any specific mutation is a rare event, and only a small fraction of the estimated thousands of human genes and conditions are currently useful as markers in estimating mutation rates. Human genetic variability, small numbers of offspring per individual, and long generation times further complicate such studies. In addition, only disorders caused by dominant mutations, some sex-linked recessive mutations, and certain chromosome aberrations can be detected in the first generation after their occurrence. Conditions caused by autosomal recessive disorders (which appear to occur more frequently than dominant disorders) or by polygenic traits may go unrecognized for many generations. Therefore, in the absence of human epidemiological data, it is appropriate to rely on data from experimental animal systems as long as the limitations of using surrogate and model systems are clearly stated.

Despite species differences in metabolism, DNA repair, and other physiological processes affecting chemical mutagenesis, the virtual universality of DNA as the genetic material and of the genetic code provides a rationale for using various nonhuman test systems to predict the intrinsic mutagenicity of test chemicals. Additional support for the use of nonhuman systems is provided by the observation that chemicals causing genetic effects in one species or test system frequently cause similar effects in other species or systems. Evidence also exists that chemicals can induce genetic damage in somatic cells of exposed humans. For example, high doses of mutagenic chemotherapeutic agents have been shown to cause chromosomal abnormalities (11), sister chromatic exchange (11), and, quite probably, point mutations in human lymphocytes exposed *in vivo* (12). While these results are not in germ cells, they do indicate that it is possible to induce mutagenic events in human cells *in vivo*. Furthermore, a wide variety of different types of mutations have been observed in humans including numerical chromosome aberrations, translocations, base-pair substitutions, and frameshift mutations. Although the cause of these mutations is uncertain, it is clear from these observations that the human germ-cell DNA is subject to the same types of

mutational events that are observed in other species and test systems.

Certain test systems offer notable advantages: cost; anatomical, histological, and/or metabolic similarities to humans; suitability for handling large numbers of test organisms; a large data base; or a basis for characterizing genetic events.

B. Test Systems

Many test systems are currently available that can contribute information about the mutagenic potential of a test compound with respect to various genetic end points. These tests have recently been evaluated through the EPA Gene-Tox Programs and the results of Phase I have been published (5). The Agency's Office of Pesticides and Toxic Substances has published various testing guidelines for the detection of mutagenic effects (13, 14).

Test systems for detecting point mutations include those in bacteria, eukaryotic microorganisms, higher plants, insects, mammalian somatic cells in culture, and germinal cells of intact mammals. Data from heritable, mammalian germ-cell tests provide the best experimental evidence that a

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chemical is a potential human germ-cell mutagen since these tests require that mutations occur in germinal cells and that they are transmitted to the next generation. To date, the most extensively used test for the induction of heritable mutation is the mouse specific-locus test which measures the induction of recessive mutations at seven loci concerned with coat color and ear morphology. While this test has a large data base compared to other germ-cell assays, it is difficult to extrapolate results to humans since recessive mutations may occur more frequently than dominants, and the impact of recessive mutations is not seen for many generations. Information on frequencies of induced mutations resulting in health disorders in the first generation may be obtained from mouse systems designed to detect skeletal abnormalities, cataracts, or general morphological abnormalities. However, these assays have been used to a relatively limited extent, and there is a need for additional studies with known, chemical germ-cell mutagens to further characterize the test systems. Because large numbers of offspring must usually be generated in the systems described above, it is not expected that many chemicals will be tested using these systems. To obtain data on a large number of environmental chemicals, it will be necessary to rely on other tests to identify and characterize hazards from gene mutations.

Test systems for detecting structural chromosome aberrations have been developed in a variety of organisms including higher plants, insects, fish, birds, and several mammalian species. Many of these assays can be performed *in vitro* or *in vivo*, and in either germ or somatic cells. Procedures available for detecting structural chromosome aberrations in mammalian germ cells include measurement of heritable translocations or dominant lethality, as well as direct cytogenetic analyses of germ cells and early embryos in rodents.

Some chemicals may cause numerical chromosome changes (i.e., aneuploidy) as their sole mutagenic effect. These agents may not be detected as mutagens if evaluated only in tests for DNA damage, gene mutations, or chromosome breakage and rearrangement. Therefore, it is important to consider tests for changes in chromosome number in the total assessment of mutagenic hazards. Although tests for the detection of variation in the chromosome number are still at an early stage of development, systems exist in such diverse organisms as fungi, Drosophila, mammalian cells in culture, and intact mammals (e.g., mouse X-chromosome loss assay). Aneuploidy can arise from disturbances in a number of events affecting the meiotic process (15, 16). Although the mechanisms by which nondisjunction occurs are not well understood, mitotic structures other than DNA may be the target molecules for at least some mechanisms of induced nondisjunction.

Other end points that provide information bearing on the mutagenicity of a chemical can be detected by a variety of test systems. Such tests measure DNA damage in eukaryotic or prokaryotic cells, unscheduled DNA synthesis in mammalian somatic and germ cells, mitotic recombination and gene conversion in yeast, and sister-chromatid exchange in mammalian somatic and germ cells. Results in these assays are useful because the induction of these end points often correlates positively with the potential of a chemical to induce mutations.

In general, for all three end points (i.e., point mutations and numerical and structural aberrations), the Agency will place greater weight on tests conducted in germ cells than in somatic cells, on tests performed *in vivo* rather than *in vitro*, in eukaryotes rather than prokaryotes, and in mammalian species rather than in submammalian species. Formal numerical weighting systems have been developed (17); however, the Agency has concluded that these do not readily accommodate such variables as dose range, route of exposure, and magnitude of response.

The Agency anticipates that from time to time somatic cell data from chemically exposed human beings will be available (e.g., cytogenetic markers in peripheral lymphocytes). When possible, the Agency will use such data in conjunction with somatic and germ cell comparisons from *in vivo* mammalian experimental systems as a component in performing risk assessments.

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The test systems mentioned previously are not the only ones that will provide evidence of mutagenicity or related DNA effects. These systems are enumerated merely to demonstrate the breadth of the available techniques for characterizing mutagenic hazards, and to indicate the types of data that the Agency will consider in its evaluation of mutagenic potential of a chemical agent. Most systems possess certain limitations that must be taken into account. The selection and performance of appropriate tests for evaluating the risks associated with human exposure to any suspected mutagen will depend on sound scientific judgment and experience, and may necessitate consultation with geneticists familiar with the sensitivity and experimental design of the test system in question. In view of the rapid advances in test methodology, the Agency expects that both the number and quality of the tools for assessing genetic risk to human beings will increase with time. The Agency will closely monitor developments in mutagenicity evaluation and will refine its risk assessment scheme as better test systems become available.

II. Qualitative Assessment (Hazard Identification)

The assessment of potential human germ-cell mutagenic risk is a multistep process. The first step is an analysis of the evidence bearing on a chemical's ability to induce mutagenic events, while the second step involves an analysis of its ability to produce these events in the mammalian gonad. All relevant information is then integrated into a weight-of-evidence scheme which presents the strength of the information bearing on the chemical's potential ability to produce mutations in human germ cells. For chemicals demonstrating this potential, one may decide to proceed with an evaluation of the quantitative consequences of mutation following expected human exposure.

For hazard identification, it is clearly desirable to have data from mammalian germ-cell tests, such as the mouse specific-locus test for point mutations and the heritable translocation or germ-cell cytogenetic tests for structural chromosome aberrations. It is recognized, however, that in most instances such data will not be available, and alternative means of evaluation will be required. In such cases the Agency will evaluate the evidence bearing on the agent's mutagenic activity and the agent's ability to interact with or affect the mammalian gonadal target. When evidence exists that an agent possesses both these attributes, it is reasonable to deduce that the agent is a potential human germ-cell mutagen.

While mammalian germ-cell assays are presently primarily performed on male animals, a chemical cannot be considered to be a non-mutagen for mammalian germ cells unless it is shown to be negative in both sexes. Furthermore, because most mammalian germ-cell assays are performed in mice, it is noteworthy that the data from ionizing radiation suggest that the female mouse immature oocyte may not be an appropriate surrogate for the same stage in the human female in mutagenicity testing. However,

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mutagenicity data on the maturing and mature oocyte of the mouse may provide a useful model for human risk assessment.

A. Mutagenic Activity

In evaluating chemicals for mutagenic activity, a number of factors will be considered: 1) genetic end points (e.g., gene mutations, structural or numerical chromosomal aberrations) detected by the test systems, 2) sensitivity and predictive value of the test systems for various classes of chemical compounds, 3) number of different test systems used for detecting each genetic end point, 4) consistency of the results obtained in different test systems and different species, 5) aspects of the dose-response relationship, and 6) whether the tests are conducted in accordance with appropriate test protocols agreed upon by experts in the field.

B. Chemical Interactions in the Mammalian Gonad

Evidence for chemical interaction in the mammalian gonad spans a range of different types of findings. Each chemical under consideration needs to be extensively reviewed since this type of evidence may be part of testing exclusive of mutagenicity per se (e.g., reproduction, metabolism, and mechanistic investigations). Although it is not possible to classify clearly each type of information that may be available on a chemical, two possible groups are illustrated.

1. *Sufficient evidence* of chemical interaction is given by the demonstration that an agent interacts with germ-cell DNA or other chromatin constituents, or that it induces such end points as unscheduled DNA synthesis, sister-chromatid exchange, or chromosomal aberrations in germinal cells.

2. *Suggestive evidence* will include the finding of adverse gonadal effects such as sperm abnormalities following acute, subchronic, or chronic toxicity testing, or findings of adverse reproductive effects such as decreased fertility, which are consistent with the chemical's interaction with germ cells.

C. Weight-of-Evidence Determination

The evidence for a chemical's ability to produce mutations and to interact with the germinal target are integrated into a weight-of-evidence judgment that the agent may pose a hazard as a potential human germ-cell mutagen. All information bearing on the subject, whether indicative of potential concern or not, must be evaluated. Whatever

evidence may exist from humans must also be factored into the assessment.

All germ-cell stages are important in evaluating chemicals because some chemicals have been shown to be positive in postgonial stages but not in gonia (18). When human exposures occur, effects on postgonial stages should be weighted by the relative sensitivity and the duration of the stages. Chemicals may show positive effects for some end points and in some test systems, but negative responses in others. Each review must take into account the limitations in the testing and in the types of responses that may exist.

To provide guidance as to the categorization of the weight of evidence, a classification scheme is presented to illustrate, in a simplified sense, the strength of the information bearing on the potential for human germ-cell mutagenicity. It is not possible to illustrate all potential combinations of evidence, and considerable judgment must be exercised in reaching conclusions. In addition, certain responses in tests that do not measure direct mutagenic end points (e.g., SCE induction in mammalian germ cells) may provide a basis for raising the weight of evidence from one category to another. The categories are presented in decreasing order of strength of evidence.

1. Positive data derived from human germ-cell mutagenicity studies, when available, will constitute the highest level of evidence for human mutagenicity.

2. Valid positive results from studies on heritable mutational events (of any kind) in mammalian germ cells.

3. Valid positive results from mammalian germ-cell chromosome aberration studies that do not include an intergeneration test.

4. Sufficient evidence for a chemical's interaction with mammalian germ cells, together with valid positive mutagenicity test results from two assay systems, at least one of which is mammalian (*in vitro* or *in vivo*). The positive results may both be for gene mutations or both for chromosome aberrations; if one is for gene mutations and the other for chromosome aberrations, both must be from mammalian systems.

5. Suggestive evidence for a chemical's interaction with mammalian germ cells, together with valid positive mutagenicity evidence from two assay systems as described under 4, above. Alternatively, positive mutagenicity evidence of less strength than defined under 4, above, when combined with sufficient evidence for a chemical's interaction with mammalian germ cells.

6. Positive mutagenicity test results of less strength than defined under 4, combined with suggestive evidence for a chemical's interaction with mammalian germ cells.

7. Although definitive proof of non-mutagenicity is not possible, a chemical could be classified operationally as a non-mutagen for human germ cells, if it gives valid negative test results for all end points of concern.

8. Inadequate evidence bearing on either mutagenicity or chemical interaction with mammalian germ cells.

III. Quantitative Assessment

The preceding section addressed primarily the processes of hazard identification, i.e., the determination of whether a substance is a potential germ-cell mutagen. Often, no further data will be available, and judgments will need to be based mainly on qualitative criteria. Quantitative risk assessment is a two-step process: determination of the heritable effect per unit of exposure (dose-response) and the relationship between mutation rate and disease incidence. The procedures that are presently accepted for the estimation of an increase in disease resulting from increased mutation have been described (3, 7, 8). Dose-response information is combined with anticipated levels and patterns of human exposure in order to derive a quantitative assessment (risk characterization).

A. Dose Response

Dose-response assessments can presently only be performed using data from *in vivo*, heritable mammalian germ-cell tests, until such time as other approaches can be demonstrated to have equivalent predictability. The morphological specific-locus and biochemical specific-locus assays can provide data on the frequencies of recessive mutations induced by different chemical exposure levels, and similar data can be obtained for heritable chromosomal damage using the heritable translocation test. Data on the frequencies of induced mutations resulting in health disorders in the first generation may be obtained from mouse systems designed to detect skeletal abnormalities, cataracts, or general morphological abnormalities. Assays that directly detect heritable health effects in the first generation may provide the best basis for predicting human health risks that result from mutagen exposure. The experimental data on induced mutation frequency are usually obtained at exposure levels much higher than those that will be experienced by human beings. An assessment of human risk is obtained by extrapolating the induced mutation frequency or the observed phenotypic

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effect downward to the approximate level of anticipated human exposure. In performing these extrapolations, the Agency will place greater weight on data derived from exposures and exposure rates that most closely simulate those experienced by the human population under study.

The Agency will strive to use the most appropriate extrapolation models for risk analysis

and will be guided by the available data and mechanistic considerations in this selection. However, it is anticipated that for tests involving germ cells of whole mammals, few dose points will be available to define dose-response functions. The Agency is aware that for at least one chemical that has been tested for mutations in mammalian germ cells, there exist departures from linearity at low exposure and exposure rates in a fashion similar to that seen for ionizing radiation that has a low linear energy transfer (19). The Agency will consider all relevant models for gene and chromosomal mutations in performing low-dose extrapolations and will choose the most appropriate model. This choice will be consistent both with the experimental data available and with current knowledge of relevant mutational mechanisms.

An experimental approach for quantitative assessment of genetic risk, which may have utility in the future, uses molecular dosimetry data from intact mammals in conjunction with mutagenicity and dosimetry data from other validated test systems (20). The intact mammal is used primarily for relating the exposure level for a given route of administration of a chemical to germ-cell dose, i.e., the level of mutagen-DNA interactions. This information is then used in conjunction with results obtained from mutagenicity test systems in which the relationship between the induction of mutations and chemical interactions with DNA can be derived. With mutagen-DNA interactions as the common denominator, a relationship can be constructed between mammalian exposure and the induced mutation frequency. The amount of DNA binding induced by a particular chemical agent may often be determined at levels of anticipated human exposure.

For some mutagenic events, DNA may not necessarily be the critical target. Interaction of chemicals with other macromolecules, such as tubulin, which is involved in the separation of chromosomes during nuclear division, can lead to chromosomal nondisjunction. At present, general approaches are not available for dose-response assessments for these types of mutations. Ongoing research should provide the means to make future assessments on chemicals causing aneuploidy.

B. Exposure Asssessment

The exposure assessment identifies populations exposed to toxic chemicals; describes their composition and size; and presents the types, magnitudes, frequencies, and durations of exposure to the chemicals. This component is developed independently of the other components of the mutagenicity assessment (2).

C. Risk Characterization

In performing mutagenicity risk assessments, it is important to consider each genetic end point individually. For example, although certain chemical substances that interact with DNA may cause both point and chromosomal mutations, it is expected that the ratio of these events may differ among chemicals and between doses for a given chemical. Furthermore, transmissible chromosomal aberrations are recoverable with higher frequencies from meiotic and postmeiotic germ-cell stages, which have a brief life span, than in spermatogonial stem cells, which can accumulate genetic damage throughout the reproductive life of an individual. For these reasons, when data are available, the Agency, to the best extent possible, will assess risks associated with all genetic end points.

Any risk assessment should clearly delineate the strengths and weaknesses of the data, the assumptions made, the uncertainties in the methodology, and the rationale used in reaching the conclusions, e.g., similar or different routes of exposure and metabolic differences between humans and test animals. When possible, quantitative risk assessments should be expressed in terms of the estimated increase of genetic disease per generation, or the fractional increase in the assumed background spontaneous mutation rate of humans (7). Examples of quantitative risk estimates have been published (7, 8, 21); these examples may be of use in performing quantitative risk assessments for mutagens.

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Part B: Response to Public and Science Advisory Board Comments

This section summarizes some of the issues raised in public and Science Advisory Board (SAB) comments on the Proposed Guidelines for Mutagenicity Risk Assessment published on November 23, 1984 (49 FR 46314). Unlike the other guidelines published on the same date, the Proposed Guidelines for Mutagenicity Risk Assessment contained a detailed section dealing with public comments received in response to the original proposal of 1980 (45 FR 74984). Several of the comments received in response to the proposed guidelines of 1984 were similar to those received in response to the proposed guidelines of 1980. Those comments are not addressed here because the position of the Agency on those issues has been presented in the responses included with the 1984 proposed guidelines (49 FR 46315- 46316).

A total of 44 comments were received in response to the proposed guidelines of 1984: 21 from manufacturers of regulated products, 10 from associations, 9 from government agencies, 2 from educational institutions, 1 from an individual, and 1 from a private consulting firm. The proposed guidelines and the public comments received were transmitted to the Agency's SAB prior to its public review of the proposed guidelines held April 22-23, 1985. The majority of the comments were favorable and expressed the opinion that the proposed guidelines accurately represent the existing state of knowledge in the field of mutagenesis. Several commentors offered suggestions for further clarification of particular issues, and many of the suggestions have been incorporated.

The two areas that received the most substantive comments were the sections concerning Weight-of-Evidence Determination and Dose Response. The comments on the proposed weight-of-evidence scheme ranged from suggestions for the elimination of a formal scheme to the expansion of the scheme to cover more potential data configurations. The SAB recommended an eight-level rank ordering scheme to define levels of evidence relating to human germ-cell mutagenicity. The Agency has incorporated this scheme into the Guidelines. Some commentors and the SAB suggested that the molecular dosimetry approach to dose-response data be presented as a concept that may be useful in the future rather than being available for use now. The Agency agrees that the data base at the present time is too sparse to recommend a general application of this approach to a wide range of chemical classes, and the Guidelines have been changed to reflect this. It should be noted, however, that the Agency strongly supports the development of molecular dosimetry methodologies as they relate to both an understanding of dose-response relationships and to methods for studying human exposure. A number of comments suggesting clarifications and editorial changes have been incorporated and the references have been expanded.

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GUIDELINES FOR THE HEALTH RISK ASSESSMENT OF CHEMICAL MIXTURES

SUMMARY: On September 24, 1986, the U.S. Environmental Protection Agency issued the following five guidelines for assessing the health risks of environmental pollutants.

Guidelines for Carcinogen Risk Assessment

Guidelines for Estimating Exposures

Guidelines for Mutagenicity Risk Assessment

Guidelines for the Health Assessment of Suspect Developmental Toxicants

Guidelines for the Health Risk Assessment of Chemical Mixtures

This section contains the Guidelines for the Health Risk Assessment of Chemical Mixtures.

The Guidelines for the Health Risk Assessment of Chemical Mixtures (hereafter "Guidelines") are intended to guide Agency analysis of information relating to health effects data on chemical mixtures in line with the policies and procedures established in the statutes administered by the EPA. These Guidelines were developed as part of an interoffice guidelines development program under the auspices of the Office of Health and Environmental Assessment (OHEA) in the Agency's Office of Research and Development. They reflect Agency consideration of public and Science Advisory Board (SAB) comments on the Proposed Guidelines for the Health Risk Assessment of Chemical Mixtures published January 9, 1985 (50 FR 1170).

This publication completes the first round of risk assessment guidelines development. These Guidelines will be revised, and new guidelines will be developed, as appropriate.

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SUPPLEMENTARY INFORMATION: In 1983, the National Academy of Sciences (NAS) published its book entitled *Risk Assessment in the Federal Government: Managing the Process*. In that book, the NAS recommended that Federal regulatory agencies establish "inference guidelines" to ensure consistency and technical quality in risk assessments and to ensure that the risk assessment process was maintained as a scientific effort separate from risk management. A task force within EPA accepted that recommendation and requested that Agency scientists begin to develop such guidelines.

General

The guidelines are products of a two-year Agencywide effort, which has included many scientists from the larger scientific community. These guidelines set forth principles and procedures to guide EPA scientists in the conduct of Agency risk assessments, and to inform Agency decision makers and the public about these procedures. In particular, the guidelines emphasize that risk assessments will be conducted on a case-by-case basis, giving full consideration to all relevant scientific information. This case-by-case approach means that Agency experts review the scientific information on each agent and use the most scientifically appropriate interpretation to assess risk. The guidelines also stress that this information will be fully presented in Agency risk assessment documents, and that Agency scientists will identify the strengths and weaknesses of each assessment by describing uncertainties, assumptions, and limitations, as well as the scientific basis and rationale for each assessment.

Finally, the guidelines are formulated in part to bridge gaps in risk assessment methodology and data. By identifying these gaps and the importance of the missing information to the risk assessment process, EPA wishes to encourage research and analysis that will lead to new risk assessment methods and data.

Guidelines for the Health Risk Assessment of Chemical Mixtures

Work on the Guidelines for the Health Risk Assessment of Chemical Mixtures began in January 1984. Draft guidelines were developed by Agency work groups composed of expert scientists from throughout the Agency. The drafts were peer-reviewed by expert scientists in the fields of toxicology, pharmacokinetics, and statistics from universities, environmental groups, industry, labor, and other governmental agencies. They were then proposed for public comment in the *FEDERAL REGISTER* (50 FR 1170). On November 9, 1984, the Administrator directed that Agency offices use the

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proposed guidelines in performing risk assessments until final guidelines become available. After the close of the public comment period, Agency staff prepared summaries of the comments, analyses of the major issues presented by the commentors, and preliminary Agency responses to those comments. These analyses were presented to review panels of the SAB on March 4 and April 22-23, 1985, and to the Executive Committee of the SAB on April 25-26, 1985. The SAB meetings were announced in the *FEDERAL REGISTER* as follows: February 12, 1985 (50 FR 5811) and April 4, 1985 (50 FR 13420 and 13421).

In a letter to the Administrator dated June 19, 1985, the Executive Committee generally concurred on all five of the guidelines, but recommended certain revisions, and requested that any revised guidelines be submitted to the appropriate SAB review panel chairman for review and concurrence on behalf of the Executive Committee. As described in the responses to comments (see Part B: Response to the Public and Science Advisory Board Comments), each guidelines document was revised, where appropriate, consistent with the SAB recommendations, and revised draft guidelines were submitted to the panel chairmen. Revised draft Guidelines for the Health Risk Assessment of Chemical Mixtures were concurred on in a letter dated August 16, 1985. Copies of the letters are available at the Public Information Reference Unit, EPA Headquarters Library, as indicated elsewhere in this section.

Following this Preamble are two parts: Part A contains the Guidelines and Part B, the Response to the Public and Science Advisory Board Comments (a summary of the major public comments, SAB comments, and Agency responses to those comments).

The SAB requested that the Agency develop a technical support document for these Guidelines. The SAB identified the need for this type of document due to the limited knowledge on interactions of chemicals in biological systems. Because of this, the SAB commented that progress in improving risk assessment will be particularly dependent upon progress in the science of interactions.

Agency staff have begun preliminary work on the technical support document and expect it to be completed by early 1987. The Agency is continuing to study the risk assessment issues raised in the guidelines and will revise these Guidelines in line with new information as appropriate.

[51 FR 34015]

References, supporting documents, and comments received on the proposed guidelines, as well as copies of the final guidelines, are available for inspection and copying at the Public Information Reference Unit (202-382-5926), EPA Headquarters Library, 401 M Street, S.W., Washington, DC, between the hours of 8:00 a.m. and 4:30 p.m.

I certify that these Guidelines are not major rules as defined by Executive Order 12291, because they are nonbinding policy statements and have no direct effect on the regulated community. Therefore, they will have no effect on costs or prices, and they will have no other significant adverse effects on the economy. These Guidelines were reviewed by the Office of Management and Budget under Executive Order 12291.

August 22, 1986

Lee M. Thomas,

Administrator

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Part A: Guidelines for the Health Risk Assessment of Chemical Mixtures

I. Introduction

The primary purpose of this document is to generate a consistent Agency approach for evaluating data on the chronic and subchronic effects of chemical mixtures. It is a procedural guide that emphasizes broad underlying principles of the various science disciplines (toxicology, pharmacology, statistics) necessary for assessing health risk from chemical mixture exposure. Approaches to be used with respect to the analysis and evaluation of the various data are also discussed.

It is not the intent of these Guidelines to regulate any social or economic aspects concerning risk of injury to human health or the environment caused by exposure to a chemical agent(s). All such action is addressed in specific statutes and federal legislation and is independent of these Guidelines.

While some potential environmental hazards involve significant exposure to only a single compound, most instances of environmental contamination involve concurrent or sequential exposures to a mixture of compounds that may induce similar or dissimilar effects over exposure periods ranging from short-term to lifetime. For the purposes of these Guidelines, mixtures will be defined as any combination of two or more chemical substances regardless of source or of spatial or temporal proximity. In some instances, the mixtures are highly complex consisting of scores of compounds that are generated simultaneously as by-products from a single source or process (e.g., coke oven emissions and diesel exhaust). In other cases, complex mixtures of related compounds are produced as commercial products (e.g., PCBs, gasoline and pesticide formulations) and eventually released to the environment. Another class of mixtures consists of compounds, often unrelated chemically or commercially, which are placed in the same area for disposal or storage, eventually come into contact with each other, and are released as a mixture to the environment. The quality and quantity of pertinent information available for risk assessment varies considerably for different mixtures. Occasionally, the chemical composition of a mixture is well characterized, levels of exposure to the population are known, and detailed toxicologic data on the mixture are available. Most frequently, not all components of the mixture are known, exposure data are uncertain, and toxicologic data on the known components of the mixture are limited. Nonetheless, the Agency may be required to take action because of the number of individuals at potential risk or because of the known toxicologic effects of these compounds that have been identified in the mixture.

The prediction of how specific mixtures of toxicants will interact must be based on an understanding of the mechanisms of such interactions. Most reviews and texts that discuss toxicant interactions attempt to discuss the biological or chemical bases of the interactions (e.g., Klaassen and Doull, 1980; Levine, 1973; Goldstein et al., 1974; NRC, 1980a; Veldstra, 1956; Withey, 1981). Although different authors use somewhat different classification schemes when discussing the ways in which toxicants interact, it generally is recognized that toxicant interactions may occur during any of the toxicologic processes that take place with a single compound: absorption, distribution, metabolism, excretion, and activity at the receptor site(s). Compounds may interact chemically, yielding a new toxic component or causing a change in the biological availability of the existing component. They may also interact by causing different effects at different receptor sites.

Because of the uncertainties inherent in predicting the magnitude and nature of toxicant interactions, the assessment of health risk from chemical mixtures must include a thorough discussion of all assumptions. No single approach is recommended in these Guidelines. Instead, guidance is given for the use of several approaches depending on the nature and quality of the data. Additional mathematical details are presented in section IV.

In addition to these Guidelines, a supplemental technical support document is being developed which will contain a thorough review of all available information on the toxicity of chemical mixtures and a discussion of research needs.

II. Proposed Approach

No single approach can be recommended to risk assessments for multiple chemical exposures. Nonetheless, general guidelines can be recommended depending on the type of mixture, the known toxic effects of its components, the availability of toxicity data on the mixture or similar mixtures,

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the known or anticipated interactions among components of the mixture, and the quality of the exposure data. Given the complexity of this issue and the relative paucity of empirical data from which sound generalizations can be constructed, emphasis must be placed on flexibility, judgment, and a clear articulation of the assumptions and limitations in any risk assessment that is developed. The proposed approach is summarized in Table 1 and Figure 1 and is detailed below. An alphanumeric scheme for ranking the quality of the data used in the risk assessment is given in Table 2.

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A. Data Available on the Mixture of Concern

For predicting the effects of subchronic or chronic exposure to mixtures, the preferred approach usually will be to use subchronic or chronic health effects data on the mixture of concern and adopt procedures similar to those used for single compounds, either systemic toxicants or carcinogens (see U.S. EPA, 1986a-1986c). The risk assessor must recognize, however, that dose-response models used for single compounds are often based on biological mechanisms of the toxicity of single compounds, and may not be as well justified when applied to the mixture as a whole. Such data are most likely to be available on highly complex mixtures, such as coke oven emissions or diesel exhaust, which are generated in large quantities and associated with or suspected of causing adverse health effects. Attention should also be given to the persistence of the mixture in the environment as well as to the variability of the mixture composition over time or from different sources of emissions. If the components of the mixture are known to partition into different environmental compartments or to degrade or transform at different rates in the environment, then those factors must also be taken into account, or the confidence in and applicability of the risk assessment is diminished.

TABLE 1.-- RISK ASSESSMENT APPROACH FOR CHEMICAL MIXTURES

1. Assess the quality of the data on interactions, health effects, and exposure (see Table 2).
   a. If adequate, proceed to Step 2.
   b. If inadequate, proceed to Step 14.

2. Health effects information is available on the chemical mixture of concern .
   a. If yes, proceed to Step 3.
   b. If no, proceed to Step 4.

3. Conduct risk assessment on the mixture of concern based on health effects data on the mixture. Use the same procedures as those for single compounds. Proceed to Step 7 (optional) and Step 12.

4. Health effects information is available on a mixture that is similar to the mixture of concern.
   a. If yes, proceed to Step 5.
   b. If no, proceed to Step 7.

5. Assess the similarity of the mixture on which health effects data are available to the mixture of concern, with emphasis on any differences in components or proportions of components, as well as the effects that such differences would have on biological activity.
   a. If sufficiently similar, proceed to Step 6.
   b. If not sufficiently similar, proceed to Step 7.

6. Conduct risk assessment on the mixture of concern based on health effects data on the similar mixture. Use the same procedures as those for single compounds. Proceed to Step 7 (optional) and Step 12.

7. Compile health effects and exposure information on the components of the mixture.

8. Derive appropriate indices of acceptable exposure and/or risk on the individual components in the mixture. Proceed to Step 9.

9. Assess data on interactions of components in the mixtures.
   a. If sufficient quantitative data are available on the interactions of two or more components in the mixture, proceed to Step 10.
   b. If sufficient quantitative data are not available, use whatever information is available to qualitatively indicate the nature of potential interactions. Proceed to Step 11.

10. Use an appropriate interaction model to combine risk assessments on compounds for which data are adequate, and use an additivity assumption for the remaining compounds. Proceed to Step 11 (optional) and Step 12.

11. Develop a risk assessment based on an additivity approach for all compounds in the mixture. Proceed to Step 12.

12. Compare risk assessments conducted in Steps 5, 8, and 9. Identify and justify the preferred assessment, and quantify uncertainty, if possible. Proceed to Step 13.

13. Develop an integrated summary of the qualitative and quantitative assessments with special emphasis on uncertainties and assumptions. Classify the overall quality of the risk assessment, as indicated in Table 2. Stop.

14. No risk assessment can be conducted because of inadequate data on interactions, health effects, or exposure. Qualitatively assess the nature of any potential hazard and detail the types of additional data necessary to support a risk assessment. Stop.

Note. -- Several decisions used here, especially those concerning adequacy of data and similarity between two mixtures, are not precisely characterized and will require considerable judgment. See text.

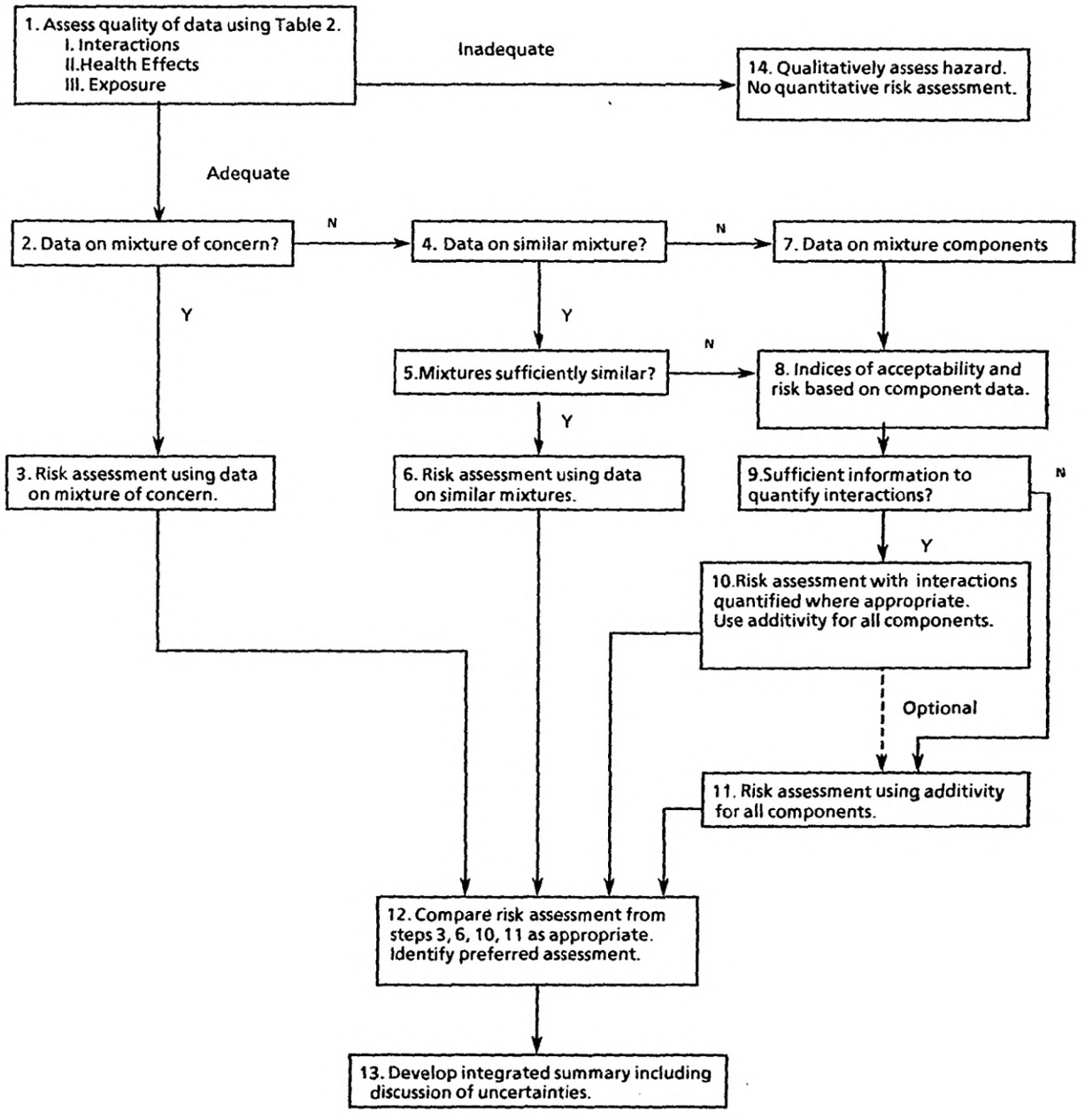

Figure 1. Flow chart of the risk assessment approach in Table 1. Note that it may be desirable to conduct all three assessments when possible (i.e., using data on the mixture, a similar mixture ,or the components) in order to make the fullest use of the available data. See text for further discussion.

TABLE 2. -- CLASSIFICATION SCHEME FOR THE QUALITY OF THE RISK ASSESSMENT OF THE MIXTURE[a]

Information on Interactions

I. Assessment is based on data on the mixture of concern.

II. Assessment is based on data on a sufficiently similar mixture.

III. Quantitative interactions of components are well characterized.

IV. The assumption of additivity is justified based on the nature of the health effects and on the number of component compounds.

V. An assumption of additivity cannot be justified, and no quantitative risk assessment can be conducted.

Health Effects Information

A. Full health effects data are available and relatively minor extrapolation is required.

B. Full health effects data are available but extensive extrapolation is required for route or duration of exposure or for species differences. These extrapolations are supported by pharmacokinetic considerations, empirical observations, or other relevant information.

C. Full health effects data are available, but extensive extrapolation is required for route or duration of exposure or for species differences. These extrapolations are not directly supported by the information available.

D. Certain important health effects data are lacking and extensive extrapolations are required for route or duration of exposure or for species differences.

E. A lack of health effects information on the mixture and its components in the mixture precludes a quantitative risk assessment.

Exposure Information[b]

1. Monitoring information either alone or in combination with modeling information is sufficient to accurately characterize human exposure to the mixture or its components.

2. Modeling information is sufficient to reasonably characterize human exposure to the mixture or its components.

3. Exposure estimates for some components are lacking, uncertain, or variable. Information on health effects or environmental chemistry suggest that this limitation is not likely to substantially affect the risk assessment.

4. Not all components in the mixture have been identified or levels of exposure are highly uncertain or variable. Information on health effects or environmental chemistry is not sufficient to assess the effect of this limitation on the risk assessment.

5. The available exposure information is insufficient for conducting a risk assessment.

B. Data Available on Similar Mixtures

If the risk assessment is based on data from a single mixture that is known to be generated with varying compositions depending on time or different emission sources, then the confidence in the applicability of the data to a risk assessment also is diminished. This can be offset to some degree if data are available on several mixtures of the same components that have different component ratios which encompass the temporal or spatial differences in composition of the mixture of concern. If such data are available, an attempt should be made to determine if significant and systematic differences exist among the chemical mixtures. If significant differences are noted, ranges of risk can be estimated based on the toxicologic data of the various mixtures. If no significant differences are noted, then a single risk assessment may be adequate, although the range of ratios of the components in the mixtures to which the risk assessment applies should also be given.

If no data are available on the mixtures of concern, but health effects data are available on a similar mixture (i.e., a mixture having the same components but in slightly different ratios, or having several common components but lacking one or more components, or having one or more additional components), a decision must be made whether the mixture on which health effects data are available is or is not "sufficiently similar" to the mixture of concern to permit a risk assessment. The determination of "sufficient similarity" must be made on a case-by-case basis, considering not only the uncertainties associated with using data on a dissimilar mixture but also the uncertainties of using other approaches such as additivity. In determining reasonable similarity, consideration should be given to any information on the components that differ or are contained in markedly different proportions between the mixture on which health effects data are available and the mixture of concern. Particular emphasis should be placed on any toxicologic or pharmacokinetic data on the components or the mixtures which would be useful in assessing the significance of any chemical difference between the similar mixture and the mixtures of concern.

Even if a risk assessment can be made using data on the mixtures of concern or a reasonably similar mixture, it may be desirable to conduct a risk assessment based on toxicity data on the

[a] See text for discussion of sufficient similarity, adequacy of data, and justification for additivity assumptions.

[b] See the Agency's Guidelines for Estimating Exposures (U.S. EPA, 1986d) for more complete information on performing exposure assessments and evaluating the quality of exposure data.

components in the mixture using the procedure outlined in section II.B. In the case of a mixture containing carcinogens and toxicants, an approach based on the mixture data alone may not be sufficiently protective in all cases. For example, this approach for a two-component mixture of one carcinogen and one toxicant would use toxicity data on the mixture of the two compounds. However, in a chronic study of such a mixture, the presence of the toxicant could mask the activity of the carcinogen. That is to say, at doses of the mixture sufficient to induce a carcinogenic effect, the toxicant could induce mortality so that at the maximum tolerated dose of the mixture, no carcinogenic effect could be observed. Since carcinogenicity is considered by the Agency to be a nonthreshold effect, it may not be prudent to construe the negative results of such a bioassay as indicating the absence of risk at lower doses. Consequently, the mixture approach should be modified to allow the risk assessor to evaluate the potential for masking, of one effect by another, on a case-by-case basis.

C. Data Available Only on Mixture Components

If data are not available on an identical or reasonably similar mixture, the risk assessment may be based on the toxic or carcinogenic properties of the components in the mixture. When little or no quantitative information is available on the potential interaction among the components, additive models (defined in the next section) are recommended for systemic toxicants. Several studies have demonstrated that dose additive models often predict reasonably well the toxicities of mixtures composed of a substantial variety of both similar and dissimilar compounds (Pozzani et al., 1959; Smyth et al., 1969, 1970; Murphy, 1980). The problem of multiple toxicant exposure has been addressed by the American Conference of Governmental Industrial Hygienists (ACGIH, 1983), the Occupational Safety and Health Administration (OSHA, 1983), the World Health Organization (WHO, 1981), and the National Research Council (NRC, 1980a, b). Although the focus and purpose of each group was somewhat different, all groups that recommended an approach elected to adopt some type of dose additive model. Nonetheless, as discussed in section IV, dose additive models are not the most biologically plausible approach if the compounds do not have the same mode of toxicologic action. Consequently, depending on the nature of the risk assessment and the available information on modes of action and patterns of joint action, the

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most reasonable additive model should be used.

1. Systemic Toxicants. For systemic toxicants, the current risk assessment methodology used by the Agency for single compounds most often results in the derivation of an exposure level which is not anticipated to cause significant adverse effects. Depending on the route of exposure, media of concern, and the legislative mandate guiding the risk assessments, these exposure levels may be expressed in a variety of ways such as acceptable daily intakes (ADIs) or reference doses (RfDs), levels associated with various margins of safety (MOS), or acceptable concentrations in various media. For the purpose of this discussion, the term "acceptable level" (AL) will be used to indicate any such criteria or advisories derived by the Agency. Levels of exposure (E) will be estimates obtained following the most current Agency Guidelines for Estimating Exposures (U.S. EPA, 1986d). For such estimates, the "hazard index" (HI) of a mixture based on the assumption of dose addition may be defined as:

$$HI = E_1/AL_1 + E_2/AL_2 + \ldots + E_i/AL_i \qquad \text{(II-1)}$$

where:

E_i = exposure level to the ith toxicant* and
AL_i = maximum acceptable level for the ith toxicant.

Since the assumption of dose addition is most properly applied to compounds that induce the same effect by similar modes of action, a separate hazard index should be generated for each end point of concern. Dose addition for dissimilar effects does not have strong scientific support, and, if done, should be justified on a case-by-case basis in terms of biological plausibility.

The assumption of dose addition is most clearly justified when the mechanisms of action of the compounds under consideration are known to be the same. Since the mechanisms of action for most compounds are not well understood, the justification of the assumption of dose addition will often be limited to similarities in pharmacokinetic and toxicologic characteristics. In any event, if a hazard index is generated, the quality of the experimental evidence supporting the assumption of dose addition must be clearly articulated.

The hazard index provides a rough measure of likely toxicity and requires cautious interpretation. The hazard index is only a numerical indication of the nearness to acceptable limits of exposure or the degree to which acceptable exposure levels are exceeded. As this index approaches unity, concern for the potential hazard of the mixture increases. If the index exceeds unity, the concern is the same as if an individual chemical exposure exceeded its acceptable level by the same proportion. The hazard index does not define dose-response relationships, and its numerical value should not be construed to be a direct estimate of risk. Nonetheless, if sufficient data are available to derive individual acceptable levels for a spectrum of effects (e.g., MFO induction,

*See the Agency's guidelines (U.S. EPA, 1986d) for information on how to estimate this value.

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variabilities of the acceptable levels are known, or if the acceptable levels are given as ranges (e.g., associated with different margins of safety), then the hazard index should be presented with corresponding estimates of variation or range. Most studies on systemic toxicity report only descriptions of the effects in each dose group. If dose-response curves are estimated for systemic toxicants, however, dose-additive or response-additive assumptions can be used, with preference given to the most biologically plausible assumption (see section IV for the mathematical details).

2. Carcinogens. For carcinogens, whenever linearity of the individual dose-response curves has been assumed (usually restricted to low doses), the increase in risk P (also called excess or incremental risk), caused by exposure d, is related to carcinogenic potency B, as:

$$P = d\,B \qquad \text{(II-2)}$$

For multiple compounds, this equation may be generalized to:

$$P = \Sigma d_i\,B_i \qquad \text{(II-3)}$$

This equation assumes independence of action by the several carcinogens and is equivalent to the assumption of dose addition as well as to response addition with completely negative correlation of tolerance, as long as $P < 1$ (see section IV). Analogous to the procedure used in equation II-1 for systemic toxicants, an index for n carcinogens can be developed by dividing exposure levels (E) by doses (DR) associated with a set level of risk:

$$HI = E_1/DR_1 + E_2/DR_2 + \ldots + E_n/DR_n \qquad \text{(II-4)}$$

Note that the less linear the dose-response curve is, the less appropriate equations II-3 and II-4 will be, perhaps even at low doses. It should be emphasized that because of the uncertainties in estimating dose-response relationships for single compounds, and the additional uncertainties in combining the individual estimate to assess response from exposure to mixtures, response rates and hazard indices may have merit in comparing risks but should not be regarded as measures of absolute risk.

3.Interactions. None of the above equations incorporates any form of synergistic or antagonistic interaction. Some types of information, however, may be available that suggest that two or more components in the mixture may interact. Such information must be assessed in terms of both its relevance to subchronic or chronic hazard and its suitability for quantitatively altering the risk assessment.

For example, if chronic or subchronic toxicity or carcinogenicity studies have been conducted that permit a quantitative estimation of interaction for two chemicals, then it may be desirable to consider using equations detailed in section IV, or modifications of these equations, to treat the two compounds as a single toxicant with greater or lesser potency than would be predicted from additivity. Other components of the mixture, on which no such interaction data are available, could then be separately treated in an additive manner. Before such a procedure is adopted, however, a discussion should be presented of the likelihood that other compounds in the mixture may interfere with the interaction of the two toxicants on which quantitative interaction data are available. If the weight of evidence suggests that interference is likely, then a quantitative alteration of the risk assessment may not be justified. In such cases, the risk assessment may only indicate the likely nature of interactions, either synergistic or antagonistic, and not quantify their magnitudes.

Other types of information, such as those relating to mechanisms of toxicant interaction, or quantitative estimates of interaction between two chemicals derived from acute studies, are even less likely to be of use in the quantitative assessment of long-term health risks. Usually it will be appropriate only to discuss these types of information, indicate the relevance of the information to subchronic or chronic exposure, and indicate, if possible, the nature of potential interactions, without attempting to quantify their magnitudes.

When the interactions are expected to have a minor influence on the mixture's toxicity, the assessment should indicate, when possible, the compounds most responsible for the predicted toxicity. This judgment should be based on predicted toxicity of each component,

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based on exposure and toxic or carcinogenic potential. This potential alone should not be used as an indicator of the chemicals posing the most hazard.

4.Uncertainties. For each risk assessment, the uncertainties should be clearly discussed and the overall quality of the risk assessment should be characterized. The scheme outlined in Table 2 should be used to express the degree of confidence in the quality of the data on interaction, health effects, and exposure.

a. Health Effects--In some cases, when health effects data are incomplete, it may be possible to argue by analogy or quantitative structure-activity relationships that the compounds on which no health effects data are available are not likely to significantly affect the toxicity of the mixture. If a risk assessment includes such an argument, the limitations of the approach must be clearly articulated. Since a methodology has not been adopted for estimating an acceptable level (e.g., ADI) or carcinogenic potential for single compounds based either on quantitative structure-activity relationships or on the results of short-term screening tests, such methods are not at present

recommended as the sole basis of a risk assessment on chemical mixtures.

b. Exposure Uncertainties--The general uncertainties in exposure assessment have been addressed in the Agency's Guidelines for Estimating Exposures (U.S. EPA, 1986d). The risk assessor should discuss these exposure uncertainties in terms of the strength of the evidence used to quantify the exposure. When appropriate, the assessor should also compare monitoring and modeling data and discuss any inconsistencies as a source of uncertainty. For mixtures, these uncertainties may be increased as the number of compounds of concern increases.

If levels of exposure to certain compounds known to be in the mixture are not available, but information on health effects and environmental persistence and transport suggest that these compounds are not likely to be significant in affecting the toxicity of the mixture, then a risk assessment can be conducted based on the remaining compounds in the mixture, with appropriate caveats. If such an argument cannot be supported, no final risk assessment can be performed until adequate monitoring data are available. As an interim procedure, a risk assessment may be conducted for those components in the mixture for which adequate exposure and health effects data are available. If the interim risk assessment does not suggest a hazard, there is still concern about the risk from such a mixture because not all components in the mixture have been considered.

c. Uncertainties Regarding Composition of the Mixture--In perhaps a worst case scenario, information may be lacking not only on health effects and levels of exposure, but also on the identity of some components of the mixture. Analogous to the procedure described in the previous paragraph, an interim risk assessment can be conducted on those components of the mixture for which adequate health effects and exposure information are available. If the risk is considered unacceptable, a conservative approach is to present the quantitative estimates of risk, along with appropriate qualifications regarding the incompleteness of the data. If no hazard is indicated by this partial assessment, the risk assessment should not be quantified until better health effects and monitoring data are available to adequately characterize the mixture exposure and potential hazards.

III. Assumptions and Limitations

A. Information on Interactions

Most of the data available on toxicant interactions are derived from acute toxicity studies using experimental animals in which mixtures of two compounds were tested, often in only a single combination. Major areas of uncertainty with the use of such data involve the appropriateness of interaction data from an acute toxicity study for quantitatively altering a risk assessment for subchronic or chronic exposure, the appropriateness of interaction data on two component mixtures for quantitatively altering a risk assessment on a mixture of several compounds, and the accuracy of interaction data on experimental animals for quantitatively predicting interactions in humans.

The use of interaction data from acute toxicity studies to assess the potential interactions on chronic exposure is highly questionable unless the mechanism(s) of the interaction on acute exposure were known to apply to low-dose chronic exposure. Most known biological mechanisms for toxicant interactions, however, involve some form of competition between the chemicals or phenomena involving saturation of a receptor site or metabolic pathway. As the doses of the toxicants are decreased, it is likely that these mechanisms either no longer will exert a significant effect or will be decreased to an extent that cannot be measured or approximated.

The use of information from two-component mixtures to assess the interactions in a mixture containing more than two compounds also is questionable from a mechanistic perspective. For example, if two compounds are known to interact, either synergistically or antagonistically, because of the effects of one compound on the metabolism or excretion of the other, the addition of a third compound which either chemically alters or affects the absorption of one of the first two compounds could substantially alter the degree of the toxicologic interaction. Usually, detailed studies quantifying toxicant interactions are not available on multicomponent mixtures, and the few studies that are available on such mixtures (e.g., Gullino et al., 1956) do not provide sufficient information to assess the effects of interactive interference.

Concerns with the use of interaction data on experimental mammals to assess interactions in humans is based on the increasing appreciation for systematic differences among species in their response to individual chemicals. If systematic differences in toxic sensitivity to single chemicals exist among species, then it seems reasonable to suggest that the magnitude of toxicant interactions among species also may vary in a systematic manner. Consequently, even if excellent chronic data are available on the magnitude of toxicant interactions in a species of experimental mammal, there is uncertainty that the magnitude of the interaction will be the same in humans. Again, data are not available to properly assess the significance of this uncertainty.

Last, it should be emphasized that none of the models for toxicant interaction can predict the magnitude of toxicant interactions in the absence of extensive data. If sufficient data are available to

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estimate interaction coefficients as described in section IV, then the magnitude of the toxicant interactions for various proportions of the same components can be predicted. The availability of an interaction ratio (observed response divided by predicted response) is useful only in assessing the magnitude of the toxicant interaction for the specific proportions of the mixture which was used to generate the interaction ratio.

The basic assumption in the recommended approach is that risk assessments on chemical mixtures are best conducted using toxicologic data on the mixture of concern or a reasonably similar mixture. While such risk

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assessments do not formally consider toxicologic interactions as part of a mathematical model, it is assumed that responses in experimental mammals or human populations noted after exposure to the chemical mixture can be used to conduct risk assessments on human populations. In bioassays of chemical mixtures using experimental mammals, the same limitations inherent in species-to-species extrapolation for single compounds apply to mixtures. When using health effects data on chemical mixtures from studies on exposed human populations, the limitations of epidemiologic studies in the risk assessment of single compounds also apply to mixtures. Additional limitations may be involved when using health effects data on chemical mixtures if the components in the mixture are not constant or if the components partition in the environment.

B. Additivity Models

If sufficient data are not available on the effects of the chemical mixture of concern or a reasonably similar mixture, the proposed approach is to assume additivity. Dose additivity is based on the assumption that the components in the mixture have the same mode of action and elicit the same effects. This assumption will not hold true in most cases, at least for mixtures of systemic toxicants. For systemic toxicants, however, most single compound risk assessments will result in the derivation of acceptable levels, which, as currently defined, cannot be adapted to the different forms of response additivity as described in section IV.

Additivity models can be modified to incorporate quantitative data on toxicant interactions from subchronic or chronic studies using the models given in section IV or modifications of these models. If this approach is taken, however, it will be under the assumption that other components in the mixture do not interfere with the measured interaction. In practice, such subchronic or chronic interactions data seldom will be available. Consequently, most risk assessments (on mixtures) will be based on an assumption of additivity, as long as the components elicit similar effects.

Dose-additive and response-additive assumptions can lead to substantial errors in risk estimates if synergistic or antagonistic interactions occur. Although dose additivity has been shown to predict the acute toxicities of many mixtures of similar and dissimilar compounds (e.g., Pozzani et al., 1959; Smyth et al., 1969, 1970; Murphy, 1980), some marked exceptions have been noted. For example, Smyth et al. (1970) tested the interaction of 53 pairs of industrial chemicals based on acute lethality in rats. For most pairs of compounds, the ratio of the predicted LD_{50} to observed LD_{50} did not vary by more than a factor of 2. The greatest variation was seen with an equivolume mixture of morpholine and toluene, in which the observed LD_{50} was about five times less than the LD_{50} predicted by dose addition. In a study by Hammond et al. (1979), the relative risk of lung cancer attributable to smoking was 11, while the relative risk associated with asbestos exposure was 5. The relative risk of lung cancer from both smoking and asbestos exposure was 53, indicating a substantial synergistic effect. Consequently, in some cases, additivity assumptions may substantially underestimate risk. In other cases, risk may be overestimated. While this is certainly an unsatisfactory situation, the available data on mixtures are insufficient for estimating the magnitude of these errors. Based on current information, additivity assumptions are expected to yield generally neutral risk estimates (i.e., neither conservative nor lenient) and are plausible for component compounds that induce similar types of effects at the same sites of action.

IV. Mathematical Models and the Measurement of Joint Action

The simplest mathematical models for joint action assume no interaction in any mathematical sense. They describe either dose addition or response addition and are motivated by data on acute lethal effects of mixtures of two compounds.

A. Dose Addition

Dose addition assumes that the toxicants in a mixture behave as if they were dilutions or concentrations of each other, thus the true slopes of the dose-response curves for the individual compounds are identical, and the response elicited by the mixture can be predicted by summing the individual doses after adjusting for differences in potency; this is defined as the ratio of equitoxic doses. Probit transformation typically makes this ratio constant at all doses when parallel straight lines are obtained. Although this assumption can be applied to any model (e.g., the one-hit model in NRC, 1980b), it has been most often used in toxicology with the log-dose probit response model, which will be used to illustrate the assumption of dose addition.

Suppose that two toxicants show the following log-dose probit response equations:

$$Y_1 = 0.3 + 3 \log Z_1 \quad \text{(IV-1)}$$
$$Y_2 = 1.2 + 3 \log Z_2 \quad \text{(IV-2)}$$

where Y_i is the probit response associated with a dose of Z_i ($i=1,2$). The potency, p, of toxicant #2 with respect to toxicant #1 is defined by the quantity Z_1/Z_2 when $Y_1 = Y_2$ (that is what is meant by equitoxic doses). In this example, the potency, p, is approximately 2. Dose addition assumes that the response, Y, to any mixture of these two toxicants can be predicted by:

$$Y = 0.3 + 3 \log (Z_1 + pZ2) \quad \text{(IV-3)}$$

Thus, since p is defined as Z_1/Z_2, equation IV-3 essentially converts Z_2 into an equivalent dose of Z by adjusting for the difference in potency. A more generalized form of this equation for any number of toxicants is:

$$Y = a_1 + b \log (f_1 + \Sigma f_i p_i) + b \log Z \quad \text{(IV-4)}$$

where:

a_1 = the y-intercept of the dose-response equation for toxicant #1
b = the slope of the dose-response lines for the toxicants
f_i = the proportion of the ith toxicant in the mixture
p_i = the potency of the ith toxicant with respect to toxicant #1 (i.e., Z_1/Z_i), and
Z = the sum of the individual doses in the mixture.

A more detailed discussion of the derivation of the equations for dose addition is presented by Finney (1971).

B. Response Addition

The other form of additivity is referred to as response addition. As detailed by Bliss (1939), this type of joint action assumes that the two toxicants act on different receptor systems and that the correlation of individual tolerances may range from completely negative ($r=-1$) to completely positive ($r=+1$). Response addition assumes that the response to a given concentration of a mixture of toxicants is completely determined by the responses to the components and the pairwise correlation coefficient. Taking P as the proportion of organisms responding to a mixture of two toxicants which evoke individual responses of P_1 and P_2, then

$P = P_1$ if $r = 1$ and $P_1 \geq P_2$ (IV-5)
$P = P_2$ if $r = 1$ and $P_1 < P_2$ (IV-6)
$P = P_1 + P_2 (1-P_1)$ if $r = 0$ (IV-7)
$P = P_1 + P_2$ if $r = -1$ and $P \leq 1$. (IV-8)

More generalized mathematical models for this form of joint action have been given by Plackett and Hewlett (1948).

C. Interactions

All of the above models assume no interactions and therefore do not incorporate measurements of synergistic or antagonistic effects. For measuring toxicant interactions for mixtures of two compounds, Finney (1942) proposed the

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following modification of equation IV-4 for dose addition:

$$Y = a_1 + b \log (f_1 + pf_2 + K[pf_1f_2]^{0.5}) + b \log Z \quad \text{(IV-9)}$$

where a_1, b, f_1, f_2, p, and Z are defined as before, and K is the coefficient of interaction. A positive value of K indicates synergism, a negative value indicates antagonism, and a value of zero corresponds to dose addition as in equation IV-4. Like other proposed modifications of dose addition (Hewlett, 1969), the equation assumes a consistent interaction throughout the entire range of proportions of individual components. To account for such asymmetric patterns of interaction as those observed by Alstott et al. (1973), Durkin (1981) proposed the following modification to equation IV-9:

$$Y = a_1 + b \log (f_1 + pf_2 + K_1f_1[pf_1f_2]^{0.5} + K_2f_2[pf_1f_2]^{0.5}) + b \log Z \quad \text{(IV-10)}$$

in which $K(pf_1f_2)^{0.5}$ is divided into two components, $K_1f_1(pf_1f_2)^{0.5}$ and $K_2f_2(pf_1f_2)^{0.5}$. Since K_1 and K_2 need not have the same sign, apparent instances of antagonism at one receptor site and synergism at another receptor site can be estimated. When K_1 and K_2 are equal, equation IV-10 reduces to equation IV-9. It should be noted that to obtain a reasonable number of degrees of freedom in the estimation of K in equation IV-9 or K_1 and K_2 in equation IV-10, the toxicity of several different combinations of the two components must be assayed along with assays of the toxicity of the individual components. Since this requires experiments with large numbers of animals, such analyses have been restricted for the most part to data from acute bioassays using insects (e.g., Finney, 1971) or aquatic organisms (Durkin, 1979). Also, because of the complexity of experimental design and the need for large numbers of animals, neither equation IV-9 nor equation IV-10 has been generalized or applied to mixtures of more than two toxicants. Modifications of response-additive models to include interactive terms have also been proposed, along with appropriate statistical tests for the assumption of additivity (Korn and Liu, 1983; Wahrendorf et al., 1981).

In the epidemiologic literature, measurements of the extent of toxicant interactions, S, can be expressed as the ratio of observed relative risk to relative risk predicted by some form of additivity assumption. Analogous to the ratio of interaction in classical toxicology studies, $S = 1$ indicates no interaction, $S > 1$ indicates synergism, and $S < 1$ indicates antagonism. Several models for both

additive and multiplicative risks have been proposed (e.g., Hogan et al., 1978; NRC, 1980b; Walter, 1976). For instance, Rothman (1976) has discussed the use of the following measurement of toxicant interaction based on the assumption of risk additivity:

$$S = (R_{11} - 1)/(R_{10} + R_{01} - 2) \qquad \text{(IV-11)}$$

where R_{10} is the relative risk from compound #1 in the absence of compound #2, R_{01} is the relative risk from compound #2 in the absence of compound #1, and R_{11} is the relative risk from exposure to both compounds. A multiplicative risk model adapted from Walter and Holford (1978, equation 4) can be stated as:

$$S = R_{11}/(R_{10}R_{01}) \qquad \text{(IV-12)}$$

As discussed by both Walter and Holford (1978) and Rothman (1976), the risk-additive model is generally applied to agents causing diseases while the multiplicative model is more appropriate to agents that prevent disease. The relative merits of these and other indices have been the subject of considerable discussion in the epidemiologic literature (Hogan et al., 1978; Kupper and Hogan, 1978; Rothman, 1978; Rothman et al., 1980; Walter and Holford, 1978). There seems to be a consensus that for public health concerns regarding causative (toxic) agents, the additive model is more appropriate.

Both the additive and multiplicative models assume statistical independence in that the risk associated with exposure to both compounds in combination can be predicted by the risks associated with separate exposure to the individual compounds. As illustrated by Siemiatycki and Thomas (1981) for multistage carcinogenesis, the better fitting statistical model will depend not only upon actual biological interactions, but also upon the stages of the disease process which the compounds affect. Consequently, there is no *a priori* basis for selecting either type of model in a risk assessment. As discussed by Stara et al. (1983), the concepts of multistage carcinogenesis and the effects of promoters and cocarcinogens on risk are extremely complex issues. Although risk models for promoters have been proposed (e.g., Burns et al., 1983), no single approach can be recommended at this time.

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Part B: Response to Public and Science Advisory Board Comments

I. Introduction

This section summarizes some of the major issues raised in public comments on the Proposed Guidelines for the Health Risk Assessment of Chemical Mixtures published on January 9, 1985 (50 FR 1170). Comments were received from 14 individuals or organizations. An issue paper reflecting public and external review comments was presented to the Chemical Mixtures Guidelines Panel of the Science Advisory Board (SAB) on March 4, 1985. At its April 22-23, 1985, meeting, the SAB Panel provided the Agency with additional suggestions and recommendations concerning the Guidelines. This section also summarizes the issues raised by the SAB.

The SAB and public commentors expressed diverse opinions and addressed issues from a variety of perspectives. In response to comments, the Agency has modified or clarified many sections of the Guidelines, and is planning to develop a technical support document in line with the SAB recommendations. The discussion that follows highlights significant issues raised in the comments, and the Agency's response to them. Also, many minor recommendations, which do not warrant discussion here, were adopted by the Agency.

II. Recommended Procedures

A. Definitions

Several comments were received concerning the lack of definitions for certain key items and the general understandability of certain sections. Definitions have been rewritten for several terms and the text has been significantly rewritten to clarify the Agency's intent and meaning.

Several commentors noted the lack of a precise definition of "mixture," even though several classes of mixtures are discussed. In the field of chemistry, the term "mixture" is usually differentiated from true solutions, with the former defined as nonhomogeneous multicomponent systems. For these Guidelines, the term "mixture" is defined as "...any combination of two or more chemicals regardless of spatial or temporal homogeneity of source" (section 1). These Guidelines are intended to cover risk assessments for any situation where the population is exposed or potentially exposed to two or more compounds of concern. Consequently, the introduction has been revised to clarify the intended breadth of application.

Several commentors expressed concern that "sufficient similarity" was difficult to define and that the Guidelines should give more details concerning similar mixtures. The Agency agrees and is planning research projects to improve on the definition. Characteristics such as composition and toxic end-effects are certainly important, but the best indicators of similarity in terms of risk assessment have yet to be determined. The discussion in the Guidelines emphasizes case-by-case judgment until the necessary research can be performed. The Agency considered but rejected adding an example, because it is not likely that any single example would be adequate to illustrate the variety in the data and types of judgments that will be required in applying this concept. Inclusion of examples is being considered for the technical support document.

B. Mixtures of Carcinogens and Systemic Toxicants

The applicability of the preferred approach for a mixture of carcinogens and systemic (noncarcinogenic) toxicants was a concern of several public commentors as well as the SAB. The Agency realizes that the preferred approach of using test data on the mixture itself may not be sufficiently protective in all cases. For example, take a simple two-component mixture of one carcinogen and one toxicant. The preferred approach would lead to using toxicity data on the mixture of the two compounds. However, it is possible to set the proportions of each component so that in a chronic bioassay of such a mixture, the presence of the toxicant could mask the activity of the carcinogen. That is to say, at doses of

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the mixture sufficient for the carcinogen to induce tumors in the small

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experimental group, the toxicant could induce mortality. At a lower dose in the same study, no adverse effects would be observed, including no carcinogenic effects. The data would then suggest use of a threshold approach. Since carcinogenicity is considered by the Agency to be a nonthreshold effect, it may not be prudent to construe the negative results of such a bioassay as indicating the absence of risk at lower doses. Consequently, the Agency has revised the discussion of the preferred approach to allow the risk assessor to evaluate the potential for masking of carcinogenicity or other effects on a case-by-case basis. Another difficulty occurs with such a mixture when the risk assessment needs to be based on data for the mixture components. Carcinogens and systemic toxicants are evaluated by the Agency using different approaches and generally are described by different types of data: response rates for carcinogens vs. effect descriptions for toxicants. The Agency recognizes this difficulty and recommends research to develop a new assessment model for combining these dissimilar data sets into one risk estimate. One suggestion in the interim is to present separate risk estimates for the dissimilar end points, including carcinogenic, teratogenic, mutagenic, and systemic toxicant components.

III. Additivity Assumption

Numerous comments were received concerning the assumption of additivity, including:

a. the applicability of additivity to "complex" mixtures;
b. the use of dose additivity for compounds that induce different effects;
c. the interpretation of the Hazard Index; and
d. the use of interaction data.

Parts of the discussion in the proposed guidelines concerning the use of additivity assumptions were vague and have been revised in the final Guidelines to clarify the Agency's intent and position.

A. Complex Mixtures

The issue of the applicability of an assumption of additivity to complex mixtures containing tens or hundreds of components was raised in several of the public comments. The Agency and its reviewers agree that as the number of compounds in the mixture increases, an assumption of additivity will become less reliable in estimating risk. This is based on the fact that each component estimate of risk or an acceptable level is associated with some error and uncertainty. With current knowledge, the uncertainty will increase as the number of components increases. In any event, little experimental data are available to determine the general change in the error as the mixture contains more components. The Agency has decided that a limit to the number of components should not be set in these Guidelines. However, the Guidelines do explicitly state that as the number of compounds in the mixture increases, the uncertainty associated with the risk assessment is also likely to increase.

B. Dose Additivity

Commentors were concerned about what appeared to be a recommendation of the use of dose additivity for compounds that induce different effects. The discussion following the dose additivity equation was clarified to indicate that the act of combining all compounds, even if they induce dissimilar effects, is a screening procedure and not the preferred procedure in developing a hazard index. The Guidelines were further clarified to state that dose (or response) additivity is theoretically sound, and therefore best applied for assessing mixtures of similar acting components that do not interact.

C. Interpretation of the Hazard Index

Several comments addressed the potential for misinterpretation of the hazard index, and some questioned its validity, suggesting that it mixes science and value judgments by using "acceptable" levels in the calculation. The Agency agrees with the possible confusion regarding its use and has revised the Guidelines for clarification. The hazard index is an easily derived restatement of dose additivity, and is, therefore, most accurate when used with mixture components that have similar toxic action. When used with components of unknown or dissimilar action, the hazard index is less accurate and should be interpreted only as a rough indication of concern. As with dose addition, the uncertainty associated with the hazard index increases as the number of components increases, so that it is less appropriate for evaluating the toxicity of complex mixtures.

D. Use of Interaction Data

A few commentors suggested that any interaction data should be used to quantitatively alter the risk assessment. The Agency disagrees. The current information on interactions is meager, with only a few studies comparing response to the mixture with that predicted by studies on components. Additional uncertainties include exposure variations due to changes in composition, mixture dose, and species differences in the extent of the interaction. The Agency is constructing an interaction data base in an attempt to answer some of these issues. Other comments concerned the use of different types of interaction data. The Guidelines restrict the use of interaction data to that obtained from whole animal bioassays of a duration appropriate to the risk assessment. Since such data are frequently lacking, at least for chronic or subchronic effects, the issue is whether to allow for the use of other information such as acute data, *in*

vitro data, or structure-activity relationships to quantitatively alter the risk assessment, perhaps by use of a safety factor. The Agency believes that sufficient scientific support does not exist for the use of such data in any but a qualitative discussion of possible synergistic or antagonistic effects.

IV. Uncertainties and the Sufficiency of the Data Base

In the last two paragraphs of section II of the Guidelines, situations are discussed in which the risk assessor is presented with incomplete toxicity, monitoring, or exposure data. The SAB, as well as several public commentors, recommended that the "risk management" tone of this section be modified and that the option of the risk assessor to decline to conduct a risk assessment be made more explicit.

This is a difficult issue that must consider not only the quality of the available data for risk assessment, but also the needs of the Agency in risk management. Given the types of poor data often available, the risk assessor may indicate that the risk assessment is based on limited information and thus contains no quantification of risk. Nonetheless, in any risk assessment, substantial uncertainties exist. It is the obligation of the risk assessor to provide an assessment, but also to ensure that all the assumptions and uncertainties are articulated clearly and quantified whenever possible.

The SAB articulated several other recommendations related to uncertainties, all of which have been followed in the revision of the Guidelines. One recommendation was that the summary procedure table also be presented as a flow chart so that all options are clearly displayed. The SAB further recommended the development of a system to express the level of confidence in the various steps of the risk assessment.

The Agency has revised the summary table to present four major options: risk assessment using data on the mixture

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itself, data on a similar mixture, data on the mixture's components, or declining to quantify the risk when the data are inadequate. A flow chart of this table has also been added to more clearly depict the various options and to suggest the combining of the several options to indicate the variability and uncertainties in the risk assessment.

To determine the adequacy of the data, the SAB also recommended the development of a system to express the level of confidence associated with various steps in the risk assessment process. The Agency has developed a rating scheme to describe data quality in three areas: interaction, health effects, and exposure. This classification provides a range of five levels of data quality for each of the three areas. Choosing the last level in any area results in declining to perform a quantitative risk assessment due to inadequate data. These last levels are described as follows:

Interactions:

An assumption of additivity cannot be justified, and no quantitative risk assessment can be conducted.

Health effects:

A lack of health effects information on the mixture and its components precludes a quantitative risk assessment.

Exposure:

The available exposure information is insufficient for conducting a risk assessment.

Several commentors, including the SAB, emphasized the importance of not losing these classifications and uncertainties farther along in the risk management process. The discussion of uncertainties has been expanded in the final Guidelines and includes the recommendation that a discussion of uncertainties and assumptions be included at every step of the regulatory process that uses risk assessment.

Another SAB comment was that the Guidelines should include additional procedures for mixtures with more than one end point or effect. The Agency agrees that these are concerns and revised the Guidelines to emphasize these as additional uncertainties worthy of further research.

V. Need for a Technical Support Document

The third major SAB comment concerned the necessity for a separate technical support document for these Guidelines. The SAB pointed out that the scientific and technical background from which these Guidelines must draw their validity is so broad and varied that it cannot reasonably be synthesized within the framework of a brief set of guidelines. The Agency is developing a technical support document that will summarize the available information on health effects from chemical mixtures, and on interaction mechanisms, as well as identify and develop mathematical models and statistical techniques to support these Guidelines. This document will also identify critical gaps and research needs.

Several comments addressed the need for examples on the use of the Guidelines. The Agency has decided to include examples in the technical support document.

Another issue raised by the SAB concerned the identification of research needs. Because little emphasis has been placed on the toxicology of mixtures until recently, the information on mixtures is limited. The SAB pointed out that identifying research needs is critical to the risk assessment process, and the EPA should ensure that these needs are considered in the research planning process. The Agency will include a section in the

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technical support document that identifies research needs regarding both methodology and data.

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GUIDELINES FOR THE HEALTH ASSESSMENT OF SUSPECT DEVELOPMENTAL TOXICANTS

SUMMARY: On September 24, 1986, the U.S. Environmental Protection Agency issued the following five guidelines for assessing the health risks of environmental pollutants.

Guidelines for Carcinogen Risk Assessment

Guidelines for Estimating Exposures

Guidelines for Mutagenicity Risk Assessment

Guidelines for the Health Assessment of Suspect Developmental Toxicants

Guidelines for the Health Risk Assessment of Chemical Mixtures

This section contains the Guidelines for the Health Assessment of Suspect Developmental Toxicants.

The Guidelines for the Health Assessment of Suspect Developmental Toxicants (hereafter "Guidelines") are intended to guide Agency analysis of developmental toxicity data in line with the policies and procedures established in the statutes administered by the EPA. These Guidelines were developed as part of an interoffice guidelines development program under the auspices of the Office of Health and Environmental Assessment (OHEA) in the Agency's Office of Research and Development. They reflect Agency consideration of public and Science Advisory Board (SAB) comments on the Proposed Guidelines for the Health Assessment of Suspect Developmental Toxicants published November 23, 1984 (49 FR 46324).

This publication completes the first round of risk assessment guidelines development. These Guidelines will be revised, and new guidelines will be developed, as appropriate.

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SUPPLEMENTARY INFORMATION: In 1983, the National Academy of Sciences (NAS) published its book entitled *Risk Assessment in the Federal Government: Managing the Process*. In that book, the NAS recommended that Federal regulatory agencies establish "inference guidelines" to ensure consistency and technical quality in risk assessments and to ensure that the risk assessment process was maintained as a scientific effort separate from risk management. A task force within EPA accepted that recommendation and requested that Agency scientists begin to develop such guidelines.

General

The guidelines are products of a two-year Agencywide effort, which has included many scientists from the larger scientific community. These guidelines set forth principles and procedures to guide EPA scientists in the conduct of Agency risk assessments, and to inform Agency decision makers and the public about these procedures. In particular, the guidelines emphasize that risk assessments will be conducted on a case-by-case basis, giving full consideration to all relevant scientific information. This case-by-case approach means that Agency experts review the scientific information on each agent and use the most scientifically appropriate interpretation to assess risk. The guidelines also stress that this information will be fully presented in Agency risk assessment documents, and that Agency scientists will identify the strengths and weaknesses of each assessment by describing uncertainties, assumptions, and limitations, as well as the scientific basis and rationale for each assessment.

Finally, the guidelines are formulated in part to bridge gaps in risk assessment methodology and data. By identifying these gaps and the importance of the missing information to the risk assessment process, EPA wishes to encourage research and analysis that will lead to new risk assessment methods and data.

Guidelines for the Health Assessment of Suspect Developmental Toxicants

Work on the Guidelines for the Health Assessment of Suspect Developmental Toxicants began in January 1984. Draft guidelines were developed by Agency work groups composed of expert scientists from throughout the Agency. The drafts were peer-reviewed by expert scientists in the field of developmental toxicology from universities, environmental groups, industry, labor, and other governmental agencies. They were then proposed for public comment in the *FEDERAL REGISTER* (49 FR 46324). On November 9, 1984, the Administrator directed that Agency offices use the proposed guidelines in performing risk assessments until final guidelines become available.

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After the close of the public comment period, Agency staff prepared summaries of the comments, analyses of the major issues presented by the commentors, and preliminary Agency responses to those comments. These analyses were presented to review panels of the SAB on March 4 and April 22-23, 1985, and to the Executive Committee of the SAB on April 25-26, 1985. The SAB meetings were announced in the *FEDERAL REGISTER* as follows: February 12, 1985 (50 FR 5811) and April 4, 1985 (50 FR 13420 and 13421).

In a letter to the Administrator dated June 19, 1985, the Executive Committee generally concurred on all five of the guidelines, but recommended certain revisions, and requested that any revised guidelines be submitted to the appropriate SAB review panel chairman for review and concurrence on behalf of the Executive Committee. As described in the responses to comments (see Part B: Response to the Public and Science Advisory Board Comments), each guidelines document was revised, where appropriate, consistent with the SAB recommendations, and revised draft guidelines were submitted to the panel chairmen. Revised draft Guidelines for the Health Assessment of Suspect Developmental Toxicants were concurred on in a letter dated July 26, 1985. Copies of the letters are available at the Public Information Reference Unit, EPA Headquarters Library, as indicated elsewhere in this section.

Following this Preamble are two parts: Part A contains the Guidelines and Part B, the Response to the Public and Science Advisory Board Comments (a summary of the major public comments, SAB comments, and Agency responses to those comments).

The SAB suggested that the Agency pursue additional follow-up work on quantitative risk assessment. Several efforts are currently underway within the Agency on quantitative risk assessment models and procedures, the relationship of maternal and developmental toxicity, and the evaluation and interpretation of postnatal studies. In addition, a document addressing research needs is being prepared to highlight those areas that are in need of further study.

The Agency is continuing to study the risk assessment issues raised in the guidelines and will revise these Guidelines in line with new information as appropriate.

References, supporting documents, and comments received on the proposed

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guidelines, as well as copies of the final guidelines, are available for inspection and copying at the Public Information Reference Unit (202-382-5926), EPA Headquarters Library, 401 M Street, S.W., Washington, DC, between the hours of 8:00 a.m. and 4:30 p.m.

I certify that these Guidelines are not major rules as defined by Executive Order 12291, because they are nonbinding policy statements and have no direct effect on the regulated community. Therefore, they will have no effect on costs or prices, and they will have no other significant adverse effects on the economy. These Guidelines were reviewed by the Office of Management and Budget under Executive Order 12291.

August 22, 1986

Lee M. Thomas,

Administrator

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Part A: Guidelines for the Health Assessment of Suspect Developmental Toxicants

I. Introduction

These Guidelines describe the procedures that the U.S. Environmental Protection Agency will follow in evaluating potential developmental toxicity associated with human exposure to environmental toxicants. In 1980, the Agency sponsored a conference that addressed issues related to such evaluations (1) and provided some of the scientific basis for these risk assessment Guidelines. The Agency's authority to regulate substances that have the potential to interfere adversely with human development is derived from a number of statutes which are implemented through multiple offices within the Agency. Because many different offices evaluate developmental toxicity, there is a need for intra-Agency consistency in the approach to assess these types of effects. The procedures described here will promote consistency in the Agency's assessment of developmental toxic effects.

The developmental toxicity assessments prepared pursuant to these Guidelines will be utilized within the requirements and constraints of the applicable statutes to arrive at regulatory decisions concerning developmental toxicity. These Guidelines provide a general format for analyzing and organizing the available data for conducting risk assessments. The Agency previously has issued testing guidelines (2, 3) that provide protocols designed to determine the potential of a test substance to induce structural and/or other abnormalities in the developing conceptus. These risk assessment Guidelines do not change any statutory or regulatory prescribed standards for the type of data necessary for regulatory action, but rather provide guidance for the interpretation of studies that follow the testing guidelines, and in addition, provide limited information for interpretation of other studies (e.g., epidemiologic data, functional developmental toxicity studies, and short-term tests) which are not routinely required, but which may be encountered when reviewing data on particular agents. Moreover, risk assessment is just one component of the regulatory process and defines the adverse health consequences of exposure to a toxic agent. The other component, risk management, combines risk assessment with the directives of the enabling regulatory legislation, together with socioeconomic, technical, political, and other considerations, to reach a decision as to whether or how much to control future exposure to the suspected toxic agent. The issue of risk management will not be addressed in these Guidelines.

The background incidence of developmental defects in the human population is quite large. For example, approximately 50% of human conceptuses fail to reach term (4); approximately 3% of newborn children are found to have one or more significant congenital malformations at birth, and by the end of the first postnatal year, about 3% more are found to have serious developmental defects (5, 6). Of these, it is estimated that 20% of human developmental defects are of known genetic transmission, 10% are attributable to known environmental factors, and the remainder result from unknown causes (7). Approximately 7.4% of children are reduced in weight at birth (i.e., below 2500 g) (8). Exposure to agents affecting development can result in multiple manifestations (malformation, functional impairment, altered growth, and/or lethality). Therefore, assessment efforts should encompass a wide array of adverse developmental end points, such as spontaneous abortions, stillbirths, malformations, early postnatal mortality, and other adverse functional or physical changes that are manifested postnatally.

Numerous agents have been shown to be developmental toxicants in animal test systems (9). Several of them have also been shown to be the cause of adverse developmental effects in humans, including alcohol, aminopterin, busulfan, chlorobiphenyls, diethylstilbestrol, isotretinoin, organic mercury, thalidomide, and valproic acid (10, 11, 12, 13). Although a number of agents found to be positive in animal studies have not shown clear evidence of hazard in humans, usually the human data available are inadequate to determine a cause and effect relationship. Comparisons of human and animal data have been made for a limited number of agents that are positive in humans (13, 14). In these comparisons, there was almost always concordance of effects between humans and at least one species tested; also, the minimally effective dose (MED) for the most sensitive animal species was approximately 0.5 to 50 times the human

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MED, not accounting for differences in the incidence of effect at the MED. Thus, there is some limited basis for estimating the risk of exposure to human development based on data from animal studies.

The National Research Council (15) has defined risk assessment as being comprised of some or all of the following components: hazard identification, dose-response assessment, exposure assessment, and risk characterization. In general, the process of assessing the risk of human developmental toxicity may be adapted to this format. However, due to special considerations in assessing developmental toxicity, which will be discussed later in these Guidelines, it is not always possible to follow the exact standards as defined for each component.

Hazard identification is the qualitative risk assessment in which all available experimental animal and human data are used to determine if an agent is likely to cause developmental toxicity. In considering developmental toxicity, these Guidelines will address not only malformations, but

also fetal wastage, growth alteration, and functional abnormalities that may result from developmental exposure to environmental agents.

The dose-response assessment defines the relationship of the dose of an agent and the occurrence of developmental toxic effects. According to the National Research Council (15), this component would usually include the results of an extrapolation from high doses administered to experimental animals or noted in epidemiologic studies to the low exposure levels expected for human contact with the agent in the environment. Since at present there are no mathematical extrapolation models that are generally accepted for developmental toxicity, the Agency, for the most part, uses uncertainty (safety) factors and margins of safety, which will be discussed in these Guidelines. Appropriate models are being sought by the Agency for application to data in this area.

The exposure assessment identifies populations exposed to the agent, describes their composition and size, and presents the types, magnitudes, frequencies, and durations of exposure to the agent.

In risk characterization, the exposure assessment and the dose-response assessment are combined to estimate some measure of the risk of developmental toxicity. As part of risk characterization, a summary of the strengths and weaknesses in each component of the assessment are presented along with major assumptions, scientific judgments, and, to the extent possible, estimates of the uncertainties.

II. Definitions and Terminology

The Agency recognizes that there are differences in the use of terms in the field of developmental toxicology. For the purposes of these Guidelines the following definitions and terminology will be used.

Developmental Toxicology--The study of adverse effects on the developing organism that may result from exposure prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the life span of the organism. The major manifestations of developmental toxicity include: 1) death of the developing organism, 2) structural abnormality, 3) altered growth, and 4) functional deficiency.

Embryotoxicity and Fetotoxicity--Any toxic effect on the conceptus as a result of prenatal exposure; the distinguishing feature between the two terms is the stage of development during which the injury occurred. The terms, as used here, include malformations and variations, altered growth, and *in utero* death.

Altered Growth--An alteration in offspring organ or body weight or size. Changes in body weight may or may not be accompanied by a change in crown-rump length and/or in skeletal ossification. Altered growth can be induced at any stage of development, may be reversible, or may result in a permanent change.

Functional Developmental Toxicology--The study of the causes, mechanisms, and manifestations of alterations or delays in functional competence of the organism or organ system following exposure to an agent during critical periods of development pre- and/or postnatally.

Malformations and Variations--A malformation is usually defined as a permanent structural change that may adversely affect survival, development, or function. The term teratogenicity, which is used to describe these types of structural abnormalities, will be used in these Guidelines to refer only to structural defects. A variation is used to indicate a divergence beyond the usual range of structural constitution that may not adversely affect survival or health. Distinguishing between variations and malformations is difficult since there exists a continuum of responses from the normal to the extreme deviant. There is no generally accepted classification of malformations and variations. Other terminology that is often used, but no better defined, includes anomalies, deformations, and aberrations.

III. Qualitative Assessment (Hazard Identification of Developmental Toxicants)

Developmental toxicity is expressed as one or more of a number of possible end points that may be used for evaluating the potential of an agent to cause abnormal development. The four types of effects on the conceptus that may be produced by developmental exposure to toxicants include death, structural abnormality, altered growth, and functional deficits. Of these, the first three types of effects are traditionally measured in laboratory animals using the conventional developmental toxicity (also called teratogenicity or Segment II) testing protocol as well as in other study protocols, such as the multigeneration study. Functional deficits are seldom evaluated in routine studies of environmental agents. This section will discuss the end points examined in routinely used protocols as well as the evaluation of data from other types of studies, including functional studies and short-term tests. Transplacental carcinogenesis, another type of developmental effect, will not be discussed in detail here since, at present, it is considered more appropriate to use the Guidelines for Carcinogen Risk Assessment (16) for assessing the human risk for these types of effects. Also, mutational events may occur as part of developmental toxicity, and in practice, are difficult to discriminate from other possible mechanisms of developmental toxicity. The Guidelines for Mutagenicity Risk Assessment (17) should be consulted in cases where genetic damage is suspected.

A. Laboratory Animal Studies of Developmental Toxicity: End Points and Their Interpretation

The most commonly used protocol for assessing developmental toxicity in laboratory animals involves the administration of a test substance to pregnant animals (usually mice, rats, or rabbits) during the period of major organogenesis, evaluation of maternal responses throughout pregnancy, and examination of the dam and the uterine contents just prior to term (2, 3, 18, 19, 20). Other protocols may use exposure periods of one to a few days to investigate periods of particular sensitivity for induction of anomalies in specific organs or organ systems (21).In

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addition, developmental toxicity may be evaluated in studies involving exposure of one or both parents prior to conception, of the conceptus during pregnancy and over several generations, or of offspring during the late prenatal and early postnatal periods. These Guidelines are intended to provide information for interpreting developmental effects related to any of these types of exposure. Since many of the end points evaluated also are related to effects on the parental reproductive systems, these Guidelines will be used in conjunction with those to be published in the future by EPA on male and female reproductive toxicity.

Study designs should include a high dose, which produces some maternal or adult toxicity (i.e., a level which at the least produces marginal but significantly reduced body weight, weight gain, or specific organ toxicity, and at the most produces no more than 10% mortality); a low dose, which demonstrates a no observed effect level (NOEL) for adult and offspring effects; and at least one intermediate dose level. A concurrent control group treated with the vehicle used for agent administration should be included. The route of exposure should be based on expected human exposure considerations, although data from other routes may sometimes be useful, especially if supported by pharmacokinetic information. Test animals should be selected based on considerations of species, strain, age, weight, and health status, and should be randomized to dose groups in order to reduce bias and provide a basis for performing valid statistical tests.

The next three sections discuss individual end points of maternal and developmental toxicity as measured in the conventional developmental toxicity study, the multigeneration study, and, on occasion, in postnatal studies. Other end points specifically related to reproductive toxicity will be covered in the relevant reproductive toxicity guidelines. The fourth section deals with the integrated evaluation of all data, including the relative effects of exposure on maternal animals and their offspring, which is important in assessing the level of concern about a particular agent.

1. End Points of Maternal Toxicity. A number of end points that may be observed as possible indicators of maternal toxicity are listed in Table 1. Maternal mortality is an obvious end point of toxicity; however, a number of other end points can be observed which may give an indication of the subtle effects of an agent. For example, in well-conducted studies, the fertility and gestation indices provide information on the general fertility rate of the animal stock used and are important indicators of toxic effects if treatment begins prior to mating or implantation. Changes in gestation length may indicate effects on the process of parturition.

Table 1.--End Points of Maternal Toxicity

Mortality
Fertility Index (no. with seminal plugs or sperm/no. mated)
Gestation Index (no. with implants/no. with seminal plugs or sperm)
Gestation Length (when allowed to deliver pups)
Body Weight
  Treatment days (at least first, middle, and last treatment days)
  Sacrifice day
Body Weight Change
  Throughout gestation
  During treatment (including increments of time within treatment period)
  Post-treatment to sacrifice
  Corrected maternal (body weight change throughout gestation minus gravid uterine weight or litter weight at sacrifice)
Organ Weights (in cases of suspected specific organ toxicity)
  Absolute
  Relative to body weight
Food and Water Consumption (where relevant)
Clinical Evaluations (on days of treatment and at sacrifice)
  Types and incidence of clinical signs
  Enzyme markers
  Clinical chemistries
Gross Necropsy and Histopathology

Body weight and the change in body weight are viewed collectively as indicators of maternal toxicity for most species, although these end points may not be as useful in rabbits, because body weight changes in rabbits are not good indicators of pregnancy status. Body weight changes may provide more information than a daily body weight measured during treatment or during gestation. Changes in weight during treatment could occur that would not be reflected in the total weight change throughout gestation, because of compensatory weight gain that may occur following treatment but before sacrifice. For this reason, changes in weight during treatment

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can be examined as another indicator of maternal toxicity.

Changes in maternal body weight corrected for gravid uterine weight at sacrifice may indicate whether the effect is primarily maternal or fetal. For example, there may be a significant reduction in weight gain throughout gestation and in gravid uterine weight, but no change in corrected maternal weight gain which would indicate primarily an intrauterine effect. Conversely, a change in corrected weight gain and no change in gravid uterine weight suggests primarily maternal toxicity and little or no intrauterine effect. An alternate estimate of maternal weight change during gestation can be obtained by subtracting the sum of the weights of the fetuses. However, this weight does not include the uterine tissue, placental tissue, or the amniotic fluid.

Changes in other end points should also be determined. For example, changes in relative and absolute organ weights may be signs of a maternal effect when an agent is suspected of causing specific organ toxicity. Food and water consumption data are useful, especially if the agent is administered in the diet or drinking water. The amount ingested (total and relative to body weight) and the dose of the agent (relative to body weight) can then be calculated, and changes in food and water consumption related to treatment can be evaluated along with changes in body weight and body weight gain. Data on food and water consumption are also useful when an agent is suspected of affecting appetite, water intake, or excretory function. Clinical evaluations of toxicity may also be used as indicators of maternal toxicity. Daily clinical observations may be useful in describing the profile of maternal toxicity. Enzyme markers and clinical chemistries may be useful indicators of exposure but must be interpreted carefully as to whether or not a change constitutes toxicity. Gross necropsy and histopathology data (when specified in the protocol) may aid in determining toxic dose levels.

2. End Points of Developmental Toxicity. Because the maternal animal, and not the conceptus, is the individual treated during gestation, data generally should be calculated as incidence per litter or as number and percent of litters with particular end points.Table 2 indicates the way in which offspring and litter end points may be expressed.

Table 2.--End Points of Developmental Toxicity.

Litters with implants

- No. implantation sites/dam
- No. corpora lutea (CL)/dam[a]
- Percent preimplantation loss

$$\frac{(\text{CL} - \text{implantations}) \times 100}{\text{CL}}$$ [a]

- No. and percent live offspring/litter
- No. and percent resorptions/litter
- No. and percent litters with resorptions

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- No. and percent late fetal deaths/litter
- No. and percent nonlive (late fetal deaths + resorptions) implants/litter
- No. and percent litters with nonlive implants
- No. and percent affected (nonlive + malformed) implants/litter
- No. and percent litters with affected implants
- No. and percent litters with total resorptions
- No. and percent stillbirths/litter

Litters with live offspring[b]

- No. and percent litters with live offspring
- No. and percent live offspring/litter
- Viability of offspring[c]
- Sex ratio/litter
- Mean offspring body weight/litter[c]
- Mean male body weight/litter[c]
- Mean female body weight/litter[c]
- No. and percent externally malformed offspring/litter
- No. and percent viscerally malformed offspring/litter
- No. and percent skeletally malformed offspring/litter
- No. and percent malformed offspring/litter
- No. and percent litters with malformed offspring
- No. and percent malformed males/litter
- No. and percent malformed females/litter
- No. and percent offspring with variations/litter
- No. and percent litters having offspring with variations
- Types and incidence of individual malformations
- Types and incidence of individual variations
- Individual offspring and their malformations and variations (grouped according to litter and dose)
- Clinical signs[c]
- Gross necropsy and histopathology

[a] Important when treatment begins prior to implantation. May be difficult in mice.

[b] Offspring refers both to fetuses observed prior to term or to pups following birth. The end points examined depend on the protocol used for each study.

[c] Measured at selected intervals until termination of the study.

When treatment begins prior to implantation, an increase in preimplantation loss could indicate an adverse effect either on the developing blastocyst or on the process of implantation itself. If treatment begins around the time of implantation (i.e., day 6 of gestation in the mouse, rat, or rabbit), an increase in preimplantation loss probably reflects normal variability in the animals being used, but the data should be examined carefully to determine whether or not the effect is dose related. If preimplantation

loss is related to dose in either case, further studies would be necessary to determine the mechanism and extent of such effects.

The number and percent of live offspring per litter, based on all litters, may include litters that have no live implants. The number and percent resorptions or late fetal deaths per litter gives some indication of when the conceptus died, and the number and percent nonlive implants per litter (postimplantation loss) is a combination of resorptions and late fetal deaths. The number and percent of litters showing an increased incidence for these end points is generally useful but may be less useful than incidence per litter because, in the former case, a litter is counted whether it has one or all resorbed, dead, or nonlive implants.

If a significant increase in postimplantation loss is found after exposure to an agent, the data may be compared not only with concurrent controls, but also with recent historical control data, since there is considerable interlitter variability in the incidence of postimplantation loss (22). If a given study control group exhibits an unusually high or low incidence of postimplantation loss compared to historical controls, then scientific judgment must be used to determine the adequacy of the studies for risk assessment purposes.

The end point for affected implants (i.e., the combination of nonlive and malformed conceptuses) gives an indication of the total intrauterine response to an agent and sometimes reflects a better dose-response relationship than does the incidence of nonlive or malformed offspring taken individually. This is especially true at the high end of the dose-response curve in cases when the incidence of nonlive implants per litter is greatly increased. In such cases, the malformation rate may appear to decrease because only unaffected offspring have survived. If the incidence of prenatal death or malformation is unchanged, then the incidence of affected implants will not provide any additional dose-response information. In studies where maternal animals are allowed to deliver pups normally, the number of stillbirths per litter should also be noted.

The number of live offspring per litter, based on those litters that have one or more live offspring, may be unchanged even though the incidence of nonlive in all litters is increased. This could occur either because of an increase in the number of litters with no live offspring, or an increase in the number of implants per litter. A decrease in the number of live offspring per litter should be accompanied by an increase in the incidence of nonlive implants per litter, unless the implant numbers differ among dose groups. In postnatal studies, the viability of live born offspring should be determined at selected intervals until termination of the study.

The sex ratio per litter, as well as the body weights of males and females, can be examined to determine whether or not one sex is preferentially affected by the agent. However, this is an unusual occurrence.

A change in offspring body weight is a sensitive indicator of developmental toxicity, in part because it is a continuous variable. In some cases, offspring weight reduction may be the only indicator of developmental toxicity; if so, there is always a question remaining as to whether weight reduction is a permanent or transitory effect. A permanent weight change may be considered more severe than a transitory change, although little is known about the long-term consequences of short-term fetal or neonatal weight changes. When fetal or neonatal weight reduction is the only indicator of developmental toxicity, data from the two-generation reproduction study (2), if available, may be useful for evaluating these parameters. Ideally, follow-up studies to evaluate postnatal viability, growth, and survival through weaning should be conducted. There are other factors that should be considered in the evaluation of fetal or neonatal weight changes. For example, in polytocous animals, fetal and neonatal weights are usually inversely correlated with litter size, and the upper end of the dose-response curve may be confounded by smaller litters and increased fetal or neonatal weight. Additionally, the average body weight of males is greater than that of females in the more commonly used laboratory animals.

Live offspring should be examined for external, visceral, and skeletal malformations. If only a portion of the litter is examined, then it is preferable that those examined be randomly selected from each litter. An increase in the incidence of malformed offspring may be indicated by a change in one or more of the following end points: the incidence of malformed offspring per litter, the number and percent of litters with malformed offspring, or the number of offspring or litters with a particular malformation that appears to increase with dose as indicated by the incidence of individual types of malformations.

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Other ways of examining the data include the incidence of external, visceral, and skeletal malformations which may indicate which general systems are affected. A listing of individual offspring with their malformations and variations may give an indication of the pattern of developmental deviations. All of these methods of expressing and examining the data are valid for determining the effects of an agent on structural development. However, care must be taken to avoid counting offspring more than once in evaluating any single end point based on number or percent of offspring or litters. The incidence of individual types of malformations and variations should be examined

for significant changes which may be masked if the data on all malformations and variations are pooled. Appropriate historical control data are helpful in the interpretation of malformations and variations, especially those that normally occur at a low incidence apparently unrelated to dose in an individual study. Although a dose-related increase in malformations is interpreted as an adverse developmental effect of exposure to an agent, the significance of anatomical variations is more difficult to determine, and must take into account what is known about developmental stage (e.g., with skeletal ossification), background incidence of certain variations (e.g., 12 or 13 pairs of ribs in rabbits), or other strain - or species-specific factors. However, if variations are significantly increased in a dose-related manner, these should also be evaluated as a possible indication of developmental toxicity. The Interagency Regulatory Liaison Group noted that dose-related increases in defects, which may occur spontaneously, are as relevant as dose-related increases in any other developmental toxicity end points (23).

3. *Functional Developmental Toxicology.* Developmental effects, which are inducible by exogenous agents, are not limited to death, structural abnormalities, and altered growth. Rather, it has been demonstrated in a number of instances that subtle alterations in the functional competence of an organ or a variety of organ systems may result from exposure during critical developmental periods that may occur between conception and sexual maturation. Often, these functional defects are observed at dose levels below those at which gross malformations are evident (24). At present, such testing is not routinely required in the United States. However, data from postnatal studies, when available, are considered very useful for the assessment of the relative importance and severity of findings in the fetus and neonate. Often, the long-term consequences of adverse developmental outcomes at birth are unknown, and further data on postnatal development and function may contribute valuable information. When regulatory statutes permit, studies designed to evaluate adverse fetal or neonatal outcomes have been requested (e.g., the Office of Pesticide Programs has sometimes requested postnatal studies where the reversibility of study findings were at issue). In some cases, useful data can be derived from well-executed multigeneration studies.

Much of the early work in functional developmental toxicology was related to behavioral evaluations, and the term "behavioral teratology" became prominent in the mid 1970s. Less work has been done on other functional systems, but sufficient data have accumulated to indicate that the cardiopulmonary, immune, endocrine, digestive, urinary, nervous, and reproductive systems are subject to alterations in functional competence (25, 26). Currently, there are no standard testing procedures, although some attempts are being made to standardize and evaluate tests and protocols (27). The functional evaluation of specific systems often involves highly specialized training and equipment. The routine use of such test procedures may not always be practical, but may be extremely important in determining the nature of a suspected alteration in terms of its biological significance and dose-response relationship.

The interpretation of data from functional developmental toxicology studies is limited due to the lack of knowledge about the underlying toxicological mechanisms and their significance. However, since such data are sometimes encountered in the risk assessment of particular agents, some guidance is provided here concerning general concepts of study design and evaluation.

a. Several aspects of study design are similar to those important in standard developmental toxicity studies (e.g., a dose-response approach with the highest dose producing minimal overt maternal or perinatal toxicity, number of litters large enough for adequate statistical power, randomization of animals to dose groups, litter generally considered the statistical unit, etc.).

b. A replicate study design provides added confidence in the interpretation of data.

c. Use of a pharmacological challenge may be valuable in evaluating function and "unmasking" effects not otherwise detectable, particularly in the case of organ systems that are endowed with a reasonable degree of functional reserve capacity.

d. Use of functional tests with a moderate degree of background variability may be more sensitive to the effects of an agent than are tests with low variability that may be impossible to disrupt without being life-threatening. Butcher et al. (28) have discussed this with relation to behavioral end points.

e. A battery of functional tests usually provides a more thorough evaluation of the functional competence of an animal; tests conducted at several ages may provide more information about maturational changes.

f. Critical periods for the disruption of functional competence include both the prenatal and the postnatal periods to the time of sexual maturation, and the effect is likely to vary depending on the time and degree of exposure.

Although interpretation of functional data may be difficult at present, there are at least three ways in which the data from these studies may be useful for risk assessment purposes: 1) to help elucidate the long-term consequences of fetal and neonatal findings; 2) to indicate the potential for an agent to cause functional alterations, and the effective doses relative to those that produce other forms of toxicity;

and 3) for existing environmental agents, to focus on organ systems to be evaluated in exposed human populations.

4. *Overall Evaluation of Maternal and Developmental Toxicity.* As discussed previously, individual end points are evaluated in developmental toxicity studies, but an integrated evaluation must be done considering all maternal and developmental end points in order to interpret the data fully. Developmental toxicity is considered to be an increase in the incidence of malformed offspring, decreased viability (prenatal or postnatal), altered growth, and/or functional deficits.

The level of concern for a developmental toxic effect is related to several issues, including the relative toxicity of an agent to the offspring versus the adult animal, and the long-term consequences of findings in the fetus or neonate. Those agents which produce developmental toxicity at a dose that is not toxic to the maternal animal are of greatest concern because the developing organism appears to be selectively affected or more sensitive than the adult. However, when developmental effects are produced only

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at maternally toxic doses, the types of developmental effects should be examined carefully, and not discounted as being secondary to maternal toxicity. Current information is inadequate to assume that developmental effects at maternally toxic doses result only from the maternal toxicity; rather, when the lowest observed effect level is the same for the adult and developing organisms, it may simply indicate that both are sensitive to that dose level. Moreover, the maternal effects may be reversible while effects on the offspring may be permanent. These are important considerations for agents to which humans may be exposed at minimally toxic levels either voluntarily or in the workplace, since several agents are known to produce adverse developmental effects at minimally toxic doses in adult humans (e.g., smoking, alcohol).

Approaches for ranking agents for their selective developmental toxicity are being developed; Schardein (10) has reviewed several of these. Of current interest are approaches that develop ratios relating an adult toxic dose to a developmental toxic dose (29, 30, 31, 32). Ratios near unity indicate that developmental toxicity occurs only at doses producing maternal toxicity; as the ratio increases, there is a greater likelihood of developmental effects occurring without maternal manifestations. Although further exploration and validation are necessary, such approaches may ultimately help in identifying those agents that pose the greatest threat and should be given higher priority for further testing (33).

5. *Short-term Testing in Developmental Toxicity.* The need for short-term tests for developmental toxicity has arisen from the large number of agents in or entering the environment, the interest in reducing the number of animals used for routine testing, and the expense of testing. Two approaches are considered here in terms of their contribution to the overall testing process: 1) an *in vivo* mammalian screen, and 2) a variety of *in vitro* systems. Currently, neither approach is considered as a replacement for routine *in vivo* developmental toxicity testing in experimental animals, and should not be used to make the final decision as to whether an agent is a positive or negative developmental toxicant; rather, such tests may be useful as tools for assigning priorities for further, more extensive testing. Although such short-term tests are not routinely required, data are sometimes encountered in the review of chemicals; the comments are provided here for guidance in the evaluation of such data.

a. *In Vivo* Mammalian Developmental Toxicity Screen. The most widely studied *in vivo* approach is that developed by Chernoff and Kavlock (34) which uses the pregnant mouse. This approach is based on the hypothesis that a prenatal injury, which results in altered development, will be manifested postnatally as reduced viability and/or impaired growth. In general, the test substance is administered over the period of major organogenesis at a single dose level that will elicit some degree of maternal toxicity. A second lower dose level may be used which potentially will reduce the chances of false positive results. The pups are counted and weighed shortly after birth, and again after 3-4 days. End points that are considered in the evaluation include: general maternal toxicity (including survival and weight gain), litter size, and viability, weight, and gross malformations in the offspring. Basic priority-setting categories for more extensive testing have been suggested: 1) agents that induce perinatal death should receive highest priority, 2) agents inducing perinatal weight changes should be ranked lower in priority, and 3) agents inducing no effect should receive the lowest priority (34). Another scheme that has been proposed applies a numerical ranking to the results as a means of prioritizing agents for further testing (35, 36).

The mouse was chosen originally for this test because of its low cost, but the procedure should be easily applicable to other species. However, the test will only predict the potential for developmental toxicity of an agent in the species utilized and does not improve the ability to extrapolate risk to other species, including humans. The Office of Toxic Substances has developed testing guidelines for this procedure (37). Although the testing guidelines are available, such procedures are not routinely

required, and further validation is currently being carried out (38).

b. *In Vitro* Developmental Toxicity Screens. Test systems that fall under the general heading of "*in vitro*" developmental toxicity screens include any system that employs a test subject other than the intact pregnant mammal. These systems have long been used to assess events associated with normal and abnormal development, but only recently have they been considered for their potential as screens in testing (39, 40, 41). Many of these systems are now being evaluated for their ability to predict the developmental toxicity of various agents in intact mammalian systems. This validation process requires certain considerations in study design, including defined end points for toxicity and an understanding of the system's ability to handle various test agents (40, 42). A list of agents for use in such validation studies has been developed (43).

6. *Statistical Considerations.* In the assessment of developmental toxicity data, statistical considerations require special attention. Since the litter is generally considered the experimental unit in most developmental toxicity studies, the statistical analyses should be designed to analyze the relevant data based on incidence per litter or on the number of litters with a particular end point. The analytical procedures used and the results, as well as an indication of the variance in each end point, should be clearly indicated in the presentation of data. Analysis of variance (ANOVA) techniques, with litter nested within dose in the model, take the litter variable into account but allow use of individual offspring data and an evaluation of both within and between litter variance as well as dose effects. Nonparametric and categorical procedures have also been widely used for binomial or incidence data. In addition, tests for dose-response trends can be applied. Although a single statistical approach has not been agreed upon, a number of factors important in the analysis of developmental toxicity data have been discussed (23, 44).

Studies that employ a replicate experimental design (e.g., two or three replicates with 10 litters per dose per replicate rather than a single experiment with 20-30 litters per dose group) allow for broader interpretation of study results since the variability between replicates can be accounted for using ANOVA techniques. Replication of effects due to a given agent within a study, as well as between studies or laboratories, provides added strength in the use of data for the estimation of risk.

An important factor to determine in evaluating data is the power of a study (i.e., the probability that a study will demonstrate a true effect), which is limited by the sample size used in the study, the background incidence of the end point observed, the variability in the incidence of the end point, and the analysis method. As an example, Nelson and Holson (45) have shown that the number of litters needed to detect a 5 or 10% change was dramatically lower for fetal weight (a continuous variable with low variability) than for resorptions (a binomial response with high variability). With the current recommendation in

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testing protocols being 20 rodents per dose group (2, 3), it is possible to detect an increased incidence of malformations in the range of 5 to 12 times above control levels, an increase of 3 to 6 times the *in utero* death rate, and a decrease of 0.15 to 0.25 times the fetal weight. Thus, even within the same study, the ability to detect a change in fetal weight is much greater than for the other end points measured. Consequently, for statistical reasons only, changes in fetal weight are often observable at doses below those producing other signs of developmental toxicity. Any risk assessment should present the detection sensitivity for the study design used and for the end point(s) evaluated.

Although statistical analyses are important in determining the effects of a particular agent, the biological significance of data should not be overlooked. For example, with the number of end points that can be observed in developmental toxicity studies, a few statistically significant differences may occur by chance. On the other hand, apparent trends with dose may be biologically relevant even though statistical analyses do not indicate a significant effect. This may be true especially for the incidence of malformations or *in utero* death where a relatively large difference is required to be statistically significant. It should be apparent from this discussion that a great deal of scientific judgment based on experience with developmental toxicity data and with principles of experimental design and statistical analysis may be required to adequately evaluate such data.

B. Human Studies

Because of the ethical considerations involved, studies with deliberate dosing of humans are not done. Therefore, dose-effect developmental toxicity data from humans are limited to those available from occupational, environmental, or therapeutic exposures. While animal studies provide dose-response data that can be used in the extrapolation of risk to humans, good epidemiologic data provide the best information for assessing human risk.

The category of "human studies" includes both epidemiologic studies and other reports of cases or clusters of events. While case reports have been important in identifying several human teratogens, they are potentially of greater value in identifying topics for further investigation (46). The data from case reports are often of an anecdotal or highly selected nature, and thus are of limited usefulness for risk assessment except when a unique defect is produced, as with thalidomide, or when the agent is

so potent as to greatly increase the incidence of a particular defect(s).

As there are many different designs for epidemiologic studies, simple rules for their evaluation do not exist. The assessment of epidemiologic studies requires a sophisticated level of understanding of the appropriate epidemiologic and statistical methods and interpretation of the findings. Factors that increase a study's usefulness for risk assessment include such things as the examination of multiple end points and exposure levels, the validity of the data, and proper control of other risk factors, effect modifiers, and confounders in the study design and/or analysis. A more in-depth discussion can be found elsewhere (47).

As described earlier, a single developmental toxicant can result in multiple end points (malformations, functional impairment, altered growth, and/or lethality). These end points can be thought of as sequential competing risks. For example, a malformed fetus spontaneously aborted would not be observed in a study of births with malformations (48). Very early conceptus losses may not be identified in human populations, whereas in most laboratory animal studies, all resorption sites can be identified. Many epidemiologic studies, especially of the case-control design, have focused on one end point, possibly missing a true effect of exposure. Furthermore, some studies have selected one type or class of malformations to study. Since an agent can result in different spectra of malformations following exposure at different times in the pregnancy (49), limiting a study to one class of malformation may give misleading results. Malformations can be meaningfully grouped only if there is a logical underlying teratogenic mechanism or pathogenetic pathway. As a minimum, malformations, deformations, and disruptions should be separated.

The power, or probability of a study to detect a true effect, is dependent upon the size of the study group, the frequency of the outcome in the general population, and the level of excess risk to be identified. Rarer outcomes, such as malformations, require thousands of pregnancies to have a high probability of detecting an increase in risk. More common outcomes, such as fetal loss, require hundreds of pregnancies to have the same probability (8, 23, 50, 51, 52, 53). The confidence one has in the results of a study with negative findings is directly related to the power of the study to detect clinically meaningful differences in incidence for the end points studied.

As in animal studies, pregnancies within the same family (or litter) are not independent events. In animal studies, the litter is generally used as the unit of measure. This approach is difficult in humans since the pregnancies are sequential, with the risk factors changing for the different pregnancies (23, 51, 54). If more than one pregnancy per family is included, and this is often necessary due to small study groups, the use of non-independent observations overestimates the true size of the population at risk and artificially increases the significance level (54).

Other criteria for evaluating epidemiologic studies include the following (23, 50, 52, 55, 56, 57, 58):

1. The potential for complete or relatively complete ascertainment of events for study. This can vary by outcome and by data source; for example, if hospital records are used, early fetal losses will be underascertained, but a more complete list of pregnancies could be obtained by interviewing the women. Congenital malformations can be more completely ascertained using hospital records than birth certificates. Studies with relatively complete ascertainment of events, or at least low probability of unbiased ascertainment, should carry more weight.

2. Validity (accuracy) of the data. Recall of past events in interviews may be faulty, while hospital files contain data recorded at the time of the event (but may be incomplete). Validation of interview data with an independent source, where possible, increases confidence in the results of the study.

3. Collection of data on other risk factors, effect modifiers, and confounders. Data on smoking, alcohol consumption, drug use, and environmental and occupational exposure, etc., during pregnancy should be examined and controlled for in the study design and/or analysis where appropriate. The analytic techniques used to control for these factors require careful consideration in their application and interpretation.

C. Other Considerations

1. *Pharmacokinetics.* Extrapolation of data between species can be aided considerably by the availability of data on the pharmacokinetics of a particular agent in the species tested and, if possible, in humans. Information on half-lives, placental metabolism and transfer, and concentrations of the parent compound and metabolites in the

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maternal animal and conceptus may be useful in predicting risk for developmental toxicity. Such data may also be helpful in defining the dose-response curve, developing a more accurate comparison of species sensitivity including that of humans (59, 60), determining dosimetry at target sites, and comparing pharmacokinetic profiles for various dosing regimens or routes of exposure. Pharmacokinetic studies in developmental toxicology are most useful if conducted in pregnant animals at the stage when developmental insults occur. The correlation of pharmacokinetic parameters and developmental toxicity data may be

useful in determining the contribution of specific pharmacokinetic parameters to the effects observed (61).

2. *Comparisons of Molecular Structure.* Comparisons of the chemical or physical properties of an agent with those of known developmental toxicants may provide some indication of a potential for developmental toxicity. Such information may be helpful in setting priorities for testing of agents or for evaluation of potential toxicity when only minimal data are available. Structure/activity relationships have not been well studied in developmental toxicology, although data are available that suggest structure-activity relationships for certain classes of chemicals (e.g., glycol ethers, steroids, retinoids). Under certain circumstances (e.g., in the case of new chemicals), this is one of several procedures used to evaluate the potential for toxicity when little or no data are available.

D. Weight-of-Evidence Determination

Information available from studies discussed previously, whether indicative of potential concern or not, must be evaluated and factored into the risk assessment. The types of data may vary from chemical to chemical, and certain types of data may be more relevant than other types in performing developmental toxicity assessments. The primary considerations are the human data (which are seldom available) and the experimental animal data. The qualitative assessment for developmental toxicity should include statements concerning the quality of the data, the resolving power of the studies, the number and types of end points examined, the relevance of route and timing of exposure, the appropriateness of the dose selection, the replication of the effects, the number of species examined, and the availability of human case reports, case series, and/or epidemiologic study data. In addition, pharmacokinetic data and structure-activity considerations, as well as other factors that may affect the quality, should be taken into account. Therefore, all data pertinent to developmental toxicity should be examined in the evaluation of a chemical's potential to cause developmental toxicity in humans, and sound scientific judgment should be exercised in interpreting the data in terms of the risk for adverse human developmental health effects.

IV. Quantitative Assessment

Risk assessment involves the description of the nature and often the magnitude of potential human risk, including a description of any attendant uncertainty. In the final phase of the risk assessment (risk characterization), the results of the qualitative evaluation (hazard identification), the dose-response, and the exposure assessments are combined to give qualitative and/or quantitative estimates of the developmental toxicity risk. A summary of the strengths and weaknesses of the hazard identification, dose-response assessment, and exposure assessment should be discussed. Major assumptions, scientific judgments, and, to the extent possible, estimates of the uncertainties in the assessment also should be presented.

A. Dose-Response Assessment

When quantitative human dose-effect data are available and with sufficient range of exposure, dose-response relationships may be examined. However, such data have rarely been available; thus, other methods have been used in developmental toxicology for estimating exposure levels that are unlikely to produce adverse effects in humans. The dose-response assessment is usually based on the evaluation of tests performed in laboratory animals. Evidence for a dose-response relationship is an important criterion in the assessment of developmental toxicity, although this may be based on limited data from standard three-dose studies. As mentioned earlier (section III. A. 2.), however, traditional dose-response relationships may not always be observed for some end points. For example, as the exposure level rises, embryo/fetolethal levels may be reached, resulting in an observed decrease in malformations with increasing dose (49, 51). The potential for this relationship indicates that dose-response relationships for individual end points as well as combinations of end points (e.g., dead and malformed combined) must be carefully examined and interpreted.

Although dose-response data are important in this area, the approaches frequently employed in attempts to extrapolate to humans has involved simply the use of uncertainty (safety) factors and margins of safety, which in some respects are conceptually similar. However, uncertainty factors and margins of safety are computed differently and are often used in different regulatory situations. The choice of approach is dependent upon many factors, including the statute involved, the situation being addressed, the data base used, and the needs of the decision-maker. The final uncertainty factor used and the acceptability of the margin of safety are risk management decisions, but the scientific issues that must be taken into account are addressed here.

The uncertainty factor approach results in a calculated exposure level believed to be unlikely to cause any toxic developmental response in humans. The size of the uncertainty factor will vary from agent to agent and will require the exercise of scientific judgment (10, 62), taking into account interspecies differences, the nature and extent of human exposure, the slope of the dose-response curve, the types of developmental effects observed, and the relative dose levels for maternal and developmental toxicity in the test species. The uncertainty factor selected is then divided into the NOEL for the most sensitive end point obtained from

the most appropriate and/or sensitive mammalian species examined to obtain an acceptable exposure level. Currently, there is no one laboratory animal species that can be considered most appropriate for predicting risk to humans (10). Each agent should be considered on a case-by-case basis.

The margin of safety approach derives a ratio of the NOEL from the most sensitive species to the estimated human exposure level from all potential sources (63). The adequacy of the margin of safety is then considered, based on the weight of evidence, including the nature and quality of the hazard and exposure data, the number of species affected, dose-response relationships, and other factors such as benefits of the agent.

Although the standard study design for a developmental toxicity study calls for a low dose that demonstrates a NOEL, there may be circumstances where a risk assessment is based on the results of a study in which a NOEL for developmental toxicity could not be identified. Rather, the lowest dose administered caused significant effect(s) and was identified as the lowest observed effect level (LOEL). In circumstances where only a LOEL is available, it may be appropriate to apply

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an additional uncertainty factor. The magnitude of this additional factor is dependent upon scientific judgment. In some instances, additional studies may be needed to strengthen the confidence in this additional uncertainty factor.

B. Exposure Assessment

The results of the dose-response assessment are combined with an estimate of human exposure in order to obtain a quantitative estimate of risk. The Guidelines for Estimating Exposures are published separately (64) and will not be discussed in detail here. In general, the exposure assessment describes the magnitude, duration, schedule, and route of exposure. This information is developed from monitoring data and from estimates based on modeling of environmental exposures. Unique considerations relevant to developmental toxicity are duration and period of exposure as related to stage of development (i.e., critical periods), and the possibility that a single exposure may be sufficient to produce adverse developmental effects (i.e., chronic exposure is not a necessary prerequisite for developmental toxicity to be manifested). Also, it should be recognized that exposure of almost any segment of the human population (i.e., fertile men and women, the conceptus, and the child up to the age of sexual maturation) may lead to risk to the developing organism.

Data on exposure to humans may be qualitative or quantitative. The qualitative data could be surrogate data, such as employment or residence histories; quantitative or dose data are frequently not available. Exposures at different stages of the reproductive process can result in different outcomes (49). In laboratory studies, these time periods can be carefully controlled. In human studies, especially retrospective ones, linking of specific time periods and specific exposures, even on a qualitative level, may be difficult due to errors of recall or record keeping (where records are available). The increased probability of misclassification of exposure status may affect the ability of a study to recognize a true effect (8, 23, 52, 65, 66).

Exposure may be defined at a specific point in time, or the cumulative lifetime exposure up to a specific point in time. Each of these definitions carries an implicit assumption about the underlying relationship between exposure and outcome. For example, a cumulative exposure measure assumes that total lifetime exposure is important, with a greater probability of effect with greater total exposure; a dichotomous exposure measure (ever exposed versus never exposed) assumes an irreversible effect of exposure; and exposure at a specific time in the reproductive process assumes that only concurrent exposure is important. The appropriate exposure depends on the outcome(s) studied, the biologic mechanism affected by exposure, and the half-life of the exposure. Unbiased misclassification of exposure, due either to poor data or to an inappropriate exposure variable, may result in missing an effect of the agent under study.

C. Risk Characterization

Many uncertainties have been pointed out in these Guidelines which are associated with the toxicological and exposure components of risk assessments in developmental toxicology. In the past, these uncertainties have often not been readily apparent or consistently presented. The presentation of any risk assessment for developmental toxicity should be accompanied by statements concerning the strength of the hazard evaluation (see section III. D. for more detail) as well as dose-response relationships, estimates of human exposure, and any other factors that affect the quality and precision of the assessment. The dose-response and exposure data are combined to estimate risk based on a NOEL for any adverse developmental effect. The uncertainty factor selected or margin of safety calculated should be sufficiently qualified as to the assumptions used and the accuracy of the estimates.

At present, there are no mathematical models that are generally accepted for estimating developmental toxicity responses below the applied dose range. This is due primarily to a lack of understanding of the biological mechanisms underlying developmental toxicity, intra/interspecies differences in the types of developmental events, the influence of maternal effects on the dose-response curve, and whether or not a threshold exists below which no effect will be

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produced by an agent. Many developmental toxicologists assume a threshold for most developmental effects; this assumption is based largely on the biological rationale that the embryo is known to have some capacity for repair of the damage or insult (49), and that most developmental deviations are probably multifactorial in nature (67). The existence of a NOEL in an animal study does not prove or disprove the existence or level of a true threshold; it only defines the highest level of exposure under the conditions of the test that are not associated with a significant increase in effect. The use of NOELs and uncertainty factors or margins of safety are attempts to ensure that the allowable levels are below those that will produce a significant increase in developmental effects.

Discussions of risk extrapolation procedures have noted that further work is needed to improve mathematical tools for developing estimates of potential human developmental risk (62, 68). Gaylor (69) has suggested an approach for controlling risk that combines the use of mathematical models for low-dose estimation of risk with the application of an uncertainty factor based on a preselected level of allowable risk. This approach is similar to approaches proposed for carcinogenesis, but does not preclude the possibility of a threshold, and may provide a more quantitative approach to controlling risk. Several such approaches are being examined. For the most part, the Agency will continue to use uncertainty factors and margins of safety as described above. Other appropriate methods for expressing risk are being sought and will be applied if considered acceptable.

These Guidelines summarize the procedures that the U.S. Environmental Protection Agency will follow in evaluating the potential for agents to cause developmental toxicity. These Guidelines will be reviewed and updated as advances are made in the field, since it is evident that our ability to evaluate and predict human developmental toxicity is imprecise. Further studies that 1) delineate the mechanisms of developmental toxicity and pathogenesis, 2) provide comparative pharmacokinetic data, and 3) elucidate the functional modalities that may be altered by exposure to toxic agents will aid in the interpretation of data and interspecies extrapolation. These types of studies, along with further evaluation of the relationship between maternal and fetal toxicity and the concept of a threshold in developmental toxicity, will provide for the development of improved mathematical models to more precisely assess risk.

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Part B: Response to Public and Science Advisory Board Comments

I. Introduction

This section summarizes some of the issues raised in public comments on the Proposed Guidelines for the Health Assessment of Suspect Developmental Toxicants published November 23, 1984 (49 FR 46324). Comments were received from 44 individuals or organizations. The Agency's initial summary of comments was presented to the Developmental Toxicity Guidelines Panel of the Science Advisory Board (SAB) at its organizational meeting on March 4, 1985. At its April 22-23, 1985, meeting, the Panel provided the Agency with its suggestions and recommendations concerning the Guidelines.

The SAB and public comments were diverse and addressed issues from a variety of perspectives. In general, the comments were favorable and in support of the Guidelines. The SAB Panel noted that the field of developmental toxicology is particularly weak with respect to quantitative assessment and recommended that further efforts be given to developing alternative methods for quantitative estimates of risk for developmental toxicity. They also indicated that further discussion of the relationship of maternal toxicity to fetal toxicity could be added. Concern was expressed that these Guidelines be coordinated with the reproductive toxicity guidelines which are currently being developed.

In response to the comments, the Agency has modified or clarified many sections of the Guidelines. For purposes of this discussion, only the most significant issues reflected by the public and SAB comments are discussed. Several minor recommendations, which do not warrant discussion here, were considered by the Agency in the revision of these Guidelines.

II. Coordination With Other Guidelines

A. Other Risk Assessment Guidelines

Several commentors raised concerns about aspects of developmental toxicity (e.g., paternally-mediated effects, effects of subchronic exposures, transplacental carcinogenesis, etc.) that were not covered in these Guidelines, and how these Guidelines will integrate with those on male and female reproductive toxicity which are still under development.

The Guidelines have been revised to indicate that developmental toxicity may result from several different types of exposure, including parental exposure prior to conception, acute or subacute exposure during organogenesis, perinatal and postnatal development to the time of sexual maturation, or subchronic exposure as would be the case in multigeneration studies. These Guidelines provide information for interpreting developmental effects related to any of the types of exposure mentioned above. End points of developmental toxicity, which are measured in multigeneration studies, have been added to Table 2 and discussed in the text. Transplacental carcinogenesis, although considered a developmental effect, will be evaluated and assessed in terms of human risk according to the Guidelines for Carcinogen Risk Assessment. Careful attention will be paid to integrating these developmental toxicity risk assessment Guidelines and the male and female reproductive toxicity risk assessment guidelines, which are currently being written, so that overlapping material is not in conflict, and no pertinent information is overlooked. Since the developmental and reproductive toxicity guidelines are being developed by Agency committees that have overlapping membership within the Agency, such integration will be ensured.

B. Coordination With Testing Guidelines

Several commentors indicated that these Guidelines did not make clear enough the fact that testing guidelines are already in place and that these guidelines were intended only for the purposes of risk assessment.

The Guidelines have been revised to indicate that they do not constitute any changes in current testing guidelines, but rather they are intended to provide guidance for the interpretation of studies that follow the testing guidelines. In addition, limited information is provided for interpretation of other studies (e.g., functional developmental toxicity studies and short-term tests) which are not routinely required or for which there are no current testing guidelines, but which may be encountered when reviewing data on particular agents.

III. Definitions

Several questions were raised about definitions of terminology, due to lack of clarity or inconsistency with other parts of these Guidelines or the testing guidelines.

As indicated in the Guidelines, there are differences in the use of terms in the field of developmental toxicology, and the terms have been defined so that the reader may understand how the terms are being used. Several minor changes in the definitions have been made

[51 FR 34040]

to make them more consistent. For example, the definition for developmental toxicology has been expanded to include the wide range of exposure situations that may result in developmental effects. The term functional teratology has been changed to functional developmental toxicology, and the term

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teratogenicity has been discussed in the section on malformations and variations.

IV. Qualitative Assessment

A. Maternal and Developmental Toxicity

Several commentors noted the need for a better discussion of how maternal toxicity affects the evaluation of developmental toxic effects.

The Agency has taken the approach in these Guidelines of discussing in detail the individual end points of maternal and offspring toxicity, then giving guidance relating to an overall evaluation of the data in Part A, section III.A.4. This approach is consistent with the philosophy reflected in the Guidelines as follows: Those agents that cause developmental effects at doses lower than those causing maternal toxicity are of greatest concern, but developmental effects at doses that also produce maternal toxicity shoud not be discounted as secondary to maternal effects. Rather, when the lowest observed effect level (LOEL) is the same for maternal and developmental toxicity, it may indicate similar sensitivities to the agent, and maternal effects may be reversible while developmental effects may be permanent.

B. Functional Developmental Toxicity

Several commentors raised concern about the premature use of functional data in the risk assessment process. On the other hand, the SAB Panel felt that these tests were very valuable in assessing developmental toxicity.

The Agency does not routinely require such testing, and these Guidelines do not suggest requirements. However, in the review of data on existing chemicals, such data are sometimes encountered and must be evaluated by the Agency. The discussion in the Guidelines is intended to delineate the current state of the art, and to indicate to what extent the data currently may be used for risk assessment purposes.

C. Short-Term Testing

Several commentors stressed the need for further refinement, validation, and comparative testing to determine the credibility of short-term tests for developmental toxicity. The appropriateness of single dose level screens for the purpose of prioritization was endorsed by the SAB Panel with the reservation that too many false positives might occur, and that positive agents in these screens would be permanently labelled as positive developmental toxicants.

Since data from these types of test procedures may be encountered in the assessment of chemicals, the Agency felt it appropriate to give guidance as to how these should be evaluated. The Guidelines have been revised to clearly indicate that these tests are not routinely required, shoud not be considered as a replacement for routine *in vivo* developmental toxicity testing in mammals, and should not be used to make the final decision as to whether an agent is a positive or negative developmental toxicant.

D. Comparisons of Molecular Structure

Comments suggested that not much is known about structure-activity relationships for developmental toxicants, and that this procedure should not be used except in the case of hormone analogs.

A statement has been added to indicate that structure-activity relationships have not been well-studied in developmental toxicology, but under certain circumstances, e.g., in the case of the premanufacturing notice process (TSCA, section 5), the evaluation of molecular structure is one of several procedures used by the Agency to evaluate potential toxicity and to support requests for testing of new chemicals.

V. Quantitative Assessment

Most comments related to the appropriateness of using uncertainty (safety) factors, margins of safety, and no observed effect levels (NOELs). Some commentors felt that the concept of threshold was not adequately discussed in the Guidelines.

These Guidelines are intended to reflect current Agency policy and practice. Although more quantitative assessment of developmental toxicity data are desirable, and efforts are currently ongoing within the Agency to evaluate other approaches, the current practice is to use the NOEL (or the LOEL if a NOEL is not available), and to apply an uncertainty factor or to calculate the margin of safety. This practice is based in large part on the lack of understanding of the biological mechanisms involved. The uncertainty factor used or acceptability of the margin of safety are considered risk management decisions, but the scientific issues that must be taken into account are discussed in these Guidelines. An experimentally determined NOEL does not prove or disprove the existence of a threshold, although many developmental toxicologists assume a threshold for most developmental effects because of known repair capabilities in developing systems and the fact that many developmental alterations are multifactorial in nature.

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51 FR 34042

GUIDELINES FOR ESTIMATING EXPOSURES

SUMMARY: On September 24, 1986, the U.S. Environmental Protection Agency issued the following five guidelines for assessing the health risks of environmental pollutants.

Guidelines for Carcinogen Risk Assessment

Guidelines for Estimating Exposures

Guidelines for Mutagenicity Risk Assessment

Guidelines for the Health Assessment of Suspect Developmental Toxicants

Guidelines for the Health Risk Assessment of Chemical Mixtures

This section contains the Guidelines for Estimating Exposures.

The Guidelines for Estimating Exposures (hereafter "Guidelines") are intended to guide Agency analysis of exposure assessment data in line with the policies and procedures established in the statutes administered by the EPA. These Guidelines were developed as part of an interoffice guidelines development program under the auspices of the Office of Health and Environmental Assessment (OHEA) in the Agency's Office of Research and Development. They reflect Agency consideration of public and Science Advisory Board (SAB) comments on the Proposed Guidelines for Exposure Assessment published November 23, 1984 (49 FR 46304).

This publication completes the first round of risk assessment guidelines development. These Guidelines will be revised, and new guidelines will be developed, as appropriate.

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SUPPLEMENTARY INFORMATION: In 1983, the National Academy of Sciences (NAS) published its book entitled *Risk Assessment in the Federal Government: Managing the Process.* In that book, the NAS recommended that Federal regulatory agencies establish "inference guidelines" to ensure consistency and technical quality in risk assessments and to ensure that the risk assessment process was maintained as a scientific effort separate from risk management. A task force within EPA accepted that recommendation and requested that Agency scientists begin to develop such guidelines.

General

The guidelines are products of a two-year Agencywide effort, which has included many scientists from the larger scientific community. These guidelines set forth principles and procedures to guide EPA scientists in the conduct of Agency risk assessments, and to inform Agency decision makers and the public about these procedures. In particular, the guidelines emphasize that risk assessments will be conducted on a case-by-case basis, giving full consideration to all relevant scientific information. This case-by-case approach means that Agency experts review the scientific information on each agent and use the most scientifically appropriate interpretation to assess risk. The guidelines also stress that this information will be fully presented in Agency risk assessment documents, and that Agency scientists will identify the strengths and weaknesses of each assessment by describing uncertainties, assumptions, and limitations, as well as the scientific basis and rationale for each assessment.

Finally, the guidelines are formulated in part to bridge gaps in risk assessment methodology and data. By identifying these gaps and the importance of the missing information to the risk assessment process, EPA wishes to encourage research and analysis that will lead to new risk assessment methods and data.

Guidelines for Estimating Exposures

Work on the Guidelines for Estimating Exposures began in January 1984. Draft guidelines were developed by Agency work groups composed of expert scientists from throughout the Agency. The drafts were peer-reviewed by expert scientists in the field of exposure assessment from universities, environmental groups, industry, labor, and other governmental agencies. They were then proposed for public comment in the *FEDERAL REGISTER* (49 FR 46304). On November 9, 1984, the Administrator directed that Agency offices use the proposed guidelines in performing risk assessments until final guidelines become available.

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After the close of the public comment period, Agency staff prepared summaries of the comments, analyses of the major issues presented by the commentors, and preliminary Agency responses to those comments. These analyses were presented to review panels of the SAB on March 4 and April 22-23, 1985, and to the Executive Committee of the SAB on April 25-26, 1985. The SAB meetings were announced in the *FEDERAL REGISTER* as follows: February 12, 1985 (50 FR 5811) and April 4, 1985 (50 FR 13420 and 13421).

In a letter to the Administrator dated June 19, 1985, the Executive Committee generally concurred on all five of the guidelines, but recommended certain revisions, and requested that any revised guidelines be submitted to the appropriate SAB review panel chairman for review and concurrence on behalf of the Executive Committee. As described in the responses to comments (see Part B: Response to the Public and Science Advisory Board Comments), each guidelines document was revised, where appropriate, consistent with the SAB recommendations, and revised draft guidelines were submitted to the panel chairmen. Revised draft Guidelines for Estimating Exposures were concurred on in a letter dated January 13, 1986. Copies of the letters are available at the Public Information Reference Unit, EPA Headquarters Library, as indicated elsewhere in this section.

Following this Preamble are two parts: Part A contains the Guidelines and Part B, the Response to the Public and Science Advisory Board Comments (a summary of the major public comments, SAB comments, and Agency responses to those comments).

The SAB requested that the Agency develop guidelines on the principles for the measurement of pollutant concentrations in the various environmental media and for the uses of environmental measurements for exposure assessment. This effort is currently underway.

The Agency also will provide technical support documents that contain detailed technical information needed to implement the Guidelines. Two of these technical reports entitled "Development of Statistical Distributions or Ranges of Standard Factors Used in Exposure Assessments" (available from the National Technical Information Service, PB85-242667) and "Methodology for Characterization of Uncertainty in Exposure Assessments" (available from the National Technical Information Service, PB85-240455) are currently available. Technical support documents will be revised periodically to reflect improvements in exposure assessment methods and new information or experience.

[51 FR 34043]

The Agency is continuing to study the risk assessment issues raised in the Guidelines and will revise these Guidelines in line with new information, as appropriate.

References, supporting documents, and comments received on the proposed guidelines, as well as copies of the final guidelines, are available for inspection and copying at the Public Information Reference Unit (202-382-5926), EPA Headquarters Library, 401 M Street, S.W., Washington, DC, between the hours of 8:00 a.m. and 4:30 p.m.

I certify that these Guidelines are not major rules as defined by Executive Order 12291, because they are nonbinding policy statements and have no direct effect on the regulated community. Therefore, they will have no effect on costs or prices, and they will have no other significant adverse effects on the economy. These Guidelines were reviewed by the Office of Management and Budget under Executive Order 12291.

August 22, 1986

Lee M. Thomas,

Administrator

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Part A: Guidelines for Estimating Exposures

I. Introduction

These Guidelines provide the Agency with a general approach and framework for carrying out human or nonhuman exposure assessments for specified pollutants. The Guidelines have been developed to assist future assessment activities and encourage improvement in those EPA programs that require, or could benefit from, the use of exposure assessments. The Guidelines are procedural. They should be followed to the extent possible in instances where exposure assessment is a required element in the regulatory process or where exposure assessments are carried out on a discretionary basis by EPA management to support regulatory or programmatic decisions.

This document, by laying out a set of questions to be considered in carrying out an exposure assessment, should help avoid inadvertent mistakes of omission. Ideally, exposure assessments are based on measured data. EPA recognizes that gaps in data will be common, but the Guidelines will nevertheless serve to assist in organizing the data that are available, including new data developed as part of the exposure assessment. In the absence of sufficient reliable data and the time to obtain appropriate measurements, exposure assessments may be based on validated mathematical models. Whenever possible, exposure assessments based on modeling should be complemented by reliable measurements. Furthermore, it is understood that the level of detail found in the exposure assessments depends on the scope of the assessment.

These Guidelines should also promote consistency among various exposure assessment activities that are carried out by the Agency. Consistency with respect to common physical, chemical, and biological parameters, with respect to assumptions about typical exposure situations, and with respect to the characterization of uncertainty of estimates, will enhance the comparability of results and enable the Agency to improve the state-of-the-art of exposure assessment over time through the sharing of common data and experiences.

It is recognized that the main objective of an exposure assessment is to provide reliable data and/or estimates for a risk assessment. Since a risk assessment requires the coupling of exposure information and toxicity or effects information, the exposure assessment process should be coordinated with the toxicity/effects assessment. This document provides a common approach to format, which should simplify the process of reading and evaluating exposure assessments and thereby increase their utility in assessing risk.

As the Agency performs more exposure assessments, the Guidelines will be revised to reflect the benefit of experience.

II. General Guidelines and Principles

A. Exposure and Dose

Exposure has been defined by Committee E-47, Biological Effects and Environmental Fate, of the American Society for Testing and Materials, as the contact with a chemical or physical agent. The magnitude of the exposure is determined by measuring or estimating the amount of an agent available at the exchange boundaries, i.e., lungs, gut, skin, during some specified time. Exposure assessment is the determination or estimation (qualitative or quantitative) of the magnitude, frequency, duration, and route of exposure. Exposure assessments may consider past, present, and future exposures with varying techniques for each phase, e.g., modeling of future exposures, measurements of existing exposure, and biological accumulation for past exposures. Exposure assessments are generally combined with environmental and health effects data in performing risk assessments.

In considering the exposure of a subject to a chemical agent, there are several related processes. The contact between the subject of concern and the agent may lead to the intake of some of the agent. If absorption occurs, this constitutes an uptake (or an absorbed dose). When biological tissue or fluid measurements indicate the presence of a chemical, exposures may be estimated from these data. Presence of a chemical in such biological samples is the most direct indication that an exposure has occurred. The route of exposure generally impacts the extent of absorption and should be considered in performing risk assessments.

[51 FR 34044]

B. Decision Path to Determine Scope of the Assessment

The first step in preparing an exposure assessment should be the circumscription of the problem at hand to minimize effort by use of a narrowing process. A decision path that describes this process is shown in Figure 1. As illustrated in Figure 1, the preliminary assessment and the in-depth assessment are two major phases in this logic path.

[51 FR 34046]

The preliminary assessment phase should commence by considering what risk is under study. Within this framework, a data base should be compiled from readily available scientific data and exposure information based on manufacturer, processor, and user practices. Next, the most likely areas of exposure (manufacturing, processing, consumer, distribution, disposal, water and food, etc.) should be identified. The preliminary exposure assessments should be based on data derived from environmental measurements. When a limited amount of measurement data is available, estimates may be based on modeling. Since a complete data search may not be possible, well identified

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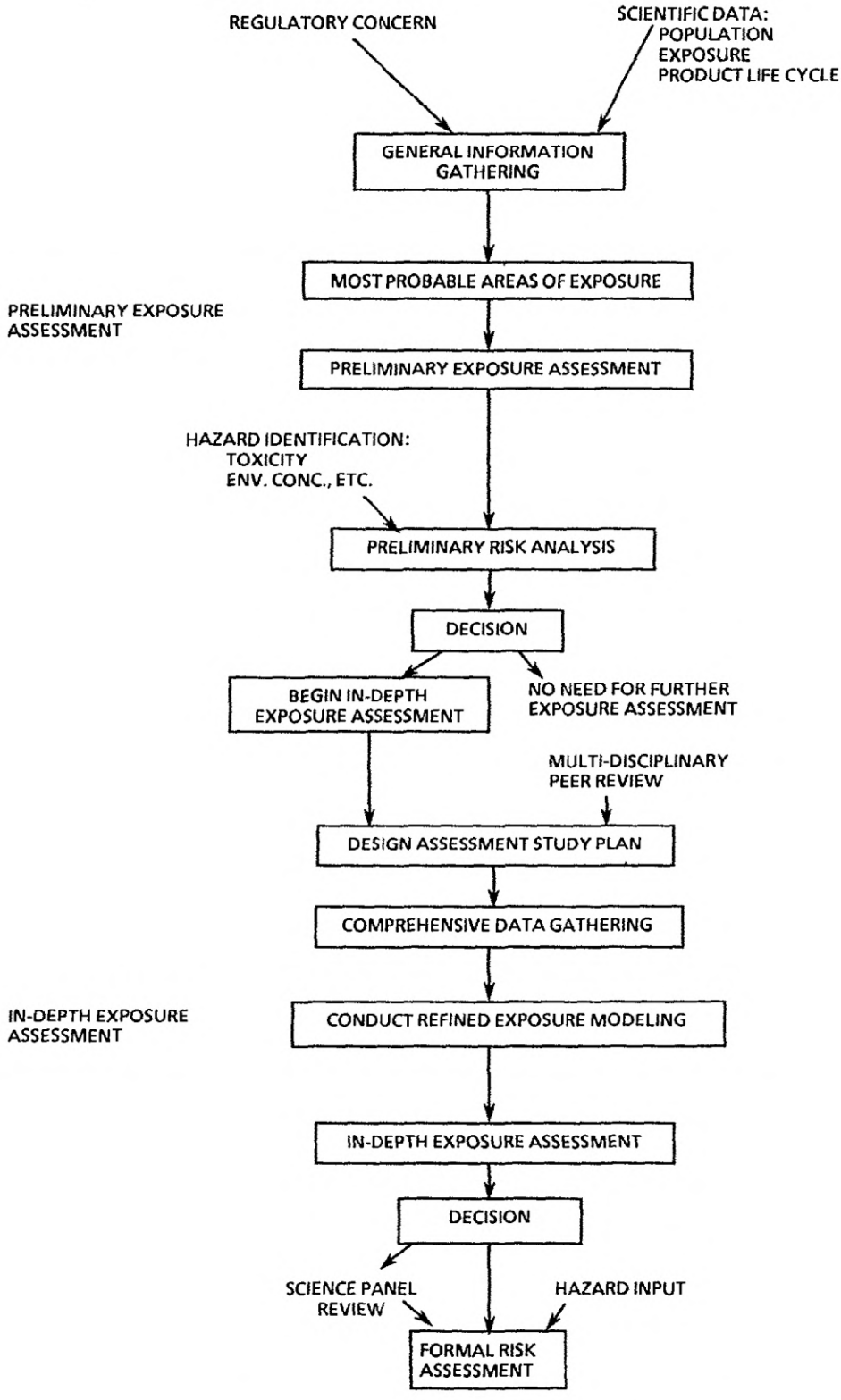

Figure 1. Decision path for exposure assessment.

assumptions and order of magnitude estimates may be used to further narrow the exposure areas of concern.

Data from this preliminary exposure assessment can then be coupled with toxicity information to perform a preliminary risk analysis. As a result of this analysis, a decision will be made that either an in-depth exposure assessment is necessary or that there is no need for further exposure information. The organization and contents of an in-depth exposure assessment are given in the following section.

In assembling the information base for either a preliminary assessment or a more detailed assessment, its adequacy should be ascertained by addressing the following considerations:

- Availability of information in every area needed for an adequate assessment;
- Quantitative and qualitative nature of the data;
- Reliability of information;
- Limitations on the ability to assess exposure.

C. Uncertainty

Exposure assessments are based on measurements, simulation model estimates, and assumptions about parameters used in approximating actual exposure conditions. Actual measurements should be used whenever possible. Both data and assumptions contain varying degrees of uncertainty which influence the accuracy of exposure assessments. Consequently, evaluation of uncertainty is an important part of all exposure assessments.

The uncertainty analyses performed will vary depending on the scope of the assessment, the quantity and quality of measurements, and the type and complexity of mathematical models used. A discussion of the types of analyses used for quantifying uncertainties in exposures is presented in the next section.

III. Organization and Contents of an Exposure Assessment

A. Overview

A suggested outline for an exposure assessment document is given in Exhibit 1. The five major topics to be addressed within most exposure assessments are as follows: Source(s), Exposure Pathways, Measured or Estimated Concentrations and Duration, Exposed Population(s), and Integrated Exposure Analysis. These five topics are appropriate for exposure assessments in general, whether the assessments are of global, national, regional, local, site specific, workplace related, or other scope. The topics are appropriate for exposure assessments on new or existing chemicals and radionuclides. They are also applicable to both single media and multimedia assessments. Since exposure assessments are performed at different levels of detail, the extent to which any assessment contains items listed in Exhibit 1 depends upon its scope. The outline is a guide to organize the data whenever they are available.

Exhibit 1.--Suggested Outline for an Exposure Assessment

1. Executive Summary
2. Introduction
   a. Purpose
   b. Scope
3. General Information for Each Chemical or Mixture
   a. Identity
      (1) Molecular formula and structure, synonyms, and Chemical Abstracts Service (CAS) number
      (2) Description of grades, contaminants, and additives
      (3) Other identifying characteristics
   b. Chemical and Physical Properties
4. Sources
   a. Characterization of Production and Distribution
   b. Uses
   c. Disposal
   d. Summary of Environmental Releases
5. Exposure Pathways and Environmental Fate
   a. Transport and Transformation
   b. Identification of Principal Pathways of Exposure
   c. Predicting Environmental Distribution
6. Measured or Estimated Concentrations
   a. Uses of Measurements
   b. Estimation of Environmental Concentrations
7. Exposed Populations
   a. Human Populations
      (1) Population size and characteristics
      (2) Population location
      (3) Population habits
   b. Nonhuman Populations (where appropriate)
      (1) Population size and characteristics
      (2) Population location
      (3) Population habits
8. Integrated Exposure Analysis
   a. Calculation of Exposure
      (1) Identification of the exposed population and critical elements of the ecosystem
      (2) Identification of pathways of exposure
   b. Human Dosimetry and Biological Measurements
   c. Development of Exposure Scenarios and Profiles
   d. Evaluation of Uncertainty
      (1) Introduction
      (2) Assessments based on limited initial data
      (3) Assessments based on subjective estimates of input variable distributions
      (4) Assessments based on data for model input variables
      (5) Assessments based on data for exposure
      (6) Summary
9. References
10. Appendices

B. Detailed Explanation of Outline

1. Executive Summary. The "Executive Summary" should be written so that it can stand on its own as a miniature report. Its main focus should be on a succinct description of the procedures used, assumptions employed, and summary tables or charts of the results. A brief discussion of the uncertainties associated with the results should be included.

2. Introduction (Purpose and Scope). This section should state the intended purpose of the exposure assessment and identify the agent being

investigated, the types of sources and exposure routes included, and the populations of concern.

3. General Information for Each Chemical or Mixture.

a. Identity.

(1) Molecular formula and structure, synonyms, and Chemical Abstracts Service number.

(2) Description of grades, contaminants, and additives.

(3) Other identifying characteristics.

b. Chemical and Physical Properties. This subsection should provide a summary description of the chemical and physical properties of the agent. Particular attention should be paid to the features that would affect its behavior in the environment.

4. Sources. The points at which a substance is believed to enter the environment should be described, along with any known rates of entry. (Points of entry may be indoors as well as outdoors; environments include indoor settings such as offices as well as outdoor environments.) A detailed exposure assessment should include a study of sources, production, uses, destruction/disposal, and environmental release of a substance. The studies

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should include a description of human activities with respect to the substance and the environmental releases resulting from those activities. It should account for the controlled mass flow of the substance from creation to destruction and provide estimates of environmental releases at each step in this flow. Seasonal variations in environmental releases should also be examined. All sources of the substance should be accounted for with the sum of the uses, destruction, and the environmental releases. The environmental releases can be described in terms of geographic and temporal distribution and the receiving environmental media, with the form identified at the various release points.

a.Characterization of Production and Distribution. All sources of the substance's release to the environment, consistent with the scope of the assessment, should be included, such as production, extraction, processing, imports, stockpiles, transportation, accidental/ incidental production as a side reaction, and natural sources. The sources should be located, and activities involving exposure to the substance should be identified.

b. Uses. The substance should be traced from its sources through various uses (with further follow-up on the products made to determine the presence of the original material as an impurity), e.g., exports, stockpile increases, etc.

c. Disposal. This subsection should contain an evaluation of disposal sites and destruction processes, such as incineration of industrial chemical waste, incineration of the substance as part of an end-use item in municipal waste, landfilling of wastes, biological destruction, or destruction in the process of using the end product. Hazardous contaminants of the substance may be included, and products containing the substance as a contaminant may be followed from production through destruction/disposal.

d. Summary of Environmental Releases. Estimates should be made of the quantities of the substance released to the various environmental media. Sources of release to the environment include production, use, distribution/transport, natural sources, disposal, and contamination of other products. Environmental releases should be presented at a reasonable level of detail. Extremely detailed exposure estimates would attempt to specify the following information for each significant emission source: location, amount of the substance being released as a function of time to each environmental medium, physical characteristics of the emission source, and the physical and chemical form of the substance being released. Evaluation of the uncertainties associated with the emission estimates should be given. A detailed discussion of the procedures for estimating uncertainty is presented in section 8.d.

5. Exposure Pathways and Environmental Fate. The exposure pathways section should address how an agent moves from the source to the exposed population or subject. For a less detailed assessment, broad generalizations on environmental pathways and fate may be made. In the absence of data, e.g., for new substances, fate estimates may have to be predicted by analogy with data from other substances. Fate estimates may also be made by using measurements and/or models and laboratory-derived process rate coefficients. At any level of detail, certain pathways may be judged insignificant and not pursued further.

For more detailed assessments involving environmental fate, the analysis of sources described previously should provide the amount and rate of emissions to the environment, and possibly the locations and form of the emissions. The environmental pathways and fate analysis follows the substance from its point of initial environmental release, through the environment, to its ultimate fate. It may result in an estimation of the geographic and temporal distribution of concentrations of the substance in the various contaminated environmental media.

a. Transport and Transformation. The substance, once released to the environment, may be transported (e.g., convected downstream in water or on suspended sediment, through the atmosphere, etc.) or physically transformed (e.g., volatilized, melted, absorbed/desorbed, etc.); may undergo chemical transformation, such as photolysis, hydrolysis, oxidation, and reduction; may undergo biotransformation, such as biodegradation; or may accumulate in one or more media. Thus, the environmental behavior of a substance should be

evaluated before exposures are assessed. Factors that should be addressed include:

- How does the agent behave in air, water, soil, and biological media? Does it bioaccumulate or biodegrade? Is it absorbed or taken up by plants?
- What are the principal mechanisms for change or removal in each of the environmental media?
- Does the agent react with other compounds in the environment?
- Is there intermedia transfer? What are the mechanisms for intermedia transfer? What are the rates of the intermedia transfer or reaction mechanisms?
- How long might the agent remain in each environmental medium? How does its concentration change with time in each medium?
- What are the products into which the agent might degrade or change in the environment? Are any of these degradation products ecologically or biologically harmful? What is the environmental behavior of the harmful products?
- Is a steady-state concentration distribution in the environment, or in specific segments of the environment, achieved? If not, can the nonsteady-state distribution be described?
- What is the resultant distribution in the environment--for different media, different types or forms of the agent, for different geographical areas, at different times or seasons?

b. Identification of Principal Pathways of Exposure. The principal pathway analysis should evaluate the sources, locations, and types of environmental releases, together with environmental behavioral factors, to determine the significant routes of human and environmental exposure to the substance. Thus, by listing the important characteristics of the environmental release (entering media, emission rates, etc.) and the agent's behavior (intermedia transfer, persistence, etc.) after release to each of the entering media, it should be possible to follow the movement of the agent from its initial release to its subsequent fate in the environment. At any point in the environment, human or environmental exposure may occur. Pathways that result in major concentrations of the agent and high potential for human or environmental contact are the principal exposure pathways.

c. Predicting Environmental Distribution. Models may be used to predict environmental distributions of chemicals. Model estimates of environmental distribution of chemicals are based on measurements whenever feasible. In predicting environmental distributions of chemicals, available measurements must be considered.

In this section an estimation is made, using appropriate models, of representative concentrations of the agent in different environmental media, and its time-dependence in specific geographical locations (e.g., river basins, streams, etc.).

6. Measured or Estimated Concentrations.

a. Uses of Measurements. Measurements are used to identify releases (source terms) and, in the

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exposure pathways and fate assessments, to quantitatively estimate both release rates and environmental concentrations. Some examples of uses of measurements are: sampling of stacks or discharge pipes for emissions to the environment, testing of products for chemical or radionuclide content, testing of products for chemical or radioactive releases, sampling of appropriate points within a manufacturing plant to determine releases from industrial processes or practices, sampling of potentially exposed populations using personal dosimeters, and sampling of solid waste for chemical or radionuclide content. These data should be characterized as to accuracy, precision, and representativeness. If actual environmental measurements are unavailable, concentrations can be estimated by various means, including the use of fate models (see previous section) or, in the case of new chemicals, by analogy with existing chemicals.

Measurements are a direct source of information for exposure analysis. Furthermore, reliable measurements can be used to calibrate or extrapolate models or calculations to assess environmental distributions. However, environmental pathway and fate analysis may be needed in addition to the measured data for the following reasons: for most pollutants, particularly organic and new chemicals, measurements are limited; analysis of measured data does not often yield relationships between environmental releases and environmental concentration distribution in media or geographic locations that have not been measured; analysis of measurements does not provide information on how and where biota influence the environmental distribution of a pollutant; and measured concentrations may not be traceable to individual sources.

b. Estimation of Environmental Concentrations. Concentrations of agents should be estimated for all environmental media that might contribute to significant exposures. Generally, the environmental concentrations are estimated from measurements, mathematical models, or a combination of the two. If environmental measurements are not limited by sample size or inaccuracies, then exposure assessments based on measurements have precedence over estimates based on models.

The concentrations must be estimated and presented in a format consistent with available dose-response information. In some cases an estimate of annual average concentration will be sufficient, while in other cases the temporal distribution of concentrations may be required. Future environmental concentrations resulting from current or past releases may also be projected. In some cases, both the temporal and geographic distributions of the concentration may be assessed.

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Moreover, if the agent has natural sources, the contribution of these to environmental concentrations may be relevant. These "background" concentrations may be particularly important when the results of tests of toxic effects show a threshold or distinctly nonlinear dose-response.

The uncertainties associated with the estimated concentrations should be evaluated by an analysis of the uncertainties of the model parameters and input variables. When the estimates of the environmental concentrations are based on mathematical models, the model results must be compared to available measurements, and any significant discrepancies should be discussed. Reliable, analytically-determined values must be given precedence over estimated values whenever significant discrepancies are found.

7. Exposed Populations. Populations selected for study may be done *a priori*, but frequently the populations will be identified as a result of the sources and fate studies. From an analysis of the distribution of the agent, populations and subpopulations (i.e., collections of subjects) at potentially high exposure can be identified, which will then form the basis for the populations studied. Subpopulations of high sensitivity, such as pregnant women, infants, chronically ill, etc., may be studied separately.

Census and other survey data may be used to identify and describe the population exposed to various contaminated environmental media. Depending on the characteristics of available toxicological data, it may be appropriate to describe the exposed population by other characteristics such as species, subspecies-age-sex distribution, and health status.

In many cases, exposed populations can be described only generally. In some cases, however, more specific information may be available on matters such as the following:

a. Human Populations

(1) Population size and characteristics (e.g., trends, sex/age distribution)

(2) Population location

(3) Population habits-- transportation habits, eating habits, recreational habits, workplace habits, product use habits, etc.

b. Nonhuman Populations (where appropriate)

(1) Population size and characteristics (e.g., species, trends)

(2) Population location

(3) Population habits

8. Integrated Exposure Analysis. The integrated exposure analysis combines the estimation of environmental concentrations (sources and fate information) with the description of the exposed population to yield exposure profiles. Data should be provided on the size of the exposed populations; duration, frequency, and intensity of exposure; and routes of exposure. Exposures should be related to sources.

For more detailed assessments, the estimated environmental concentrations should be considered in conjunction with the geographic distribution of the human and environmental populations. The behavioral and biological characteristics of the exposed populations should be considered, and the exposures of populations to various concentration profiles should be estimated. The results can be presented in tabular or graphic form, and an estimate of the uncertainty associated with them should be provided.

a. Calculation of Exposure. The calculation of exposure involves two major aspects:

(1) Identification of the exposed population and critical elements of the ecosystem.

The estimate of environmental concentrations also should give the geographical areas and environmental media contaminated. The stated purpose of the assessment should have described the human and environmental subjects for which exposures are to be calculated. If the subjects are not listed, the contaminated geographical areas and environmental media can be evaluated to determine subject populations. The degree of detail to be used in defining the exposed population distribution depends on the concentration gradient over geographic areas.

(2) Identification of pathways of exposure.

(a) Identification and description of the routes by which the substances travel from production site, through uses, through environmental releases/sources, through transport and fate processes, to the target population.

(b) Quantitative estimates of the amounts of the chemical following each exposure pathway. Such estimates allow the various pathways to be put in the perspective of relative importance.

From the geographic and temporal distribution of environmental

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concentrations, the exposed population, the behavioral characteristics, and the critical elements of the ecosystem, exposure distributions can be estimated. The results of exposure calculation should be presented in a format that is consistent with the requirements of the dose-response functions which may later be used in a risk assessment. For example, when health risks caused by exposure over extended durations are considered, average daily exposure over the duration of exposure usually is calculated. When lifetime risks are considered, average daily exposure over a lifetime usually is calculated. In contrast, when health risks caused by exposures over short durations are considered, exposure rates are calculated over short time intervals to ensure that peak risks are defined. Many exposure assessments are based on the average exposure occurring over the exposure period. The range of possible exposures is usually divided into intervals,

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and the exposures within each interval are counted. The results can be presented in tabular form or as a histogram.

The population residing in a specific geographic area may be exposed to a substance from several exposure routes. For each exposure route, exposure of individuals in these populations may be determined by summing the contribution of all sources to the exposure route. When exposures involve more than one exposure route, the relative amounts of a substance absorbed is usually route dependent. Consequently, total absorbed dose estimates must account for these differences. Because EPA regulates sources of releases, the contribution to exposures from each type of source being considered should be displayed. Exposure estimates should be presented for each significant exposure route, and the results should be tabulated in such a way that total externally applied and absorbed dose can be determined.

b. Human Dosimetry and Biological Measurements. Biological measurements of human body fluids and tissues for substances or their metabolites can be used to estimate current or past exposure to chemicals. When analytical methods are available, chemicals that have been absorbed into the body can be measured in body tissue and fluid. Such measurements may be used to estimate human exposure if the chemical substances leave in the body reliable indicators of exposure. Furthermore, although a compound may be relatively easy to detect in body tissue, for some compounds, attributing body burdens to specific environmental releases may be difficult because of limited ability to obtain environmental measurements or appropriate metabolic data.

c. Development of Exposure Scenarios and Profiles. Depending on the scope of the exposure assessment, the total exposure may be fractionated into one or more "exposure scenarios" to facilitate quantification. As an example, Table 1 lists seven very broad scenarios: Occupational, Consumer, Transportation, Disposal, Food, Drinking Water, and Ambient. For each of the scenarios, the major topics necessary to quantify exposure include sources, pathways, measurements, and population characteristics. Investigation of only one scenario may be necessary for the scope of some assessments. For example, a pesticide application exposure assessment may consider the occupational scenario which would address the exposure to applicators and populations in the vicinity of the site. An exposure assessment around a hazardous waste site may focus on the disposal scenario. The exposure assessment

TABLE 1.--EXPOSURE ASSESSMENT INFORMATION NEEDS FOR VARIOUS EXPOSURE SCENARIOS

Exposure scenario	Sources	Fate	Population Characteristics	Measurement
Occupational (chemical production).	Site/plant locations, in-plant/on-site materials balance.	Physical and chemical properties models.	Workers, families, population around sites/plants.	In-plant/on-site releases, ambient levels surrounding site/plants; human dosimetry.
Consumer (direct use of chemical or inadvertent use).	Consumption rates, distribution pattern amounts in products.	Physical and chemical properties, shelf life release rates, models.	Consumers	Levels in products releases.
Transportation / storage/spills.	Patterns of distribution and transportation; models for spills.	Physical and chemical properties, environmental fate models.	Storage, transportation workers, general population in area.	Releases, ambient levels.
Disposal (include incineration, landfill).	Materials balance around disposal method, efficiency,releases to environment.	Fate within disposal process; environmental fate of releases; models.	Workers at site of disposal, general population around site.	Releases, levels at various points within process, ambient levels.
Food	Food chain, packaging, additives.	Food chain models, fate during preparation or processing of food.	General population, nonhuman population.	Levels in food, feedstuff; food chain sampling.
Drinking water	Groundwater, surface water, distribution system.	Leach rates from pipes, chlorination processes, fate in water; models.	General population.	Levels in drinking water, groundwater, surface water, treatment plants.
Ambient	Releases to environment; air, land, water.	Environmental fate models.	General population, nonhuman population.	Ambient air, water, soil, etc.; human dosimetry.

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also may consider other scenarios. The more extensive and comprehensive the scope, the more scenarios are usually involved.

It will usually be advantageous in performing an exposure assessment to identify exposure scenarios, quantify the exposure in each scenario, and then integrate the scenarios to estimate total exposure. In this "integrated exposure analysis," the summation of independent exposures from different scenarios (keeping exposure routes separate) often will result in a breakout of exposure by subpopulations, since the individual scenarios usually treat exposure by subpopulation. Therefore, the integration of the scenarios, or integrated exposure analysis, will often result in an exposure profile.

For each exposed subpopulation, exposure profiles should include the size of the group, the make-up of the group (age, sex, etc.), the source of the agent, the exposure pathways, the frequency and the intensity of exposure by each route (dermal, inhalation, etc.), the duration of exposure, and the form of the agent when exposure occurs. Assumptions and uncertainties associated with each scenario and profile should be clearly discussed.

d. Evaluation of Uncertainty.

(1) Introduction. Often an exposure assessment progresses through several stages of refinement. The purpose of these Guidelines is to present methods appropriate for characterization of uncertainty for assessments at various stages of refinement, from assessments based on limited initial data to those based on extensive data.

The appropriate method for characterizing uncertainty for an exposure assessment depends upon the underlying parameters being estimated, the type and extent of data available, and the estimation procedures utilized.

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The uncertainty of interest is always with regard to the population characteristic being estimated. For example, when the population distribution of exposures is being estimated, characterization of uncertainty addresses the possible differences between the estimated distribution of exposure and the true population distribution of exposure.

An exposure assessment quantifies contact of a substance with affected population members (human or nonhuman subjects). The measure of contact (e.g., environmental level or absorbed dose) depends upon what is needed to predict risk. An integrated exposure assessment quantifies this contact via all routes of exposure (inhalation, ingestion, and dermal) and all exposure pathways (e.g., occupational exposure, exposure from consumption of manufactured goods, etc.). The exposed population generally is partitioned into subpopulations such that the likely exposure of all members of a subpopulation is attributable to the same sources. The exposure for each member of a subpopulation is then the sum of exposures over a fixed set of sources and pathways. The measured or estimated exposures for members of a subpopulation are ideally used to estimate the subpopulation distribution of exposure or characteristics thereof. However, a lack of sufficient information sometimes precludes estimation of the subpopulation distributions of exposure and only summary measures of this distribution, such as the mean, minimum, maximum, etc., are estimated. In each case, characterization of uncertainty for the exposure assessment primarily addresses limitations of the data and the estimation procedures. The proportions of the population members in the individual subpopulations are usually estimated and can be used (by combining estimated distributions for the subpopulations) to estimate the distribution of exposure for the total population. Uncertainty concerning the sizes of the subpopulations should be addressed by discussing limitations of the data and estimation methods as well as by tabulating confidence interval estimates for the population sizes whenever possible.

(2) Assessments based on limited initial data. The initial exposure assessment for a substance may be based on limited data for exposure and/or input variables for an exposure prediction model (i.e., an equation that expresses exposure as a function of one or more input variables). These data might be either extant data or data produced by an initial small-scale study. The limited initial data frequently are insufficient to permit estimation of the entire distribution of exposure. Instead, summary measures of this distribution, such as the mean, minimum, and maximum, are usually estimated.

If the assessment is based on measured exposures, the methods used to characterize uncertainty depend mainly upon whether or not the data result from a probability sample for which the probability of inclusion is known for each sample member. Characterization of uncertainty for an assessment based on a probability sample of exposures is discussed later in section 8.d.(5). If the measured exposures are not based on a probability sample, acknowledgement that no strictly valid statistical inferences can be made beyond the units actually in the sample is one aspect of the characterization of uncertainty. If inference procedures are implemented, the assumptions upon which these inferences are based (e.g., treatment of the sample as if it were a simple random sample, or assumption of an underlying model) should be explicitly stated and justified. The data collection methods and inherent limitations of the data should also be discussed.

An initial exposure assessment also may be based on limited data, such as estimated ranges, for input variables for an exposure prediction model. The exposure prediction model would be derived from a postulated exposure scenario that describes the pathways from sources to contact with population members. If the data were only sufficient to support estimates of the ranges of the input variables, the exposure assessment might be limited

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to a sensitivity analysis. The purpose of the sensitivity analysis would be to identify influential model input variables and develop bounds on the distribution of exposure. A sensitivity analysis would estimate the range of exposures that would result as individual model input variables were varied from their minumum to their maximum possible values with the other input variables held at fixed values, e.g., their midranges. The overall minimum and maximum possible exposures usually would be estimated also. For an exposure assessment of this type, the uncertainty would be characterized by describing the limitations of the data used to estimate possible ranges of model input variables and by discussing justification for the model. Justification of the model should include a description of the exposure scenario, choice of model input variables, and the functional form of the model. Sensitivity to the model formulation also can be investigated by replicating the sensitivity analysis for plausible alternative models.

The sensitivity analysis can be enhanced by computing the predicted exposures that result from all possible input variable combinations. If each input variable has only a finite set of possible values, the set of all possible combinations of the input variables can be formed, and the predicted exposure can be computed for each combination. These exposure predictions can be used to form a distribution of exposures by counting the number of occurrences at each exposure level or interval of exposures. This is equivalent to estimating the distribution of exposures that results from treating all input variable combinations as equally likely. This procedure can also be applied by transforming continuous input variables into discrete ones and representing them by equally spaced points. In the limit, as the equal spaces become small and the number of points becomes large, the distribution of exposure that results from counting occurrences of exposure levels is equivalent to estimating the distribution of exposures that results from statistically independent, continuous input variables with uniform distributions on the estimated ranges. This estimated distribution of exposure values can be produced by Monte Carlo simulation, one of the methods of mathematical statistics. The Monte Carlo method consists of randomly generating input variate values and using these to compute corresponding exposure levels, generating an exposure distribution via many iterations. Interpretation of statistics based on this exposure distribution would be in terms of the equally likely input variable combinations. For example, the 95th percentile of this distribution would be the exposure level exceeded by only 5% of the exposures resulting from treating all combinations of input variable values as equally likely. Although this distribution of exposures cannot be interpreted as an estimate of the population distribution (unless the input variables actually are statistically independent and uniformly distributed), it provides additional information for making regulatory decisions. Characterization of uncertainty would include a discussion of limitations of the data and justification for the model as discussed above. Sensitivity to model formulation could also be investigated by estimating the distribution of exposure that results from using the

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same uniform input variable distributions with plausible alternative models and comparing the estimated percentiles.

(3) Assessments based on subjective estimates of input variable distributions. If a model has been formulated that expresses exposure as a function of one or more input variables, the methods of mathematical statistics, such as Monte Carlo simulation, can be used to estimate the population distribution of exposure from an estimate of the joint distribution of the model input variables. Ideally, model input variables should be represented by empirically-validated probability distributions. In some cases, it may be possible to formulate an estimate of the joint distribution of model input variables from discussions with subject matter experts (e.g., via histograms for statistically-independent input variables). The estimated population distribution of exposure will be equivalent to the distribution discussed in section 8.d.(2) for equally likely combinations of input variable values only when the input variable distributions supported are independent uniform distributions. When qualitative knowledge of input variable distributions is used to estimate the population distribution of exposure, uncertainty is characterized by discussing justification for the presumed model and input variable distributions. Alternative models and/or alternative input variable distributions also should be discussed. Sensitivity to these alternatives can be investigated by estimating the distributions of exposure that result from plausible alternatives and comparing the percentiles of the estimated exposure distributions. All available data, even if data are limited, should be used to validate the presumed input variable distributions and the predicted distribution of exposure.

(4) Assessments based on data for model input variables. The exposure assessment based on an estimate of the joint probability distribution for model input variables can be refined by collecting sample survey data for model input variables for a sample of population members. The population distribution of exposure can then be estimated by computing the expected exposure for each sample member based on the model. These expected exposures can be used to directly compute confidence interval estimates for percentiles of the exposure distribution. Alternatively, the sample survey data can be used to compute joint confidence interval estimates for percentiles of the input variable

distribution, which can then be used to generate confidence interval estimates for percentiles of the exposure distribution. In either case, the interval estimates for percentiles of the exposure distribution are a useful quantitative characterization of uncertainty.

Characterization of uncertainty for the exposure assessment would contain a thorough discussion of limitations of the data and justification for the model used to compute expected exposures. The design of the sample survey used to produce the data base should also be discussed. If a probability sample were not used, the lack of a probability sample would be an additional source of uncertainty. Any assumptions used in computing the confidence interval estimates, such as independence of model input variables, should be explicitly stated and justified. Sensitivity to model formulation can be investigated by estimating the distribution of exposure for plausible alternative models and comparing the estimated percentiles, if sample survey data have been collected for the input variables of the alternative models. Appropriate available data for exposure should be used to validate the predicted distribution of exposure. If specific probability distributions have been presumed for any model input variables, the data for these variables should be used to test for goodness of fit for these distributions.

(5) Assessments based on data for exposure. A major reduction in the uncertainty associated with an exposure assessment can be achieved by directly measuring the exposure for a sufficiently large sample of members of the affected population. This reduction in uncertainty is achieved by eliminating the use of a model to predict exposure. The measured exposure levels can be used to directly estimate the population distribution of exposure and confidence interval estimates for percentiles of the exposure distribution. Direct confidence interval estimates also can be computed for other characteristics of the exposure distribution, such as the mean exposure.

These confidence interval estimates are then the primary characterization of uncertainty for the exposure assessment. Limitations of the data and design of the sample survey used to collect the data also should be discussed. If the sample was not a probability sample, this would again be an additional source of uncertainty.

(6) Summary. A summary of the primary methods recommended for characterizing uncertainty in exposure assessments is presented in Table 2. Virtually all exposure assessments, except those based on measured exposure levels for a probability sample of population members, rely upon a model to predict exposure. The model may be any mathematical function, simple or complex, that expresses an individual's exposure as a function of one or more input variables. Whenever a model that has not been validated is used as the basis for an exposure assessment, the uncertainty associated with the exposure assessment may be substantial. The primary characterization of uncertainty is at least partly qualitative in this case, i.e., it includes a description of the assumptions inherent in the model and their justification. Plausible alternative models should be discussed. Sensitivity of the exposure assessment to model formulation can be investigated by replicating the assessment for plausible alternative models.

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When an exposure assessment is based on directly measured exposure levels for a probability sample of population members, uncertainty can be greatly reduced and described quantitatively. In this case, the primary sources of uncertainty are measurement errors and sampling errors. The effects of these sources of error are measured quantitatively by confidence interval estimates of percentiles of the exposure distribution. Moreover, the sampling errors can be limited by taking a large sample.

Whenever it is not feasible to take a large sample, it is sometimes possible to obtain at least some data for exposure and model input variables. These data should be used to assess goodness of fit of the model and/or presumed distributions of input variables. This substantially reduces the amount of quantitative uncertainty for estimation of the distribution of exposure and is strongly recommended. It is recognized, however, that it may not be feasible to collect such data.

9.References. The references should contain a listing of all reports, documents, articles, memoranda, contacts, etc. that have been cited in the report.

10.Appendices. The appendices may contain such items as memoranda and letters that are not readily accessible, other tables of measurements, detailed lists of emission sources, detailed tables of exposures, process flow diagrams, mathematical model formulations, or any other item that may be needed to describe or document the exposure assessment.

Part B: Response to Public and Science Advisory Board Comments

I. Introduction

This section summarizes some of the issues raised in public comments on the Proposed Guidelines for Exposure Assessment published November 23, 1984 (49 FR 46304). Comments were received from 29 individuals or organizations. The Agency's initial summary of comments was presented to the Exposure Assessment Guidelines Review Group of the Science Advisory Board (SAB) on March 4, 1985. At its April 22-23, 1985, meeting, the panel provided the Agency with suggestions and recommendations concerning the Guidelines.

The SAB and public commentors expressed diverse opinions and addressed issues from a variety of perspectives. While most commentors supported the Guidelines, two urged withdrawal of the

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TABLE 2.--SUMMARY OF PRIMARY METHODS FOR CHARACTERIZING UNCERTAINTY FOR ESTIMATING EXPOSURES

Type and extent of data	Population characteristic being estimated	Primary methods for characterizing uncertainty	
		Qualitative methods	Quantitative methods
Measured exposures for a large sample of population members.	Distribution of exposure.	1. Limitations of the survey design and measurement techniques.	1. Confidence interval estimates for percentiles of the exposure distribution. 2. Goodness of fit for exposure models, if any have been postulated.
Measured exposures for a small sample of population members.	Summary parameter(s) of the exposure distribution, e.g., mean or a percentile.	1. Limitations of the survey design and. measurement techniques.	1. Confidence interval estimate for the summary parameter(s). 2. Goodness of fit for exposure models,. if any have been postulated.
Measured model input variables for a large sample of population members.	Distribution of exposure.	1. Limitations of the survey.design and measurement techniques. 2. Validity of the exposure model.	1. Confidence interval estimates for percentiles of the exposure distribution. 2. Goodness of fit for input variable distribution functions, if any have been postulated. 3. Estimated distribution of exposure based on alternative models.
Estimated distributions of model input variables.	Distribution of exposure.	1. Validity of the exposure model. 2. Limitations of the data. or other basis for the input variable distributions.	1. Confidence interval estimates for percentiles of the exposure distribution. 2. Goodness of fit for input variable distributions, if input variable data are available. 3. Estimated distribution of exposure based on alternative models.
Limited data for model input variables.	Minimum, maximum, and range of the exposure distribution.	1. Limitations of the data. 2. Validity of the exposure model.	If input variable data are very limited, e.g., some extant data collected for other purposes, quantitative characterization of uncertainty may not be possible.

document. The SAB Panel recommended that supplementary guidelines be written on the use of measurements in preparing exposure assessments. In addition, the Panel wished to see a greater emphasis in the current Guidelines on the use of measured data rather than models in generating exposure assessments. The Panel recommended that the technical support document entitled "Methodology for Characterization of Uncertainty in Exposure Assessments" be expanded with additional examples.

In response to the comments, the Agency has modified or clarified many sections of the Guidelines, and is planning to develop supplementary guidance in line with the SAB recommendations. The discussion that follows highlights significant issues raised in the comments, and the Agency's response to them. Also, many minor recommendations, which do not warrant discussion here, were adopted by the Agency.

II. General Information

A. Acceptable Latitude of Approach

Some commentors believe the Guidelines are too general and allow too much latitude in choice of approach and do not assure that "all" data, sources, limitations, etc. are considered before an exposure assessment is conducted. Others suggested that the Agency specify models to be used while others thought that only measured data should be allowed.

The Guidelines were developed to provide assistance in carrying out exposure assessments. The approach suggested is deliberately general in order to accommodate the development of exposure assessments with different levels of detail depending on the scope of the assessment. The Agency does not agree with the inclusion of such restrictive terminology as "in all cases." We cannot foresee all possible cases. We believe reasonable flexibility is a necessary ingredient for the proper implementation of the Guidelines while relying on uncertainty and sensitivity analyses to put the quality of the approach in perspective.

B. Technical Nature of Guidelines

Some commentors believe the language of the document is too technical for the lay person to understand; one commentor expressed misgivings concerning the "state-of-the-art" methods available for conducting exposure assessments.

While the Agency recognizes that the public has an interest in the Guidelines and invites comments from the public, the Guidelines are intended for use by technical/professional people. Providing guidelines written in lay terms would result in insufficient technical specifications to the professionals in the development of scientifically acceptable exposure assessments.

The Agency believes that the suggested procedures and methods in the Guidelines are commonly accepted. The Guidelines do not suggest the use of ad hoc, untested, and unvalidated procedures, but stress the use of the best scientific methods available with maximum analysis of existing data. This is both a scientific and practical approach that reflects the level of consensus within the Agency.

[51 FR 34053]

C. Measurements vs. Modeling

Some commentors support the use of measurements alone to develop an exposure assessment. Some believed there should be no data restraints; others thought all data should be validated. Other commentors argued for the use of simulation model estimates without measurements. One commentor objected to the use of unvalidated models to perform exposure assessments. In its review, the SAB strongly encouraged the Agency to develop a supplement to the current Guidelines on the development and use of measurements for exposure assessments.

The Agency encourages the use of validated measurements when available. The Guidelines specifically state that "Reliable, analytically determined values should be given precedence over estimated values. . ." and analytically determined values ". . .can be used to calibrate. . . models. . .to assess environmental distribution." Furthermore, in practice, exposure assessments performed by the Agency use published models with varying degrees of testing and validation. It is our belief that transport process models have been adequately validated over many years in most cases.

Furthermore, the Agency has revised the Guidelines to reflect the SAB suggestions that exposure assessments based on reliable measured data are preferred over model estimates whenever feasible.

III. Data Availability and Uncertainty Analysis

A. Information Uses

Some commentors asked for guidance in the use of information that may be false and how to deal with the potential situation when different models give different results. Others asked for model selection criteria.

The Guidelines clearly state the considerations that need to be addressed when assembling information bases for exposure assessments. Two considerations are: qualitative and quantitative nature of the data and the reliability of the information. Whether the exposure assessment is based on measurements or simulation model estimates, an evaluation of uncertainties associated with the data including source data and assumptions is necessary and important.

When there is uncertainty in the scientific facts, it is Agency policy to err on the side of public safety. The Agency intends to be realistic, but will not arbitrarily select midranges of environmental distributions that may compromise human health. In addition, quality assurance is an important matter that requires detailed attention. The collection of measured data and the development of methods to collect measurements are done by another office within the EPA. These issues will be handled by the Office of Acid Deposition, Environmental Monitoring, and Quality Assurance as they develop the supplemental guidelines for measurement of exposure.

Substantial work is currently being done on the development of mathematical model selection criteria. Results of these efforts will be published as a technical support document containing detailed information to further implement the Guidelines.

B. Worst-Case Estimates

A few commentors were concerned that worst-case estimates would be used when data are nonexistent or limited. The Guidelines do not encourage the use of worst-case assessments, but rather the development of realistic assessments based on the best data available.

A technical support document and a substantial section of the Guidelines currently discuss evaluation of uncertainty in order to produce objective assessments using the best (not worst-case) estimates available either for preliminary or in-depth exposure assessments. However, the Agency will err on the side of public health when evaluating uncertainties when data are limited or nonexistent.

IV. Evaluation of Uncertainties

A. Uncertainty Analysis

Many commentors felt that the sections of the Guidelines that dealt with uncertainty needed amplification while some sections as written were confusing. Some urged that uncertainty evaluation be presented and documented for each section within a specific exposure scenario in order to judge the overall plausibility of the assessment in reaching regulatory decisions.

Since the accuracy of an exposure assessment is influenced by the degrees of uncertainty contained in both data and assumptions, the Guidelines call for the evaluation of these uncertainties. The technical support document, Methodology for

Characterization of Uncertainty in Exposure Assessments (available from the National Technical Information Service, PB85-240455), describes in detail how such analyses can be performed. The Guidelines suggest that the uncertainty characterization include a discussion of the limitations of the data and estimation procedures as the justification for the model chosen. A sensitivity analysis of the exposure assessment is appropriate if the data were only able to support the estimates of ranges of the input variables. By identifying model input variables that determine the bounds on the distribution of exposure, the range of exposure, which results as individual model input variables are varied from minimum to maximum possible values as other variables remain constant, constitutes the sensitivity analysis. Further sensitivity of model formulation can be examined by repeating the sensitivity analysis for plausible alternative models.

Nothing in the Guidelines precludes estimation of uncertainty for each specific exposure scenario. The Agency has encouraged the evaluation of uncertainty in each aspect of the exposure assessment, which could impact the total risk estimate. It is important to estimate the level of uncertainty in risk assessments so that decisions based on risk assessment will reflect total uncertainty. The information presented in the Guidelines or the technical support documents properly and adequately describes the extent and quality of appropriate uncertainty analysis. Recognizing that the basis for the decision to refine a preliminary exposure assessment involves risk management, the Agency, at the suggestion of many commentors, decided to strike from the Guidelines the paragraph beginning "If the maximum possible exposure. . . ." in section III.B.8.d.(2).

B. Population Characterization

The Guidelines state that identification of populations and subpopulations at potentially high exposure forms the basis of the populations to be studied. Separate studies of sensitive subpopulation can also be included. Population characteristics, such as age and/or sex distributions, can be derived from the use of geographic and activity-specific data. Uncertainty related to estimation of a population characteristic include a discussion of the data limitations and the estimation procedures. In addition, uncertainty in estimating sizes of sensitive subpopulations should include estimates of confidence intervals.

Some commentors suggested the inclusion of additional characteristics, such as occupational and life style factors, and the inclusion of additional guidance concerning potential pitfalls when conducting population exposure

[51 FR 34054]

assessments. Others expressed concern that the exposure of a particular subpopulation would be combined with other exposures to produce an average exposure level for the general population.

The section describing population characterization encompasses, in general terms, the many characteristics that may be available, including life style factors, to describe exposed populations. The Agency agrees that there are difficulties associated with epidemiologic studies. The relationship between exposure assessments and epidemiologic studies is currently being investigated and will be the subject of a future technical support document and the further refinement of the Guidelines.

V. Clarification of Terminology

A. Exposure vs. Dose

Commentors expressed concern with the American Society for Testing and Materials (ASTM) definition of exposure. Concern was also raised about the assertion that exposures can be estimated when biological tissues for fluid measurements indicate the presence of a chemical. Some commentors found difficulty in the wording of the last sentence in section II.A., specifically "The route of exposure. . .impacts. . .the overall exposure. . . ."

It is the Agency's opinion that the members who served on the ASTM Committee E-47 had expertise in exposure assessment. The scientists and engineers cumulatively possessed many years of experience in exposure assessment. In addition, no technical society has presented an alternate definition of exposure. The Agency will consider changing the definition if a reasonable alternate definition is written and agreed upon by the scientific community.

The Agency agrees with the commentors who were concerned that the wording provided in the Guidelines that the presence of a chemical in biological tissue can be used to estimate exposure is not correct in all cases. Consequently, the word "can" was changed to "may" to reflect the current level of understanding between tissue residue and exposure (II.A., 2nd paragraph, 4th sentence). The Agency agrees with several commentors' concerns that the route of exposure impacts the overall absorbed dose, not the overall exposure, and the Guidelines reflect this change (II.A., last sentence).

B. Mixtures and Synergism

Some commentors thought more discussion was necessary on the effect of chemical mixtures and potential synergistic effect on exposure. The Guidelines for the Health Risk Assessment of Chemical Mixtures includes a discussion of chemical synergism. The Agency recognizes the need to do further work in the area of exposure to mixtures. It is recommended that this be identified as an area requiring further research.

REC 6232

These Guidelines stress the need to determine the products into which the chemical might degrade or react in the environment and to determine if any of these products are ecologically or biologically harmful.

C. Removal and Creation Steps

Some commentors urged that more emphasis be placed on changes that occur once the materials have entered the ambient environment. Other commentors argued that our current understanding will not allow a comprehensive treatment, particularly for metabolic processes.

These Guidelines state the need to address how a chemical agent moves from the source to the exposed population, which may result in the estimation of geographic and temporal distributions in various environmental media. The Guidelines also state the need to know such factors as, for example, whether the chemical agent bioaccumulates or by what mechanism the agent is removed from each medium and the role of any degradation products on ecological safety. We have already stated that guidance for analysis of metabolism data is an area of ongoing research which includes consideration of metabolism data in the calculation of whole organism dose from one species to another.

VI. Purpose, Philosophy, and Results

Several commentors raised questions related to the basic style of the Guidelines. Among the issues raised were:

- the role of exposure assessment in risk assessment/risk management (many comments directed to appropriateness of Figure 1);
- statutory/regulatory authority and uses of results; and
- the need for peer review of assessments and periodic updating of Guidelines.

A deliberate effort to separate risk assessment from risk management has been made. The management of complex issues such as procedural issues, which include coordination or linkage among divisions in the Agency, are best dealt with by management and not in Guidelines.

The decision pathway (Figure 1) was included in the Guidelines at the recommendation of the SAB. It has drawn many comments. The changes suggested would include additional detail and steps that would diminish the value of the graphic. However, the figure has been truncated to remove risk management steps.

In order to remain consistent with the separation of risk assessment and risk management, any directions to consider applicable laws or regulatory decisions have been stricken from the Guidelines.

The Agency agrees that peer review is an important aspect of the assessment process. However, emergency cases may not allow peer review in preliminary assessments. All nonemergency exposure assessments have been peer reviewed and will continue to be peer reviewed. Finally, it is clearly stated in the Guidelines that periodic revision of the document will be done to reflect the benefit of experience and knowledge.

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Exhibit C



Guidance Document

First, Second, and Third Tier Review of Toxic Air Pollution Sources (Chapter 173-460 WAC)

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Publication and Contact Information

This document is available on the Department of Ecology's website at www.ecy.wa.gov/biblio/0802025.html.

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Introduction

Ecology and local air quality agencies use first, second and third tier review to regulate emissions of toxic air pollutants. Hundreds of potentially toxic chemicals are released into the air each year in Washington. Excess exposures to these chemicals can cause serious illnesses and premature deaths. Widespread exposure probably accounts for some of the occurrences of various types of cancers within our population.

This publication is to help toxic air pollution sources understand and use the first, second, and third tier review sections of the notice of construction application. Requirements for first, second, and third tier review are found in Chapter 173-460 Washington Administrative Code (WAC).

First Tier Review

What is first tier review?

First tier review is part of a notice of construction application for a new or modified toxic air pollutant source. It compares your project emissions to the toxic air pollutant values listed in WAC 173-460-150.

How do I know if I need to do a first tier review?

You will need to do a first tier review if potential emissions from your project exceed the de minimis emission levels specified in WAC 173-460-150. Your potential emissions are the expected worst-case emissions from your facility, considering its physical and operational design.

How do I get first tier review?

You do not need to submit a separate petition for first tier review. The notice of construction application you file with the permitting agency serves as your petition for first tier review. Typically, the permitting agency will conduct a first tier review on every notice of construction application it receives.

What issues must I address before the order can be issued?

You must show that the emission increases from all new or modified emission units are below the acceptable source impact level (ASIL):

- after application of best available control technology for air toxics (tBACT); and
- at any location outside of your property boundary.

You can find the ASILs in WAC 173-460-150.

How can I show that emissions are below the ASIL?

You can show emissions are below the ASIL by:

- demonstrating that the emissions are at or below the small quantity emission rates (SQER);
- using a screening model (such as AERSCREEN); or
- using a refined air dispersion model (such as AERMOD).

What can I do if emissions exceed the ASIL?

You have several options, including:

- revise the project and application;
- negotiate an enforceable limit;
- off-set the emissions by reducing emissions from another on-site emission unit;
- submit a second tier petition;
- submit a third tier petition; or
- withdraw the application.

How do I off-set the new emissions by reducing them at another emission unit?

You must meet several criteria in order to get this option approved:

- the emission reductions must be actual reductions;
- the reductions must be modeled against all affected receptors; and
- when the emission increases and reductions are modeled together at the receptor, the modeling must demonstrate that the off-set proposal results in emission values lower than the ASIL.

Who approves a first tier analysis?

Your permitting agency will review the first tier analysis and either approve or deny it.

What happens if my first tier analysis is approved?

If your permitting agency approves the first tier analysis, it will include the approval decision in an "Order of Approval." For permits issued by Ecology, guidelines for issuing this order and requirements for notifying the public are in WAC 173-400-110. Other permitting agencies may have their own guidelines. The order may contain the following:

- emission limits for each toxic air pollutant (TAP) subject to review;
- a method of assuring compliance with TAP limits (usually monitoring, reporting, and operation restrictions);
- a statement of the Best Available Control Technology for Air Toxics (tBACT) for each TAP; and
- enforcement criteria for voluntary emission reductions, including monitoring, record-keeping, and reporting requirements.

What happens if my first tier analysis is not approved?

If emission increases still exceed the ASIL and other options do not work, you can submit a petition for second tier review.

Are there any exemptions from the first tier review process?

Yes. A list of exemptions from new source review is in WAC 173-400-110. Also, your permitting agency might have its own list of exemptions. Exemptions for toxic air pollutants and criteria pollutants are related because the permit process procedures, definitions, and exemptions are the same for both.

Exemptions are divided into two broad categories:

- emission unit and activity exemptions; and
- exemptions based on emissions.

To see if your project is exempt, read the emission unit and activity listing in WAC 173-400-110(4 and 5), and contact your permitting agency. De minimis emission values for toxic air pollutants are in WAC 173-460-150. You must consider all of the new or modified emission units together. For the project to be exempt, emissions from all of the individual emission units added together must be below the de minimis values.

Second Tier Review

What is second tier review?

Like first tier review, second tier review is part of a notice of construction application for a new or modified toxic air pollutant source. You need to do a second tier review if any of your project's toxic air pollutant emissions exceed the ASIL after you have completed a first tier review. In this step of the notice of construction application process, the applicant submits a health impacts assessment to Ecology. Ecology will review the health risks associated with your project.

How do I get second tier review?

Submit a petition for second tier review to Ecology, with a copy to the permitting agency that has jurisdiction. The application form includes the Health Impact Assessment Checklist and is available at: http://www.ecy.wa.gov/biblio/ecy070415.html

What is the review process for a second tier petition?

Ecology's air toxics engineer, toxicologist, and air quality modeler work together on second tier petitions. The review process includes:

- pre-application conference;
- a second tier petition and payment of applicable fees;
- HIA protocol; and
- HIA document.

Pre-application conference

After Ecology is notified that a proposed project requires second tier review, Ecology recommends you have a pre-application conference with Ecology staff before you submit a second tier petition. The pre-application conference:

- helps you identify regulatory issues before you commit a significant amount of time and resources toward a specific course of action;
- lets you know early in the process what you need to address in the Health Impact Assessment, which can avoid unnecessary delays later on; and
- helps you identify the review criteria for your project, so that you can present your proposal accurately.

You and your consulting team need to attend the conference. The team typically includes an engineer, plant operations manager, and other specialists involved in your proposal. You and your team will meet with an Air Quality Program engineer, toxicologist, and air quality modeler.

The permit writer who reviewed your first tier analysis will also attend, whether they work for Ecology or a local air quality agency.

At the conference, you, your team, and Ecology staff will review the following information:

- required permits, approvals, and fees;
- protocol for the health impact analysis;
- the refined air dispersion modeling methods used to estimate TAP levels;
- typical project review timelines;
- application regulations;
- the public hearing process; and
- any other questions you might have.

The amount of information Ecology can give you at the conference depends on the level of detail you provide about the project. Because the conference takes place early in the process, Ecology will not be able to anticipate all the relevant project details. Ecology will give you a protocol to follow that tells you what to do next.

The conference **will not** provide:

- a detailed toxicology analysis or modeling review; or
- a final recommendation on a proposal.

To schedule a pre-application conference, call Matt Kadlec at (360) 407-6817 or Gary Palcisko at (360) 407-7338. They will work with you to find a time that works for everyone. The conference is typically held at Ecology's Headquarters building at:

300 Desmond Drive SE
Lacey, WA 98503

Second tier review petition and fees

After the pre-application conference, the applicant submits to Ecology a petition and applicable fees for second tier review, with a copy to the permitting agency that has jurisdiction. The application form includes the Health Impact Assessment Checklist and is available at: http://www.ecy.wa.gov/biblio/ecy070415.html. You can find more information on applicable fees starting on page 31.

HIA protocol

The applicant must also submit an HIA protocol. Ecology will review the HIA protocol after the applicant submits the $10,000 initial fee with the HIA protocol and completed second tier application. Basic information required for HIA protocol is included later in this document.

HIA document

After Ecology approves the HIA Protocol, the applicant prepares and submits an HIA document. Ecology toxicologists will review the HIA to determine if health impacts are adequately characterized. Ecology will provide substantive and non-substantive comments on the HIA document and will request the applicant revise the HIA document if necessary. This process can be repeated until the applicant prepares an acceptable final HIA document. Ecology's project engineer or delegate will review portions of the HIA that involve the project's engineering specifications. Likewise, Ecology's dispersion modeler will review portions of the HIA that involve toxic air pollutant (TAP) concentration modeling. Following confirmations by the engineer and modeler, Ecology's project toxicologist will review risk assessment portions of the HIA. The toxicologist will then communicate to all parties the results of the HIA review.

Once an acceptable HIA document has been prepared, Ecology will prepare a brief staff report which summarizes Ecology's review of the HIA and includes recommendation(s) to the local permitting authority about the petition. Ecology will:

- post the applicant's final HIA document, Ecology's staff report, and Ecology's cover letter on Ecology's air toxics review web page (http://www.ecy.wa.gov/programs/air/Tier2/Tier2_infosite.html);
- make a final recommendation for approval or denial of the project; and
- send the recommendation to you and the permitting agency, which issues the actual approval order.

Ecology's decision on the second tier petition must be included in the final decision on the notice of construction application.

Who approves a petition for second tier review?

Only Ecology staff can review, approve, or deny a second tier petition.

What materials should I provide, and when?

In the pre-application conference, you will be given a protocol for preparing the required documentation for the second tier petition. After the pre-application conference, the permitting agency (either a local air quality agency or one of Ecology's regional offices) will provide a preliminary order of approval directly to Ecology. Then, follow this protocol to provide information:

Provide to Ecology:

- the results of the refined air dispersion modeling for all pollutants that exceed the SQERs; and
- a full copy of the second tier petition (containing a Health Impacts Assessment).

Provide to the permitting agency that reviewed your first tier analysis:

- a full copy of the second tier petition.

Is public involvement required?

Yes. Public involvement is required for any project that needs a second tier review. It may be limited to a public notice and public comment period, or Ecology may determine that a public hearing is needed. If a public hearing is held, Ecology and the permitting agency will hold a joint public hearing to streamline the public review process. Ecology staff will explain the second tier recommendation at the public hearing. You and your consultants should be prepared to explain your project and answer questions at the public hearing.

What can I do if Ecology does not approve the second tier petition?

If Ecology denies the second tier petition, the permitting agency may not approve the project. At that point, you have the following options:

- revise the project and application;
- propose emission reductions from an off-site emission unit;
- submit a third tier petition; or
- withdraw the application.

My project triggers second tier review. Are there any exemptions from the second tier review process?

No. If your project triggers second tier review, you must submit a second tier petition to Ecology before your project can be approved. If you think that your project will not meet the approval criteria of a second tier review, you may opt to submit a third tier petition instead of a second tier petition.

Third Tier Review

What is third tier review?

You can submit a petition for third tier review if the health risks from your project exceed the second tier review thresholds. In third tier review, your petition requests that the director of Ecology approve the project based on a risk management analysis.

How do I submit a petition for third tier review?

Submit your petition for third tier review to Ecology, with a copy to the permitting agency that has jurisdiction.

What materials should I provide, and when?

The materials required for a third tier review are the same as for a second tier review. You may submit the third tier petition at the same time you submit the second tier petition. Prior denial of a second tier petition submitted under WAC 173-460-090 is not required. The permitting agency (either a local air quality agency or one of Ecology's regional offices) will provide a preliminary order of approval directly to Ecology. Then follow this protocol to provide information:

Provide to Ecology:

- the results of the refined air dispersion modeling for all pollutants that exceed the SQERs;
- a full copy of the third tier petition (containing a health impacts assessment); and
- a description of environmental benefits of the proposal.

Provide to the permitting authority that reviewed your first tier analysis:

- a full copy of the third tier petition.

In addition to the above documentation, you may propose voluntary measures to reduce community exposure to pollutants emitted by your project. Voluntary measures might include voluntary reduction of emissions from existing unmodified emissions units at your facility or at another facility.

What is the review process for a third tier petition?

Ecology's air toxics engineer, toxicologist, and air quality modeler work together to prepare a recommendation to the director of Ecology to either approve or deny a third tier petition. Within 30 days after you've submitted the petition, Ecology will:

- review it for completeness; and
- provide you a letter stating the petition is complete or listing needed information if it is not complete.

Within 60 days after determining that your petition is complete, Ecology will:

- write a draft technical support document and send it to you and the permitting agency for review and comment;
- address any questions or concerns brought up during review;
- together with you, initiate a minimum 30-day public notice and public comment period;
- together with you, schedule a public hearing.

After the public hearing, Ecology will review and address all comments. Ecology will then prepare the final recommendation and technical support document, and send them to you and the permitting authority, which issues the actual approval order.

Ecology's final recommendation on the third tier petition must be included in the final decision on the notice of construction application.

What criteria will Ecology follow to approve or deny a petition for third tier review?

Before approving your third petition, Ecology's director must find that the following conditions are met:

- proposed emission controls represent at least tBACT;
- a health impact assessment addressing all of Ecology's requirements has been completed; and
- approval of the project will result in a greater environmental benefit to the state of Washington.

Is public involvement required?

Yes. Public involvement is required for any project that needs a third tier review. The public involvement process must include a public notice and public comment period, as well as a public hearing. The purpose of the public hearing is to present the results of the third tier review and to

answer any questions from the public. You and your consultants should be prepared to explain your project and answer questions at the public hearing.

What can I do if Ecology does not approve the third tier petition?

If Ecology denies the third tier petition, the permitting agency may not approve the project. At that point, you have the following options:

- revise the project and application;
- propose emission reductions from an off-site emission unit; or
- withdraw the application.

My project triggers third tier review. Are there any exemptions from the third tier review process?

No. If your project triggers third tier review, you must submit a third tier petition before your project can be approved.

Health Impact Assessment

This section helps toxic air pollution sources prepare a health impact assessment (HIA) as part of second tier or third tier review, as required in Chapter 173-460 WAC. Ecology's Air Quality Program recommends that permit applicants preparing an HIA refer to the Air Toxics Hot Spots Program Guidance Manual for Preparation of Health Risk Assessments, published in March 2015 by the Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. (See the citation list at the end of this document.)

The guidance manual addresses the techniques used to assess health risks of airborne contaminants released by new or modified stationary sources like those permitted in Washington. Most of the techniques described in the Hot Spots Program Guidance Manual are common to other regulatory risk assessment applications. However, applicants may need additional analyses depending on their unique circumstances. Applicants should contact Ecology before beginning work on their HIA in order to assure that all WAC 173-460-090 requirements will be satisfied. In general, using the Hot Spots Program Guidance Manual risk assessment procedures and report presentation will speed up Ecology's review. It will also minimize the chance that applicants will need to revise and resubmit their HIA.

What is an HIA?

An HIA looks at how emissions of toxic air pollutants from a specific project will affect public health. It involves several steps, including hazard identification, exposure analysis, toxic response, and risk characterization.

Who needs to submit an HIA?

Second and third tier petitions always need an HIA.

How do I submit an HIA?

When you submit a petition for a second or third tier review, the HIA will be included in your pre-application conference.

Why do I need a pre-application conference?

Pre-application conferences help you learn about regulatory issues before you commit a significant amount of time and resources to a specific course of action. At the pre-application conference, Ecology will tell you what issues need to be addressed in the HIA. This will help you avoid unnecessary costs and delays.

What documentation do I submit with an HIA?

Because each HIA is tailored to fit a specific project, each one may require different documentation. Generally, you will need to include:

- A map of the site and neighborhood showing:
    - location of new or modified emission points;
    - local zoning of the affected area;
    - locations of and distances (in meters) between the sources; and
    - residences, businesses, roadways, public properties, and public or private facilities serving population subgroups such as schools, nursing homes, hospitals, and for certain TAPs, private and public drinking water wells (note the well depth).

- Hazard identification, including:
    - a list of all TAPs (as defined in Chapter 173-460 WAC) that will be emitted by the facility, and
    - a physical description of those TAPs.

For details, refer to the sections below titled "Dispersion Modeling Protocol and Report Contents," "Contents of the Health Impact Assessment," and "Outline of the Health Impact Assessment Report."

What do I need to submit about the TAP concentrations?

You must show how you derived the TAP concentration levels. Include the following:

- emission rates, in grams per unit of time, at the maximum possible rate;
- modeled concentration estimates in $\mu g/m^3$ or ppb (disclose the emissions factors used in modeling);
- any available monitoring measurement results; and
- any uncertainties and assumptions in deriving concentration levels.

You must also disclose the cross-media transport of the emissions in the environment, the environmental persistence, the degradation pathways, and the final fate of the toxic air pollutants. This means describe the movement of proposed toxic air emissions from air into water and/or soil which people may be exposed to. Generally, the inhalation pathway of exposure is the largest contributor to the total dose. However, there are situations where a non-inhalation pathway contributes substantially to total dose. You can get detailed guidance on this subject from a variety of authorities, for example EPA's Guidelines for Exposure Assessment (1992) and Exposure Factors Handbook (2011) and OEHHA's Air Toxics Hot Spots Program Guidance Manual for Preparation of Health Risk Assessments (2015, chapter five). (See the citation list at the end of this document.)

What materials must I include to assess exposure?

You must identify the TAP exposure pathways, including the following:

- Disclose the total daily intake of TAPs attributable to the project source as well as the background sources. EPA has some ambient air concentration estimates in their NATA database.
- Estimate the durations of exposure, including long-term averages, short-term peaks and worst-case scenarios. Detail the exposure parameters associated with sensitive population subgroups. You can get detailed guidance on this subject from a variety of authorities, including EPA's Guidelines for Exposure Assessment (1992) and Exposure Factors Handbook (2011) and OEHHA's Air Toxics Hot Spots Program Guidance Manual for Preparation of Health Risk Assessments, (2015, chapter five). (See the citation list at the end of this document.) Identify the potentially exposed populations. Give special emphasis to any subpopulations that might be unusually susceptible to any TAPs emitted by your project.
- Using the information on the location of potentially exposed populations, show the TAP concentrations at the points where people might be exposed to the pollutants in question.

What issues do I need to address in the toxicity discussion?

The toxicity discussion should focus on the effects relevant to the proposed toxic air pollutant concentrations. The following issues should be thoroughly discussed:

- toxic effects of the toxic air pollutants;
- exposure levels associated with specific effects;
- exposure patterns and duration of exposure as established by studies of the toxic effects;
- any quantitative, chronic toxicity values including:
    - inhalation reference concentration or similar hazard-based concentrations;
    - cancer unit risk factor estimates;
    - slope factor or carcinogenic potency estimates; and
- any quantitative intermediate and short-term acute toxicity values.

What issues do I need to address in the risk/hazard assessment section?

Provide a discussion of offsetting reductions in risk that might accrue to society as a result of completing the proposed facility modification. This typically includes a:

- qualitative discussion of the risks;
- quantitative discussion of the risks with appropriate toxicity measures, calculated cancer risks, and the hazard index;
- discussion of uncertainties in the risk assessment;

- discussion of acceptability of risk with regard to guidelines in Chapter 173-460 WAC; and
- discussion of the extent to which the proposed facility might affect human health.

What issues do I need to address in the uncertainty section?

There is always some level of uncertainty associated with risk assessment. While uncertainty encompasses those factors that are not known, and could be eliminated or reduced with scientific studies, we are not asking you to conduct original research. We want you to disclose your level of confidence in the data used to substantiate your conclusions.

Risk can be over or underestimated because of many factors, including:

- extrapolation of toxicity data in animals to humans;
- uncertainty in the estimation of emissions;
- uncertainty in the air dispersion models;
- interactive effects of exposure to more than one carcinogen or toxicant;
- uncertainty in the exposure estimates; and
- uncertainty about the extent of toxicant susceptibility variation within human populations.

The HIA mentions subpopulations. What is an example of a sensitive or understudied subpopulation?

Children are a subpopulation whose hematological nervous, endocrine, and immune systems are still developing. They may be more sensitive to the effects of carcinogens on their developing systems. These sensitivities are not included in the worker population and risk estimates based on occupational epidemiological data, which are based on adult populations.

Who reviews the HIA?

Ecology's Air Quality Program toxicologists review HIAs. While the toxicologists are reviewing the HIA, the engineer and dispersion modeling staff review other portions of the second or third tier petition. They determine if tBACT and refined modeling are sufficient.

Note that though Ecology's toxicologists review HIA documentation; they are not authorized to prepare the applicant's assessment.

What can I do if Ecology does not approve the HIA?

You have the following options:

- revise the project and application;
- propose emission reductions from an off-site or on-site emission unit;
- submit a third tier petition (See WAC 173-460-100); or
- withdraw the application.

Where can I get more information on the HIA?

Contact either of the Air Quality Program toxicologists:

Matt Kadlec
(360) 407-6817
matt.kadlec@ecy.wa.gov

Gary Palcisko
(360) 407-7338
gary.palcisko@ecy.wa.gov

Contents of the Health Impact Assessment Protocol

Applicants must submit a Health Impacts Assessment Protocol before submitting a draft HIA. The protocol ensures that the applicant will submit sufficient information and is intended to prevent delays caused by incomplete analyses. The protocol should contain a description of how the applicant intends to estimate the health impacts posed by TAPs subject to second tier review. Generally, an applicant will need to provide an air quality analysis that demonstrates compliance with both national ambient air quality standards and toxics review. The following items need to be included in the Health Impact Assessment Protocol:

Emissions Estimate

- Quantify short- and long-term emission rates,
  - mass per hour, day, year;
- Report emission factors and their source and justification;
- Report applicable emission standards and ASILs;
- Provide background concentrations, if known.

Source Characteristics

- Site plan showing fence line, emission units, and other structures;
- Modeling parameters.

Model and Model Assumptions

- AERMOD is to be used in most situations.

Meteorology

- Identify representative surface meteorological data.
  - 5 years of continuous quality-assured/quality-controlled meteorological data/QC'd upper air data

Receptor Grid

- Recommended receptor grid spacing to ensure that sampling error does not reduce the maximum computed concentration by more than 10%:

Distance from Source [m]	Grid Spacing [m]
0 – 150	12.5
150 – 400	25
400 – 900	50
900 - 2000	100
2000 - 4500	300
> 4500	600

Deposition

- For some TAPs, applicants may need to estimate deposition so that multi-pathway exposures can be assessed. These TAPs include:
    - 4,4'-Methylene dianiline
    - Creosotes
    - Diethylhexylphthalate
    - Hexachlorocyclohexanes
    - PAHs
    - PCBs
    - Cadmium & compounds
    - Chromium VI and compounds
    - Inorganic arsenic and compounds
    - Beryllium and compounds
    - Lead and compounds
    - Mercury and compounds
    - Nickel
    - Fluorides (including hydrogen fluoride)
    - Dioxins and furans

Model Output/Results

- Files provided to Ecology
- Modeling results to be used to demonstrate compliance or assess risk

Receptors

- Identify receptors where the ASIL is exceeded.
  - Identify maximally-exposed residential, workplace receptors and point(s) of maximum impact. (**Note**: Maximally-impacted receptors around a site can vary depending on concentration averaging time.)

Short-term and long-term risk-based exposure concentrations

Depending on which chemicals are being evaluated and the type of receptor that is impacted, short-term and/or long-term ambient concentrations are needed.

- Short-term = typically 1-hr., 8-hr., 24-hr. concentrations
- Long-term = typically annual average concentration

Acute and chronic non-cancer hazard (1-hr., 8-hr., 24-hr., annual exposure concentrations)

For all non-carcinogenic toxic air pollutants exceeding their SQERs:

- Identify relevant short-term and long-term non-cancer toxicity values for chemicals exceeding SQERs
  - For example: EPA RfCs, OEHHA RELs, ATSDR MRL

- Calculate Hazard Quotients (HQ)
  - Exposure concentration ($\mu g/m^3$) divided by risk-based concentration ($\mu g/m^3$)

- For multiple chemicals with similar toxic effects (i.e., same tissue or organ system), calculate Hazard Index
  - Sum hazard quotients with same averaging time and similar toxic effects for all toxic air pollutants that exceed the SQER

- Determine the frequency and geographic extent that short- and long-term concentrations exceed relevant toxicity values (i.e., HQs > 1)

Cancer risk (annual exposure concentrations)

For all carcinogenic toxic air pollutants exceeding their ASILs and SQERs:

- Identify existing inhalation unit risk factors or cancer potency factors
- Calculate lifetime increased cancer risk from exposure to each TAP
- Calculate the sum of cancer risks for all chemicals emitted in excess of SQER to produce the total increased cancer risk from project
- Identify population exposed in excess of one per million and estimate total population risk from project

Outline of the Health Impact Assessment Report

In general, the HIA should provide information about:

- Project description
- Emissions
- Air dispersion modeling
- ASIL screening
- Risk assessment
  - Hazard identification, exposure, dose-response (which criteria are used to estimate risk), risk characterization, uncertainty
  - Discussion of acceptability of risk

Recommended Outline of an HIA

Note: Not every item below will be required in every HIA report. Ecology staff will discuss the specific requirements of your HIA report during the pre-application meeting.

Project description

- Project overview
- Physical location
  - Address, city, county
  - Land use (zoning) in areas adjacent to project
  - Site map showing emission points, property boundary, off-site receptors (outside any limited public access boundary maintained around the facility, and the locations of any buildings and their usage (i.e., housing, business, school, etc.))

SQER and ASIL comparison

- Comparison of facility emission rates of TAPs to their respective SQER
  - Model concentrations of those that exceed their SQER
  - Compare results to their ASIL(s)
- Refined dispersion modeling to estimate off-site concentration of those TAPs to their respective ASILs
- If a chemical exceeds its ASIL at an off-site location, then a health impact assessment is performed.

Hazard identification

- Identification of the TAPs that may pose a threat to human health (those that exceed ASILs and those that exceed SQERs with similar effects).
- Physical description of the TAP (s) emitted in amounts greater than their SQER and overview of each chemical's toxicity (i.e., affected tissue/organ and the critical effect. For example, acrolein: Eyes and respiratory tract; eye irritation and respiratory epithelium lesions).
- Potential for cross-media transport in the environment, environmental persistence, degradation pathways, and final fate of the TAP(s). Provide public water solubility data, and degradation half-lives in air, water, and soil.

Identification of places with potentially-exposed people (off-site)

- For example, residences, businesses, parks, schools, hospitals within the geographic extent where estimated concentrations are greater than the ASIL.

Discussion of TAP concentrations

- Using the information on location of potentially-exposed populations, TAP concentrations that exceed ASIL(s) should be given at points where humans might come into contact with the TAP(s).
- Derivation of the concentration levels should be discussed.
- Concentration estimates, in $\mu g/m^3$ by modeling and emissions factors used in modeling.
  - Averaging times may vary depending on the project and potentially-exposed receptors, but examples are:
    - Maximum 1-hr., 8-hr., and 24-hr. exposure – for chemicals that have the potential to cause acute effects over a short time
    - Annual average exposure – for chemicals that have the potential to cause cancer or other chronic effects
    - Display results on maps

Exposure assessment

- Identification of TAP exposure pathways
- Development of total daily intake attributable to source and background sources (existing ambient air concentration estimates for some pollutants are available in EPA's NATA)
  - Durations of exposure, including long-term averages, short-term peaks, and worst-case scenarios
  - Exposures at maximally-effected residence(s), business(es), and fence line (limited public access boundary) places
  - Exposure parameters associated with sensitive population subgroups. For example, situations where children may be frequently exposed may warrant child-specific exposure parameters.

Toxicity (should focus on effects relevant to proposed TAP concentrations)

- Description of toxic effect(s)
- Exposure levels associated with effect(s)
- Exposure pattern and duration of exposure in studies of toxic effects
- Any quantitative, chronic toxicity values
  - Inhalation reference concentration or similar hazard-based concentrations
  - Cancer unit risk factor estimates
  - Oral risk based concentrations for substances evaluated through multi-pathways of exposure
- Quantitative intermediate/short-term toxicity values
- Discussion of how the site-specific toxicity value considers exposure duration and frequency at the site

Risk/hazard characterization

- Qualitative discussion of the risk(s)
- Quantitative discussion of the risk(s)
  - With appropriate measure(s) of toxicity
  - Calculated cancer risk(s)
- Hazard quotients and hazard indexes, if there are any co-acting combinations of TAPs. (Critical effect –specific hazard indexes for TAPs emitted at rates above their SQERs for any co-acting combination of such TAPs.)

Discussion of uncertainty and variability of numeric values used in the HIA

A HIA is composed of many numeric values – each with its own uncertainty and/or variability. Uncertainty is that which is not known about a factor that influences its value. Variability occurs when a quantity that is repeatedly measured exhibits values that differ. It can be quantified using descriptive statistics such as the range.

Discussion of acceptability of risk with regard to guidelines in Chapter 173-460 WAC

- Increased cancer risk is no more than 10 per million
- Non-cancer hazard quotients or indexes are less than one, or Ecology determined that non-cancer hazards are acceptable

Second and Third Tier Review Timeline

Step 1: Applicant submits to Ecology:

- full copy of the second or third tier petition (including all of the elements discussed in the HIA protocol);
- results of the refined air dispersion modeling for all pollutants that exceed the ASILs;
- preliminary order of approval issued by the permitting agency (The permitting agency will generally provide the preliminary order of approval directly to Ecology. The permitting agency is either a local air quality agency or one of Ecology's regional offices.); and
- description of environmental benefits of the proposal (for a **third tier petition**).

Step 2: Within 30 days after receiving the petition, Ecology will:

- review it for completeness; and
- issue a letter stating the petition is complete or list all information needed to complete the petition.

Step 3: Within 60 days after determining a petition is complete, Ecology will:

- write a draft technical support document and send it to the applicant and permitting agency for review and comment;
- address any questions or concerns brought up during that review;
- for a **second tier petition**, make a final decision to recommend approval or denial of the project, and send the **final second tier** recommendation to the applicant and the permitting agency;
- for a **third tier petition**, prepare a third tier review recommendation and technical support document for public comment, and send them to the applicant and the permitting agency.

Step 4: Permitting agency initiates a public comment period on the draft notice of construction approval

After receiving Ecology's recommendation on the second or third tier petition, the permitting agency and the applicant must:

- provide a minimum 30-day public notice and a public comment period before approving or denying a notice of construction application involving second or third tier review;
- include the draft notice of construction approval order and Ecology's recommendation on the second or third tier petition as part of the public review documents;

- hold a public hearing to discuss the third tier petition and to answer questions from the public; and
- in consultation with Ecology, address any questions or concerns brought up during the public comment period.

Step 5: Final approval or denial of the project by the permitting agency

- If Ecology recommends approval of the project, the permitting agency may approve the notice of construction application.
- If Ecology recommends denial of the project, the permitting agency may not approve the project.

Second and Third Tier Review Fees

Purpose

This section explains second and third tier review fees and key process changes to applicants and consultants who submit health impact assessments under Chapter 173-460 WAC. These changes were prompted by a 2011 fee rule that changes the way Ecology collects fees and charges time for work spent reviewing health impact assessment documents.

Background

Beginning July 1, 2011, Ecology changed the fee schedule for permitting activities covered under our new source review program. These fee increases, which were authorized by the 2011 legislature, must support the cost of issuing a permit. Ecology accomplishes this by collecting an initial fee with the application that will cover a set number of review hours (base hours), depending on application type and a $95 per hour fee for the hours above base needed to complete the review and issue the permit. A notice summarizing all of the changes made by Ecology to the permitting fees regulation is available at http://www.ecy.wa.gov/biblio/1102028.html.

How the 2011 Fee Structure Affects Second and Third Tier Review

Under the 2011 fee structure, each member of Ecology's toxics review team will provide approximately 2 hours of pre-application assistance to the applicant. Time spent on pre-application assistance will not be counted toward the permit fee (not toward the initial fee or any additional fee) billed to the applicant, and will be provided in the form of one meeting between the applicant and Ecology, as well as any required advanced preparation for that meeting. Our goal in this pre-application assistance is to provide you with the majority of the information you need to prepare your health impact assessment protocol for submission to Ecology.

Once Ecology has provided information in the meeting, we will still be available to offer limited guidance to you as you prepare your protocol; however, the next step is for you to submit a health impact assessment (HIA) protocol along with the initial review fee of $10,000. The fee must be submitted with the protocol to Ecology's fiscal office before Ecology will review or approve the HIA protocol.

The HIA protocol must be accompanied by a completed application for second or third tier review. The application form includes the Health Impact Assessment Checklist and is available at http://www.ecy.wa.gov/biblio/ecy070415.html.

Alternate Method for Continuing Discussions with Ecology

It is our goal that you know how to proceed to develop the HIA by the end of the pre-application meeting. If you think your project needs more than a 2-hour meeting with Ecology, you have three choices:

- Submit the Application for Second Tier Review or Third Tier Review along with your $10,000 check. Ecology will meet with you to help you prepare your HIA and we will track our time against your initial fee.
- Enter into a contract with Ecology for additional upfront work. The rate is $95 per hour. We charge the same rate for working on your project under either option.
- Request Ecology stop working on the project once the 2 hours of "free" (included in the initial review fee) pre-application assistance are used up.

The Initial Fee You Submit May Not Cover the Cost of Processing Your Petition

The $10,000 initial fee you submit covers up to 106 hours of Ecology's review time. Ecology will track the number of hours spent on your project and will notify you when we approach the 106 hours covered by the initial fee. If the total number of review hours exceeds 106 hours, Ecology will bill you $95 per hour for each additional hour worked. We will bill you at the end of the process just before we issue a final decision. You must pay the bill before Ecology will issue a decision on your petition.

Public Hearing

The applicant is responsible for costs associated with a public hearing, if one is held. This includes staff time to prepare for the public hearing, travel time to and from the public hearing, time spent conducting the public hearing, time spent responding to public comments, and publications costs for a newspaper notice.

Changes to HIA Review Procedure

Ecology's goal is to complete our review of the HIA in a timely manner so that applicants are not charged additional hourly charges. To accomplish this goal, Ecology has changed the way we review the health impact assessment. The primary changes to our review procedure include:

- Ecology will provide the minimum amount of pre-application assistance necessary to advise the applicant of the demonstrations and submittals necessary to meet permitting requirements (one meeting lasting about 2 hours).

- Ecology will review the HIA protocol after the applicant submits the $10,000 initial fee with the HIA protocol and complete second or third tier application. The HIA protocol review process can be one of continuous improvement, until an acceptable HIA protocol has been prepared.

- Based on the approved HIA protocol, the applicant will prepare and submit an HIA document for review by Ecology.
- Ecology will provide substantive and non-substantive comments on the HIA document and will request the applicant revise the HIA document, as necessary. This process can be one of continuous improvement, until an acceptable final HIA document has been prepared by the applicant. Ecology's project engineer or delegate will review portions of the HIA that involve the project's engineering specifications. Likewise, Ecology's meteorological modeler will review portions of the HIA that involve toxic air pollutant (TAP) concentration modeling. Following confirmations by the engineer and modeler, Ecology's project toxicologist will review risk assessment portions of the HIA. The toxicologist will then communicate to all parties the results of their review of the HIA.
- Once an acceptable HIA document has been prepared, Ecology will prepare a brief staff report which summarizes Ecology's review of the HIA and includes a recommendation(s) to the local permitting authority regarding the petition.
- Ecology will post the applicant's final HIA document and Ecology's staff report and cover letter on Ecology's air toxics review web page.

Who to Contact for More Information

For more information, contact:

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Citations

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Exhibit D

EPA/630/R-03/003F
March 2005

Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens

Risk Assessment Forum
U.S. Environmental Protection Agency
Washington, DC 20460

TR 3466

REC 6270

DISCLAIMER

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PREFACE

U.S. Environmental Protection Agency (EPA or the Agency) cancer risk assessments may be conducted differently than envisioned in this Supplemental Guidance for many reasons including, for example, new information, new scientific understanding, or different science policy judgment. The practice of risk assessment with respect to accounting for early-life exposures to toxicants continues to develop, and specific components of this Supplemental Guidance may become outdated or may otherwise require modification in individual settings. It is EPA's intent to use, to the extent practicable and consistent with Agency statutes and regulations, the best available science in its risk assessments and regulatory actions, and this Supplemental Guidance is not intended to provide any substantive or procedural obstacle in achieving that goal. Therefore, the Supplemental Guidance has no binding effect on EPA or on any regulated entity. Where EPA does use the approaches in the Supplemental Guidance in developing risk assessments, it will be because EPA has decided in the context of that risk assessment that the approaches from the Supplemental Guidance are suitable and appropriate. This judgment will be tested through peer review, and the risk assessment will be modified to use different approaches if appropriate.

This Supplemental Guidance is intended for guidance only. It does not establish any substantive "rules" under the Administrative Procedure Act or any other law and has no binding effect on EPA or any regulated entity, but instead represents a non-binding statement of policy.

The Supplemental Guidance addresses a number of issues pertaining to cancer risks associated with early-life exposures generally, but provides specific guidance on potency adjustment only for carcinogens acting through a mutagenic mode of action. This guidance recommends for such chemicals, a default approach using estimates from chronic studies (i.e., cancer slope factors) with appropriate modifications to address the potential for differential risk of early-lifestage exposure. Default adjustment factors are meant to be used only when no chemical-specific data are available to assess directly cancer susceptibility from early-life exposure to a carcinogen acting through a mutagenic mode of action.

The Agency considered both the advantages and disadvantages of extending the recommended, age dependent adjustment factors for carcinogenic potency to carcinogenic agents for which the mode of action remains unknown. EPA recommends these factors only for carcinogens acting through a mutagenic mode of action based on a combination of analysis of available data and long-standing science policy positions that set out the Agency's overall approach to carcinogen risk assessment, e.g., the use of a linear, no threshold extrapolation procedure in the absence of data in order to be health protective. In general, the Agency prefers

to rely on analyses of data rather than on general defaults. When data are available for a susceptible lifestage, they should be used directly to evaluate risks for that chemical and that lifestage on a case-by-case basis. In the case of nonmutagenic carcinogens, when the mode of action is unknown, the data were judged by EPA to be too limited and the modes of action too diverse to use this as a category for which a general default adjustment factor approach can be applied. In this situation per the Agency's *Guidelines for Carcinogen Risk Assessment*, a linear low-dose extrapolation methodology is recommended. It is the Agency's long-standing science policy position that use of the linear low-dose extrapolation approach (without further adjustment) provides adequate public health conservatism in the absence of chemical-specific data indicating differential early-life susceptibility or when the mode of action is not mutagenicity.

The Agency expects to produce additional supplemental guidance for other modes of action, as data from new research and toxicity testing indicate it is warranted. EPA intends to focus its research, and to work collaboratively with its federal partners, to improve understanding of the implications of early life exposure to carcinogens. Development of guidance for estrogenic agents and chemicals acting through other processes resulting in endocrine disruption and subsequent carcinogenesis, for example, might be a reasonable priority in light of the human experience with diethylstilbesterol and the existing early-life animal studies. It is worth noting that each mode of action for endocrine disruption will probably require separate analysis.

As the Agency examines additional carcinogenic agents, the age groupings may differ from those recommended for assessing cancer risks from early-life exposure to chemicals with a mutagenic mode of action. Puberty and its associated biological changes, for example, involve many biological processes that could lead to changes in susceptibility to the effects of some carcinogens, depending on their mode of action. The Agency is interested in identifying lifestages that may be particularly sensitive or refractory for carcinogenesis, and believes that the mode of action framework described in the Agency's *Guidelines for Carcinogen Risk Assessment* is an appropriate mechanism for elucidating these lifestages. For each additional mode of action evaluated, the various age groupings determined to be at differential risk may differ from those described in this Supplemental Guidance. For example, the age groupings selected for the age-dependent adjustments were initially selected based on the available data, i.e., for the laboratory animal age range representative of birth to < 2 years in humans. More limited data and information on human biology are being used to determine a science-informed policy regarding 2 to < 16 years. Data were not available to refine the latter age group. If more data become available regarding carcinogens with a mutagenic mode of action, consideration may be given to further refinement of these age groups.

Access to data and other information relating to the Cancer Guidelines (U.S. EPA, 2005) and this Supplemental Guidance will be through EPA's Risk Assessment Forum website, under Publications, Guidelines, Guidelines for Cancer Risk Assessment. The URL is http://www.epa.gov/cancerguidelines. The data and results of analyses are available in spreadsheets.

1. INTRODUCTION

Cancer risk to children in the context of the U.S. Environmental Protection Agency's cancer guidelines (U.S. EPA, 2005) includes both early-life exposures that may result in the occurrence of cancer during childhood and early-life exposures that may contribute to cancers later in life. The National Research Council (NRC, 1994) recommended that "EPA should assess risks to infants and children whenever it appears that their risks might be greater than those of adults." This document focuses on cancer risks from early-life exposure compared with those from exposures occurring later in life. Evaluating childhood cancer and childhood exposures resulting in cancer later in life are related, but separable, issues.

Historically, the focus on cancer has been as a disease associated with aging, resulting from extended exposure duration with prolonged latency periods before the cancers appear. Because much of cancer epidemiology addresses occupational exposures and because rodent cancer studies are designed to last approximately a lifetime (two years) beginning after sexual maturity, the cancer database used by EPA and other agencies for risk assessment focuses on adults. However, extensive literature demonstrates that exposures early in life (i.e., transplacental or *in utero*, early postnatal, lactational) in animals can result in the development of cancer (reviewed in Toth, 1968; Della Porta and Terracini, 1969; Druckery, 1973; Rice, 1979; Vesselinovitch et al., 1979; Rice and Ward, 1982; Vesselovitch et al., 1983; Anderson et al., 2000). Thus, one element in extending analyses to children is to evaluate the extent to which exposures early in life would alter the incidence of cancers observed later in life, compared with the incidence observed with adult-only exposures (Anderson et al., 2000; NRC, 1993).

The causes of cancer encompass a variety of possible risk factors, including genetic predisposition (Tomlinson et al., 1997), diet, lifestyle, associations with congenital malformations (Bosland, 1996), and exposure to biological and physical agents and chemicals in the environment. In some cases, tumors in adults and children have been compared (Anderson et al., 2000; Ginsberg et al., 2002). Children and adults generally develop the same spectrum of tumors when they have inherited gene and chromosomal mutations, such as Li-Fraumeni syndrome (Birch et al., 1998). With ionizing radiation, which operates through a mutagenic mode of action, both the young and the old develop many of the same tumors, with the difference being that children are more susceptible for a number of tumor types (NRC, 1990; U.S. EPA, 1994; UNSCEAR, 2000). Studies with anticancer drugs (cytotoxic and immunosuppressive) demonstrate a similar spectrum of tumors (Hale et al., 1999; Kushner et al., 1998; Larson et al., 1996; Nyandoto et al., 1998). Various viral infections, such as Epstein Barr and hepatitis B, lead to lymphoma and liver cancer, respectively, in both age groups (Lindahl et

al., 1974; Mahoney, 1999). These observations in humans indicate that the mode of action for these agents would be the same or similar for adults and children.

Although there are similarities between childhood and adult tumors, significant differences are also known to exist (Grufferman, 1998; Israel, 1995). Tumors of childhood generally consist more of embryonic cell tumors, while adults have more carcinomas. Leukemias, brain and other nervous system tumors, lymphomas (lymph node cancers), bone cancers, soft tissue sarcomas, kidney cancers, eye cancers, and adrenal gland cancers are the most common cancers of children, while skin, prostate, breast, lung, and colorectal cancers are the most common in adults (Ries et al., 1999; U. S. Cancer Statistics Working Group, 2002). Some tumors are unique to the young, including several with well established genetic bases, such as tumors of the kidney (Wilms' tumor) or eye (retinoblastoma) (Anderson et al., 2000; Israel, 1995).

The relative rarity in the incidence of childhood cancers and a lack of animal testing guidelines with perinatal[1] exposure impede a full assessment of children's cancer risks from exposure to chemicals in the environment. Unequivocal evidence of childhood cancer in humans occurring from chemical exposures is limited (Anderson et al., 2000). Established risk factors for the development of childhood cancer include radiation and certain pharmaceutical agents used in chemotherapy (Reise, 1999). There is some evidence in humans for adult tumors resulting from perinatal exposure. Pharmacological use of diethylstilbesterol (DES) during pregnancy to prevent miscarriages induced clear cell adenocarcinoma of the vagina in a few daughters exposed *in utero* though this tumor was not observed in exposed mothers (Hatch et al., 1998; Robboy et al., 1984; Vessey, 1989). In addition to the limited human data, there are examples of transplacental carcinogens in animal studies, such as recent studies with nickel and arsenic (Diwan et al., 1992; Waalkes et al., 2003), as well as studies suggesting that altered development can affect later susceptibility[2] to cancer induced by exposure to other chemicals (Anderson et al., 2000; Birnbaum and Fenton, 2003).

Infrequently, perinatal exposure in animals has been shown to induce tumors of different types than those observed with adult exposures. Studies with saccharin (Cohen et al., 1995; Whysner and Williams, 1996; IARC, 1999) and ascorbate (Cohen et al., 1998; Cohen et al., 1995; NTP, 1983) found cancer when exposures were initiated in the perinatal period. In

[1] Perinatal is defined as the time around birth and may include both prenatal (prior to birth) and postnatal (after birth) periods.

[2] Susceptibility is defined here as an increased likelihood of an adverse effect, often discussed in terms of relationship to a factor that can be used to describe a human subpopulation (e.g., lifestage, demographic feature, or genetic characteristic). The terms "susceptibility" and "sensitivity" are used with a variety of definitions in published literature making it essential that readers are aware of these differences in terminology across documents.

contrast, studies submitted to the Food and Drug Administration of approximately a dozen other food additives and colorings that were not adult carcinogens did not indicate cancer, even when perinatal exposures occurred (U.S. EPA, 1996). When observed, the differences between childhood and adult cancers suggest the importance of evaluating the impacts of maternal exposures during pregnancy as well as exposures to children (Anderson et al., 2000). The effects of maternal exposures and transplacental carcinogens require separate evaluation and are not quantitatively evaluated in the analysis presented below.

The limited human information described briefly above is supported by a number of animal bioassays that include both perinatal and adult exposures to chemicals. Standard animal bioassays generally begin dosing after the animals are 6-8 weeks old, when many organs and systems are almost fully developed, though substantial growth in body size continues thereafter (as more fully discussed in Hattis et al., 2005). The literature can be divided roughly into three types of exposure scenarios: those that include *repeated* exposures for the early postnatal to juvenile period, as compared with chronic later-life dosing; *lifetime* (i.e., combined perinatal and adult) exposure as compared with chronic later-life dosing; and those that include more *acute* exposures, such as a single intraperitoneal (ip) or subcutaneous injection, for both early-life and later-life dosing. In the early-life exposure studies that are available, perinatal exposure usually induces higher incidence of tumors later in life than the incidence seen in standard bioassays where adult animals only were exposed; some examples include diethylnitrosamine (DEN) (Peto et al., 1984), benzidine (Vesselinovitch et al., 1979), DDT (Vesselinovitch et al., 1979), and polybrominated biphenyls (PCBs) (Chhabra et al., 1993a). Reviews comparing early-life carcinogenesis bioassays with standard bioassays for a limited number of chemicals (McConnell, 1992; Miller et al., 2002; U.S. EPA, 1996) have concluded:

- The same tumor sites usually are observed following either perinatal or adult exposure.
- Perinatal exposure in conjunction with adult exposure usually increases the incidence of tumor bearing animals or reduces the latent period before tumors are observed.

There is limited evidence to inform the mode(s) of action leading to differences in tumor type and tumor incidence following early-life exposure and exposure later in life. Differences in the capacity to metabolize and clear chemicals at different ages can result in larger or smaller internal doses of the active agent(s), either increasing or decreasing risk (Ginsberg et al., 2002; Renwick, 1998). There is reason to surmise that some chemicals with a mutagenic mode of action, which would be expected to cause irreversible changes to DNA, would exhibit a greater effect in early-life versus later-life exposure. Several studies have shown increased susceptibility

of weanling animals to the formation of DNA adducts following exposure to vinyl chloride (Laib et al., 1989; Morinello et al., 2002a; Morinello et al., 2002b). Additionally, even though not used quantitatively in the analyses in this document, a recent analysis of *in vivo* transplacental micronucleus assays indicated that fetal tissues generally are more sensitive than maternal tissues for induction of micronuclei from mutagenic chemicals (Hayashi et al., 2000), providing qualitative support for the early-life susceptibility. Similarly, the neonatal mouse model for carcinogenesis, which uses two doses prior to weaning followed by observation of tumors at one year, shows carcinogenic responses for mutagenic agents (Flammang et al., 1997; McClain et al., 2001). These results are consistent with the current understanding of biological processes involved in carcinogenesis, which leads to a reasonable expectation that children can be more susceptible to carcinogenic agents than adults (Anderson et al., 2000; Birnbaum and Fenton, 2003; Ginsberg, 2003; Miller et al., 2002; Scheuplein et al., 2002). Some aspects potentially leading to childhood susceptibility include the following issues.

- More frequent cell division during development can result in enhanced fixation of mutations due to the reduced time available for repair of DNA lesions and clonal expansion of mutant cells gives a larger population of mutants (Slikker et al, 2004).
- Some embryonic cells, such as brain cells, lack key DNA repair enzymes.
- Some components of the immune system are not fully functional during development (Holladay and Smialowicz, 2000; Holsapple et al., 2003).
- Hormonal systems operate at different levels during different lifestages (Anderson et al., 2000).
- Induction of developmental abnormalities can result in a predisposition to carcinogenic effects later in life (Anderson et al., 2000; Birnbaum and Fenton, 2003; Fenton and Davis, 2002).

The methodology that has been generally used by the U.S. EPA to estimate cancer risk associated with oral exposures relies on estimation of the lifetime average daily dose, which can account for differences between adults and children with respect to exposure factors such as eating habits and body weight. However, susceptibility differences with respect to early lifestages are not taken into consideration because cancer slope factors[3] are based upon effects

[3] Cancer slope factor – An upper bound estimate of the increased cancer risk from a lifetime exposure to an agent. This estimate, usually expressed in units of proportion (of a population) affected per unit exposure (e.g., mg/kg-day or ug/m^3), is generally reserved for use in the low-dose region of the dose-response relationship. It is often the statistical upper bound on the potency and therefore the risk. "Upper bound" in this context is a plausible

observed following exposures to adult humans or sexually mature animals. Since a much larger database exists for chemicals inducing cancer in adult humans or sexually mature animals, it is necessary to determine whether adjustment of such adult-based cancer slope factors would be appropriate when assessing cancer risks associated with exposures early in life. The analysis undertaken here addresses this issue, focusing upon studies that define the potential duration and degree of increased susceptibility that may arise from childhood, defined as early-life (typically postnatal and juvenile animal) exposures. Some of these analyses, along with a more complete description of the procedures used, have been published (Barton et al., 2005). The analysis presented in this Supplemental Guidance and in the published article form the basis for developing Supplemental Guidance for evaluating cancer susceptibility associated with early-life exposures.

upper limit to the true probability.

2. PROCEDURES

This section describes the steps taken to assess potential susceptibility to early-life exposure to carcinogenic compounds compared with adult and whole-life exposure. The readily available literature was reviewed to identify animal studies that compared tumor incidence between early-life and adult-only exposures or between early-life-and-adult and adult-only exposures. Studies were categorized by length of exposure; those studies with quantitative information to estimate tumor incidence over time for early-life and adult exposures were identified. These studies provided the basis for quantitatively estimating the difference in susceptibility between early-life and adult exposures, as described below. Finally, summaries of available human data for radiation exposure were reviewed in the context of tumor incidence from early-life versus later-in-life exposure.

2.1. DATA SOURCES FOR ANIMAL STUDIES

Studies in the literature included in this analysis are those that report tumor response from experiments that included both early-life and adult exposure as separate experimental groups. Initial studies for consideration were identified through review articles and a search of the National Toxicology Program (NTP) database. Reviews of the literature regarding cancer susceptibility from early-life exposure in animals include McConnell (1992), Ginsberg (2003), Anderson et al. (2000), Miller et al. (2002) and U.S. EPA (1996). A literature search was conducted utilizing key words and MeSH headings (Medline) from studies identified in the available reviews. The list of chemicals included in this analysis for quantitative evaluation is shown in Table 1a and 1b.

Abstracts or papers were reviewed to determine if a study provided information that could be used for quantitative analysis. The criteria used to decide if a study could be included in the quantitative analysis were:

- Exposure groups at different post-natal ages in the same study or same laboratory, if not concurrent (to control for a large number of potential cross-laboratory experimental variables including pathological examinations),

- Same strain/species (to eliminate strain-specific responses confounding age-dependent responses),

- Approximately the same dose within the limits of diets and drinking water intakes that obviously can vary with age (to eliminate dose-dependent responses confounding age-dependent responses),

- Similar latency period following exposures of different ages (to control for confounding latency period for tumor expression with age-dependent responses), arising from sacrifice at >1 year for all groups exposed at different ages, where early-life exposure can occur up to about 7 weeks. Variations of around 10 to 20% in latency period are acceptable,

- Postnatal exposure for juvenile rats and mice at ages younger than the standard 6 to 8 week start for bioassays; prenatal (*in utero*) exposures are not part of the current analysis. Studies that have postnatal exposure were included (without adjustment) even if they also involved prenatal exposure,

- "Adult" rats and mice exposure beginning at approximately 6 to 8 weeks old or older, i.e. comparable to the age at initiation of a standard cancer bioassay (McConnell, 1992). Studies with animals only at young ages do not provide appropriate comparisons to evaluate age-dependency of response (e.g., the many neonatal mouse cancer studies). Studies in other species were used a supporting evidence, because they are relatively rare and the determination of the appropriate comparison ages across species is not simple, and

- Number of affected animals and total number of animals examined are available or reasonably reconstructed for control, young, and adult groups (i.e., studies reporting only percent response or not including a control group would be excluded unless a reasonable estimate of historical background for the strain was obtainable).

Tables 2 and 3 include information on the methods and results from the animal studies identified in Table 1b. Pertinent information on species, sex, dosing regimen, and tumor incidence is given. Additionally, the "Notes" column includes general information about the relationship between tumor incidence, animal age at first dosing, and sex. The data in Tables 2 and 3 were used for the calculations, described below, for estimating potentially increased cancer risk from early-life exposure.

The available literature includes a wide range of exposure scenarios. This range is due in part to the lack of a defined protocol for early-life testing and the difficulty of standardizing and administering doses preweaning. As noted previously, the literature can be divided roughly into three types of exposure scenarios: those that include repeated exposures for the early postnatal to juvenile period, as compared with chronic later-life dosing; lifetime (i.e., combined perinatal and adult) exposure as compared with chronic later-life dosing; and those that include more acute exposures, such as a single intraperitoneal (ip) or subcutaneous injection, for both early-life and later-life dosing. Table 2 includes the studies that had early postnatal to juvenile exposures, adult chronic exposures, and lifetime exposures. Table 3 includes studies with acute exposures. A discussion of the implications of the different exposure scenarios is included in Section 3.

Studies were identified for more than 50 chemicals not included in Tables 2 and 3 that demonstrated carcinogenesis following perinatal exposure, but did not directly compare exposures at different ages. A large number of studies address *in utero* exposures only. More than 100 chemicals (with both negative and positive findings) have been studied in the neonatal mouse assay, but this assay does not have a comparable adult exposure (Flammang et al., 1997; McClain et al., 2001; Fujii, 1991). Studies across laboratories often varied in their use of animal strains (e.g., for AZT studies, Diwan et al., 1999 used CD-1 mice, while NTP, 1999 used $B6C3F_1$ mice). Studies of tamoxifen use two Wistar-derived strains and had very different periods for tumor expression, i.e., sacrifice at 20 months for adult-exposed rats and natural death up to 35 months for juvenile-exposed rats, with uterine tumors observed in animals dying after 22 months (Carthew et al., 2000; Carthew et al., 1996; Carthew et al., 1995). Due to these factors, the chemicals that belong to this group were not evaluated quantitatively. In addition, there were studies assessing radiation in animals (Covelli et al., 1984; Di et al., 1990; Sasaki et al., 1978). The radiation data were not analyzed in depth, in part because there are recognized differences in toxicokinetics and toxicodynamics between radiation and chemicals with a mutagenic mode of action for carcinogenesis. Even though the data on A-bomb survivors provide information for many different cancer sites in humans with a single exposure involving all ages, a number of national and international committees of experts have analyzed and modeled these data to develop risk estimates for various specific applications. Furthermore, lack of uniformity regarding radiation doses, gestational age at exposure, and the animal strains used make it difficult to make comparisons across studies (Preston et al., 2000).

2.2. EVALUATING THE MODE OF ACTION OF CARCINOGENS

Evaluation of the mode of action of a carcinogen was based upon a weight-of-evidence approach. Multiple modes of action are associated with the chemicals in this database, but a number are associated with mutagenicity (i.e., benzo(a)pyrene, benzidine, dibenzanthracene, diethylnitrosamine, dimethylbenz(a)anthracene, dimethylnitrosamine, ethylnitrosourea, 3-methylcholanthrene, methylnitrosourea, safrole, urethane, and vinyl chloride). Determination of carcinogens that are operating by a mutagenic mode of action entails evaluation of short-term testing results for genetic endpoints, metabolic profiles, physicochemical properties, and structure-activity relationship (SAR) analyses in a weight-of-evidence approach (Dearfield et al., 1991; U.S. EPA, 1986, 1991; Waters et al., 1999), as has been done for several chemicals (e.g., Dearfield et al., 1999; McCarroll et al., 2002; U.S. EPA, 2000a). Key data for a mutagenic mode of action may be evidence that the carcinogen or a metabolite is DNA reactive and/or has the ability to bind to DNA. Also, such carcinogens usually produce positive effects in multiple test

systems for different genetic endpoints, particularly gene mutations and structural chromosome aberrations, and in tests performed *in vivo* which generally are supported by positive tests *in vitro*. Additionally, carcinogens may be identified as operating via a mutagenic mode of action if they have similar properties and SAR to established mutagenic mode of action.

2.3. QUANTITATIVE METHODS

To estimate the potential difference in susceptibility between early-life and adult exposure, we calculated the estimated ratio of the cancer potency from early-life exposure compared to the estimated cancer potency from adult exposure. The cancer potency was estimated from a one-hit model, or a restricted form of the Weibull model, which is commonly used to estimate cumulative incidence for tumor onset. The general form of the equation is:

P(dose) = 1-[1-P(0)]exp(-cancer potency*dose)

The ratio of juvenile to adult cancer potencies were calculated by fitting this model to the data for each age group. The model fit depended upon the design of the experiment that generated the data. Two designs should be handled separately: experiments in which animals are exposed either as juveniles or as adults (with either a single or multiple dose in each period), and experiments in which exposure begins either in the juvenile or in the adult period, but once begun, continues through life.

For the first case, the model equations are:

$$P_A = P_0 + \left(1 - P_0\right)\left(1 - \mathrm{e}^{-m_A \delta_A}\right) \qquad (1)$$
$$P_J = P_0 + \left(1 - P_0\right)\left(1 - \mathrm{e}^{-m_A \mathrm{e}^{\lambda} \delta_J}\right)$$

where:

subscripts A and J refer to the adult and juvenile period, respectively,
λ is the natural logarithm of the juvenile:adult cancer potency ratio,
P_0 is the fraction of control animals with the particular tumor type being modeled,
P_x is the fraction of animals exposed in age period x with the tumor,
m_A is the rate of accumulation of "hits" per unit of time for adults, i.e., the cancer potency, and
δ_x is the duration or number of exposures during age period x.

For a substantial number of data sets (acute exposures), $\delta_J = \delta_A = 1$. We are interested in

determining λ, which is the logarithm of the estimated ratio of juvenile to adult cancer potencies, a measure of potential susceptibility for early-life exposure.

For the second kind of design, the model equations should take into account that exposures that were initiated in the juvenile period continue through the adult period. The model equations for the fraction of animals exposed only as adults with tumors in this design are the same as in the first design, but the fraction of animals whose first exposure occurred in the juvenile period is:

$$P_J = P_0 + (1 + P_0)\left(1 - e^{-m_A e^{\lambda}(\delta_J - \delta_A) - m_A \delta_A}\right) \quad (2)$$

All symbols in (eq. 2) have the same interpretation as their counterparts in (eq. 1), but now δ_J includes the duration of exposure during the juvenile period as well as the subsequent adult period.

Parameters in these models were estimated using Bayesian methods (see, for example, Carlin and Louis, 2000), and all inferences about the ratios were based on the marginal posterior distribution of λ. Some of these analyses, including a more complete description of the procedures (including the potential effect of alternative Bayesian priors that have been examined) have been published (Barton et al., 2005). The data for estimating each ratio were in the form of numbers of animals tested and number affected for each of control, juvenile-exposed, and adult-exposed animals, and duration of exposure for each of the juvenile-exposed and adult-exposed groups. A few data sets had separate control groups for the juvenile-exposed and adult-exposed groups, and equations 1 and 2 were modified accordingly. The likelihood for the parameters in the model was the product of three (or four, if there were two control groups) binomial probabilities: for the number of animals with tumors in the control group(s), for the juvenile-exposed group, and for the adult-exposed group. The prior for P_0 (the fraction of control animals with a particular tumor) was right triangular (right angle at the origin), based on the assumption that control incidences should be relatively low. (The base of the distribution is one, as P_0 can not exceed one. As this is a probability distribution, the area of the triangle is one. Therefore, its height at the origin must be 2.) The effect of exposure in adults is quantified by the extra risk, Q, where the probability that an animal has a tumor is $P_0 + (1 - P_0)Q$. So, from equations 1, $Q = 1 - e^{-m_A \delta_A}$, Q was given a uniform prior on the interval (0,1), reflecting total ignorance about the extra risk of adult exposure. Finally, the prior for λ was Gaussian with mean 0 (corresponding to a median or geometric mean ratio of one) and standard deviation 3. The prior for the log ratio of juvenile to adult cancer potency has some influence over the posterior estimates for the ratio of juvenile to adult potency. The magnitude of that influence depends on

the amount of support in the data for different values of the log ratio. The prior also effectively downweights extremely large or small values for the juvenile to adult potency ratio. Three priors for the standard deviation were evaluated (Barton et al., 2005, see Appendix), with the intent of finding the largest prior, i.e., one that would contain the least informative assumption for the prior. A standard deviation of 9 was tried, but some of the intervals would not converge. A standard deviation of 3 worked well, allowed ratio estimates to be derived, with all of the data of interest. An intermediate value of 6 was also examined to ascertain if a less informative prior could be used. While the intervals converged, a sensitivity analysis showed that this value for the standard deviation resulted in sufficient down-weighting of the ratios with limited information that these data would not influence the result. This was considered an unreasonable bias, so a standard deviation of 3 was used for the further analyses. A further discussion of these analyses can be found in Barton et al. (2005).

The posterior distribution for the unknown parameters in these models is the product of the likelihood from the data and the priors (the "unnormalized" prior), divided by a normalization constant that is the integral of the unnormalized prior over the ranges of all the parameters. This normalization constant was computed using numerical integration, as were posterior means and variances and marginal posterior quantiles for the log-ratio λ. All numerical computations were carried out in the R statistical programming language (version 1.8.1; R Development Core Team, 2003).

This method produced a posterior mean ratio of the early-life to adult cancer potency, which is an estimate of the potential susceptibility of early-life exposure to carcinogens. If the ratio was greater than one, this indicated that the experiment found that there was greater susceptibility from early-life exposure. If the ratio was less than one, this indicated that the experiment found that there was less susceptibility from early-life exposure. Summaries of the individual ratios from each of the dose groups from the different experiments for different groupings were also calculated (for example for all acute exposures of chemicals that are carcinogenic by a mutagenic mode of action). The summary ratios were constructed from the individual ratios within a group, by variance-weighting the means of each ratio. The individual, posterior means were weighted by using reciprocals of their posterior variance. This weighting procedure is commonly used because it gives greater weight to those studies for which the variances, i.e., the uncertainties, are smaller. Because the ratios were calculated as log ratios (see eq. 1), exponentiating the resulting inverse-variance-weighted mean yielded inverse-variance-weighted geometric means of ratios.

2.4. IONIZING RADIATION

A supporting role was assigned to the available human radiation data, where cancer incidence in adults who were children at the time of the atomic bomb (A-bomb) exposure was compared with cancer incidence in adults who were older at the time of exposure. Although there are recognized differences in toxicokinetics and toxicodynamics between radiation and chemical carcinogens with a mutagenic mode of action, the data on A-bomb survivors provide information for many different cancer sites in humans with a single exposure involving all ages. In addition to the richness of the data, a number of national and international committees of experts have analyzed and modeled these data to develop risk estimates for various specific applications.

The report of the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR, 2000, with Scientific Annexes) lists more than 80 studies, in addition to the reports of the Japanese A-bomb survivors, in which at least one type of cancer was measured in humans who were exposed either intentionally or accidentally to some form of ionizing radiation. However only the A-bomb survivor reports have relevant information on incidence of early-life exposures. One of the more recent papers cited in the UNSCEAR report, by Thompson et al. (1994), contains detailed data on the incidence of 21 different cancers in 37,270 exposed A-bomb survivors (42,702 unexposed). Also, EPA has used data from the A-bomb survivors to develop age-specific relative risk coefficients using various methods for transporting the risk from the Japanese population to the U.S. population (U.S. EPA, 1994). It is beyond the scope of this effort to present all of the radiation data or a discussion of the various analyses and modeling efforts. Rather, information relevant to comparing cancer risks from juvenile versus adult exposure from UNSCEAR (2000) and U.S. EPA (1994; 1999) is presented as representative findings to determine whether the radiation data are similar qualitatively to the chemical findings. More detailed data on the A-bomb survivors can be found in Delongchamp et al. (1997) and Preston et al. (2000).

As previously noted, several studies have assessed radiation in animal studies (Covelli et al., 1984; Di et al., 1990; Sasaki et al., 1978). However, lack of uniformity regarding radiation doses, gestational age at exposure, and the animal strains used make it difficult to compare the experimental data on cancer induction after prenatal irradiation (Preston et al., 2000).

3. RESULTS

3.1. QUALITATIVE EVALUATION OF THE DATABASE

The question addressed in this analysis was whether, and how, available quantitative scientific data could inform risk assessment policy choices for adjusting cancer slope factors when they are used in the assessment of cancer risk from childhood exposure. Cancer slope factors are, with few exceptions, based on adult human epidemiology or standard chronic adult rodent bioassays, which do not address the impacts of early-life exposures. Thus, the critical data are either human epidemiological data on childhood exposures resulting in adult cancer or research studies with rodents involving early postnatal exposures. The major human data available are from radiation exposures (studies summarized in Tables 9-11), with very limited data available for humans exposed during childhood to chemicals (reviewed in Anderson et al., 2000; Miller et al., 2002).

A review of the literature identified several hundred references reporting more than 50 chemicals that have been shown to be able to cause cancer following perinatal exposure (Table 1a) (reviewed in Toth, 1968; Della Porta and Terracini, 1969; Druckery, 1973, Rice, 1979; Vesselinovitch et al., 1979; Rice and Ward, 1982; Vesselovitch et al.; 1983; Fujii, 1991; Anderson et al., 2000). Studies (or groups of studies from a single laboratory on a given chemical) that directly provided quantitative data on carcinogenesis following early postnatal exposures and adult exposures to chemicals in animals were identified for 18 chemicals, listed in Table 1b, 2, and 3. Of the identified studies, there were 11 chemicals involving repeated exposures during early postnatal and adult lifestages (Table 1b) and 8 chemicals using acute exposures (typically single doses) at different ages (Table 1b). Some of the studies evaluated single tissues or organs for tumors (e.g., only liver), while others evaluated multiple tissues and organs (Tables 2 and 3). Mice, rats, or both species and sometimes multiple strains were tested. These studies serve as the basis for the quantitative analyses presented later in the results.

In addition to the studies identified in Table 1b, studies were identified with early postnatal and early-life exposures that were evaluated qualitatively but not quantitatively. Some of these studies are notable and provide important supporting information. Two recent studies used transgenic mouse models for human tumors. Increased multiplicity of colon tumors was observed following earlier versus later azoxymethane exposures (Paulsen et al., 2003). Shortened mammary tumor latency following estradiol exposure occurred when exposures occurred between 8 and 18 weeks as opposed to earlier or later, which is generally consistent with the incidence results analyzed for DMBA (Yang et al., 2003). Several notable examples exist of developmental windows leading to cancer susceptibilities that were not observable in

adults. Several potent estrogenic chemicals including DES, tamoxifen, and genistein produce uterine tumors with early postnatal exposures of mice, though there also appear to be strain-dependent differences in the tumor sites in adult mice (Gass et al., 1964; Greenman et al., 1990; Newbold et al., 1990, 1997, 1998, 2001). Developmental susceptibilities are believed to play a key role in effects observed with saccharin (Cohen et al., 1995; Whysner and Williams, 1996) and ascorbate (Cohen et al., 1998; NTP, 1983), with bladder tumors arising when early-life exposures occurred. Studies with several species, including rat, mouse, and opossum, indicate that nervous systems tumors associated with exposures to ENU and several other chemicals appear to be highly dependent upon exposures occurring within certain windows, particularly prenatal ones (Rice, 1979; Rice and Ward, 1982; Jurgelski et al., 1979).

Analyses of the difference in cancer risk from exposures during different lifetime periods ideally should address both the period of potential susceptibility and the magnitude of the susceptibility. Available studies used a variety of study designs (see Tables 2 and 3), which can be valuable because they provide different information (Figure 1). However, variations in study design can result in a lack of comparability across chemicals, and can limit information on the consistency of effects with different chemicals acting through different modes of action. The acute dosing (largely single dose) studies (Table 3) are valuable because they involve identical exposures with explicitly defined doses and time periods demonstrating that differential tumor incidences arise exclusively from age-dependent susceptibility. These studies address both the period and magnitude of susceptibility. They were not as appropriate for quantitative adjustments for the cancer potency estimates because of their limitations, including that most used subcutaneous or ip injection that historically have not been considered quantitatively relevant routes of environmental exposure for human cancer risk assessment by EPA, and that these routes of exposure are expected to have only partial or a complete absence of first pass metabolism that is likely to affect potency estimates.

The repeated dosing studies with exposures during early postnatal or adult lifetime provide useful information on the relative impact of repeated exposures at different lifestages and may be more likely to have exposure occur during a window of susceptibility, if there is one. One notable difference in study designs was that studies with repeated early postnatal exposure were included in the analysis even if they also involved earlier maternal and/or prenatal exposure, while studies addressing only prenatal exposure were not otherwise a part of this analysis. Another notable difference among studies involved the tissues that were evaluated for tumors: some studies focused on a single tissue, particularly liver, while others evaluated multiple tissues.

Comparisons within a single repeated dosing study may have limitations for evaluating

differential susceptibility because exposures to the chemical can differ during the different lifestages, particularly when dietary or drinking water exposures are involved. A notable example is the PCB study (Chhabra et al., 1993a), in which mobilization of such lipid-soluble chemicals into mother's milk would be expected to result in infants receiving much larger exposures than other lifestages. While lactational transfer is just as relevant to human nursing offspring, this difference in exposure obscures the extent to which the early lifestage is quantitatively more susceptible (i.e., part of the increased early-life cancer risk arises from higher exposure than during the adult period). Maternal metabolism of compounds such as diphenylhydantoin (DPH) (Chhabra et al., 1993b) also may result in lower exposure during lactation, potentially underestimating the early-lifestage risk, if the parent compound is the active form of the chemical. Similar issues exist due to normal age-dependent changes in food and water consumption. Ascribing differential effects observed in animal studies solely to lifestage susceptibility must be done carefully as there may also be differences in the exposures. There are substantial and clear benefits, therefore, from experimental consistency when comparisons are made directly within a study (e.g., same species and strain, consistent pathological evaluation).

One issue to note is the rationale for the organization of the available data. It was observed that the results across a broad range of chemicals with a variety of modes of action were somewhat variable. Therefore, consistent with the approach of the EPA cancer guidelines (U.S. EPA, 2005), an approach based on mode of action appeared to be a common framework for analysis. Variability in lifestage-dependent susceptibility and susceptibility across a range of modes of action was further supported by theoretical analyses using multistage and two-stage models of carcinogenesis (Goddard and Krewski, 1995; Murdoch et al., 1992).

3.2. QUANTITATIVE EVALUATION OF THE DATABASE

As described in the Section 2.3, the potential difference in susceptibility between early-life and adult exposure was calculated as the estimated ratio of cancer potency from early-life exposure over the cancer potency from adult exposure. Tables 4-7 present the results of the quantitative analysis using the studies that were determined qualitatively to have appropriate study designs (Tables 2 and 3) containing sufficient information to analyze. Based on the studies available, the calculations were organized into four tables: (1) compounds acting through a primarily mutagenic mode of action, where the compound was administered by a chronic dosing regimen to adults and repeated dosing in the early postnatal period (Table 4); (2) compounds acting through a primarily nonmutagenic mode of action, where the compound was administered by a chronic dosing regimen to adults and repeated dosing in the early postnatal period (Table 5);

(3) compounds acting through a primarily mutagenic mode of action, where the compounds were administered by an acute dosing regimen (Table 6); and (4) compounds acting primarily through either a mutagenic or nonmutagenic mode of action with chronic adult dosing and repeated early postnatal dosing (Table 7). In these tables, the 2.5% and 97.5% are percentiles of the posterior distribution. For a Bayesian distribution, these percentiles function in a manner similar to the 95% confidence limits for other types of statistical analyses. The results are discussed below, followed by a description of results from analyses of studies of humans exposed to radiation.

3.2.1. Carcinogens with a Mutagenic Mode of Action

The most informative database on early-lifestage susceptibility exists for chemicals with a well-accepted mutagenic mode of action (e.g., diethylnitrosamine, vinyl chloride). This database includes both single-dose studies and repeated-dose studies involving periods of postnatal and/or chronic exposure. These studies help define the periods of increased vulnerability and the magnitude of the susceptibility. The acute dosing studies demonstrate that the age-dependent responses are not due to differences in exposure, because these studies explicitly control the exposure.

3.2.1.1. *Early Postnatal, Juvenile, and Adult Repeated Dosing Studies of Chemicals with a Mutagenic Mode of Action*

Studies comparing repeated dosing for early-life, adult, or lifetime exposures exist for six carcinogens with a mutagenic mode of action [benzidine, diethylnitrosamine (DEN), 3-methylcholanthrene, safrole, urethane, and vinyl chloride]; DEN also had acute dosing studies. Lifetime (i.e., combined juvenile and adult) compared to adult exposure studies were analyzed for DEN, safrole, and urethane, while studies comparing juvenile with adult exposures were analyzed for benzidine, 3-methylcholanthrene, safrole, and vinyl chloride. These chemicals all require metabolic activation to the active carcinogenic form. Analysis of the tumors arising per unit time of exposure found that juvenile exposures with each chemical could be more effective than adult exposures were at inducing tumors (Tables 4 and 7; Figure 2, a graphic representation of the posterior, unweighted geometric means and their 95% confidence intervals, for the ratios of juvenile to adult cancer potency for carcinogens acting through a mutagenic mode of action). The weighted geometric mean for repeat and lifetime exposures is 10.4; for acute exposures the weighted geometric mean value is 1.5. For benzidine and safrole, there was a notable sex difference, with high liver tumor incidence observed for early postnatal exposures of male, but not female, mice. For both the acute and the repeated/lifetime data, the 95th percentile of the individual, unweighted geometric means is above 10 (Figure 2).

This analysis focused upon the duration of exposure as a surrogate for dose, essentially assuming that the doses animals received during the different periods of these studies were similar. This assumption is a limitation of the analysis because these studies involved exposures via lactation (i.e., dosing the mother prior to weaning), drinking water, diet, or inhalation, which have the potential to deliver different doses at different lifestages. However, the range of the magnitudes of the tumor incidence ratios of juvenile to adult exposures is similar (Table 8) for the repeated dosing studies (0.12 – 111, weighted geometric mean 10.5, 42% of ratios greater than 1), lifetime dosing studies (0.18 – 79, weighted geometric mean 8.7, 67% of ratios greater than 1), and acute dosing studies (0.01 – 178, weighted geometric mean 1.5, 55% of ratios greater than 1), suggesting that these differences in dosing are not the sole determinant of the increased incidence of early tumors, i.e., uncertainty and variability remain. Because these comparisons include different chemicals with different tissue specificities, it may be informative to consider liver as a target organ affected by all of these chemicals. The range of the magnitudes of the liver tumor incidence ratios of juvenile to adult exposures is similar for the repeated dosing studies (0.12 – 111, weighted geometric mean 41.8, 86% of ratios greater than 1, Table 4), lifetime dosing studies (0.47 – 79, weighted geometric mean 14.9, 80% of ratios greater than 1, Table 7), and acute dosing studies (0.1 – 40, weighted geometric mean 8.1, 77% of ratios greater than 1, Table 8). Thus, the repeated dose studies support the concept that early-lifestage exposure to carcinogenic chemicals with a mutagenic mode of action would lead to an increased tumor incidence compared with adult exposures of a similar duration and dose.

3.2.1.2. *Acute Dosing Studies of Chemicals with a Mutagenic Mode of Action*

Acute dosing studies are available for eight carcinogens with a mutagenic mode of action that were administered to mice or rats [benzo[a]pyrene (BaP), dibenzanthracene (DBA), Diethylnitrosamine (DEN), dimethylbenzanthracene (DMBA), dimethylnitrosamine (DMN), ethylnitrosourea (ENU), methylnitrosourea (NMU), and urethane (also known as ethyl carbamate)] (Table 1b). Except for ENU and NMU, these compounds require metabolic activation to their active carcinogenic forms. These acute dosing studies generally compared a single exposure during the first few weeks of life with the identical or similar exposure in young adult animals (Tables 3 and 6). Many of these studies compared exposures during the preweaning period (i.e., approximately day 21 for rats and mice) with effects around week 6, which is approximately the age at which typical chronic bioassays begin dosing animals. These studies largely were by subcutaneous or ip injection, which historically have not been considered quantitatively relevant routes of environmental exposure for human cancer risk assessment by EPA. For purposes of comparing age-dependent susceptibilities to tumor development, these

data are highly relevant. The injection route typically alters the pharmacokinetic time courses of the parent compound and the metabolites compared with oral or other exposures due to altered kinetics of absorption and metabolism. However, for these compounds and the systemic organ effects observed, there are several pharmacokinetic reasons to believe that the age-dependent trends would be similar with other routes of exposure. These compounds are expected to be reasonably well absorbed orally, comparable with injection routes, and largely require metabolic activation, so partial or complete absence of first pass metabolism in the injection studies would be similar to or underestimate metabolic activation when compared with oral exposure.

The early exposures often resulted in higher incidence of tumors than later exposures, with increased early susceptibilities up to 178-fold (unweighted ratios in Table 6 range from 0.011 to 178, with a weighted geometric mean of 1.5, and 55% of ratios greater than 1, Figure 2, Table 8). Examples of the general age-dependent decline in susceptibility of tumor response include BaP (liver tumors), DEN (liver tumors), ENU (liver and nervous system tumors), and urethane (liver and lung tumors). While generally the Day 1 and Day 15 time points were higher than later time points, in several cases similar tumor incidence was observed at both these early times (e.g., ENU-induced kidney tumors, Tables 6 and 8).

While the degree of susceptibility generally declines during the early postnatal period through puberty into early adulthood, there are exceptions due perhaps to pubertal periods of tissue development (e.g., mammary tissues) or very early development of xenobiotic metabolizing enzymes. One such exception was the increased incidence of mammary tumors in 5-8 week old rats given DMBA, compared with older or younger rats (Meranze et al., 1969; Russo et al., 1979). Meranze et al. (1969) reported 8% mammary tumors following a single dose of DMBA at less than two weeks, 56% if given once to animals between 5 and 8 weeks old, and 15% when given once to 26 week old rats. Thus, a ratio of 7.1 is obtained when comparing susceptibilities of 5–8 week and 26-week-old rats (Table 6) compared to a ratio of 0.2 when comparing the exposure at 2 weeks versus 26 weeks. A similar effect was observed by Russo et al. (1979); see Table 3. This observation corresponds well with pubertal development of the mammary tissue, with ovarian function commencing between 3 and 4 weeks (after the < 2 week time point in the Meranze et al., 1969 study), and mammary ductal growth and branching occurring such that it is approximately two-thirds complete by week 5, consistent with the 5–8 week susceptible period of Meranze et al. (Silberstein, 2001). While this differs from the general trend previously discussed, it indicates susceptibility later in the juvenile period rather than earlier. Another example of deviation from the general trend toward an age-dependent decline is DEN-induced lung tumors that were somewhat lower in incidence following exposure on day 1 than observed for the day 15 or day 42 exposures (Vesselinovitch et al., 1975) (Tables 3 and 6).

There are substantial differences in the early-life susceptibility of different tissues observed in the acute studies (Table 8). It should be noted that the target tissues vary with chemical, so the number of chemicals for which data are available varies for each tissue. Several tissues have weighted geometric mean ratios of greater than 1 including kidney, leukemia, liver, lymph, mammary, nerve, reticular tissue, thymic lymphoma, and uterus/vagina. Some of these, such as the nerve and mammary tumors, appear to have a very specific window of susceptibility, as noted above, and the ratios were much higher if the exposure occurred during this window. Tissues with weighted mean ratios less than 1 include forestomach, harderian gland, ovaries, and thyroid. Lung has a weighted geometric mean of 1. Many of the studies produced very high lung tumor responses regardless of age, so the results are difficult to interpret, as illustrated by the dose-response data with urethane in Rogers (1951) in which the increased early susceptibility is only apparent when the dose is low. The large numbers of studies with high lung tumor responses at all ages contribute to the differences in the weighted geometric means for the acute and for the repeated dosing studies.

Overall, the acute dosing studies support the concept that early-lifestage exposure to carcinogenic chemicals with a mutagenic mode of action would lead to an increased incidence of tumors compared with adult exposures of a similar dose and duration. These studies generally use the same dose and duration at all ages, and thus do not have the type of issues discussed for the repeated dosing studies. On the other hand, the acute dosing studies have limitations that were sufficient to decide that they should not be included in the quantitative adjustment of cancer potency. First, as mentioned in the previous paragraph, the large number of studies of lung tumors with almost 100% response observed at all doses and all ages would significantly bias the median ratio toward unity for a reason based on study design rather than biology. Second, cancer potency estimates are usually derived from chronic exposures. Therefore, any adjustment to those potencies should be, if possible, from similar exposures. Third, most exposures of concern to the Agency are from repeated or chronic exposures rather than acute exposures. Finally, many of the acute studies used ip exposures, which is not the usual route of exposure for environmental chemicals. Thus, the repeated and lifetime studies are more appropriate for the purpose of this analysis.

3.2.2. Carcinogens With Modes of Action Other Than Mutagenicity

Studies comparing tumors observed at the same sites following early postnatal and chronic adult exposures in a single protocol were available for six chemicals that do not act through a mutagenic mode of action [amitrole, dichlorodiphenyltrichloroethane (DDT), dieldrin, ethylene thiourea (ETU), diphenylhydantoin (DPH), polybrominated biphenyls (PBB)] (Table 5).

These chemicals cause tumors through several different, not necessarily well defined, modes of action. For example, thyroid hormone disruption by ETU causes thyroid tumors; some PBBs act through aryl hydrocarbon (Ah) receptors, while others are phenobarbital-like pleiotrophic inducers of liver enzymes and liver tumors. Three of these studies evaluated only mouse liver tumors (amitrole, DDT, dieldrin), while the other three evaluated a large number of tissues in both mice and rats (ETU, DPH, PBB). These studies generally included a combined perinatal and adult exposure as well as the separate perinatal or adult-only groups. It should be noted that no acute perinatal dosing studies of carcinogenesis were identified for these agents; such protocols are generally considered largely non-responsive for modes of action other than mutagenicity and potent estrogenicity (e.g., DES).

For five chemicals (amitrole, DDT, dieldrin, PBB and DPH), the same tumors were observed from early and/or adult exposures, though the studies for amitrole, DDT, and dieldrin only evaluates the animals for liver tumors. With ETU, no tumors in mice or rats were observed following perinatal exposure alone (except a small, not-statistically-significant increase in male rat thyroid tumors), while thyroid tumors were observed in adult rats and thyroid, liver, and pituitary tumors in adult mice. Analysis of the incidence of tumors per time of exposure shows early-lifestage susceptibilities. The range of the magnitudes of the tumor incidence ratios of juvenile to adult exposures is similar for the repeated dosing studies (0.06–13.3, weighted geometric mean 2.2, 27% of ratios greater than 1, Tables 5 and 8) and lifetime dosing studies (0.15–36, weighted geometric mean 3.4, 21% of ratios greater than 1, Tables 7 and 8). These ranges and means are similar to those for chemicals with a mutagenic mode of action, though the means and maximums are somewhat lower. Again, liver tumors are common to these chemicals. The range of the magnitudes of liver tumor incidence ratios of juvenile to adult exposures also is similar for the repeated dosing studies (0.06–13.3, weighted geometric mean 2.6, 43% of ratios greater than 1, Tables 5 and 8) and lifetime dosing studies (0.15–36, weighted geometric mean 5.8, 33% of ratios greater than 1, Tables 7 and 8).

The major factor that complicates the interpretation of the results is that these studies, except with DDT and dieldrin, involved dietary feeding initially to the mother, which potentially could increase or decrease the dose received by the pups. Due to the maternal dosing during pregnancy and lactation, the extent to which offspring received similar doses during different early and adult lifestages is particularly uncertain for DPH, ETU, and PBBs. Oral gavage doses in young animals were selected to approximate the average daily dose in adult dietary studies based on standard estimates of feed consumption in the studies with DDT and dieldrin, while the amitrole study involved dietary feeding postnatally to the mother so the young were dosed via lactation. In addition, DDT, dieldrin, and some PBBs are more persistent in the body than are

most chemicals, leading to a prolonged exposure even following limited dosing. Thus, these studies provide evidence that early lifestages can be more susceptible to exposures to chemicals causing cancer through a variety of modes of action other than mutagenicity. However, the studies with ethylene thiourea, which acts via thyroid disruption, indicate that this is not necessarily the case for all modes of action.

3.2.3. Ionizing Radiation

As mentioned previously, the UNSCEAR, Annex I (2000) includes information derived from a wide range of both intentional (generally diagnostic or therapeutic medical) and accidental radiation exposures. Only information derived from the Japanese population (referred to as the Life Span Study in the UNSCEAR Annex I) is presented here. A statistically significant excess cancer mortality associated with radiation has been found among the bomb survivors for the following types of cancer: esophagus, stomach, colon, liver, lung, bone and connective tissue, skin, breast, urinary tract, and leukemia. Tables 9 and 10 are extracted from the tables in UNSCEAR, Annex I. The excess relative risk (ERR) is the increased cancer rate relative to an unexposed population; an ERR of 1 corresponds to a doubling of the cancer rate. Because of the low numbers of cancers in individual sites within narrow age groups, the ERRs for the various solid tumors and leukemia were presented only as less than or greater than 20 years of age at the time of exposure. The larger number of thyroid tumors enable a more detailed breakout shown in Table 10. Most sites show greater risks in the younger than in the older ages.

The U.S. EPA (1994) document presents a methodology for estimation of cancer risks in the U.S. population due to low-LET (linear energy transfer) radiation exposures using data from the Atomic Bomb Survivor Study (ABSS) as well as from selected medical exposures. The report developed mortality risk coefficients using several models that took into account age and gender dependence of dosimetry, radiogenic risk, and competing causes of death as well as transporting of risks across populations. The risk projections were updated using more recent vital statistics in a report that also included an uncertainty analysis (U.S. EPA, 1999). Details of the derivation of these coefficients are available at http://www.epa.gov/radiation/docs/rad_risk.pdf .

Table 11 contains the calculated age-specific risk coefficients derived from the application of the various models to the ABSS data. For most of the sites in the table, the risk coefficients are higher in the earlier age groups; liver, bone, skin, and kidney coefficients are age-independent and only esophageal cancer coefficients increase with increasing age. Also of note is that the coefficients generally are higher for females. Similar to the information from the UNSCEAR (2000) Annex, most sites show greater risks in the younger ages than the older ages.

However, a comparison of the two tables seems to show reversal of risks for some sites as a function of age at exposure. While the high sampling variability in the epidemiological data for some ages may contribute to this apparent reversal, the choice of risk models and associated parameters also is a factor.

4. DISCUSSION

The challenge for this analysis was how to use the existing, but limited, scientific database on early postnatal and juvenile exposures to carcinogens to inform a science policy decision on whether, and if so how, to assess the risk from childhood exposures to chemicals for which we have evidence of carcinogenicity only in adult humans or sexually mature laboratory animals. The database overall is of limited size (particularly compared with the number of chemicals that have been studied in adult occupational epidemiological studies or chronic bioassays). The majority of the human data involves exposures to ionizing radiation or DES (Anderson et al., 2000). More than 50 chemicals have been demonstrated to cause cancer following perinatal exposures in animals (without adult exposures), but only a subset of the chemicals have comparative studies across ages. The comparative experimental studies used 18 chemicals, 12 of which had mutagenic modes of action and 6 of which had data from repeated or lifetime exposures. Other analyses of similar data have found similar results (Hattis et al. 2005), but have focused on other aspects of the data, e.g., gender differences.

Previously published or internal U.S. EPA analyses have concluded that the standard animal bioassay protocols usually do not miss chemicals that would have been identified as carcinogens if perinatal exposures had been undertaken (McConnell, 1992; Miller et al., 2002; U.S. EPA, 1996). Given the increased complexity and costs of chronic bioassays with perinatal exposures, a limited number of such studies have been performed. However, these are the studies that largely constitute the available database for this analysis. In addition to the chronic bioassays with perinatal exposures, there are studies with acute dosing at different lifestages and a large number of studies with perinatal exposures without a directly comparative adult study.

Two other kinds of information can contribute toward developing a scientifically informed policy: theoretical analyses and analyses of stop studies.[4] Theoretical analyses suggest that the differential susceptibility would depend in part on the mode of action (i.e., at what step in the cancer process(s) the chemical was acting) and that the use of the average daily exposure prorated over a lifetime may underestimate or overestimate the cancer risk when exposures are time-dependent (Goddard and Krewski, 1995; Murdoch et al., 1992). Evidence for old-age-dependent promotion of basophilic foci in rats by peroxisome proliferators appears to provide a concrete example consistent with these theoretical analyses (Cattley et al., 1991; Kraupp-Grasl et al., 1991). The stop studies performed by the National Toxicology Program began exposure at the standard post-weaning age, but stopped exposure after varying periods of months. Other groups of animals were exposed for a full two years; all animals were evaluated

[4] Stop studies are studies in which exposure is halted after a predetermined period.

for tumors at the end of two years regardless of the duration of exposure (Halmes et al., 2000). Related data also are available from the stop studies with vinyl chloride (Drew et al., 1983). Analysis by Halmes et al. (2000) showed that, for six of the eleven chemicals and half the tumor sites, the assumption that the cancer risk would be equal when the product of concentration and time (i.e., C x T) was constant was incorrect, and usually underestimated risk, as more of the risk came from the beginning of the exposure rather than the end. This dependence of risk on both duration and intensity of exposure did not appear to be correlated with mutagenicity. It should be noted that these stop studies all involved exposures early in the life of the animal (as opposed to a limited number of cancer studies that looked at later periods of life; e.g., Drew et al., 1983), but the extent to which the differences in tumor outcome result from increased susceptibility in these early periods or the extended period for expression of the cancer cannot be evaluated. These stop studies also used doses as high as or higher than the highest dose used in the two-year exposure. This latter factor clearly had a significant effect for two chemicals, causing tumors at higher doses that were not observed at lower doses. These results suggest that pharmacokinetic or other dose-rate dependencies can make the effects of exposures at high doses different from those exposures at lower doses. While not directly informative about early childhood exposures, these studies provide a perspective on the common cancer risk assessment practice of averaging exposures over a lifetime, especially those that include earlier lifestages. Thus, alternative methods for estimating risks from short-term exposures during childhood should be considered.

Information on different lifestage susceptibilities to cancer risks for humans exists for ionizing radiation. The effects of chemical mutagens at different lifestages on cancer induction are derived from laboratory animal studies. While the induction of cancer by ionizing radiation and the induction of cancer by chemical mutagens are not identical processes, both involve direct damage to DNA as critical causal steps in the process. In both cases, the impacts of early exposure can be greater than the impacts of later exposures, probably due to some combination of early-lifestage susceptibility and the longer periods for observation of effects. As indicated in Tables 9 and 10, A-bomb survivors exhibited different lifestage dependencies at different tumor sites, though the total radiation-related incidence of tumors showed a general slow decline with age at exposure. However, as previously noted, there are apparent differences at some sites between the two tables. In addition to the sampling and modeling differences, the excess risk values in Table 9 are based on Japanese baselines while the coefficients in Table 10 reflect UNSCEAR's effort to transport the risks from the Japanese population to that of the United States. However, it is clear that the total radiation-related tumor incidence showed a general slow decline with age at exposure.

The studies in rodents of chemicals with mutagenic modes of action similarly support a

general decline in induced cancer risk with age at exposure and similarly show some differences for individual tumor sites. In general, the earliest two or three postnatal weeks in mice and rats appeared to be the most susceptible, though some degree of increased susceptibility through puberty in rats (beginning around 5–7 weeks) and mice (beginning around 4–6 weeks) for some types of tumors exists.

All the acute dosing studies that demonstrated carcinogenicity with animals of different ages used chemicals with a mutagenic mode of action (Tables 4 and 6). These studies provide the clearest demonstrations of periods of differential susceptibility because the exposure rate is constant at the different ages. The repeated dose studies also include several of the most informative studies for assessing perinatal carcinogenesis, notably those on vinyl chloride and DEN (Tables 2 and 4). The vinyl chloride studies by Maltoni and colleagues are part of a large series of studies on this compound that included exposures to different concentrations for varying durations, including some at early lifestages (Maltoni et al., 1984). The DEN study by Peto et al. (1984) used a unique chronic study design in which groups of rats were exposed to multiple drinking water concentrations starting at 3, 6, or 20 weeks of life. This design provides information on the susceptibility of early exposure periods within a nearly lifetime exposure.

Beyond the analysis described here, there are conceptual biological rationales that would suggest DNA-damaging agents would have greater impacts on early lifestages. Growth involves substantial levels of cell replication, even in organs that in adults are only very slowly replicating, thus increasing the likelihood that a cell will undergo division before the DNA damage caused by the mutagen has been repaired. Increased replication also can lead to a greater division of initiated cells, leading to a larger number of initiated cells per specified dose. These periods of cell replication can vary for different tissues. For example, DMBA appears to be more effective at initiating mammary tumors in 6-8 week old rats, which are undergoing development of that tissue, than during earlier or later periods (Meranze et al., 1969). While tumor promotion processes can be very dependent upon the duration of promotion, initiation processes can occur in relatively brief periods (e.g., the single-dose studies in animals or radiation exposure in humans). Most tumors take extended periods to develop, making damage that occurs earlier in life more likely to result in tumors prior to death than would exposures that occur later in life. While some of these observations may also pertain to other modes, all of them (with some differences among tumor sites) appear to be potentially relevant to a greater susceptibility to mutagenic modes of action during early-life stages (vs. later-life stages).

The information on lifestage susceptibility for chemicals inducing cancers through modes of action other than direct DNA interaction is more varied, showing an increase in tumor incidence during perinatal exposure versus exposures of mature animals (e.g., polybrominated

biphenyls induced liver tumors), no tumors from perinatal exposure (e.g., ethylene thiourea induced thyroid tumors), no effect of combined perinatal and adult exposure (e.g., DPH liver tumors in rats and female mice), and different tumors from perinatal exposure versus adult exposure (e.g., DES, ascorbate). These variations are likely a result of the modes of action of these chemicals and the pharmacokinetic differences in doses during different periods of life. No studies were evaluated that were directly comparable to the single-dose studies with mutagens, which clearly show significant differences in tumor responses after explicitly controlled doses at different lifestages.

Some evidence for an effect of early-lifestage exposures on tumor incidence was observed in studies with polybrominated biphenyls, amitrole, DDT, dieldrin, and diphenylhydantoin. These studies show increased incidence of tumors in mice from perinatal exposure, though only those for polybrominated biphenyls were statistically significant. (A nonstatistically significant increase also was observed in male rats with polybrominated biphenyls.) Combined perinatal and adult exposures generally gave statistically significant increases, though not necessarily for each sex and species (rat and mice) in the diphenylhydantoin and polybrominated biphenyl studies.

There are important demonstrations of chemicals acting through modes of action other than mutagenic to cause different tumor types with early-lifestage exposures compared with exposures for adults, e.g., tamoxifen and DES (Carthew et al., 2000; Carthew et al., 1996, Gass et al., 1964; Newbold et al., 1990, 1997, 1998). In addition, studies with *in utero* exposure to atrazine (Fenton and Davis, 2002), DES, and arsenic (Waalkes et al., 2003) indicate that early-life exposures to compounds can alter susceptibility of endocrine and reproductive organs. Three of these compounds (i.e., DES, genistein, and tamoxifen) bind to the estrogen receptor. Ongoing studies on ethinyl estradiol, nonylphenol, and genistein by the National Toxicology Program will add to this database for estrogens (Laurenzana et al., 2002; Newbold et al., 2001). These studies will evaluate cancer incidence in offspring exposed *in utero*, during lactation, and through adulthood via diet. A study with genistein found uterine tumor development to be dependent upon early-lifestage exposures (Newbold et al., 2001). Another recent study of estrogen found a shorter latency for mammary tumors in mice exposed at 8 and 12 weeks as compared to mice exposed at 4 or 18 weeks, indicating a susceptible period between 8 to 12 weeks of exposure (Yang, 2003). Thus, there is an actively growing database from which to consider issues of childhood exposure and cancer for compounds acting through the estrogen receptor or other mechanisms of endocrine disruption.

The ability to estimate with any accuracy the juvenile to adult cancer potency ratio depends very much on the experimental design used. The lifetime design has less ability to

distinguish increased susceptibility from early-life exposure than the other types of designs. Consider two different experimental designs. In the first, the "lifetime" design, a group of animals are exposed starting as juveniles, and exposure continues through adulthood. A second group are exposed only in adulthood, and the juvenile:adult ratio results from a comparison of tumor incidences in the two groups. In the second, the "repeated" design, one group of animals is exposed only during the juvenile period, and is then followed through adulthood to assess tumor incidence, and a second group of animals is exposed only through adulthood. The lifetime design turns out to be a particularly insensitive design for estimating the juvenile:adult ratio.

The following example demonstrates the magnitude of the problem: Suppose the risk per day of exposure of a chemical is ten fold greater in the juvenile period as in the adult period, and animals exposed through adulthood at a particular dose level have an extra risk of 60% for having at least one tumor, while 1% of control animals have tumors. The adult exposure period is 94 weeks, while the juvenile exposure period is 4 weeks. Thus, in the lifetime design, the group of animals exposed as juveniles will receive a total of 98 weeks of exposure, (4 in juvenile and 94 in adult), while those receiving the adult-only exposure receive 94 weeks of exposure. In the repeated design, animals exposed as juveniles receive only 4 weeks of exposure, while the adults receive 94 weeks, just as in the lifetime design. Each group starts with 50 animals. Under these assumptions, using equations (1) and (2) from Section 2.3, the expected number of animals with tumors in the three treatment groups (control, juvenile-exposed, adult-exposed groups) in the two designs is:

	Number of animals with tumors		
	Control	**Early-life exposure**	**Adult exposure**
Lifetime	1	36	30
Repeated	1	16	30

Notice that in the "lifetime" design, only six more juvenile-exposed animals have tumors than in the adult-exposed group, whereas in the "repeated" design, 16 juvenile-exposed animals have tumors. The data in the lifetime design are consistent with the hypothesis of no tumors being induced during the juvenile period: the ratios 36/50 and 30/50 are not statistically significantly different. In other words, the data from the lifetime design are statistically consistent with the hypothesis of *no risk at all* during the juvenile period, even though the real response is a 10 times greater risk from early-life exposure. The difference between the results from the two different study designs is due to the one-hit model: each additional week of a long exposure contributes less than the previous week to the total number of animals with tumors.

Note that, even if the one-hit model is not correct, chronic exposure probably results in a non-statistically significant increase for the lifetime exposure including juveniles as compared with only adult exposure.

The proper measure of relative potency of an exposure in the juvenile period relative to an exposure in the adult period is the ratio of doses in the two periods that give the same incidence of tumors. However, most of the data sets used in this report contained only one non-control dose, precluding the extensive dose-response modeling that would be required to estimate this ratio of doses. However, this document largely considered chemicals for which a mutagenic mode of action has been established and for which a linear, no-threshold dose-response function is assumed for the low-dose range being considered for risk assessment. In the case of the linear dose-response function, the analysis of the relative response from the same dose will produce the same value as ratio of doses that produces the same incidence of tumors.

For a one-hit dose-response equation, the probability of developing a tumor after the same dose and duration in the juvenile or adult period is

$$P_a = 1 - (1 - P_0)e^{-m_a x}$$
$$P_j = 1 - (1 - P_0)e^{-m_j x}$$

for dose x. Suppose we want to calculate the dose D_a or D_j that results in a given incidence of tumors after an adult or juvenile exposure. From equation 1, D_a and D_j equal:

$$D_a = \frac{-\ln\left(\frac{1-P_c}{1-P_0}\right)}{m_a}$$
$$D_j = \frac{-\ln\left(\frac{1-P_c}{1-P_0}\right)}{m_j}$$

Thus, the ratio $D_a/D_j = m_j/m_a$, the ratio calculated in this document.

In summary, this analysis supports the conclusion that there can be greater susceptibility for the development of tumors as a result of exposures to chemicals acting through a mutagenic mode of action, when the exposures occur in early lifestages as compared with later lifestages. Thus, this Supplemental Guidance recommends for chemicals with a mutagenic mode of action for carcinogenesis when chemical-specific data on early-life exposure are absent, a default

approach using estimates from chronic studies (i.e., cancer slope factors) with appropriate modifications to address the potential for differential risk of early-lifestage exposure. For chemicals acting through a non-mutagenic mode of action, e.g., hormonally mediated carcinogens, the available data suggest that other approaches may need to be developed for addressing cancer risk estimates from childhood exposures. This is a particular concern because the tumors arising from hormonally active chemicals appear to involve different sites when exposure is during early-life versus adulthood, an effect that has been observed relatively infrequently. Development of such approaches would require additional research to provide an expanded scientific basis for their support, including additional research and the possible development of new toxicity testing protocols that consider early lifestage dosing.

The current data do also not allow analysis of some issues of potential interest for risk assessment, e.g., potential increased risk of childhood cancer, from *in utero* or childhood exposures. Assessing the role of environmental exposures on childhood cancers is difficult, but additional research could include epidemiological studies or experimental studies with animals genetically designed to express cancers analogous to human childhood cancers. Rigorous quantification of exposure doses at different lifestages and in rodent pups in experimental studies would be useful for evaluating whether there is greater childhood susceptibility. Pharmacokinetic modeling could better define the internal doses to improve determination of the magnitude of increased susceptibility.

5. GUIDANCE FOR ASSESSING CANCER RISKS FROM EARLY-LIFE EXPOSURE

Consistent with the approach and recommendations of the U.S. EPA cancer risk assessment guidelines (U.S. EPA, 2004), any assessment of cancer susceptibility will begin with a critical analysis of the available information. Figure 3 shows the proposed steps in the process. The potential for increased susceptibility to cancer from early-life exposure, relative to comparable exposure later in life, generally warrants explicit consideration for each assessment.

When developing quantitative estimates of cancer risk, the Agency recommends integration of age-specific values for both exposure and toxicity/potency where such data are available and appropriate. Children, in general, are expected to have some exposures that differ from those of adults (either higher or lower), due to differences in size, physiology, and behavior. For example, children are generally assumed to eat more food and drink more water relative to their body weight than adults. Children's normal activities, such as putting their hands into their mouths or playing on the ground, can result in exposures to contaminants that adults do not encounter. Moreover, children and adults exposed to the same concentration of an agent in food, water, or air may receive different (higher or lower) internal doses due to differences, for example, in intake, metabolism, or absorption rates. Children are less likely than adults to be exposed to products typically used in industrial settings and often have more limited diets than adults. When assessing risks, if the data are available and relevant, it is important to include exposure that is measured or modeled for all lifestages, including exposures during childhood and during adulthood. EPA continues to develop better tools for assessing childhood exposure differences, such as the *Child-Specific Exposure Factors Handbook* (U.S. EPA, 2002a), and models, such as Stochastic Human Exposure and Dose Simulation (SHEDS) and Consolidated Human Activity Database (CHAD) (McCurdy et al., 2000; Zartarian et al., 2000)

Mode-of-action studies can be a source of data on quantitative differences between children and adults (Figure 3, Box 1). If the available information is sufficient to establish the agent's mode of action for early-life and adult exposures, then the implications for early-life exposure of that mode of action are used to develop separate risk estimates for childhood exposure. Pertinent information can be obtained both from agent-specific studies and from other

studies that investigate the general properties of the particular mode of action. All data indicating quantitative differences between children and adults are considered in developing those portion(s) of the risk estimates for exposure estimates that include childhood exposure. Some examples include the potential for children to have a different internal dose of the active agent or a change in a key precursor event (see Section 2.4.3.4 of the *Guidelines for Cancer Risk Assessment*).

When the mode of action cannot be established (Figure 3, Box 2), the policy choice would be to use linear extrapolation to lower doses such that risk estimates are based on a lifetime average daily exposure without further adjustment. No general adjustment is recommended at this time. This policy choice is consistent with past U.S. EPA practice that has been favorably evaluated over the years. The result would be expected to produce plausible upper bound risk estimates, based on the use of linear extrapolation as a default in the absence of information on the likely shape of the dose-response curve.

When a mode of action other than mutagenicity is established, if it is nonlinear (Figure 3, Box 3) or linear (Figure 3, Box 4), no general adjustment is recommended at this time. Although the available studies (discussed previously) indicates that higher or lower cancer risks may result from early-life exposure, there is insufficient information or analyses currently available to determine a general adjustment at this time. As other modes of action become better understood, this information may include data on quantitative differences between children and adults. If such data are available, an analysis of the differences could be used to adjust risk estimates for childhood exposure. EPA expects to expand this Supplemental Guidance to specifically address modes of action other than mutagenicity when sufficient data are available and analyzed.

When the data indicate a mutagenic mode of action,[5] the available studies (discussed

5 Determination of chemicals that are operating by a mutagenic mode of action entails evaluation of test results for genetic endpoints, metabolic profiles, physicochemical properties, and structure-activity analyses in a weight-of-evidence approach (Waters et al., 1999). Established protocols are used to generate the data (Cimino, 2001; OECD, 1998; U.S. EPA, 2002b); however, it is recognized that newer methods and technologies such as those arising from genomics can provide useful data and insights to a mutagenic mode of action. Carcinogens acting through a mutagenic mode of action generally interact with DNA and can produce such effects as DNA adducts and/or breakage. Carcinogens with a mutagenic mode of action often produce positive effects in multiple test systems for different genetic endpoints, particularly gene mutations and structural chromosome aberrations, and in tests performed *in vivo,* which generally are supported by those performed *in vitro*. This mode of action is addressed in more detail in Section 2.3.5 of EPA's cancer guidelines (U.S. EPA, 2005).

above) indicate higher cancer risks resulting from a given exposure occurring early in life when compared with the same amount of exposure during adulthood. However, chemical-specific data relating to mode of action (e.g., toxicokinetic or toxicodynamic information) may suggest that even though a compound has a mutagenic mode of action, higher cancer risks may not result. Such data should be considered before applying the age-dependent adjustment factors.

If the available, chemical-specific information includes an epidemiologic study of the effects of childhood exposure or an animal bioassay involving early-life exposure (Figure 3, Box 5), then these studies are analyzed to develop risk estimates (i.e., cancer slope factors) that specifically address any potential for differential potency in early lifestages. An example is the IRIS assessment of vinyl chloride (U.S. EPA, 2000b; c).

In the absence of early-life studies on a specific chemical under consideration (Figure 3, Box 6), the extrapolation from the point of departure to lower doses employs linear extrapolation (see Section 3.3.1 of the U.S. EPA [2005] cancer guidelines). This choice is based on mode-of-action data indicating that mutagens can give rise to cancers with an apparently low-dose linear response. Adjustments to the resultant risk estimates are specified with regard to childhood exposures. This approach is adopted because risk estimates based on an average daily exposure prorated over a lifetime do not consider the potential for higher cancer risks from early-life exposure.

The adjustments described below reflect the potential for early-life exposure to make a greater contribution to cancers appearing later in life. The 10-fold adjustment represents an approximation of the weighted geometric mean tumor incidence ratio from juvenile or adult exposures in the repeated dosing studies (see Table 8). This adjustment is applied for the first 2 years of life, when toxicokinetic and toxicodynamic differences between children and adults are greatest (Ginsberg et al., 2002; Renwick, 1998). Toxicokinetic differences from adults, which are greatest at birth, resolve by approximately 6 months to 1 year, while higher growth rates extend for longer periods. The 3-fold adjustment represents an intermediate level of adjustment that is applied after 2 years of age through <16 years of age. This upper age limit represents middle adolescence following the period of rapid developmental changes in puberty and the conclusion of growth in body height in NHANES data (Hattis et al., 2005). Efforts to map the approximate start of mouse and rat bioassays (i.e., 60 days) to equivalent ages in humans ranged from 10.6 to 15.1 years (Hattis et al., 2005). Data are not available to calculate a specific dose-response adjustment factor for the 2 to <16-year age range, so EPA selected the 3-fold

adjustment because it reflects a midpoint, i.e., approximately half the difference between 1 and 10 on a logarithmic scale ($10^{1/2}$), between the 10-fold adjustment for the first two years of life and no adjustment (i.e., 1-fold) for adult exposure. EPA also recognizes that exposures occurring near the end of life may have little effect on lifetime cancer risk, but lacks adequate data at present to provide an adjustment for this "wasted dose" effect. Similarly, since most of the studies involved only one latency period, the potential effect of early-life exposure on latency for the observed tumors could not be evaluated. The lack of data on effect on latency also limited the types of analyses that could be performed, e.g., more complex dose-response functions, such as multi-stage or clonal expansion models, could not be evaluated. Thus, the potential effects of early-life exposures on latency were not evaluated. Finally, as the adjustment factors are derived from a weighted geometric mean of the data evaluated, these adjustment will both over-estimate and under-estimate the potential potency for early-life exposure for chemicals with a mutagenic mode of action for carcinogenesis. An examination of the data in the tables demonstrates that some of the ratios were less than one, while others exceeded 10. For this reason, the Supplemental Guidance emphasizes that chemical-specific data should be used in preference to these default adjustment factors whenever such data are available.

The following adjustments represent a practical approach that reflects the results of the preceding analysis, which concluded that cancer risks generally are higher from early-life exposure than from similar exposure durations later in life:

- For exposures before 2 years of age (i.e., spanning a 2-year time interval from the first day of birth up until a child's second birthday), a 10-fold adjustment.

- For exposures between 2 and <16 years of age (i.e., spanning a 14-year time interval from a child's second birthday up until their sixteenth birthday), a 3-fold adjustment.

- For exposures after turning 16 years of age, no adjustment.

Clearly other age groups, such as an age group experiencing pubertal changes in physiology, or approximately ages 9 - 15, may experience changes in biological processes that could lead to modifications in the susceptibility to the effects of some carcinogens, depending on the mode of action. This Supplemental Guidance focuses on carcinogens with a mutagenic mode

of action. For any mode of action, the Agency is interested in identifying lifestages that may be particularly sensitive or refractory for carcinogenesis, and believes that the mode of action framework as described by EPA's cancer guidelines (U.S. EPA, 2005), is an appropriate mechanism for elucidating these lifestages. In general, the Agency's analyses of lifestages that may be susceptible will depend on three factors: (1) establishing the mode of action for carcinogenesis; (2) using knowledge about the biological and toxicological key events in that mode of action that are likely to be affected by lifestages; and (3) the availability, or development, of data that allow analysis of the effects of chemicals acting by that mode of action during the relevant ages. For each mode of action evaluated, therefore, the various age groupings determined to be at a differential risk, which may differ significantly from those proposed for the mutagenic mode of action, are expected to be evaluated independently of other modes of action. When data, including well established mode of action data, are available that allow specific evaluation of lifestage differences in toxicokinetics or toxicodynamics that would lead to lesser or greater susceptibility from early-life exposures to carcinogens, then those data should be used, as generally discussed in EPA's cancer guidelines (U.S. EPA, 2005), in preference to the default procedures described in this Supplemental Guidance.

The 10-fold and 3-fold adjustments in slope factor are to be combined with age-specific exposure estimates when estimating cancer risks from early life exposure to carcinogens that act through a mutagenic mode of action. It is important to emphasize that these adjustments are combined with corresponding age-specific estimates of exposure to assess cancer risk. For example, for a 70-year lifetime, where there are data showing negligible exposure to children, the estimated cancer risk from childhood exposure would be also negligible and the lifetime cancer risk would be reduced to that resulting from the relevant number of years of adult exposure (in the absence of specific information, 55 years). Where there are data (measured or modeled) for childhood exposures, the age-group specific exposure values are used along with the corresponding adjustments to the slope factor. Where there are no relevant data or models for childhood exposures and only lifetime average exposure data are available, the lifetime exposure data are used with the adjustments to the slope factor for each age segment.

It is recognized that, when the exposure is fairly uniform over a lifetime, the effect of these adjustments on estimated lifetime cancer risk are small relative to the overall uncertainty of

such estimates. These adjustments can be applied when estimating the cancer risk resulting from childhood exposure. These adjustments are applied when developing risk estimates from conventional animal bioassays or epidemiologic studies of effects of adult exposure. Some examples follow in the next section.

The Agency has also carefully considered both the advantages and disadvantages to extending the default potency adjustment factors to carcinogenic chemicals for which the mode of action remains unknown. It is the Agency's long-standing science policy position that use of the linear low-dose extrapolation approach (without further adjustment) provides adequate public health conservatism in the absence of chemical-specific data indicating differential early-life susceptibility. At the present time, therefore, EPA is recommending these age-dependent adjustment factors only for carcinogens acting through a mutagenic mode of action based on a combination of analysis of available data and the above-mentioned science policy position. In general, the Agency prefers to rely on analyses of data, rather than general defaults. When data are available for a susceptible lifestage, they should be used directly to evaluate risks for that chemical and that lifestage on a case-by-case basis. In this analysis, the data for non-mutagenic carcinogens, when the mode of action is unknown, were judged to be too limited and the modes of action too diverse to use this as a category for which a general default adjustment factor approach can be applied.

6 COMBINING LIFESTAGE DIFFERENCES IN EXPOSURE AND DOSE-RESPONSE WHEN ASSESSING CARCINOGEN RISK - SOME EXAMPLES FOR CARCINOGENS THAT ACT THROUGH A MUTAGENIC MODE OF ACTION

It is important for the risk assessor to consider lifestage differences in both exposure and dose-response when assessing cancer risk resulting from early-life exposures. As discussed in Section 5, age dependent adjustments factors (ADAFs) in dose response (i.e., slope factors) are combined with age specific exposure estimates when assessing cancer risks. This is a departure from the way cancer risks have historically been based upon the premise that risk is proportional to the daily average of lifetime dose. This Supplemental Guidance recommends an integrative approach that can be used to assess total lifetime risk resulting from lifetime or less-than-lifetime exposure during a specific portion of a lifetime.

The following examples can help demonstrate how to apply this guidance by integrating potential lifestage differences in exposure and/or dose-response (potency), and also demonstrate what the resulting impacts are on calculated risks. These hypothetical examples consider risks from both lifetime, as well as less-than-lifetime oral exposures. Risks associated with inhalation exposure to carcinogens that act via a mutagenic mode of action are calculated in similar fashion by applying the appropriate ADAF(s) along with the corresponding inhalation unit risk estimate, using pertinent estimates of exposure concentration.

Note again, ADAFs are only to be used for agents with a mutagenic mode of action for carcinogenesis when chemical-specific data are absent. For all modes of action, when chemical-specific data are available for early-life exposure, those data should be used.

6.1 CALCULATING LIFETIME RISKS ASSOCIATED WITH LIFETIME EXPOSURES

Example 1: Consider a scenario of exposure to a carcinogen with a **nonmutagenic** mode of action. Suppose the oral cancer slope factor derived from a typical animal study (i.e., where dosing begins after puberty) is estimated to be 2 per mg/kg-d, and the exposure rate remains constant throughout life at 0.0001 mg/kg-d (this is equivalent to saying the daily average of lifetime dose rate is equal to 0.0001 mg/kg-d). The risk from lifetime exposure is calculated by multiplying the slope factor and the exposure rate:

$$\text{Risk} = (2 \text{ per mg/kg-d}) \times (0.0001 \text{ mg/kg-d})$$

$= \quad 2 \times 10^{-4}$

Example 2: Now consider the same exposure scenario for a carcinogen with a **mutagenic** mode of action for which the oral cancer slope factor, derived from a typical animal study where dosing begins after puberty, is also estimated to be 2 per mg/kg-d. In this case, ADAFs are used, as follows.

a. To calculate lifetime risk for a population with average life expectancy of 70 years, sum the risk associated with each of the three relevant time periods:

- Risk during the first 2 years of life (where the ADAF = 10);
- Risk for ages 2 through < 16 (ADAF = 3); and
- Risk for ages 16 until 70 years (ADAF = 1).

Thus, risk equals the sum of:

- Risk for birth through < 2 yr = (2 per mg/kg-d) x 10 (ADAF) x (0.0001 mg/kg-d) x 2yr/70yr
  $= 0.6 \times 10^{-4}$
- Risk for ages 2 through < 16 = (2 per mg/kg-d) x 3 (ADAF) x (0.0001 mg/kg-d) x (13yr/70yr)
  $= 1.1 \times 10^{-4}$
- Risk for ages 16 until 70 = (2 per mg/kg-d) x 1 (ADAF) x (0.0001 mg/kg-d) x (55yr/70yr)
  $= 1.6 \times 10^{-4}$

Risk $= 0.6 \times 10^{-4} + 1.1 \times 10^{-4} + 1.6 \times 10^{-4}$

$= 3.3 \times 10^{-4}$

b. If exposure varies with age, then such differences are also included. Now suppose the same example as immediately above, except that exposure for ages 1 through <12 was twice as high as exposure for all other ages. In this case, sum the risk associated with each of the five relevant time periods in which exposure rates and/or potencies (slope

factors) vary:

Risk equals the sum of:

- Risk for birth through < 1 yr (1yr) = (2 per mg/kg-d) x 10 (ADAF) x 0.0001 mg/kg-d x 1yr/70yr
  $= 0.3 \times 10^{-4}$
- Risk for ages 1 through < 2 (1yr) = (2 per mg/kg-d) x 10 (ADAF) x 0.0002 mg/kg-d x 1yr/70 yr
  $= 0.6 \times 10^{-4}$
- Risk for ages 2 through < 12 (10yr) = (2 per mg/kg-d) x 3 (ADAF) x 0.0002 mg/kg-d x 10yr/70yr
  $= 1.7 \times 10^{-4}$
- Risk for ages 12 through < 16 (4yr) = (2 per mg/kg-d) x 3 (ADAF) x 0.0001 mg/kg-d x 4yr/70yr
  $= 0.3 \times 10^{-4}$
- Risk for ages 16 until 70 years (55yr) = (2 per mg/kg-d) x 1 (ADAF) x 0.0001 mg/kg-d x 55yr/70yr
  $= 1.6 \times 10^{-4}$

Risk $= 0.3 \times 10^{-4} + 0.6 \times 10^{-4} + 1.7 \times 10^{-4} + 0.3 \times 10^{-4} + 1.6 \times 10^{-4}$
$= 4.5 \times 10^{-4}$

6.2 CALCULATING LIFETIME RISKS ASSOCIATED WITH LESS THAN LIFETIME EXPOSURES

If exposure only occurs for a limited number of years (for example, consider a family that lives near a source of exposure for a five-year period of time before moving away), it is critical to combine lifestage differences in exposure and dose-response for the relevant time interval. The examples presented below demonstrate how adjusting potency and/or exposure can affect the assessment of cancer risk.

Example 3: If exposure to a carcinogen with a mutagenic mode of action with an oral slope factor equal to 2 per mg/kg-d occurs during adulthood for only 5 years, the daily average of lifetime dose is time weighted to apportion risk for the number of years of exposure by a factor of 5/70:

$$\text{Risk} = (2 \text{ per mg/kg-d}) \times (0.0001 \text{ mg/kg-d}) \times (5\text{yr}/70\text{yr})$$
$$= 1.4 \times 10^{-5}$$

Example 4: If this 5-year exposure occurs during childhood, the risk calculations are adjusted to consider the potential for higher potency from early-life exposure. Assessors should remember that the age dependent adjustment factors for carcinogens with a mutagenic mode of action are applied only to exposure periods occurring up to age 16.

a. For a child exposed between ages 5 and 10, only a 3-fold ADAF is applied because the exposure occurs entirely between ages 2 and <16 years:

$$\text{Risk} = 3 \text{ (ADAF)} \times (2 \text{ per mg/kg-d}) \times (0.0001 \text{ mg/kg-d}) \times (5 \text{ yr}/70 \text{ yr})$$
$$= 4.3 \times 10^{-5}$$

b. For an exposure between ages 13 and <18, a 3-fold ADAF is applied only to the 3-year portion occurring before age 16:

Risk equals the sum of:

- Risk for ages 13 through < 16 (3yr) $= 3 \text{ (ADAF)} \times (2 \text{ per mg/kg-d}) \times (0.0001 \text{ mg/kg-d}) \times (3 \text{ yr}/70 \text{ yr})$
  $= 2.6 \times 10^{-5}$
- Risk for ages 16 through < 18 (2yr) $= 1 \text{ (ADAF)} \times (2 \text{ per mg/kg-d}) \times (0.0001 \text{ mg/kg-d}) \times (2 \text{ yr}/70 \text{ yr})$
  $= 0.6 \times 10^{-5}$

$$\text{Risk} = 2.6 \times 10^{-5} + 0.6 \times 10^{-5}$$

$= 3.2 \times 10^{-5}$

c. For a child exposed from birth through age 5, different ADAFs are applied to the periods before and after age 2:

Risk equals the sum of:

- Risk for birth through < 2 (2yr) $= 10 \text{ (ADAF)} \times (2 \text{ per mg/kg-d}) \times (0.0001 \text{ mg/kg-d}) \times (2 \text{ yr}/70 \text{ yr})$
  $= 5.7 \times 10^{-5}$
- Risk for ages 2 through < 5 (3yr) $= 3 \text{ (ADAF)} \times (2 \text{ per mg/kg-d}) \times (0.0001 \text{ mg/kg-d}) \times (3 \text{ yr}/70 \text{ yr})$
  $= 2.6 \times 10^{-5}$

Risk $= 5.7 \times 10^{-5} + 2.6 \times 10^{-5}$
$= 8.3 \times 10^{-5}$

Example 5: Lifetime risk calculations based on less-than-lifetime exposure to a carcinogen with a mutagenic mode of action include any lifestage changes in potency as well as exposure. In this example, again consider a scenario of 5 years of exposure to a carcinogen with a mutagenic mode of action, but suppose that the exposure rate is found to vary from 0.0002 mg/kg-d during the first 2 years of life, to 0.0001 mg/kg-d during the last 3 years.

a. For a child exposed between birth and age 5, sum the risk associated with the two relevant time periods:

Risk equals the sum of:

- Risk for birth through < 2 (2yr) = 10 (ADAF) x (2 per mg/kg-d) x (0.0002 mg/kg-d) x (2 yr/70 yr)
  $= 11.4 \times 10^{-5}$
- Risk for ages 2 through < 5 (3yr) = 3 (ADAF) x (2 per mg/kg-d) x (0.0001 mg/kg-d) x (3 yr/70 yr)
  $= 2.6 \times 10^{-5}$

Risk $= 11.4 \times 10^{-5} + 2.6 \times 10^{-5}$
$= 1.4 \times 10^{-4}$

b. For comparison, a similar risk calculation for 5 years of exposure later in life (after age 16) in which the first 2 years of exposure are double that of the next 3 years are carried out without any adjustment for potency:

Risk equals the sum of:

- Risk for first 2 years of adult exposure = 1 (ADAF) x (2 per mg/kg-d) x (0.0002 mg/kg-d) x (2yr/70yr)
  $= 1.1 \times 10^{-5}$
- Risk for final 3 years of adult exposure = 1 (ADAF) x (2 per mg/kg-d) x (0.0001 mg/kg-d) x (3yr/70yr)
  $= 0.9 \times 10^{-5}$

Risk $= 1.1 \times 10^{-5} + 0.9 \times 10^{-5}$
$= 2 \times 10^{-5}$

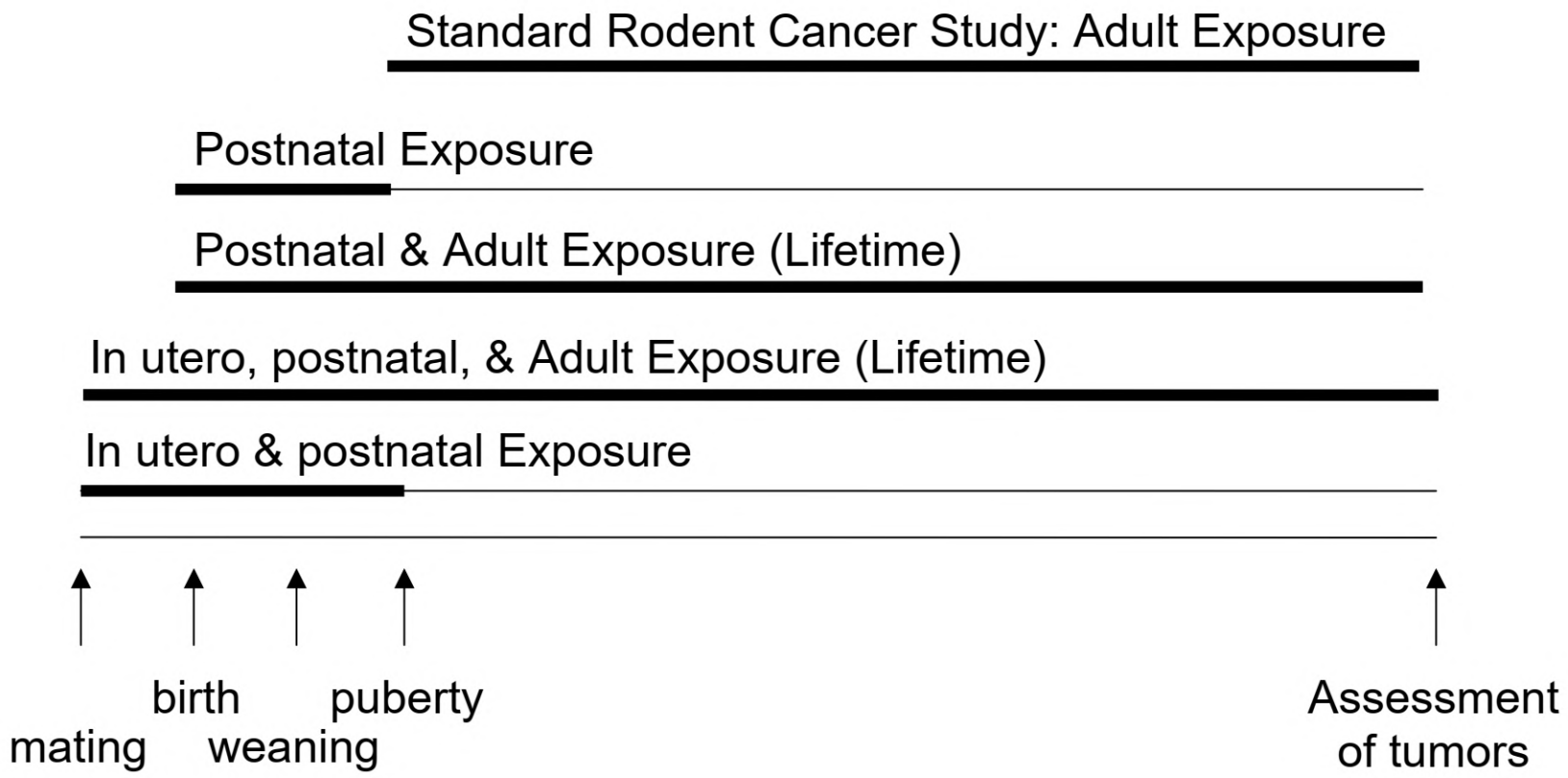

Figure 1. Study designs.

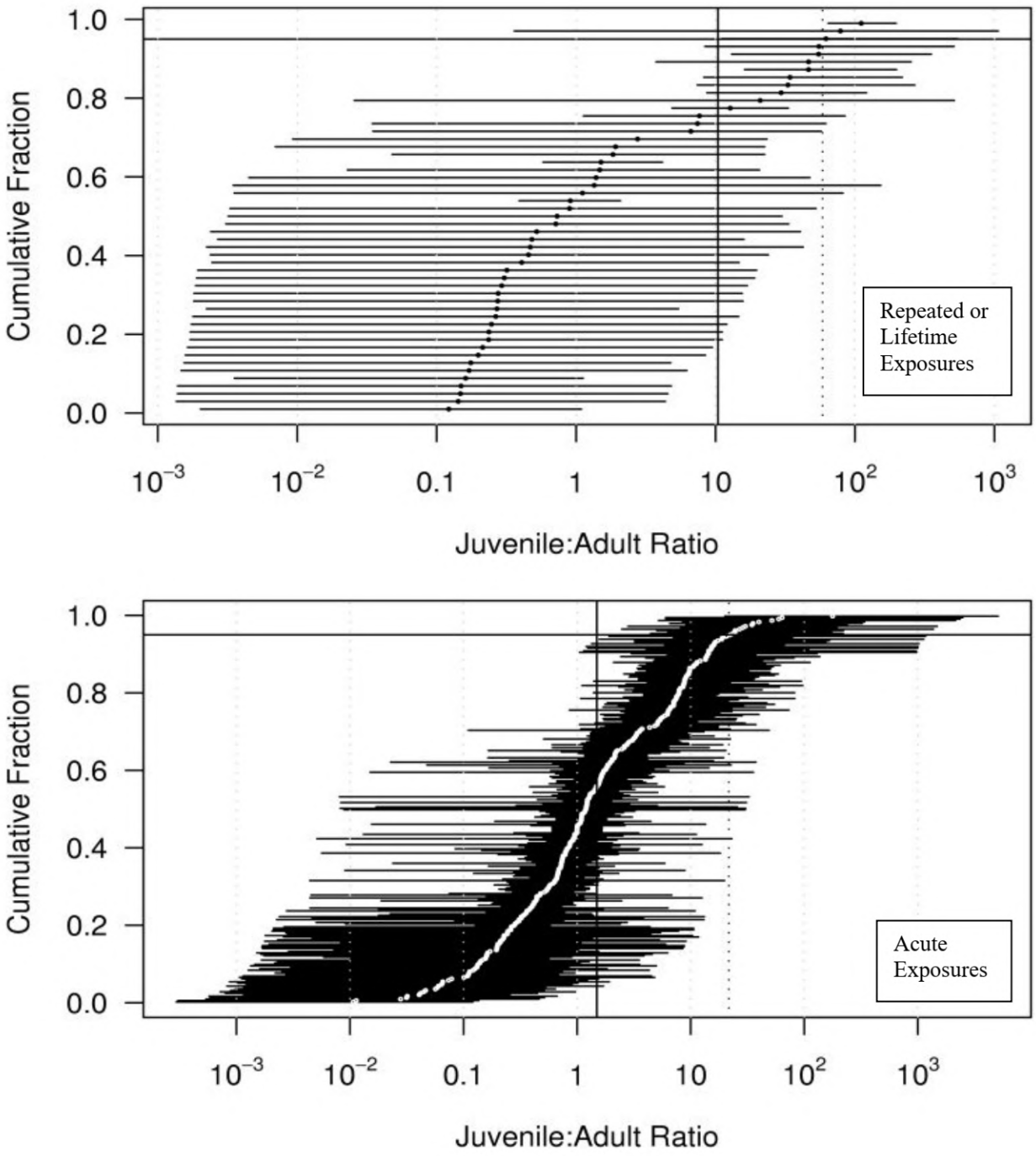

Figure 2: Posterior, unweighted geometric means and 95% confidence intervals for the ratios of juvenile to adult cancer potency for carcinogens acting primarily through a mutagenic mode of action. The top panel is for repeated and lifetime exposure studies (geometric mean in black), the bottom panel is for acute exposure studies mutagens (geometric mean in white). The horizontal lines to the left and right of each geometric mean correspond to 95% confidence limits. The vertical dark line represents the inverse-variance weighted geometric mean of the posterior geometric means. The horizontal dark line represents the 95th percentile of the unweighted distribution, with the vertical, dotted line establishing it value.

Figure 3. Flow chart for early-life risk assessment using mode of action framework

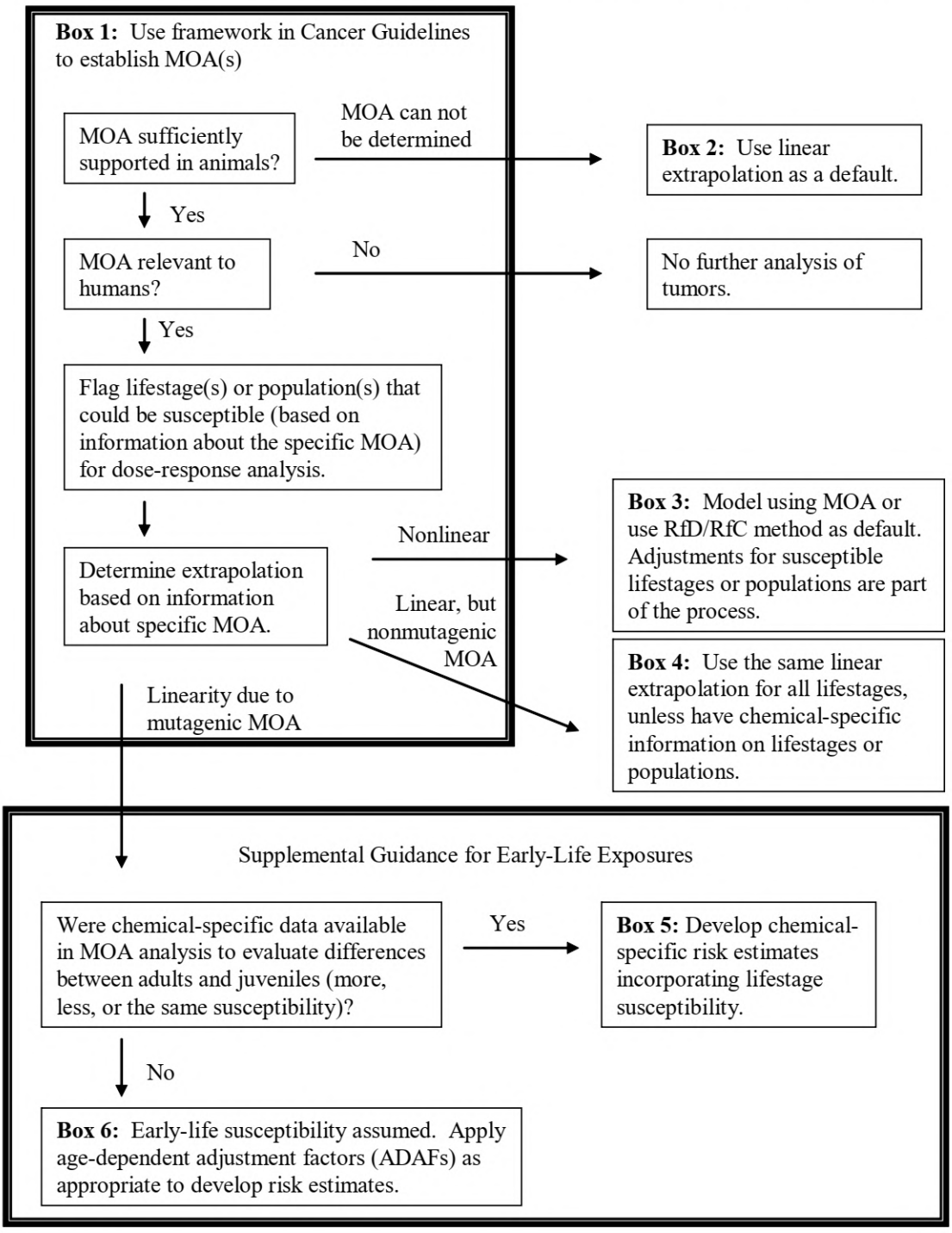

Table 1a. Chemicals that have been found to have carcinogenic effects from prenatal or postnatal exposure in animals as identified in different review articles

Chemical name	Review articles including prenatal and postnatal exposure					Chemicals selected for quantitative analysis
	Fujii (1991)	McClain et al. (2001)	Anderson et al. (2000)	Della Porta and Terracini (1969)	Other literature	
4-Acetylaminobiphenyl (AAB)	X					
4-Aminoazobenzene (AB)	X					
3-Amino-1,4,-dimethyl-5H-pyrido[4,3-b]indole (Trp-P-1)	X					
2-Aminodipyridol[1,2-a:3',2'-d]imidazole (Glu-P-2)	X					
2-Amino-6-methyldipyridol[1,2-a:3',2'-d]imidazole (Glu-P-1)	X					
3-Amino-1-methyl-5H-pyrido[4,3-b]indole (Trp-P-2)	X					
Amitrole						X
Arsenic					X	
5-Azacytidine			X			
3'-Azido-3'-deoxythymidine (AZT)			X			
Azoxymethane			X			
Benz[*a*]anthracene				X		
Benzidine			X			X
Benzo[*a*]pyrene (BaP)	X			X		X
1-(4'Bromophenylazo)-1-phenyl-1-hydroperoxymethane (BPH)	X					
N-Butyl-N-(3-carboxypropyl)nitrosamine (BCPN)	X					
N-Butyl-N-(3 hydroxbutyl)nitrosamine (BBN)	X					
Butylnitrosourea (BNU)	X					
Cyclophosphamide		X				
Dibenz[*a,h*]anthracene (DBA)				X		X
Dibutylnitrosamine (DBN)	X					
Dichlorodiphenyltrichloroethane (DDT)						X
Dieldrin						X
2-Diethylaminoethyl-2,2-dephenylvalerate hydrochloride (SKF 525A)	X					

Table 1a. Chemicals that have been found to have carcinogenic effects from prenatal or postnatal exposure in animals as identified in different review articles (continued)

Chemical name	Review articles including prenatal and postnatal exposure					Chemicals selected for quantitative analysis
	Fujii (1991)	McClain et al. (2001)	Anderson et al. (2000)	Della Porta and Terracini (1969)	Other literature	
Diethylnitrosamine (DEN)	X		X			X
Diethylstilbesterol (DES)			X			
4-Dimethylaminoazobenzene				X		
1,2-Dimethylhydrazine (DMH)	X					
7,12-Dimethylbenz[*a*]anthracene (DMBA)	X		X	X		X
Dimethylnitrosamine (DMN)	X		X	X		X
5',5'-Diphenylhydantoin (DPH)						X
Estradiol	X	X				
6-Ethoxy-2,2,4-trimethyl-1,2-dihydroquinoline (Santoquin)	X					
Ethylene thiourea (ETU)						X
Ethyl methane sulphonate				X		
Ethylnitrosobiuret			X			
Ethylnitrosourea (ENU)			X			X
N-2-Fluorenylacetamide (FAA)	X			X		
Genistein					X	
3-Hydroxyl-4-acetylaminobiphenyl (N-OH-AAB)	X					
N-2-Hydroxy-N-2-fluorenylacetamide (N-OH-FAA)	X					
2-Hydroxypropyl-propylnitrosamine			X			
9-Methylanthracene				X		
Methyl-2-benzylhydrazine			X			
Methylcholanthrene			X	X		
3-Methyl-4-dimethylaminoabenzene (3'ME-DAB)	X					
4-(Methylnitrosoamino)-1-(3-pyridyl)-1-butanone (NNK)			X			
Methylnitrosourea (NMU)			X			
Methylnitrosourethane			X			
1-Methyl-3-nitro-1-nitrosoguanidine (MNNG)	X					

Table 1a. Chemicals that have been found to have carcinogenic effects from prenatal or postnatal exposure in animals as identified in different review articles (continued)

Chemical name	Review articles including prenatal and postnatal exposure					Chemicals selected for quantitative analysis
	Fujii (1991)	McClain et al. (2001)	Anderson et al. (2000)	Della Porta and Terracini (1969)	Other literature	
2-Naphthylamine				X		
2-Naphthylhydroxyamine				X		
Nickel acetate			X			
N-Nitrosobuylamine			X			
4-Nitroquinoline-1-oxide			X	X		
N-Nitrosomethyl(2-oxopropyl)amine			X			
2-Oxopropyl-propylnitrosamine			X			
1-Phenyl-3,3',-dimethylhydrzine			X			
1-Phenyl-3,3,-dimethyltriazene			X			
Polybrominated biphenyls (PBBs)						X
Safrole (3,4-methylenedioxyally benzene)	X		X			X
Soot	X					
Sterigmatocystin	X					
Tamoxifen					X	
1,3,5-Trimethyl-2,4,6-tris[3,5-di-tert-butyl-4-hydroxybenzyl]benzene (Ionox 33)	X					
Urethane (ethyl carbamate)			X	X		X
Vinyl chloride						X

Table 1b. List of chemicals considered in this analysis. (These are chemicals for which both early-life and adult exposure are reported in the same animal experiment.)

Chemical	References	Study type	Mutagenic mode of action
Amitrole	Vesselinovitch (1983)	Repeat dosing	
Benzidine	Vesselinovitch et al. (1975b)	Repeat dosing	X
Benzo[*a*]pyrene (BaP)	Vesselinovitch et al. (1975a)	Acute exposure	X
Dibenzanthracene (DBA)	Law (1940)	Acute exposure	X
Dichlorodiphenyltrichloroethane (DDT)	Vesselinovitch et al. (1979)	Repeat dosing Lifetime exposure	
Dieldrin	Vesselinovitch et al. (1979)	Repeat dosing Lifetime exposure	
Diethylnitrosamine (DEN)	Peto et al. (1984)	Lifetime exposure	X
	Vesselinovitch et al. (1984)	Acute exposure	
Dimethylbenz[*a*]anthracene (DMBA)	Meranze et al. (1969)	Acute exposure	X
	Pietra et al. (1961)	Acute exposure	
	Walters (1966)	Acute exposure	
Dimethylnitrosamine (DMN)	Hard (1979)	Acute exposure	X
Diphenylhydantoin, 5,5- (DPH)	Chhabra et al. (1993b)	Repeat dosing Lifetime exposure	
Ethylnitrosourea (ENU)	Naito et al. (1981)	Acute exposure	X
	Vesselinovitch et al. (1974)	Acute exposure	
	Vesselinovitch (1983)	Acute exposure	
Ethylene thiourea (ETU)	Chhabra et al. (1992)	Repeat dosing Lifetime exposure	
3-Methylcholanthrene (3-MU)[a]	Klein (1959)	Repeat dosing	X
Methylnitrosourea (NMU)	Terracini and Testa (1970) Terracini et al. (1976)	Acute exposure Acute exposure	X
Polybrominated biphenyls (PBBs)	Chhabra et al. (1993a)	Repeat dosing Lifetime exposure	
Safrole	Vesselinovitch et al. (1979)	Repeat dosing Lifetime exposure	X
Urethane	Chieco-Bianchi et al. (1963) Choudari Kommineni et al. (1970) De Benedictis et al. (1962) Fiore-Donati et al. (1962)	Acute exposure Acute exposure Acute exposure Acute exposure	X
	Klein (1966)	Acute exposure Lifetime exposure	
	Liebelt et al. (1964)	Acute exposure	
	Rogers (1951)	Acute exposure	
Vinyl chloride (VC)	Maltoni et al. (1984)	Repeat dosing	X

[a] Formerly known as 20-methylcholanthrene.

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
Amitrole	Mice ($B6C3F_1$)	liver	Control	None	Control: 0 ppm	N/A	90 weeks	1/98 (1%)	0/96 (0%)	Incidences are mice with adenomas or carcinomas.	Vesselinovitch (1983)
			Gestation day 12	Diet, to mothers	500 ppm	Gestation day 12 to delivery		6/74 (8%)[b]	0/83 (0%)[b]		
			Newborn	Diet, to mothers	500 ppm	Birth until weaning		10/45 (22%)[b]	0/55 (0%)[b]		
			At weaning	Diet, to offspring	500 ppm	From weaning to 90 weeks		20/55 (36%)[b]	9/49 (18%)[b]		
Benzidine	Mice ($B6C3F_1$)	liver	Control	None	Control: 0 ppm	N/A	90 weeks	1/98 (1%)	0/100 (0%)	Higher sensitivity in males during perinatal period, in females during adulthood. Incidences are mice with adenomas or carcinomas.	Vesselinovitch et al. (1975b) Vesselinovitch et al. (1979a)
			Gestation day 12	Diet, to mothers	150 ppm	Gestation day 12 to delivery		17/55 (31%)[c]	2/62 (3%)[d]		
			Newborn	Diet, to mothers	150 ppm	Birth until weaning		62/65 (95%)[c]	2/43 (5%)[d]		
			At weaning	Diet, to offspring	150 ppm	From weaning to 90 weeks		22/50 (44%)[c]	47/50 (94%)[c]		
			Gestation day 12	Diet, to mothers	150 ppm	Gestation day 12 until weaning		49/49 (100%)[c]	12/48 (25%)[c]		
			Gestation day 12	Diet, to mothers	150 ppm	Gestation day 12 until 90 weeks		50/50 (100%)[c]	47/50 (94%)[c]		
DDT Dichlorodiphenyl-trichloroethane	Mice ($B6C3F_1$)	liver	Control	None	Control: 0 ppm	N/A	90 weeks	1/50 (2%)	—		Vesselinovitch et al. (1979b)
			Week 1	Gavage, daily	230 µg	Weeks 1–4		5/49 (10%)[d]	—		
			Week 5	Diet, daily	150 ppm	Weeks 5–90		8/49 (16%)[d]	—		
			Week 1	Gavage, daily until 4 weeks, then in diet	230 µg 150 ppm (diet)	Weeks 1–90		10/50 (20%)[c]	—		

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
Dieldrin	Mice ($B6C3F_1$)	liver	Control	None	Control: 0 ppm	N/A	90 weeks	1/58 (2%)	—		Vesselinovitch et al. (1979b)
			Week 1	Gavage, daily	12.5 µg	Weeks 1–4		3/46 (7%)[b]	—		
			Week 5	Diet, daily	10 ppm	Weeks 5–90		7/60 (12%)[b]	—		
			Week 1	Gavage, daily until 4 weeks, then in diet	12.5 µg 10 ppm	Weeks 1–90		21/70 (30%)[a]	—		
DEN[e] Diethylnitrosamine	Rats (Colworth)	liver	Control		Control	N/A		29/384 (8%)		Highest tumor rate when dosed at earlier ages. Incidents are rats with adenomas or carcinomas.	Peto et al. (1984)
			Week 3	Diet (in drinking water), daily	16 different doses combined[f]	From week 3 until death	6 months–3 years	105/180 (58%)[b]			
			Week 6			From week 6 until death		714/1440 (50%)[b]			
			Week 20			From week 20 until death		76/180 (42%)[b]			
		esophagus	Control		Control	N/A		0/384 (0%)			
			Week 3	Diet (in drinking water), daily	16 different doses combined[g]	From week 3 until death		77/180 (43%)[b]			
			Week 6			From week 6 until death		663/1440 (46%)[b]			
			Week 20			From week 20 until death		88/180 (49%)[b]			

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
DPH Diphenylhydantoin, 5,5-	Rats (F344/N)	liver	Control	Control	0 ppm	N/A	2 years	0/50 (0%)	0/50 (0%)	In rats, perinatal exposure ranged from 63 to 630 ppm, and adult exposures ranged from 240 to 2,400 ppm. In mice, perinatal exposure ranged from 21 to 210 ppm. Adult exposure ranged from 30 to 300 ppm in males and 60 to 600 ppm in females. Tumor incidences are animals with adenomas or carcinomas.	Chhabra et al. (1993b)
			Perinatal	Diet, daily	630 ppm	Perinatal through 8 weeks		1/50 (2%)[d]	0/49 (0%)[d]		
			8 weeks		800 ppm	8 weeks–2 years		2/50 (4%)[d]	1/50 (2%)[d]		
			8 weeks		2,400 ppm	8 weeks–2 years		4/50 (8%)[d]	1/50 (2%)[d]		
			Perinatal		630–800	Perinatal through 2 years		1/49 (2%)[d]	0/50 (0%)[d]		
			Perinatal		630–2,400 ppm	Perinatal through 2 years		5/49 (10%)[c]	0/50 (0%)[d]		
	Mice ($B6C3F_1$)	liver	Control	Control male	0 ppm	N/A	2 years	29/50 (58%)			
			Perinatal	Diet, male	210 ppm	Perinatal through 8 weeks		33/50 (66%)[d]			
			8 weeks		100 ppm	8 weeks–2 years		29/49 (59%)[d]			
			8 weeks		300 ppm	8 weeks–2 years		26/49 (53%)[d]			
			Perinatal		210–100 ppm	Perinatal through 2 years		35/49 (71%)[d]			
			Perinatal		210–300 ppm	Perinatal through 2 years		41/50 (82%)[c]			
			Control	Control female	0 ppm	N/A	2 years		5/48 (10.4%)[d]		
			Perinatal	Diet, female	210 ppm	Perinatal through 8 weeks			12/49 (24.5%)[d]		
			8 weeks		200 ppm	8 weeks–2 years			14/49 (28%)[c]		
			8 weeks		600 ppm	8 weeks–2 years			30/50 (60%)[c]		
			Perinatal		210–200 ppm	Perinatal through 2 years			16/50 (32%)[c]		
			Perinatal		210–600 ppm	Perinatal through 2 years			34/50 (68%)[c]		

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
ETU Ethylene thiourea	Rats (F344/N)	thyroid	Control	Control	0 ppm	N/A	2 years	1/49 (2%)	3/50 (6%)	Tumor incidences are animals with adenomas or carcinomas.	Chhabra et al. (1992)
			Perinatal	Diet, daily	90 ppm	Perinatal through 8 weeks		4/49 (8%)[d]	3/50 (6%)[d]		
			8 weeks		83 ppm	8 weeks–2 years		12/46 (26%)[c]	7/44 (16%)[d]		
			8 weeks		250 ppm	8 weeks–2 years		37/50 (74%)[c]	30/49 (61%)[c]		
			Perinatal		90–83 ppm	Perinatal through 2 years		13/50 (26%)[c]	9/47 (19%)[d]		
			Perinatal		90–250 ppm	Perinatal through 2 years		48/50 (96%)	37/50 (74%)		
	Mice ($B6C3F_1$)	liver	Control	Control	0 ppm	N/A	2 years	20/49 (41%)	4/50 (8%)		
			Perinatal	Diet, daily	330 ppm	Perinatal through 8 weeks		13/49 (26.5%)[d]	5/49 (10%)[d]		
			8 weeks		330 ppm	8 weeks–2 years		32/50 (64%)[c]	44/50 (88%)[c]		
			8 weeks		1,000 ppm	8 weeks–2 years		46/50 (92%)[c]	48/50 (96%)[c]		
			Perinatal		330–330 ppm	Perinatal through 2 years		34/49 (69%)[c]	46/50 (92%)[c]		
			Perinatal		330–1,000 ppm	Perinatal through 2 years		47/49 (6%)[c]	49/50 (98%)[c]		
		thyroid	Control	Control	0 ppm	N/A		1/50 (2%)	0/50 (0%)		
			Perinatal	Diet, daily	330 ppm	Perinatal through 8 weeks		1/46 (2%)[d]	1/49 (2%)[d]		
			8 weeks		330 ppm	8 weeks–2 years		1/49 (2%)[d]	2/50 (4%)[d]		
			8 weeks		1,000 ppm	8 weeks–2 years		29/50 (58%)[c]	38/50 (76%)[c]		

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
ETU Ethylene thiourea (continued)			Perinatal		330–330 ppm	Perinatal through 2 years		2/48 (4%)[d]	10/49 (20%)[c]		
			Perinatal		330–1,000 ppm	Perinatal through 2 years		35/49 (71%)[c]	38/50 (76%)[c]		
		pituitary	Control	Control	0 ppm	N/A		0/44 (0%)	11/47 (23%)		
			Perinatal	Diet, daily	330 ppm	Perinatal through 8 weeks		0/42 (0%)[d]	11/48 (23%)[d]		
			8 weeks		330 ppm	8 weeks–2 years		0/42 (0%)[d]	19/49 (39%)[d]		
			8 weeks		1,000 ppm	8 weeks–2 years		8/41 (19.5%)[c]	26/49 (53%)[c]		
			Perinatal		330–330 ppm	Perinatal through 2 years		0/45 (0%)[d]	26/47 (55%)[c]		
			Perinatal		330–1,000 ppm	Perinatal through 2 years		4/39 (10%)[d]	24/47 (51%)[c]		

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death		Tumor incidence		Reference
							M	F	M	F	
3-Methylcholanthrene (formerly known as 20-methylcholanthrene)	Mice (Albino)	liver	Control	gavage, 3× per week	NA	NA	475 days	480 days	3/39 (7.7%)	0/36 (0%)	Klein (1959)
			8 days		0.25 mg/g	10×	311 days	321 days	21/25 (84%)[b]	7/30 (23.3%)[b]	
			90 days		0.25 mg/g	10×	330 days	366 days	1/26 (3.8%)[b]	0/29 (0%)[d]	
		lung	Control		NA	NA	475 days	480 days	17/39 (43.6%)	14/36 (38.9%)	
			8 days		0.25 mg/g	10×	311 days	321 days	25/25 (100%)[b]	28/30 (93.3%)[b]	
			90 days		0.25 mg/g	10×	330 days	366 days	25/26 (96.2%)[b]	27/29 (93.1%)[b]	
		fore-stomach	Control		NA	NA	475 days	480 days	0/39 (0%)	0/36 (0%)	
			8 days		0.25 mg/g	10×	311 days	321 days	12/25 (48%)[b]	12/30 (40%)[b]	
			90 days		0.25 mg/g	10×	330 days	366 days	13/26 (50%)[b]	8/29 (27.6%)[b]	
		skin	Control		NA	NA	475 days	480 days	0/39 (0%)	0/36 (0%)	
			8 days		0.25 mg/g	10×	311 days	321 days	4/25 (16%)[b]	4/30 (13.3%)[b]	
			90 days		0.25 mg/g	10×	330 days	366 days	1/26 (3.8%)[b]	1/25 (4%)[b]	

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
PBBs Polybrominated biphenyls	Rats (F344/N)	liver[g]	Control	Control	0 ppm	N/A	2 years	1/50 (2%)	0/50 (0%)	Findings suggest that combined perinatal and adult exposure increases PBB-related hepatocellular carcinogenicity relative to adult-only exposure in mice and female rats. Apparent association between increasing incidences of MCL and exposure to PBB in male and female rats. Tumor incidences are animals with adenomas or carcinomas.	Chhabra et al. (1993a)
			Perinatal	Diet	10 ppm	Perinatal–8 weeks		5/50 (10%)[d]	0/50 (0%)[d]		
			8 weeks		10 ppm	8 weeks–2 years		12/49 (24%)[c]	12/50 (24%)[c]		
			8 weeks		30 ppm	8 weeks–2 years		41/50 (82%)[c]	39/50 (78%)[c]		
			Perinatal		10–10 ppm	Perinatal–2 years		16/50 (32%)[c]	39/50 (78%)[c]		
			Perinatal		10–30 ppm	Perinatal–2 years		41/50 (82%)[c]	47/50 (94%)[c]		
		Mono-nuclear cell leukemia (MCL)	Control	Control	0 ppm	N/A	2 years	25/50 (50%)	14/50 (28%)		
			Perinatal	Diet	10 ppm	Perinatal–8 weeks		31/50 (62%)[d]	13/50 (26%)[d]		
			8 weeks		10 ppm	8 weeks–2 years		33/50 (66%)[c]	22/50 (44%)[d]		
			8 weeks		30 ppm	8 weeks–2 years		31/50 (62%)[d]	23/50 (46%)[c]		
			Perinatal		10–10 ppm	Perinatal–2 years		37/50 (74%)[c]	27/50 (54%)[c]		
			Perinatal		10–30 ppm	Perinatal–2 years		37/50 (74%)[c]	25/50 (50%)[c]		
	Mice ($B6C3F_1$)	liver[g]	Control	Control	0 ppm	N/A	2 years	16/50 (32%)	5/50 (10%)		
			Perinatal	Diet	30 ppm	Perinatal–8 weeks		40/50 (80%)[c]	21/50 (42%)[c]		
			8 weeks		10 ppm	8 weeks–2 years		48/49 (98%)[c]	42/50 (84%)[c]		
			8 weeks		30 ppm	8 weeks–2 years		48/50 (96%)[c]	47/48 (98%)[c]		
			Perinatal		10 ppm	Perinatal–2 years		46/49 (94%)[c]	44/50 (88%)[c]		
			Perinatal		30–30 ppm	Perinatal–2 years		50/50 (100%)[c]	47/47 (100%)[c]		

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
Safrole	Mice ($B6C3F_1$)	liver	Control	None	None	N/A	90 weeks	3/100 (3%)	0/100 (0%)	Highest tumor rate in males due to preweaning treatment. Highest tumor rate in females due to susceptibility in adulthood. Tumor incidences are mice with adenomas or carcinomas.	Vesselinovitch et al. (1979b)
			Day 12 of gestation	Gavage, to mothers	120 µg/g body weight	4× (days 12, 14, 16, 18)		2/61 (3%)[d]	0/65 (0%)[d]		
			Newborn	Gavage, to mothers, on alternate days	120 µg/g body weight	From birth until weaning		28/83 (34%)[c]	2/80 (3%)[d]		
			At weaning	Gavage, to offspring, 2× weekly	120 µg/g body weight	From weaning until 90 weeks		4/35 (11%)[d]	22/36 (61%)[c]		
			Day 12 of gestation	Gavage, to mothers, alternate days	120 µg/g body weight	From gestation until weaning		22/68 (32%)[b]	1/72 (1%)[b]		
			Day 12 of gestation	Gavage, to mothers, alternate days until weaning; Gavage, to offspring, 2× weekly	120 µg/g body weight	From gestation until 90 weeks		19/37 (51%)[b]	37/46 (80%)[b]		
Urethane	Mice ($B6AF_1/J$)	liver	1 week	gavage	2.5 mg/pup	1×	39–40 weeks	Tumor incidence[a]		No tumor data for controls.	Klein (1966)
								M	F		
								12/37 (33%)[b]	0/40 (0%)[b]		
			1 week		2.5 mg/pup	16× (1× at 1 week; 3× weekly for 5 weeks beginning at 4 wks of age)	39 weeks	11/33 (33%)[b]	0/31 (0%)[b]		
			4 weeks		2.5 mg/pup	15× (3× weekly for 5 weeks beginning at 4 weeks of age)	41 weeks	0/37 (0%)[b]	0/31 (0%)[b]		

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
VC Vinyl chloride	Rats (Sprague-Dawley)	liver angio-sarcoma	Control	Control	0 ppm	N/A	135 weeks	0/22 (0%)	0/29 (0%)	Higher tumor risk when exposed at birth, higher for females.	Maltoni et al. (1984)
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk, 5 weeks	124 weeks	5/18 (28%)[b]	12/24 (50%)[b]		
					10,000 ppm			6/24 (25%)[b]	9/20 (45%)[b]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	3/17 (18%)[b]	10/25 (40%)[b]		
					10,000 ppm			3/21 (14%)[b]	4/25 (16%)[b]		
		zymbal gland	Control	Control	0 ppm	N/A	135 weeks	0/28 (0%)	0/29 (0%)		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk, 5 weeks	124 weeks	1/12 (8%)[b]	1/17 (6%)[b]		
					10,000 ppm			1/17 (6%)[b]	0/17 (0%)[b]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	3/29 (10%)[b]	4/30 (13%)[b]		
					10,000 ppm			10/30 (33%)[b]	6/30 (20%)[b]		
		leukemia	Control	Control	0 ppm	N/A	135 weeks	0/27 (0%)	1/29 (3%)		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk, 5 weeks	124 weeks	N/A	1/7 (14%)[b]		
					10,000 ppm			2/6 (33%)[b]	0/15 (0%)[b]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	N/A	0/29 (0%)[b]		
					10,000 ppm			0/27 (0%)[b]	2/29 (7%)[b]		
		nephro-blastoma	Control	Control	0 ppm	N/A	135 weeks	0/22 (0%)	0/29 (0%)		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk, 5 weeks	124 weeks	0/15 (0%)[b]	0/21 (0%)[b]		
					10,000 ppm			0/19 (0%)[b]	0/17 (0%)[b]		

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
VC Vinyl chloride (continued)			Week 13		6,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	4/18 (22%)[b]	1/26 (4%)[b]		
					10,000 ppm			3/21 (14%)[b]	2/25 (8%)[b]		
		angio-sarcomas: other sites	Control	Control	0 ppm	N/A	135 weeks	0/29 (0%)	0/29 (0%)		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk, 5 weeks	124 weeks	1/15 (7%)[b]	0/21 (0%)[b]		
					10,000 ppm			0/19 (0%)	0/17 (0%)[b]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	1/29 (3%)[b]	2/30 (7%)[b]		
					10,000 ppm			2/30 (7%)[b]	1/30 (3%)[b]		
		angiomas and fibromas: other sites	Control	Control	0 ppm	N/A	135 weeks	0/28 (0%)	2/29 (7%)[b]		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk, 5 weeks	124 weeks	1/15 (7%)[b]	0/21 (0%)[b]		
					10,000 ppm			2/19 (11%)[b]	1/17 (6%)[b]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	2/29 (7%)[b]	2/30 (7%)[b]		
					10,000 ppm			2/29 (7%)[b]	1/29 (3%)[b]		
		hepatoma	Control	Control	0 ppm	N/A	135 weeks	0/19 (0%)	0/28 (0%)		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk, 5 weeks	124 weeks	9/18 (50%)[b]	11/24 (46%)[b]		
					10,000 ppm			13/24 (54%)[b]	7/20 (35%)[b]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	0/10 (0%)[b]	1/17 (6%)[b]		
					10,000 ppm			1/8 (13%)[b]	0/16 (0%)[b]		

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
VC Vinyl chloride (continued)		skin carcinomas	Control	Control	0 ppm	N/A	135 weeks	0/20 (0%)	1/29 (3%)		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk, 5 weeks	124 weeks	1/10 (10%)[b]	1/14 (7%)[b]		
					10,000 ppm			1/16 (6%)[b]	0/15 (0%)[b]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	0/15 (0%)[b]	2/19 (11%)[b]		
					10,000 ppm			2/13 (15%)[b]	1/21 (5%)[b]		
		neuro-blastoma	Control	Control	0 ppm	N/A	135 weeks	0/22 (0%)	0/29 (0%)		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk, 5 weeks	124 weeks	0/18 (0%)[b]	0/29 (0%)[b]		
					10,000 ppm			0/22 (0%)[b]	0/19 (0%)[b]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	2/21 (10%)[b]	1/27 (4%)[b]		
					10,000 ppm			2/22 (9%)[b]	5/26 (19%)[b]		

[a] Where not delineated by gender, data combined by study authors or gender not specified. Where percentages only are given, number of subjects not specified.
[b] Not evaluated by authors.
[c] Significant compared with controls.
[d] Evaluated but not significant compared with controls.
[e] Reported as NDEA (N-nitrosodiethylamine) in the original document.
[f] Results from each dose are not available.
[g] Tumors were adenomas or carcinomas.

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
BaP Benzo[*a*]pyrene	Mice ($B6C3F_1$)	liver	Control	Control	None	N/A	142 weeks	7/100 (7%)	1/100 (1%)	In general, hepatomas developed with significantly higher incidence ($p<0.01$) in mice that were treated within 24 hours of birth or at 15 days of age than they did in similarly treated animals at 42 days of age. + higher for males.	Vesselinovitch et al. (1975a)
			Day 1	i.p.	75 µg/g body weight	1×	86 weeks (m) 129 weeks (f)	26/47 (55%)[b]	3/45 (7%)[b]		
					150 µg/g body weight	1×	81 weeks (m) 121 weeks (f)	51/63 (81%)[b]	8/45 (18%)[b]		
			Day 15	i.p.	75 µg/g body weight	1×	93 weeks (m) 116 weeks (f)	36/60 (60%)[b]	4/55 (7%)[b]		
					150 µg/g body weight	1×	81 weeks (m) 90 weeks (f)	32/55 (58%)[b]	4/55 (7%)[b]		
			Day 42	i.p.	75 µg/g body weight	1×	108 weeks(m)	7/55 (13%)[b]	0/47 (0%)[b]		
					150 µg/g body weight	1×	87 weeks (m)	4/47 (9%)[b]	0/46 (0%)[b]		
	Mice ($C3AF_1$)	liver	Control	Control	None	N/A	142 weeks	8/100 (8%)	1/100 (1%)	+ higher for males. "Age at death" is the average age at which tumors were observed.	
			Day 1	i.p.	75 µg/g body weight	1×	80 weeks (m) 91 weeks (f)	21/62 (34%)[b]	1/45 (2%)[b]		
					150 µg/g body weight	1×	69 weeks (m) 701 weeks (f)	24/52 (46%)[b]	1/56 (2%)[b]		
			Day 15	i.p.	75 µg/g body weight	1×	90 weeks (m) 102 weeks (f)	15/56 (27%)[b]	1/49 (2%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
BaP Benzo[*a*]pyrene (continued)					150 µg/g body weight	1×	77 weeks (m) 62 weeks (f)	12/53 (23%)[b]	1/57 (2%)[b]		
			Day 42	i.p.	75 µg/g body weight	1×		0/30 (0%)[b]	0/32 (0%)[b]		
					150 µg/g body weight	1×	79 weeks (m)	1/32 (3%)[c]	0/40 (0%)[b]		
	Mice ($B6C3F_1$)	lung	Control	Control	Control	N/A	142 weeks	13/100 (13%)	9/100 (9%)	Both sexes developed lung tumors with higher incidence when treated with BaP at birth than at 15 or 42 days of age ($p<0.05$).	
			Day 1	i.p.	75 µg/g body weight	1×	103 weeks (m) 126 weeks (f)	20/47 (43%)[b]	22/45 (49%)[b]		
					150 µg/g body weight	1×	84 weeks (m) 112 weeks (f)	37/63 (59%)[b]	28/45 (62%)[b]		
			Day 15	i.p.	75 µg/g body weight	1×	103 weeks (m) 122 weeks (f)	15/60 (25%)[b]	18/55 (33%)[b]		
					150 µg/g body weight	1×	82 weeks (m) 101 weeks (f)	20/55 (36%)[b]	18/45 (40%)[b]		
			Day 42	i.p.	75 µg/g body weight	1×	119 weeks (m) 131 weeks (f)	20/55 (36%)[b]	12/47 (26%)[b]		
					150 µg/g body weight	1×	95 weeks (m) 118 weeks (f)	18/47 (38%)[b]	8/46 (17%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
BaP Benzo[*a*]pyrene (continued)	Mice ($C3AF_1$)	lung	Control	Control	None	N/A	142 weeks	60/100 (60%)	50/100 (50%)	Of the two mouse strains tested, $C3AF_1$ mice developed significantly more tumors than did the $B6C3F_1$ mice ($p<0.001$).	Vesselinovitch et al. (1975a)
			Day 1	i.p.	75 µg/g body weight	1×	78 weeks (m) 82 weeks (f)	58/62 (93%)[b]	42/45 (93%)[b]		
					150 µg/g body weight	1×	70 weeks (m) 73 weeks (f)	48/52 (92%)[b]	52/56 (93%)[b]		
			Day 15	i.p.	75 µg/g body weight	1×	87 weeks (m) 98 weeks (f)	52/56 (93%)[b]	46/49 (94%)[b]		
					150 µg/g body weight	1×	75 weeks (m) 79 weeks (f)	50/53 (94%)[b]	52/57 (91%)[b]		
			Day 42	i.p.	75 µg/g body weight	1×	91 weeks (m) 93 weeks (f)	28/30 (93%)[b]	28/32 (87%)[b]		
					150 µg/g body weight	1×	85 weeks (m) 83 weeks (f)	28/32 (87%)[b]	36/40 (90%)[b]		
DBA Dibenzanthracene	Mice (Caracul × P stock)	lung	Control	Control	None	N/A	228 days	1/31 (3.2%)			Law (1940)
			Day 1	i.p.	4 mg per cm^3 vehicle	1×	181 days	24/24 (100%)[b]			
			2 months	s.c.	4 mg per cm^3 vehicle	1×	189 days	2/29 (6.9%)[b]			

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
DEN Diethylnitrosamine	Mice ($B6C3F_1$)	liver	Control	Control	Vehicle (0.01 mL trioctanoin/g body weight)	4×	142 weeks (m) 137 weeks (f)	7/98 (7%)	1/100 (1%)	Animals treated as newborns and infants developed significantly more liver tumors than animals that were treated as young adults. Newborns and infant females developed liver tumors at a later age than similarly treated males. Incidences for malignant tumors only.	Vesselinovitch et al. (1984)
			Day 1	i.p. (3-, 6- and 6-day intervals)	1.5 µg/g body weight	4×	67 weeks (m) 90 weeks (f)	37/51 (73%)[b]	45/64 (70%)[b]		
					3 µg/g body weight	4×	65 weeks (m) 80 weeks (f)	40/58 (69%)[b]	44/65 (68%)[b]		
			Day 15		1.5 µg/g body weight	4×	86 weeks (m) 117 weeks (f)	41/57 (72%)[b]	40/71 (56%)[b]		
					3 µg/g body weight	4×	76 weeks (m) 96 weeks (f)	48/69 (70%)[b]	46/62 (74%)[b]		
			Day 42		1.5 µg/g body weight	4×	117 weeks (m) 135 weeks (f)	9/49 (18%)[b]	1/47 (2%)[b]		
					3 µg/g body weight	4×	123 weeks (m) 133 weeks (f)	6/38 (16%)[b]	4/57 (7%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
DEN Diethylnitrosamine (continued)	Mice ($C3AF_1$)	liver	Control	Control	Vehicle (0.1 trioctanoin/g body weight)	4×	123 weeks (m) 131weeks (f)	8/99 (8%)	1/97 (1%)	Highest tumor rate when dosed at early ages. Newborns and infant females developed liver tumors at a lower incidence than similarly treated males. + higher for males.	Vesselinovitch et al. (1984)
			Day 1	i.p. (3-, 6- and 6-day intervals)	1.5 µg/g body weight	4×	64 weeks (m) 84 weeks (f)	23/32 (72%)[b]	11/39 (28%)[b]		
					3 µg/g body weight	4×	59 weeks (m) 76 weeks (f)	39/58 (67%)[b]	26/50 (52%)[b]		
			Day 15		1.5 µg/g body weight	4×	82 weeks (m) 102 weeks (f)	22/46 (48%)[b]	8/65 (12%)[b]		
					3 µg/g body weight	4×	74 weeks (m) 94 weeks (f)	35/54 (65%)[b]	22/62 (35%)[b]		
			Day 42		1.5 µg/g body weight	4×	105 weeks (m) 106 weeks (f)	12/56 (22%)[b]	0/53 (0%)[b]		
					3 µg/g body weight	4×	105 weeks (m) 103 weeks (f)	9/57 (16%)[b]	0/56 (0%)[b]		
	Mice ($B6C3F_1$)	lung	Control	Control	Vehicle (0.1 trioctanoin/g body weight)	4×	142 weeks (m) 137 weeks (f)	13/98 (13%)	9/100 (9%)	The mice treated as newborns showed lung tumors earlier than animals exposed at other times. It is not known whether this was due to actual earlier emergence of tumors or	

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
DEN Diethylnitrosamine (continued)			Day 1	i.p. (3-, 6- and 6-day intervals)	1.5 µg/g body weight	4×	70 weeks (m) 91 weeks (f)	29/51 (57%)[b]	49/64 (77%)[b]	to their earlier detection caused by shorter survival.	
					3 µg/g body weight	4×	68 weeks (m) 81 weeks (f)	34/58 (59%)[b]	42/65 (65%)[b]		
			Day 15		1.5 µg/g body weight	4×	87 weeks (m) 115 weeks (f)	51/57 (89%)[b]	61/71 (86%)[b]		
					3 µg/g body weight	4×	77 weeks (m) 97 weeks (f)	51/69 (74%)[b]	53/62 (85%)[b]		
			Day 42		1.5 µg/g body weight	4×	123 weeks (m) 129 weeks (f)	38/49 (78%)[b]	38/47 (81%)[b]		
					3 µg/g body weight	4×	121 weeks (m) 127 weeks (f)	33/38 (87%)[b]	43/57 (75%)[b]		
	Mice ($C3AF_1$)	lung	Control	Control	Vehicle (0.1 trioctanoin/g body weight)	4×	142 weeks (m) 137weeks (f)	60/99 (61%)	50/97 (52%)	Of the two strains, $C3AF_1$ mice developed lung tumors with a higher incidence and multiplicity than $B6C3F_1$ hybrids.	
			Day 1	i.p. (3-, 6- and 6-day intervals)	1.5 µg/g body weight	4×	65 weeks (m) 84 weeks (f)	30/32 (94%)[b]	38/39 (97%)[b]		
					3 µg/g body weight	4×	59 weeks (m) 76 weeks (f)	49/58 (84%)[b]	46/50 (92%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
DEN Diethylnitrosamine (continued)			Day 15		1.5 µg/g body weight	4×	80 weeks (m) 101 weeks (f)	42/46 (91%)[b]	61/65 (94%)[b]		
					3 µg/g body weight	4×	74 weeks (m) 92 weeks (f)	50/54 (93%)[b]	57/62 (92%)[b]		
			Day 42		1.5 µg/g body weight	4×	104 weeks (m) 110 weeks (f)	55/56 (98%)[b]	52/53 (98%)[b]		
					3 µg/g body weight	4×	101 weeks (m) 102 weeks (f)	56/57 (98%)[b]	54/56 (96%)[b]		
	Mice ($B6C3F_1$)	liver	Control	Control	None	N/A	90 weeks	1/98 (1%)	0/96 (0%)	Infant animals of both sexes (Day 15) were more sensitive than similarly exposed adults.	Vesselinovitch and Mihailovich (1983)
			Gestation day 18	i.p.	1.5 µg/g body weight	1×		2/50 (4%)[b]	1/51 (2%)[b]		
			Day 15	i.p. (3-, 6- and 6-day intervals)	1.5 µg/g body weight	4×		47/51 (92%)[b]	60/64 (94%)[b]		
			Day 42		1.5 µg/g body weight	4×		13/49 (26%)[b]	3/47 (6%)[b]		
			Day 1	i.p.	1.5 µg/g body weight	1×	73 weeks	15/59 (25%)[b]	—	At the 1.5-µg dose level, 1-day-old mice developed significantly fewer liver tumors than similarly treated infants (Day 15) ($p<0.025$). Tumor incidence in treated groups versus controls was not evaluated.	Vesselinovitch et al. (1979a)
					5 µg/g body weight	1×		29/45 (64%)[b]	—		
					10 µg/g body weight	1×		24/25 (96%)[b]	—		
			Day 15	i.p.	1.5 µg/g body weight	1×		13/24 (54%)[b]	—		
					5 µg/g body weight	1×		40/54 (74%)[b]	—		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
DEN Diethylnitrosamine (continued)					10 µg/g body weight	1×		25/25 (100%)[b]	—		
DMBA Dimethyl-benz[*a*]anthracene	Rats (Sprague-Dawley)	mammary adeno-sarcoma	Day 20	Gavage	10 mg/100 g body weight	1×	Week 25	—	3/6 (50%)[b]	36 of 42 (86%) animals dosed at age 20 days died soon after. Highest number of tumors per animal was in the 46-day group, with decreasing numbers in the older animals. Animals were sacrificed 22 weeks after treatment.	Russo et al. (1979)
			Day 30		10 mg/100 g body weight	1×	Week 26	—	14/15 (93%)[b]		
			Day 40		10 mg/100 g body weight	1×	Week 27	—	8/9 (89%)[b]		
			Day 46		10 mg/100 g body weight	1×	Week 28	—	8/8 (100%)[b]		
			Day 55		10 mg/100 g body weight	1×	Week 29	—	33/34 (97%)[b]		
			Day 70		10 mg/100 g body weight	1×	Week 32	—	5/8 (63%)[b]		
			Day 140		10 mg/100 g body weight	1×	Week 42	—	10/15 (67%)[b]		
			Day 180		10 mg/100 g body weight	1×	Week 47	—	14/26 (54%)[b]		
	Rats (Wistar)	mammary carcinoma[d]	Control 5–8 weeks	Control	None	N/A	17 months	0/22 (0%)	0/25 (0%)	Highest tumor rate in females exposed at 5–8 weeks. Animals were observed for 16 months following treatment.	Meranze et al. (1969)
			Control 26 weeks	Control	None	N/A	20 months	0/31 (0%)	2/20 (10%)		
			< Week 2	Gavage	0.5–1.0 mg	1×	Week 40–56	0/23 (0%)[b]	4/50 (8%)[b]		
			Week 5–8		15 mg	1×	Week 14–55	0/23 (0%)[b]	14/25 (56%)[b]		
			Week 26		15 mg	1×	Week 32–73	0/34 (0%)[b]	4/26 (15%)[b]		
	Rats (Wistar, castrated)	mammary carcinoma	Week 5–8	Gavage	15 mg	1×	Week 14–55	0/21 (0%)[b]	0/22 (0%)[b]		
			Week 26		15 mg	1×	Week 32–73	0/33 (0%)[b]	0/26 (0%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
DMBA Dimethyl-benz[*a*]anthracene (continued)	Rats (Wistar)	Total tumors	Control 5–8 weeks	Control	None	N/A	17 months	0/22 (0%)	0/25 (0%)	Total tumors includes leukemia.	
			Control 26 weeks	Control	None	N/A	20 months	2/31 (6%)	5/20 (25%)		
			< Week 2	Gavage	0.5–1.0 mg	1×	Week 40–56	16/23 (70%)[b]	36/50 (72%)[b]		
			Week 5–8		15 mg	1×	Week 14–55	7/23 (30%)[b]	16/25 (64%)[b]		
			Week 26		15 mg	1×	Week 32–73	12/34 (35%)[b]	13/26 (50%)[b]		
	Mice (BALB/c)	lung	Control: Day 1	Control s.c.	Aqueous gelatine	1×	40 weeks	0/12 (0%)	7/23 (30%)	15 µg DMBA gave rise to a significantly greater incidence of lung tumors when administered to newborn mice than to suckling or young adults.	Walters (1966)
			Day 1	s.c.	15 µg	1×	40 weeks[f]	14/14 (100%)[b]	24/24 (100%)[b]		
			Week 2–3 (suckling)	s.c.	15 µg	1×	42–43 weeks	12/23 (52%)[b]	16/22 (73%)[b]		
				s.c.	30 µg (60 µg total)	2×	42–43 weeks	14/14 (100%)[b]	24/24 (100%)[b]		
			Adult[e]	s.c.	15 µg	1×	48-49 weeks	6/12 (50%)[b]	15/33 (45%)[b]		
				s.c.	30 µg (60 µg total)	2×	48-49 weeks	9/10 (90%)[b]	21/23 (91%)[b]		
				s.c.	30 µg (180 µg total)	6×	48-49 weeks	12/12 (100%)[b]	13/13 (100%)[b]		
	Mice (Swiss)	lymphoma	Control	Control	None	N/A	31–52 weeks	3/408 (0.7%)		Higher tumor rates at younger age of exposure. Only one treatment group was exposed i.p.; others were exposed by s.c. injection..	Pietra et al. (1961)
			Day 1	i.p.	30–40 µg	1×	13–33 weeks	6/31 (19%)[b]			
			Day 1	s.c.	30–40 µg	1×	12–27 weeks	8/27 (30%)[b]			
			Week 8	s.c.	900 µg	1×	30 weeks	1/13 (8%)[b]			

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
DMBA Dimethyl-benz[*a*]anthracene (continued)	Mice (Swiss)	lung	Control	Control	None	N/A	31–52 weeks	4/408 (0.9%)			
			Day 1	i.p.	30–40 µg	1×	13–33 weeks	24/31 (77%)[b]			
			Day 1	s.c.	30–40 µg	1×	12–27 weeks	23/27 (85%)[b]			
			Week 8	s.c.	900 µg	1×	30 weeks	2/13 (15%)[b]			
DMN Dimethyl-nitrosamine	Rats (Wistar)	kidney carcinoma	Day 1	i.p.	20 mg/kg	1×	≥5 months	1/33 (3)[b]		In the neonatal group, the dose was reduced to 20 mg/kg to achieve approximately equivalent numbers of survivors. No control group.	Hard (1979)
			Day 21		30 mg/kg	1×		5/39 (13)[b]			
			Month 1		30 mg/kg	1×		2/33 (6)[b]			
			Month 1.5		30 mg/kg	1×		1/28 (4)[b]			
			Month 2		30 mg/kg	1×		1/26 (4)[b]			
			Month 3		30 mg/kg	1×		10/27 (37)[b]			
			Month 4		30 mg/kg	1×		7/32 (22)[b]			
			Month 5		30 mg/kg	1×		0/14 (0)[b]			
	Rats (Wistar)	kidney adenoma	Day 1	i.p.	20 mg/kg	1×	≥5 months	1/33 (3)[b]			
			Day 21		30 mg/kg	1×		13/39 (33)[b]			
			Month 1		30 mg/kg	1×		11/33 (33)[b]			
			Month 1.5		30 mg/kg	1×		13/28 (48)[b]			
			Month 2		30 mg/kg	1×		11/26 (42)[b]			
			Month 3		30 mg/kg	1×		18/27 (67)[b]			
			Month 4		30 mg/kg	1×		17/32 (53)[b]			
			Month 5		30 mg/kg	1×		6/14 (43)[b]			

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a] M	Tumors[a] F	Comments	Reference
DMN Dimethyl-nitrosamine (continued)	Rats (Wistar)	kidney mesenchymal tumors	Day 1	i.p.	20 mg/kg	1×	≥5 months	8/33 (24)[b]		Mesenchymal tumors were most frequent in the three youngest age groups (z test, $p < 0.001$).	
			Day 21		30 mg/kg	1×		18/39 (46)[b]			
			Month 1		30 mg/kg	1×		23/33 (70)[b]			
			Month 1.5		30 mg/kg	1×		5/28 (19)[b]			
			Month 2		30 mg/kg	1×		2/26 (8)[b]			
			Month 3		30 mg/kg	1×		3/27 (11)[b]			
			Month 4		30 mg/kg	1×		7/32 (22)[b]			
			Month 5		30 mg/kg	1×		0/14 (0)[b]			
	Rats (Wistar)	kidney cortical epithelial tumors	Day 1	i.p.	20 mg/kg	1×	≥5 months	2/33 (6)[b]			Hard (1979)
			Day 21		30 mg/kg	1×		16/39 (41)[b]			
			Month 1		30 mg/kg	1×		12/33 (36)[b]			
			Month 1.5		30 mg/kg	1×		14/28 (52)[b]			
			Month 2		30 mg/kg	1×		11/26 (42)[b]			
			Month 3		30 mg/kg	1×		18/27 (67)[b]			
			Month 4		30 mg/kg	1×		21/32 (66)[b]			
			Month 5		30 mg/kg	1×		6/14 (43)[b]			
	Rats (Wistar)	Total tumors	Day 1	i.p.	20 mg/kg	1×	≥5 months	11/33 (33)[b]			
			Day 21		30 mg/kg	1×		25/39 (64)[b]			
			Month 1		30 mg/kg	1×		25/33 (76)[b]			
			Month 1.5		30 mg/kg	1×		17/28 (63)[b]			
			Month 2		30 mg/kg	1×		13/26 (50)[b]			
			Month 3		30 mg/kg	1×		18/27 (67)[b]			
			Month 4		30 mg/kg	1×		22/32 (69)[b]			
			Month 5		30 mg/kg	1×		7/14 (50)[b]			

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
ENU Ethylnitrosourea	Rats	nervous system	Day 1	Injection	20 mg/kg	1×		100%[b]		Susceptibility to neuro-oncogenic effect declined with increasing age.	Maekawa and Mitsumori (1990)
			Day 30	Injection	20 mg/kg	1×		61%[b]			
	Mice ($B6C3F_1$)	liver	Control	Control	None	N/A	90 weeks	1/98 (1%)	0/96 (0%)	Both male and female mice were responsive to exposure during prenatal and infant life.	Vesselinovitch (1983)
			Gestation day 18	i.p.	60 µg/g body weight	1×		28/52 (54%)[b]	18/49 (37%)[b]		
			Day 15		60 µg/g body weight	1×		41/50 (82%)[b]	28/51 (55%)[b]		
			Day 42		60 µg/g body weight	1×		10/50 (20%)[b]	5/50 (10%)[b]		
	Rats (Wistar)	nerve tissue	Control	Control	None	N/A	4–7 months	0/16 (0%)	0/10 (0%)	Highest tumor rate seen when exposed during gestation or soon after birth. Statistically significant decrease in tumor incidence with increasing age of exposure.	Naito et al. (1981)
			Gestation day 16	i.p.	40 mg/kg	1×		26/26 (100%)[b]	18/18 (100%)[b]		
			Day 1	s.c.	40 mg/kg	1×		12/12 (100%)[g]	16/16 (100%)[g]		
			Week 1		40 mg/kg	1×		12/17 (71%)[b]	18/20 (90%)[b]		
			Week 2		40 mg/kg	1×		10/14 (71%)[b]	14/18 (78%)[b]		
			Week 3		40 mg/kg	1×		6/13 (46%)[b]	5/17 (29%)[b]		
			Week 4		40 mg/kg	1×		8/15 (53%)[b]	2/10 (20%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
ENU Ethylnitrosourea (continued)	Mice ($B6C3F_1$)	lung	Day 1	i.p.	60 µg/g body weight	1×		49/55 (89%)[b]	49/50 (98%)[b]		Vesselinovitch et al. (1974)
			Day 15			1×		50/55 (91%)[b]	47/55 (85%)[b]		
			Day 42			1×		53/59 (90%)[b]	44/51 (86%)[b]		
			Day 1		120 µg/g body weight	1×		36/38 (95%)[b]	54/60 (90%)[b]		
			Day 15			1×		45/49 (92%)[b]	43/50 (86%)[b]		
			Day 42			1×		52/54 (96%)[b]	50/57 (88%)[b]		
	Mice ($C3AF_1$)	lung	Day 1		60 µg/g body weight	1×		46/47 (98%)[g]	51/51 (100%)[g]		
			Day 15			1×		49/49 (100%)[g]	57/59 (97%)[g]		
			Day 42			1×		59/59 (100%)[g]	57/57 (100%)[g]		
			Day 1		120 µg/g body weight	1×		63/64 (98%)[g]	53/57 (93%)[g]		
			Day 15			1×		54/56 (96%)[g]	50/56 (89%)[g]		
			Day 42			1×		59/59 (100%)[g]	48/48 (100%)[g]		
	Mice ($B6C3F_1$)	liver	Day 1	i.p.	60 µg/g body weight	1×		50/54 (93%)[g]	28/43 (65%)[g]		
			Day 15			1×		55/56 (98%)[g]	33/54 (61%)[g]		
			Day 42			1×		12/40 (30%)[b]	6/39 (15%)[b]		
			Day 1		120 µg/g body weight	1×		29/34 (85%)[g]	32/53 (60%)[g]		
			Day 15			1×		45/48 (94%)[g]	29/43 (67%)[g]		
			Day 42			1×		17/49 (35%)[g]	4/50 (8%)[g]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
ENU Ethylnitrosourea (continued)	Mice ($C3AF_1$)	liver	Day 1	i.p.	60 µg/g body weight	1×		42/45 (93%)[g]	19/41 (46%)[g]		
			Day 15			1×		42/50 (84%)[g]	19/48 (40%)[g]		
			Day 42			1×		7/29 (24%)[b]	4/50 (8%)[b]		
			Day 1		120 µg/g body weight	1×		55/62 (89%)[g]	19/45 (42%)[g]		
			Day 15			1×		35/45 (78%)[g]	15/35 (43%)[g]		
			Day 42			1×		8/33 (24%)[b]	3/33 (9%)[b]		
	Mice ($B6C3F_1$)	kidney	Day 1	i.p.	60 µg/g body weight	1×		11/48 (23%)[b]	5/49 (10%)[b]		
			Day 15			1×		6/41 (15%)[b]	7/31 (23%)[b]		
			Day 42			1×		4/40 (10%)[b]	3/37 (8%)[b]		
			Day 1		120 µg/g body weight	1×		10/30 (33%)[g]	14/53 (26%)[b]		
			Day 15			1×		17/37 (46%)[g]	19/49 (39%)[b]		
			Day 42			1×		8/40 (20%)[b]	11/39 (28%)[b]		
	Mice ($C3AF_1$)	kidney	Day 1	i.p.	60 µg/g body weight	1×		7/44 (16%)[b]	6/45 (13%)[b]		
			Day 15			1×		7/41 (17%)[b]	8/46 (17%)[b]		
			Day 42			1×		3/42 (42%)[b]	3/43 (7%)[b]		
			Day 1		120 µg/g body weight	1×		4/52 (7%)[b]	6/29 (21%)[g]		
			Day 15			1×		8/35 (23%)[b]	12/29 (41%)[g]		
			Day 42			1×		6/41 (71%)[b]	3/39 (8%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
ENU Ethylnitrosourea (continued)	Mice (B6C3F1)	Harderian	Day 1		60 µg/g body weight	1×		7/40 (17%)[b]	5/43 (12%)[b]		
			Day 15			1×		10/51 (20%)[b]	17/59 (29%)[b]		
			Day 42			1×		14/50 (28%)[b]	14/45 (31%)[b]		
			Day 1		120 µg/g body weight	1×		9/30 (30%)[g]	6/52 (12%)[b]		
			Day 15			1×		15/41 (37%)[g]	8/31 (26%)[b]		
			Day 42			1×		25/48 (52%)[g]	14/49 (29%)[b]		
	Mice ($C3AF_1$)	Harderian	Day 1		60 µg/g body weight	1×		3/25 (12%)[b]	4/35 (11%)[b]		
			Day 15			1×		1/9 (11%)[b]	6/38 (16%)[b]		
			Day 42			1×		12/48 (25%)[b]	5/33 (15%)[b]		
			Day 1		120 µg/g body weight	1×		3/52 (6%)[b]	1/25 (4%)[b]		
			Day 15			1×		6/46 (13%)[b]	2/52 (4%)[b]		
			Day 42			1×		5/29 (17%)[b]	2/11 (18%)[b]		
	Mice ($B6C3F_1$)	stomach	Day 1		60 µg/g body weight	1×		3/48 (6%)[b]	4/43 (9%)[b]		
			Day 15			1×		10/42 (24%)[g]	7/45 (16%)[b]		
			Day 42			1×		9/51 (18%)[g]	8/36 (22%)[b]		
			Day 1		120 µg/g body weight	1×		2/29 (7%)[b]	9/53 (17%)[b]		
			Day 15			1×		10/35 (29%)[g]	12/33 (36%)[b]		
			Day 42			1×		12/53 (23%)[g]	12/50 (24%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
ENU Ethylnitrosourea (continued)	Mice ($C3AF_1$)	stomach	Day 1		60 µg/g body weight	1×		2/39 (5%)[b]	7/45 (16%)[b]		
			Day 15			1×		7/45 (16%)[g]	7/38 (18%)[b]		
			Day 42			1×		14/55 (25%)[g]	7/49 (14%)[b]		
			Day 1		120 µg/g body weight	1×		8/60 (13%)[b]	9/44 (20%)[b]		
			Day 15			1×		16/51 (31%)[g]	11/42 (26%)[b]		
			Day 42			1×		19/48 (40%)[g]	13/37 (35%)[b]		
	Mice ($B6C3F_1$)	malignant lymphomas	Day 1		60 µg/g body weight	1×		2/55 (4%)[b]	6/52 (12%)[g]		
			Day 15			1×		3/56 (5%)[b]	14/59 (24%)[g]		
			Day 42			1×		9/59 (15%)[b]	17/59 (29%)[g]		
			Day 1		120 µg/g body weight	1×		8/39 (20%)[b]	15/65 (23%)[g]		
			Day 15			1×		14/60 (23%)[b]	17/58 (29%)[g]		
			Day 42			1×		12/59 (20%)[b]	14/60 (23%)[g]		
	Mice ($C3AF_1$)	malignant lymphomas	Day 1		60 µg/g body weight	1×		6/49 (12%)[b]	8/49 (16%)[g]		
			Day 15			1×		3/49 (6%)[b]	13/61 (21%)[g]		
			Day 42			1×		6/60 (10%)[b]	9/55 (16%)[g]		
			Day 1		120 µg/g body weight	1×		3/66 (5%)[b]	10/58 (17%)[g]		
			Day 15			1×		10/56 (18%)[b]	18/60 (30%)[g]		
			Day 42			1×		3/49 (6%)[b]	13/50 (26%)[g]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumor incidence[a]		Comments	Reference
								M	F		
NMU Methylnitrosourea	Mice ($BC3F_1$)	Total tumors	Control	Control	N/A	N/A	60 weeks	1/20 (5%)	0%	Control mice did not exhibit tumors in target sites except a single hepatoma in a male control mouse.	Terracini and Testa (1970)
		lung	Day 1	i.p.	50 µg/g body weight	1×	60 weeks	12/15 (80%)[b]	16/19 (84%)[b]		
			5 weeks		50 µg/g body weight	1×	60 weeks	10/26 (39%)[b]	10/35 (29%)[b]		
		lympho-sarcoma	Day 1		50 µg/g body weight	1×	60 weeks	23/39 (59%)[b]	23/45 (51%)[b]		
			5 weeks		50 µg/g body weight	1×	60 weeks	11/35 (31%)[b]	21/45 (47%)[b]		
		liver	Day 1		50 µg/g body weight	1×	60 weeks	10/12 (83%)[b]	1/17 (6%)[b]		
			5 weeks		50 µg/g body weight	1×	60 weeks	0%[b]	0%[c]		
		kidney	Day 1		50 µg/g body weight	1×	60 weeks	3/15 (20%)[b]	3/18 (17%)[b]		
			5 weeks		50 µg/g body weight	1×	60 weeks	2/21 (10%)[b]	0%[c]		
		fore-stomach	Day 1		50 µg/g body weight	1×	60 weeks	0%[b]	4/17 (24%)[b]		
			5 weeks		50 µg/g body weight	1×	60 weeks	8/22 (36%)[b]	12/18 (67%)[b]		
	Rats (Wistar)	mammary	Day 1	i.p.	50 µg/g body weight	1×	60 weeks	0%[b]	4/14 (29%)[b]	Tumor incidence for control rats was based on previous experiments (Della Porta et al., 1968) and was not specifically reported in this paper.	Terracini and Testa (1970)
			5 weeks		50 µg/g body weight	1×	60 weeks	0%[b]	3/5 (60%)[b]		
		lympho-sarcoma	Day 1		50 µg/g body weight	1×	60 weeks	1/10 (10%)[b]	0%[b]		
			5 weeks		50 µg/g body weight	1×	60 weeks	2/8 (25%)[b]	1/11 (9%)[b]		
		kidney (ana-plastic)	Day 1		50 µg/g body weight	1×	60 weeks	14/18 (78%)[b]	9/13 (69%)[b]		
			5 weeks		50 µg/g body weight	1×	60 weeks	2/5 (40%)[b]	5/12 (42%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumor incidence[a]		Comments	Reference
								M	F		
NMU Methylnitrosourea (continued)		kidney (adenoma)	Day 1		50 µg/g body weight	1×	60 weeks	3/14 (21%)[b]	2/6 (33%)[b]		
			5 weeks		50 µg/g body weight	1×	60 weeks	¼ (25%)[b]	0%[b]		
		forestomach	Day 1		50 µg/g body weight	1×	60 weeks	4/14 (29%)[b]	3/6 (50%)[b]		
			5 weeks		50 µg/g body weight	1×	60 weeks	0%[c]	0%[b]		
		intestine	Day 1		50 µg/g body weight	1×	60 weeks	3/10 (30%)[b]	2/2 (100%)[b]		
			5 weeks		50 µg/g body weight	1×	60 weeks	2/4 (50%)[b]	0%[b]		
	Mice (C3Hf/Dp)	thymus	control	i.p.	NA	NA	120 wks[**]	0/34 (0%)	0/25 (0%)	[*]Age at death from thymic lymphoma reported specifically for some, but not all, dose groups. [**]Control mice were sacrificed at 120 wks. [***]Age of death for all mice in this dose group, regardless of cancer type.	Terracini et al. (1976)
			Day 1		25 µg NMU/g body weight	1×	29 ± 8.4 wks	2/16 (13%)[b]	5/25 (20%)[b]		
			Day 70		25 µg NMU/g body weight	1×	120 wks (M)[***] 100 wks (F)	0/20 (0%)[c]	1/20 (5%)[b]		
			Day 1		50 µg NMU/g body weight	1×	16.5 ± 0.7 wks	16/24 (67%)[b]	30/44 (68%)[b]		
			Day 21		50 µg NMU/g body weight	1×	24.5 ± 2.5 wks	14/44 (32%)[b]	18/38 (47%)[b]		
			Day 70		50 µg NMU/g body weight	1×	31.4 ± 4.4 wks	9/30 (30%)[b]	6/41 (15%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death		Tumor incidence		Reference
							M	F	M	F	
NMU Methylnitrosourea (continued)	Mice (C3Hf/Dp)	extra-thymic lymphoma	control	i.p.	NA	NA	120 weeks	120 weeks	1/34 (3%)	2/25 (8%)	Terracini et al. (1976)
			Day 1		25 µg NMU/g body weight	1×	100 weeks	90 weeks	2/16 (13%)[b]	1/25 (4%)[b]	
			Day 70		25 µg NMU/g body weight	1×	120 weeks	100 weeks	0/20 (0%)[b]	0/20 (0%)[b]	
			Day 1		50 µg NMU/g body weight	1×	70 weeks	80 weeks	0/24 (0%)[b]	0/44 (0%)[b]	
			Day 21		50 µg NMU/g body weight	1×	100 weeks	90 weeks	1/44 (2%)[b]	0/38 (0%)[b]	
			Day 70		50 µg NMU/g body weight	1×	110 weeks	90 weeks	1/30 (3%)[b]	0/41 (0%)[b]	
		lung	control	i.p.	NA	NA	120 weeks	120 weeks	4/34 (12%)	6/25 (24%)	
			Day 1		25 µg NMU/g body weight	1×	100 weeks	90 weeks	7/16 (44%)[b]	13/25 (52%)[b]	
			Day 70		25 µg NMU/g body weight	1×	120 weeks	100 weeks	12/20 (60%)[b]	8/20 (40%)[b]	
			Day 1		50 µg NMU/g body weight	1×	70 weeks	80 weeks	5/24 (21%)[b]	11/44 (25%)[b]	
			Day 21		50 µg NMU/g body weight	1×	100 weeks	90 weeks	23/44 (52%)[b]	15/38 (39%)[b]	
			Day 70		50 µg NMU/g body weight	1×	110 weeks	90 weeks	18/30 (60%)[b]	24/41 (59%)[b]	
		liver	control	i.p.	NA	NA	120 weeks	120 weeks	13/34 (38%)	1/25 (4%)	Terracini et al. (1976)
			Day 1		25 µg NMU/g body weight	1×	100 weeks	90 weeks	9/16 (56%)[g]	2/25 (8%)[b]	
			Day 70		25 µg NMU/g body weight	1×	120 weeks	100 weeks	12/20 (60%)[g]	2/20 (10%)[b]	
			Day 1		50 µg NMU/g body weight	1×	70 weeks	80 weeks	4/24 (17%)[g]	3/44 (7%)[b]	
			Day 21		50 µg NMU/g body weight	1×	100 weeks	90 weeks	21/44 (48%)[g]	1/38 (2.6%)[b]	

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death		Tumor incidence		Reference
							M	F	M	F	
NMU Methylnitrosourea (continued)	Mice (C3Hf/Dp)		Day 70		50 µg NMU/g body weight	1×	110 weeks	90 weeks	8/30 (27%)[g]	2/41 (5%)[b]	
		stomach	control	i.p.	NA	NA	120 weeks	120 weeks	0/34 (0%)	5/25 (20%)	
			Day 1		25 µg NMU/g body weight	1×	100 weeks	90 weeks	2/16 (13%)[b]	10/25 (40%)[b]	
			Day 70		25 µg NMU/g body weight	1×	120 weeks	100 weeks	3/20 (15%)[b]	7/20 (35%)[b]	
			Day 1		50 µg NMU/g body weight	1×	70 weeks	80 weeks	2/24 (8%)[b]	1/44 (2%)[b]	
			Day 21		50 µg NMU/g body weight	1×	100 weeks	90 weeks	19/44 (43%)[b]	9/38 (24%)[b]	
			Day 70		50 µg NMU/g body weight	1×	110 weeks	90 weeks	8/30 (27%)[b]	21/41 (51%)[b]	
		kidney	control	i.p.	NA	NA	120 weeks	120 weeks	0/34 (0%)	0/25 (0%)	Terracini et al. (1976)
			Day 1		25 µg NMU/g body weight	1×	100 weeks	90 weeks	0/16 (0%)[b]	0/25 (0%)[b]	
			Day 70		25 µg NMU/g body weight	1×	120 weeks	100 weeks	0/20 (0%)[b]	0/20 (0%)[b]	
			Day 1		50 µg NMU/g body weight	1×	70 weeks	80 weeks	0/24 (0%)[b]	4/44 (9%)[b]	
			Day 21		50 µg NMU/g body weight	1×	100 weeks	90 weeks	1/44 (2%)[b]	4/38 (11%)[b]	
			Day 70		50 µg NMU/g body weight	1×	110 weeks	90 weeks	5/30 (17%)[b]	7/41 (17%)[b]	

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death		Tumor incidence		Reference
							M	F	M	F	
NMU Methylnitrosourea (continued)	Mice (C3Hf/Dp)	ovary	control	i.p.	NA	NA	120 weeks	120 weeks	NA	3/25 (12%)	
			Day 1		25 µg NMU/g body weight	1×	100 weeks	90 weeks	NA	2/25 (8%)[b]	
			Day 70		25 µg NMU/g body weight	1×	120 weeks	100 weeks	NA	4/20 (20%)[b]	
			Day 1		50 µg NMU/g body weight	1×	70 weeks	80 weeks	NA	0/44 (0%)[b]	
			Day 21		50 µg NMU/g body weight	1×	100 weeks	90 weeks	NA	9/38 (24%)[b]	
			Day 70		50 µg NMU/g body weight	1×	110 weeks	90 weeks	NA	16/41 (39%)[b]	
		mammary	control	i.p.	NA	NA	120 weeks	120 weeks	NA	2/25 (8%)	Terracini et al. (1976)
			Day 1		25 µg NMU/g body weight	1×	100 weeks	90 weeks	NA	1/25 (4%)[b]	
			Day 70		25 µg NMU/g body weight	1×	120 weeks	100 weeks	NA	0/20 (0%)[b]	
			Day 1		50 µg NMU/g body weight	1×	70 weeks	80 weeks	NA	0/44 (0%)[b]	
			Day 21		50 µg NMU/g body weight	1×	100 weeks	90 weeks	1/44 (2%)[b]	0/38 (0%)[b]	
			Day 70		50 µg NMU/g body weight		110 weeks	90 weeks	NA	4/41 (9.8%)[b]	
		uterus or vagina	control	i.p.	NA	NA	120 weeks	120 weeks	NA	1/25 (4%)	
			Day 1		25 µg NMU/g body weight	1×	100 weeks	90 weeks	NA	1/25 (4%)[b]	
			Day 70		25 µg NMU/g body weight	1×	120 weeks	100 weeks	NA	6/20 (30%)[b]	
			Day 1		50 µg NMU/g body weight	1×	70 weeks	80 weeks	NA	0/44 (0%)[b]	
			Day 21		50 µg NMU/g body weight	1×	100 weeks	90 weeks	NA	1/38 (3%)[b]	
			Day 70		50 µg NMU/g body weight		110 weeks	90 weeks		7/41 (17%)[b]	

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
Urethane	Mice (SWR)	lung adenoma	Newborn	s.c.	0.18 mg/g body weight	1×	10 weeks	100%[b]		The average number of tumors per mouse increased linearly with dose.	Kaye and Trainin (1966)
			11–22 weeks	s.c.	0.25 mg/g body weight	1×	23–34 weeks	0%[b]			
	Mice (C3H/f)	liver	Control	Control	None	N/A	493 days (m) 553 days (f)	14/97 (14%)	1/77 (1%)		Liebelt et al. (1964)
			Day 1	i.p.	0.8 mg/g body weight	1×	481 days (m) 434 days (f)	27/30 (90%)[g]	18/39 (46%)[g]		
			8–10 weeks	i.p.	1 mg/g body weight	1×	321 days (m) -	6/25 (24%)[c]	0/32 (0%)[c]		
		lung	Control	Control	None	N/A	493 days (m) 553 days (f)	0/97 (0%)	0/77 (0%)	The number of lung tumors among the controls was not provided.	
			Day 1	i.p.	0.8 mg/g body weight	1×	401 days (m) 408 days (f)	14/30 (46%)[g]	19/39 (48%)[g]		
			8–10 weeks	i.p.	1 mg/g body weight	1×	506 days (m) -	2/25 (8%)[c]	0/32 (0%)[c]		
		reticular tissue	Control	Control	None	N/A	493 days (m) 553 days (f)	2/97 (2%)	6/77 (8%)		
			Day 1	i.p.	0.8 mg/g body weight	1×	285 days (m) 343 days (f)	4/30 (13%)[c]	22/39 (56%)[g]		
			8–10 weeks	i.p.	1 mg/g body weight	1×	- 453 days (f)	0/25 (25%)[c]	4/32 (13%)[c]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a] M	Tumors[a] F	Comments	Reference
Urethane (continued)	Mice (Swiss)	leukemia	Control	Control	None	N/A	8–10 months	1%		Highest tumor rates when dosed at birth. Exposure to newborns was followed by 21.6% leukemia, occurring at a mean age of 105 days.	Fiore-Donati et al. (1962)
			Day 1	s.c.	2 mg in 0.05 mL aqueous solution	1×		13/60 (22%)[b]			
			Day 5		4 mg in 0.05 mL aqueous solution	1×		7/39 (18%)[b]			
			Day 40		20 mg in 0.1 mL aqueous solution	1×		2/63 (3%)[b]			
	Mice (Swiss)	lung adenoma	Control 2 weeks	Control	None	N/A	9 weeks	0/15 (0%)	—	The proportion of animals with adenomas decreased steadily with age of exposure.	Rogers (1951)
			Control 4 weeks	Control	None	N/A	11 weeks	0/14 (0%)	—		
			Control 6 weeks	Control	None	N/A	13 weeks	1/15 (7%)	—		
			Control 8 weeks	Control	None	N/A	15 weeks	2/15 (13%)	—		
			Control 10 weeks	Control	None	N/A	17 weeks	0/15 (0%)	—		
			2 weeks	i.p.	1 mg/g body weight	1×	9 weeks	24/24 (100%)[b]	—		
			4 weeks	i.p.	1 mg/g body weight	1×	11 weeks	23/25 (92%)[b]	—		
			6 weeks	i.p.	1 mg/g body weight	1×	13 weeks	22/25 (88%)[b]	—		
			8 weeks	i.p.	1 mg/g body weight	1×	15 weeks	21/25 (84%)[b]	—		
			10 weeks	i.p.	1 mg/g body weight	1×	17 weeks	19/25 (76%)[b]	—		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
Urethane (continued)	Mice (Swiss)	lung adenoma	3 weeks	i.p.	0.25 mg/g body weight	1×	12 weeks	16/19 (84%)[b]	—		
					0.5 mg/g body weight	1×	12 weeks	16/20 (80%)[b]	—		
					1 mg/g body weight	1×	12 weeks	18/20 (90%)[b]	—		
			8 weeks	i.p.	0.25 mg/g body weight	1×	17 weeks	4/17 (24%)[b]	—		
					0.5 mg/g body weight	1×	17 weeks	15/16 (94%)[b]	—		
					1 mg/g body weight	1×	17 weeks	18/18 (100%)[b]	—		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumor incidence[a]		Comments	Reference
								M	F		
Urethane (continued)	Mice (Swiss)	liver	Control	Control	N/A	N/A	360–720 days	10/227 (4.4%)	4/222 (8.22%)		Chieco-Bianchi et al. (1963)
			Day 1	s.c.	1 mg/g body weight	1×	180 days	1/20 (5%)[g]	0/20 (0%)[c]		
			Day 1	s.c.	1 mg/g body weight	1×	240 days	2/17 (12%)[g]	0/12 (0%)[c]		
			Day 1	s.c.	1 mg/g body weight	1×	300 days	5/18 (28%)[g]	0/16 (0%)[c]		
			Day 1	s.c.	1 mg/g body weight	1×	360 days	11/20 (55%)[g]	0/23 (0%)[c]		
			Day 1	s.c.	1 mg/g body weight	1×	420 days	13/15 (87%)[g]	2/22 (9%)[g]		
			Day 1	s.c.	1 mg/g body weight	1×	480 days	17/23 (74%)[c]	2/25 (8%)[c]		
			Day 5	s.c.	1 mg/g body weight	1×	420 days	9/13 (69.2%)[b]	2/11 (18.2%)[b]		
			Day 20	s.c.	1 mg/g body weight	1×	420 days	1/13 (8%)[b]	0/16 (0%)[b]		
			Day 40	s.c.	1 mg/g body weight	1×	420 days	0/11 (0%)[b]	0/9 (0%)[b]		
	Mice (Swiss)	skin	Control	Control	N/A	N/A	180–550 days	30/712 (4.21%)		Croton oil treatment initiated at 40 days of age.	Chieco-Bianchi et al. (1963)
			Day 1	s.c.	1 mg urethane/g body weight; 5% croton oil	single dose urethane, croton oil applied 2×/week for 10 mos	660 days	26/59 (44.1%)[g]			

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumor incidence[a]		Comments	Reference
								M	F		
Urethane (continued)			Day 40	s.c.	1 mg urethane/g body weight; 5% croton oil	single dose urethane, croton oil applied 2×/week for 10 mos	700 days	8/41 (19.5%)[b]			
	Mice ($B6AF_1/J$)	liver	Control	gavage	N/A	N/A	71 weeks	1/25 (4%)	0/25 (0%)		Klein (1966)
			Day 1		1 mg/g body weight	1×	66 weeks	9/20 (45%)[g]	9/26 (35%)[g]		
			Day 7		1 mg/g body weight	1×	67 weeks	20/22 (91%)[g]	20/26 (77%)[g]		
			Day 14		1 mg/g body weight	1×	68 weeks	16/20 (80%)[g]	10/23 (43%)[g]		
			Day 21		1 mg/g body weight	1×	69 weeks	13/23 (57%)[g]	1/20 (5%)[g]		
			Day 28		1 mg/g body weight	1×	70 weeks	4/24 (17%)[g]	1/20 (5%)[g]		
		lung	Control	gavage	1 mg/g body weight	1×	71 weeks	9/25 (36%)	6/25 (24%)		
			Day 1		1 mg/g body weight	1×	66 weeks	20/20 (100%)[b]	25/26 (96%)[b]		
			Day 7		1 mg/g body weight	1×	67 weeks	22/22 (100%)[b]	26/26 (100%)[b]		
			Day 14		1 mg/g body weight	1×	68 weeks	19/20 (95%)[b]	19/23 (83%)[b]		
			Day 21		1 mg/g body weight	1×	69 weeks	23/23 (100%)[b]	19/20 (95%)[b]		
			Day 28		1 mg/g body weight	1×	70 weeks	24/24 (100%)[b]	20/20 (100%)[b]		
	Mice ($B6AF_1/J$)	Harderian gland	Control	gavage	1 mg/g body weight	1×	71 weeks	0/25 (0%)	0/25 (0%)		Klein (1966)
			Day 1		1 mg/g body weight	1×	66 weeks	0/20 (0%)[c]	1/26 (4%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumor incidence[a]		Comments	Reference
								M	F		
Urethane (continued)			Day 7		1 mg/g body weight	1×	67 weeks	0/22 (0%)[c]	1/26 (4%)[b]		
			Day 14		1 mg/g body weight	1×	68 weeks	0/20 (0%)[c]	2/23 (9%)[b]		
			Day 21		1 mg/g body weight	1×	69 weeks	1/23 (4%)[b]	0/20 (0%)[c]		
			Day 28		1 mg/g body weight	1×	70 weeks	0/24 (0%)[c]	0/20 (0%)[c]		
		forestomach	Control	gavage	1 mg/g body weight	1×	71 weeks	0/25 (0%)	1/25 (4%)		
			Day 1		1 mg/g body weight	1×	66 weeks	0/20 (0%)[c]	3/26 (12%)[b]		
			Day 7		1 mg/g body weight	1×	67 weeks	1/22 (5%)[b]	1/26 (4%)[b]		
			Day 14		1 mg/g body weight	1×	68 weeks	1/20 (5%)[b]	4/23 (17%)[b]		
			Day 21		1 mg/g body weight	1×	69 weeks	0/23 (0%)[c]	1/20 (5%)[b]		
			Day 28		1 mg/g body weight	1×	70 weeks	2/24 (8%)[b]	1/20 (5%)[b]		

[a] Where not delineated by gender, data combined by study authors or gender not specified. Where percentages only are given, number of subjects not specified.
[b] Not evaluated by authors.
[c] Evaluated but not significant compared with controls.
[d] Study also included mammary fibroadenomas and fibromas as well as other types of cancers.
[e] 8–9 weeks old.
[f] Includes survivors up to 40 weeks only.
[g] Significant compared with controls.

i.p. = intraperitoneal injection; s.c. = subcutaneous injection

Table 4. Ratio of early-life to adult cancer potencies for studies with repeated exposures of juvenile and adult animals to carcinogens with a mutagenic mode of action*

Compound	Species (strain)	Sex	Dose	Tumor	Unweighted geometric mean	2.5%	Median	97.5%	Reference
Benzidine	Mice ($B6C3F_1$)	male		liver	111	64	**110**	198	Vesselinovitch et al. (1975b)
		female		liver	0.16	0.004	**0.22**	1.1	
3-MU 3-Methylcholanthrene (formerly known as 20-methylcholanthrene)	Mice (Albino)	male	0.25 mg/g	hepatoma	33	7.4	**30**	268	Klein (1959)
		female	0.25 mg/g	hepatoma	7.7	1.1	**7.1**	85	
		male	0.25 mg/g	forestomach	0.91	0.39	**0.91**	2.1	
		female	0.25 mg/g	forestomach	1.5	0.58	**1.5**	4.2	
		male	0.25 mg/g	skin	1.8	0.048	**2.1**	22	
		female	0.25 mg/g	skin	1.5	0.023	**1.8**	21	
Safrole	Mice ($B6C3F_1$)	male		liver	47	16	**44**	198	Vesselinovitch et al. (1979b)
		female		liver	0.12	0.002	**0.18**	1.1	
VC Vinyl chloride	Rats (Sprague-Dawley)	male	6,000 ppm	liver-angiosarcoma	6.7	0.035	**9.8**	57	Maltoni et al. (1984)
		male	10,000 ppm	liver-angiosarcoma	7.4	0.035	**11**	62	
		female	6,000 ppm	liver-angiosarcoma	13	4.9	**13**	33	
		female	10,000 ppm	liver-angiosarcoma	30	8.7	**29**	121	
		male	6,000 ppm	zymbal gland	0.73	0.0032	**1.1**	30	
		male	10,000 ppm	zymbal gland	0.27	0.0022	**0.4**	5.4	
		female	6,000 ppm	zymbal gland	0.48	0.0027	**0.7**	16	
		female	10,000 ppm	zymbal gland	0.15	0.0014	**0.19**	4.5	
		male	10,000 ppm	leukemia	21	0.026	**37**	514	
		female	6,000 ppm	leukemia	1.3	0.0035	**1.7**	153	
		female	10,000 ppm	leukemia	0.29	0.0019	**0.35**	17	
		male	6,000 ppm	nephroblastomas	0.15	0.0014	**0.19**	4.8	
		male	10,000 ppm	nephroblastomas	0.17	0.0015	**0.21**	6.2	
		female	6,000 ppm	nephroblastomas	0.28	0.0018	**0.33**	16	
		female	10,000 ppm	nephroblastomas	0.24	0.0017	**0.29**	11	
		male	6,000 ppm	angiosarcomas-other sites	0.9	0.0033	**1.26**	53	
		male	10,000 ppm	angiosarcomas-	0.25	0.0017	**0.30**	12	

Table 4. Ratio of early-life to adult cancer potencies for studies with repeated exposures of juvenile and adult animals to mutagenic chemicals (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Unweighted geometric mean	2.5%	Median	97.5%	Reference
				other sites					
VC Vinyl chloride (continued)		female	6,000 ppm	angiosarcomas-other sites	0.24	0.0017	**0.29**	11	
		female	10,000 ppm	angiosarcomas-other sites	0.32	0.0019	**0.38**	20	
		male	6,000 ppm	angiomas & fibromas-other sites	0.72	0.0031	**1.0**	33	
		male	10,000 ppm	angiomas & fibromas-other sites	1.4	0.0045	**2.36**	47	
		female	6,000 ppm	angiomas & fibromas-other sites	0.27	0.0018	**0.33**	16	
		female	10,000 ppm	angiomas & fibromas-other sites	0.52	0.0024	**0.63**	41	
		male	6,000 ppm	hepatoma	62	11	**58**	543	
		male	10,000 ppm	hepatoma	34	8.2	**32**	218	
		female	6,000 ppm	hepatoma	55	13	**51**	352	
		female	10,000 ppm	hepatoma	55	8.4	**53**	513	
		male	6,000 ppm	skin carcinomas	1.1	0.0035	**1.5**	82	
		male	10,000 ppm	skin carcinomas	0.41	0.0024	**0.56**	15	
		female	6,000 ppm	skin carcinomas	0.46	0.0024	**0.59**	24	
		female	10,000 ppm	skin carcinomas	0.31	0.0019	**0.37**	19	
		male	6,000 ppm	neuroblastoma	0.21	0.0016	**0.26**	9.5	
		male	10,000 ppm	neuroblastoma	0.20	0.0016	**0.24**	8.5	
		female	6,000 ppm	neuroblastoma	0.27	0.0018	**0.32**	15	
		female	10,000 ppm	neuroblastoma	0.14	0.0014	**0.18**	4.4	

* The 2.5% and 97.5% are percentiles of the posterior distribution. For a Bayesian distribution, these percentiles function in a manner similar to the 95% confidence limits for other types of statistical analyses.

Table 5. Ratio of early-life to adult cancer potencies for studies with repeated exposures of juvenile and adult animals to chemicals with a nonmutagenic mode of action*

Compound	Species (strain)	Sex	Dose	Tumor	Ratio of juvenile to adult potency				Reference
					Unweighted geometric mean	2.5%	Median	97.5%	
Amitrole	Mice ($B6C3F_1$)	male	NA	liver	13	5.1	**14**	30	Vesselinovitch (1983)
		female	NA	liver	0.14	0.0013	**0.18**	3.9	
DDT	Mice ($B6C3F_1$)	male	NA	liver	1.3	0.0044	**2.5**	25	Vesselinovitch et al. (1979a)
Dieldrin	Mice ($B6C3F_1$)	male	NA	liver	0.75	0.0031	**1.2**	27	Vesselinovitch et al. (1979a)
DPH	Rats (F344/N)	male	630	liver	0.4	0.0024	**0.54**	16	Chhabra et al. (1993b)
		female	630	liver	0.24	0.0017	**0.29**	12	
	Mice ($B6C3F_1$)	male	210	liver	1.5	0.0040	**2.4**	71	
		female	210	liver	1.3	0.0056	**2.6**	15	
ETU	Rats (F344/N)	male	90	thyroid	0.37	0.0029	**0.61**	5.4	Chhabra et al. (1992)
		female	90	thyroid	0.23	0.0018	**0.3**	7.0	
	Mice ($B6C3F_1$)	male	330	liver	0.091	0.0011	**0.12**	1.9	
		female	330	liver	0.057	0.0010	**0.081**	0.65	
		male	330	thyroid	0.41	0.0022	**0.52**	25	
		female	330	thyroid	0.4	0.0024	**0.55**	16	
		male	330	pituitary	0.32	0.0019	**0.38**	22	
		female	330	pituitary	0.24	0.0018	**0.32**	6.9	
PBB	Rats (F344/N)	male	10	liver	0.59	0.0041	**1.1**	6.6	Chhabra et al. (1993a)
		female	10	liver	0.063	0.0009	**0.079**	1.2	
		male	10	mononuclear cell leukemia	0.79	0.0035	**1.4**	18	
		female	10	mononuclear cell leukemia	0.21	0.0017	**0.28**	6.0	
	Mice ($B6C3F_1$)	male	30	liver	3.9	1.9	**3.9**	7.5	
		female	30	liver	1.0	0.37	**1.05**	2.1	

* The 2.5% and 97.5% are percentiles of the posterior distribution. For a Bayesian distribution, these percentiles function in a manner similar to the 95% confidence limits for other types of statistical analyses.

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action*

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
BaP*	Mice ($B6C3F_1$)	male	75 µg/kg	liver	1 day	9.3	2.9	**8.4**	55	Vesselinovitch et al. (1975a)
					15 days	11	3.5	**9.6**	61	
		female	75 µg/kg		1 day	1.2	0.0083	**1.6**	31	
					15 days	1.7	0.015	**2.1**	36	
		male	150 µg/kg		1 day	29	8.2	**26**	194	
					15 days	15	4.1	**13**	109	
		female	150 µg/kg		1 day	8.8	1.4	**8.1**	94	
					15 days	1.2	0.0082	**1.6**	30	
	Mice ($C3AF_1$)	male	75 µg/kg	liver	1 day	11	2.1	**10**	112	
					15 days	7.5	1.1	**7.0**	83	
		female	75 µg/kg		1 day	0.2	0.0018	**0.26**	9.1	
					15 days	0.2	0.0017	**0.24**	8.5	
		male	150 µg/kg		1 day	14	3.0	**12.8**	130	
					15 days	3.6	0.11	**3.8**	49	
		female	150 µg/kg		1 day	0.2	0.0017	**0.24**	8.8	
					15 days	0.2	0.0017	**0.24**	8.7	
	Mice ($B6C3F_1$)	Male	75 µg/kg	lung	1 day	1.2	0.45	**1.2**	3.4	
					15 days	0.2	0.0046	**0.31**	1.4	
		female	75 µg/kg	lung	1 day	2.8	1.096	**2.7**	9.5	
					15 days	1.4	0.41	**1.4**	5.1	
		Male	150 µg/kg	lung	1 day	2.2	1.0	**2.1**	5.4	
					15 days	0.8	0.2	**0.82**	2.3	
		female	150 µg/kg	lung	1 day	7.9	2.6	**7.2**	43	
					15 days	3.7	1.1	**3.4**	22	
	Mice ($C3AF_1$)	male	75 µg/kg	lung	1 day	1.2	0.47	**1.2**	3.2	
					15 days	1.1	0.43	**1.08**	3.1	

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
BaP* (continued)		female	75 µg/kg	lung	1 day	1.6	0.66	**1.55**	4.0	
					15 days	1.6	0.71	**1.63**	4.2	
		male	150 µg/kg	lung	1 day	1.5	0.57	**1.5**	5.0	
					15 days	1.9	0.71	**1.8**	6.0	
		female	150 µg/kg	lung	1 day	1.3	0.61	**1.3**	2.9	
					15 days	1.2	0.54	**1.1**	2.6	
DBA	Mice			lung		178	20	**143**	5100	Law (1940)
DEN**	Mice ($B6C3F_1$)	male	6 µg/kg	liver	1 day	9.0	3.5	**8.3**	37	Vesselinovitch et al. (1984)
					15 days	8.9	3.5	**8.2**	36	
		female	6 µg/kg	liver	1 day	35	9.1	**31**	239	
					15 days	25	6.3	**226**	175	
		male	12 µg/kg	liver	1 day	9.6	3.3	**8.8**	50	
					15 days	9.8	3.4	**8.9**	51	
		female	12 µg/kg	liver	1 day	16	5.9	**15**	67	
					15 days	19	7.1	**18**	79	
	Mice ($C3AF_1$)	male	6 µg/kg	liver	1 day	7.3	2.9	**6.9**	26	
					15 days	3.5	1.4	**3.3**	13	
		female	6 µg/kg	liver	1 day	17	3.2	**16**	166	
					15 days	6.4	0.86	**6.0**	73	
		male	12 µg/kg	liver	1 day	11	3.7	**9.5**	53	
					15 days	9.8	3.4	**8.9**	50	
		female	12 µg/kg	liver	1 day	40	8.5	**36**	340	
					15 days	25	5.0	**22**	221	
	Mice ($B6C3F_1$)	male	6 µg/kg	lung	1 day	0.5	0.27	**0.52**	0.93	
					15 days	1.6	0.95	**1.6**	2.7	
		female	6 µg/kg	lung	1 day	0.9	0.54	**0.89**	1.5	
					15 days	1.2	0.76	**1.2**	2.0	

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
DEN** (continued)		male	12 µg/kg	lung	1 day	0.4	0.21	**0.40**	0.73	
					15 days	0.7	0.39	**0.66**	1.1	
		female	12 µg/kg	lung	1 day	0.7	0.44	**0.73**	1.2	
					15 days	1.4	0.88	**1.4**	2.3	
	Mice ($C3AF_1$)	male	6 µg/kg	lung	1 day	0.7	0.22	**0.67**	1.7	
					15 days	0.5	0.21	**0.56**	1.3	
		female	6 µg/kg	lung	1 day	1.1	0.45	**1.1**	2.5	
					15 days	0.7	0.36	**0.74**	1.5	
		male	12 µg/kg	lung	1 day	0.3	0.084	**0.33**	0.76	
					15 days	0.6	0.26	**0.62**	1.4	
		female	12 µg/kg	lung	1 day	0.7	0.35	**0.75**	1.6	
					15 days	0.7	0.37	**0.75**	1.5	
DMBA#	Rats (Wistar)	male		total	2 vs 5–8 wks	3.3	1.3	**3.2**	10	Meranze et al. (1969)
					2 vs 26 wks	3.2	1.3	**3.1**	9.7	
		female		total	2 vs 5–8 wks	1.3	0.68	**1.3**	2.5	
					2 vs 26 wks	3.3	1.2	**3.0**	16	
				mammary	2 vs 5–8 wks	0.0	0.0012	**0.056**	0.26	
					2 vs 26 wks	0.2	0.0023	**0.29**	5.3	
					5 vs 26 wks	7.1	1.8	**6.4**	55	
	Mice (Balb/c)	male	15 µg	lung	1 day	30	2.8	**22**	1482	Walters (1966)
					15–19 days	1.0	0.28	**1.0**	3.5	
		male	30 µgx2	lung	15–19 days	14	1.056	**10**	978	
		female	15 µg	lung	1 day	60	6.0	**46**	2350	
					15–19 days	3.1	0.51	**3.0**	22	
		female	30 µgx2	lung	15–19 days	15	1.2	**11**	1004	
	Mice (Swiss)			lymphoma		2.7	0.60	**2.5**	19	Pietra et al. (1961)
				lung		9.1	2.9	**8.7**	40	

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
DMN***	Rats (Wistar)		3 wks	total	1 month	0.7	0.41	**0.73**	1.3	Hard (1979)
					1.5 months	1.1	0.58	**1.1**	2.1	
					2 months	1.5	0.75	**1.5**	3.0	
					3 months	0.9	0.50	**0.94**	1.8	
			24 hr		1 month	0.3	0.13	**0.28**	0.6	
					1.5 months	0.4	0.18	**0.42**	0.9	
					2 months	0.6	0.24	**0.56**	1.3	
					3 months	0.4	0.16	**0.36**	0.78	
			1 month		1.5 months	1.5	0.80	**1.52**	3.0	
					2 months	2.0	1.0	**2.0**	4.2	
					3 months	1.3	0.69	**1.3**	2.5	
ENU	Mice ($B6C3F_1$)	male		liver		7.8	3.9	**7.7**	18	Vesselinovitch (1983)
		female				7.1	2.9	**6.9**	21	
	Rats (Wistar)	male		nerve tissue	1 day	27	2.5	**20**	1374	Naito et al. (1981)
					1 week	1.6	0.61	**1.6**	4.6	
					2 weeks	1.6	0.58	**1.6**	4.8	
					3 weeks	0.7	0.12	**0.72**	2.3	
		female			1 day	64	6.0	**50**	2488	
					1 weeks	9.6	2.6	**8.9**	59	
					2 weeks	6.2	1.6	**5.7**	40	
					3 weeks	0.7	0.0090	**0.89**	8.9	
	Mice ($B6C3F_1$)	male	60 µg/g	lung	1	1.0	0.60	**1.0**	1.7	Vesselinovitch et al. (1974)
					15	1.1	0.66	**1.1**	1.8	
		female	60 µg/g	lung	1	2.1	1.17	**2.1**	4.1	
					15	1.0	0.60	**1.0**	1.7	
		male	120 µg/g	lung	1	1.0	0.60	**1.0**	1.7	

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
					15	1.1	0.66	**1.0**	1.8	
ENU (continued)		female	120 µg/g	lung	1	2.1	1.2	**2.1**	4.1	
					15	1.0	0.60	**1.0**	1.7	
	Mice ($C3AF_1$)	male	60 µg/g	lung	1	8.7	2.7	**8.0**	48	
					15	52	5.2	**39**	2141	
		female	60 µg/g	lung	15	0.7	0.32	**0.72**	1.6	
		male	120 µg/g	lung	1	0.9	0.38	**0.92**	2.2	
					15	0.7	0.28	**0.67**	1.6	
		female	120 µg/g	lung	1	0.5	0.24	**0.54**	1.2	
					15	0.4	0.18	**0.42**	0.92	
	Mice ($B6C3F_1$)	male	60 µg/g	liver	1	8.8	4.2	**8.5**	22	
					15	14	6.2	**14**	37	
		female	60 µg/g	liver	1	6.3	2.6	**6.1**	18	
					15	5.6	2.4	**5.4**	16	
		male	120 µg/g	liver	1	5.2	2.5	**5.1**	11	
					15	7.6	3.9	**7.5**	17	
		female	120 µg/g	liver	1	11	4.1	**11**	46	
					15	14	4.9	**13**	55	
	Mice ($C3AF_1$)	male	60 µg/g	liver	1	12	4.7	**11**	43	
					15	8.1	3.2	**7.6**	29	
		female	60 µg/g	liver	1	7.5	2.6	**7.0**	32	
					15	4.8	1.8	**4.6**	18	
		male	120 µg/g	liver	1	9.8	4.1	**9.3**	32	
					15	6.6	2.7	**6.3**	23	
		female	120 µg/g	liver	1	5.4	1.7	**5.0**	25	
					15	5.4	1.7	**5.1**	25	
	Mice ($B6C3F_1$)	male	60 µg/g	kidney	1	2.2	0.73	**2.1**	8.0	
					15	1.2	0.29	**1.2**	5.1	

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
		female	60 µg/g	kidney	1	0.7	0.024	**0.85**	5.9	
					15	2.6	0.61	**2.5**	15	
ENU (continued)		male	120 µg/g	kidney	1	1.7	0.65	**1.7**	4.4	
					15	2.6	1.14	**2.6**	6.4	
		female	120 µg/g	kidney	1	0.9	0.37	**0.87**	2.0	
					15	1.4	0.67	**1.4**	3.2	
	Mice ($C3AF_1$)	male	60 µg/g	kidney	1	1.8	0.17	**1.9**	15	
					15	2.0	0.25	**2.0**	16	
		female	60 µg/g	kidney	1	1.0	0.016	**1.3**	13	
					15	2.1	0.16	**2.2**	20	
		male	120 µg/g	kidney	1	0.2	0.0029	**0.24**	1.5	
					15	1.5	0.38	**1.5**	5.9	
		female	120 µg/g	kidney	1	2.3	0.17	**2.4**	20	
					15	7.1	1.8	**6.5**	47	
	Mice ($B6C3F_1$)	male	60 µg/g	Harderian	1	0.3	0.018	**0.41**	1.4	
					15	0.5	0.075	**0.52**	1.4	
		female	60 µg/g	Harderian	1	0.1	0.0025	**0.16**	0.74	
					15	0.8	0.35	**0.84**	2.0	
		male	120 µg/g	Harderian	1	0.4	0.13	**0.42**	0.96	
					15	0.6	0.26	**0.57**	1.2	
		female	120 µg/g	Harderian	1	0.1	0.0030	**0.18**	0.85	
					15	0.7	0.17	**0.77**	2.1	
	Mice ($C3AF_1$)	male	60 µg/g	Harderian	1	0.1	0.0023	**0.20**	1.3	
					15	0.1	0.0016	**0.18**	1.8	
		female	60 µg/g	Harderian	1	0.4	0.019	**0.52**	2.5	
					15	0.8	0.15	**0.85**	3.4	
		male	120 µg/g	Harderian	1	0.1	0.0010	**0.086**	1.0	
					15	0.3	0.0050	**0.40**	2.8	

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
		female	120 µg/g	Harderian	1	0.1	0.0012	**0.094**	1.2	
					15	0.1	0.0012	**0.081**	0.90	
ENU (continued)	Mice ($B6C3F_1$)	male	60 µg/g	stomach	1	0.3	0.0091	**0.34**	2.4	
					15	1.9	0.61	**1.82**	8.7	
		female	60 µg/g	stomach	1	0.2	0.0083	**0.26**	1.1	
					15	0.2	0.0072	**0.24**	1.0	
		male	120 µg/g	stomach	1	0.2	0.0059	**0.20**	0.90	
					15	1.2	0.50	**1.2**	2.9	
		female	120 µg/g	stomach	1	0.6	0.19	**0.60**	1.5	
					15	1.6	0.67	**1.6**	3.7	
	Mice ($C3AF_1$)	male	60 µg/g	stomach	1	0.0	0.0009	**0.063**	0.51	
					15	0.3	0.023	**0.41**	1.3	
		female	60 µg/g	stomach	1	0.8	0.085	**0.89**	3.5	
					15	1.1	0.19	**1.1**	4.5	
		male	120 µg/g	stomach	1	0.2	0.010	**0.19**	0.56	
					15	0.7	0.32	**0.70**	1.5	
		female	120 µg/g	stomach	1	0.4	0.14	**0.46**	1.2	
					15	0.6	0.24	**0.64**	1.5	
NMU	Mice ($BC3F_1$)	male	50 µg/g	lung adenomas	1	3.4	1.3	**3.3**	9.3	Terracini and Testa (1970)
		female	50 µg/g	lung adenomas	1	6.3	2.4	**6.0**	23	
		male	50 µg/g	lymphosarcoma	1	2.5	1.1	**2.4**	6.4	
		female	50 µg/g	lymphosarcoma	1	1.1	0.49	**1.1**	2.4	
		male	50 µg/g	hepatoma	1	35	6.5	**32**	324	
		female	50 µg/g	hepatoma	1	0.3	0.0023	**0.39**	13	
		male	50 µg/g	renal adenoma	1	0.9	0.0093	**1.2**	13	
		female	50 µg/g	renal adenoma	1	1.3	0.0081	**1.7**	33	
		male	50 µg/g	forestomach	1	0.0	0.0006	**0.039**	0.52	
		female	50 µg/g	forestomach	1	0.1	0.0027	**0.15**	0.69	

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
	Mice (C3Hf/Dp)	male	25 µg/g	thymic lymphoma	1	1.9	0.048	**2.1**	23	
NMU (continued)		female	25 µg/g	thymic lymphoma	1	1.2	0.0089	**1.5**	30	
		male	25 µg/g	lung adenomas	1	1.0	0.013	**1.2**	11	
		female	25 µg/g	lung adenomas	1	0.4	0.018	**0.46**	1. 7	
		male	25 µg/g	liver tumor	1	0.2	0.0016	**0.21**	4.6	
		female	25 µg/g	liver tumor	1	0.3	0.0026	**0.39**	4.4	
		male	25 µg/g	Stomach	1	0.5	0.0045	**0.67**	6.8	
		female	25 µg/g	Stomach	1	0.3	0.0046	**0.43**	3.8	
				ovarian	1	0.1	0.0014	**0.17**	3.5	
				uterine/vaginal	1	8.6	1.1	**8.1**	97	
		male	50 µg/g	thymic lymphoma	1	7.9	3.1	**7.4**	30	
		female	50 µg/g	thymic lymphoma	1	3.1	1.3	**3.0**	7.8	
		male	50 µg/g	lung adenomas	1	0.04	0.0008	**0.058**	0.45	
		female	50 µg/g	lung adenomas	1	0.1	0.0012	**0.084**	0.53	
		male	50 µg/g	liver tumor	1	0.2	0.0021	**0.33**	7.8	
		female	50 µg/g	liver tumor	1	0.1	0.0011	**0.13**	4.5	
		male	50 µg/g	Stomach	1	0.01	0.0003	**0.013**	0.12	
		female	50 µg/g	Stomach	1	0.1	0.0022	**0.15**	0.96	
				ovarian	1	0.0	0.0003	**0.014**	0.14	
				uterine/vaginal	1	0.0	0.0005	**0.034**	0.46	
		male	50 µg/g	thymic lymphoma	21	4.3	1. 6	**4.1**	17	
		female	50 µg/g	thymic lymphoma	21	1.0	0.39	**1.0**	2.6	
		male	50 µg/g	lung adenomas	21	0.1	0.0022	**0.22**	1.1	
		female	50 µg/g	lung adenomas	21	0.7	0.30	**0.75**	1.7	

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
		male	50 µg/g	liver tumor	21	0.1	0.0013	**0.15**	4.3	
		female	50 µg/g	liver tumor	21	0.9	0.0051	**1.4**	23	
NMU (continued)		male	50 µg/g	stomach	21	0.1	0.001	**0.08**	0.64	
		female	50 µg/g	stomach	21	1.8	0.77	**1.8**	4.7	
				ovarian	21	0.0	0.0007	**0.055**	0.97	
				uterine/vaginal	21	1.7	0.59	**1.7**	6.4	
Urethane	Mice (Swiss)	male	1 mg/g	liver	1	24	4.4	**21**	220	Chieco-Bianchi et al. (1963)
		female	1 mg/g	liver	1	0.4	0.0044	**0.54**	13	
		male	1 mg/g	liver	5	14	2.4	**13**	137	
		female	1 mg/g	liver	5	1.2	0.017	**1.4**	26	
		male	1 mg/g	liver	20	0.2	0.0018	**0.28**	10	
		female	1 mg/g	liver	20	0.1	0.0011	**0.12**	4.8	
		both	1 mg/g	skin	1	0.2	0.0027	**0.32**	5.4	
Urethane + croton oil	Mice (Swiss)	both	1 mg/g	skin	1	2.9	1.2	**2.8**	8.2	
Urethane	Rats (MRC Wistar-derived)	male/ female	16%×6	neurilemmomas	1	0.2	0.0028	**0.33**	4.5	Choudari Kommineni et al. (1970)
		male/ female	16%×6	neurilemmomas	28	0.4	0.0045	**0.51**	6.3	
		male/ female	16%×6	liver	1	7.9	1.4	**7.1**	82	
		male/ female	16%×6	liver	28	0.2	0.0026	**0.4**	11.7	
		male/ female	16%×6	thyroid	1	0.0	0.0006	**0.039**	0.67	
		male/ female	16%×6	thyroid	28	0.1	0.0011	**0.1**	1.5	
	Mice (Swiss)	male/ female	1 mg/g	lung	1	15	1.2	**11**	997	De Benedictis et al. (1962)
	Mice (Swiss)			leukemia		6.7	1.7	**6.1**	45	Fiore-Donati et al.

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
						5.1	1.1	**4.7**	38	(1962)
Urethane (continued)	Mice ($B6AF_1/J$)	male	1 mg/g	liver	21	5.1	1.4	**4.7**	30	Klein (1966)
		female	1 mg/g	liver	21	0.2	0.0019	**0.26**	6.0	
				Harderian gland	1	0.3	0.0021	**0.33**	11	
					7	0.3	0.0021	**0.33**	11	
					14	0.6	0.0044	**0.85**	20	
		male	1 mg/g	Harderian gland	21	0.3	0.0024	**0.41**	13	
		male	1 mg/g	forestomach	1	0.1	0.0009	**0.079**	1.9	
		female	1 mg/g	forestomach	1	0.4	0.0028	**0.49**	11	
		male	1 mg/g	forestomach	7	0.1	0.0017	**0.19**	3.5	
		female	1 mg/g	forestomach	7	0.1	0.0013	**0.16**	5.0	
		male	1 mg/g	forestomach	14	0.2	0.0018	**0.21**	3.9	
		female	1 mg/g	forestomach	14	0.8	0.0056	**1.1**	18	
		male	1 mg/g	forestomach	21	0.1	0.0008	**0.072**	1.7	
		female	1 mg/g	forestomach	21	0.2	0.0015	**0.2**	6.3	
				lung	1	1.0	0.36	**0.95**	2.5	
		male	1 mg/g	lung	14	0.8	0.26	**0.8**	2.3	
		female	1 mg/g	lung	14	0.4	0.16	**0.45**	1.1	
					21	0.9	0.31	**0.86**	2.4	
	Mice (C3H/f)	male	1 mg/g	liver	1	14	4.0	**12**	81	Liebelt et al. (1964)
		female	1 mg/g	liver	1	16	3.2	**15**	155	
		male	1 mg/g	lung	1	5.9	1.7	**5.6**	28	
		female	1 mg/g	lung	1	22	4.5	**20**	203	
		male	1 mg/g	reticular tissue	1	2.0	0.023	**2.3**	38	
		female	1 mg/g	reticular tissue	1	8.6	2.3	**7.7**	60	
	Mice (Swiss)		1 mg/g	pulmonary adenomas	2 vs 4 weeks	14	1.1	**10.1**	965	Rogers (1951)

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
			1 mg/g	pulmonary adenomas	2 vs 6 weeks	16	1.3	**11.3**	1025	
Urethane (continued)			1 mg/g	pulmonary adenomas	2 vs 8 weeks	19	1.6	**13.3**	1126	
			1 mg/g	pulmonary adenomas	2 vs 10 weeks	21	1.9	**14.5**	1168	
			0.25 mg/g	adenomas	3 vs 8 weeks	7.1	2.3	**6.7**	29	
			0.5 mg/g	adenomas	3 vs 8 weeks	0.7	0.29	**0.67**	1.6	
			1.0 mg/g	adenomas	3 vs 8 weeks	0.7	0.28	**0.68**	1.6	

* The 2.5% and 97.5% are percentiles of the posterior distribution. For a Bayesian distribution, these percentiles function in a manner similar to the 95% confidence limits for other types of statistical analyses.

Table 7. Ratio of early-life to adult cancer potencies for studies with lifetime exposures starting with juvenile and adult animals to carcinogens with mutagenic or nonmutagenic modes of action*

Compound	Species (strain)	Sex	Dose	Tumor	Unweightedg eometric mean	2.5%	Median	97.5%	Reference
Mutagenic compounds									
DEN	Rats (Colworth)		multiple	liver	2.8	0.0093	**5.6**	23	Peto et al. (1984)
				esophagus	0.18	0.0015	**0.23**	4.8	
Safrole	Mice ($B6C3F_1$)	male		liver	50	3.7	**50**	253	Vesselinovitch et al. (1979b)
		female		liver	4.0	0.007	**4.0**	23	
Urethane	Mice ($B6AF_1/J$)	male	2.5 mg/pup	liver	79	0.36	**102**	1,064	Klein (1966)
		female	2.5 mg/pup	liver	0.47	0.0022	**0.55**	42	
Nonmutagenic compounds									
DDT	Mice ($B6C3F_1$)			liver	23	0.0023	**0.58**	23	Vesselinovitch et al. (1979a)
Dieldrin	Mice ($B6C3F_1$)			liver	91	0.014	**14**	91	Vesselinovitch et al. (1979a)
DPH	Rats (F344/N)	male	630:800	liver	0.31	0.0019	**0.37**	18	Chhabra et al. (1993b)
			630:2,400	liver	0.36	0.0021	**0.45**	17	
		female	630:800	liver	0.33	0.0019	**0.39**	21	
			630:2,400	liver	0.33	0.0019	**0.39**	21	
	Mice ($B6C3F_1$)	male	210:100	liver	0.71	0.0028	**0.93**	49	
			210:300	liver	14	0.03	**23**	214	
		female	210:200	liver	0.32	0.002	**0.42**	13	
			210:600	liver	0.35	0.0023	**0.53**	8.8	
ETU	Rats (F344/N)	male	90:83	thyroid	0.23	0.0017	**0.3**	7.3	Chhabra et al. (1992)
			90:250	thyroid	9.1	1.1	**10.5**	27	
		female	90:83	thyroid	0.37	0.0021	**0.46**	19	
			90:250	thyroid	0.61	0.0034	**1.1**	10	

Table 7. Ratio of early-life to adult cancer potencies for studies with lifetime exposures starting with juvenile and adult animals to carcinogens with mutagenic or nonmutagenic modes of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Unweighted geometric mean	2.5%	Median	97.5%	Reference
ETU (continued)	Mice ($B6C3F_1$)	male	330:330	liver	0.37	0.0022	**0.5**	14	
			330:1,000	liver	0.48	0.0027	**0.75**	12	
		female	330:330	liver	0.33	0.0023	**0.5**	7.8	
			330:1,000	liver	0.42	0.0025	**0.65**	11	
		male	330:330	thyroid	0.44	0.0022	**0.52**	34	
			330:1,000	thyroid	0.63	0.0035	**1.12**	10	
		female	330:330	thyroid	5.2	0.011	**10**	108	
			330:1,000	thyroid	0.18	0.0016	**0.24**	4.2	
		male	330:330	pituitary	0.40	0.0021	**0.47**	32	
			330:1,000	pituitary	0.18	0.0015	**0.22**	5.7	
		female	330:330	pituitary	0.21	0.0016	**0.26**	10	
			330:1,000	pituitary	0.27	0.0019	**0.36**	9.0	
PBB	Rats (F344/N)	male	10:10	liver	0.39	0.0023	**0.56**	13	Chhabra et al. (1993a)
			10:30	liver	0.18	0.0016	**0.25**	4.3	
		female	10:10	liver	36	15	**36**	86	
			10:30	liver	3.1	0.023	**4.6**	22	
		male	10:10	mononuclear cell leukemia	0.51	0.0025	**0.69**	23	
		male	10:30	mononuclear cell leukemia	0.77	0.0031	**1.1**	35	
		female	10:10	mononuclear cell leukemia	0.54	0.0026	**0.74**	24	
		female	10:30	mononuclear cell leukemia	0.34	0.0021	**0.45**	15	
	Mice ($B6C3F_1$)	male	30:30	liver	8.9	0.015	**12.2**	1,076	
		female	30:30	liver	4.4	0.0075	**6.2**	786	
		male	10:10	liver	0.15	0.0014	**0.2**	3.9	

Table 7. Ratio of early-life to adult cancer potencies for studies with lifetime exposures starting with juvenile and adult animals to carcinogens with mutagenic or nonmutagenic modes of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Unweighted geometric mean	2.5%	Median	97.5%	Reference
		female	10:10	liver	0.29	0.0021	**0.43**	7.0	

* The 2.5% and 97.5% are percentiles of the posterior distribution. For a Bayesian distribution, these percentiles function in a manner similar to the 95% confidence limits for other types of statistical analyses.

Table 8. Summary of quantitative estimates of ratio of early-life to adult cancer potencies

Dose	Tissue	Number of chemicals	Inverse-weighted geometric mean ratio	Unweighted Minimum	Unweighted Maximum	Number of ratios	Percentage >1
Chemicals with mutagenic mode of action							
Repeated		4	10.5	0.12	111	45	42
Lifetime		3	8.7	0.18	79	6	67
	Combined repeated and lifetime	**6**	**10.4**	**0.12**	**111**	**51**	**45**
Acute	**Combined**	11	1.5	0.01	178	268	55
	Forestomach	3	0.076	0.01	1.9	32	16
	Harderian	2	0.48	0.06	0.8	20	0.0
	Kidney	2	1.6	0.17	7.1	18	78
	Leukemia	1	5.9	5.1	6.7	2	100
	Liver	5	8.1	0.10	40	70	77
	Lung	7	1.1	0.04	178	77	56
	Lymph	2	1.8	1.1	2.7	3	100
	Mammary (wk 5 vs wk 26)	1	7.1	NA	NA	1	100
	Mammary (wk 2 vs wk 5–8 or 26)	1	0.071	NA	NA	2	0
	Nerve	2	2.3	0.24	64	8	75
	Nerve (Day 1 comparison)	2	10	0.24	64	3	67
	Ovarian	1	0.033	0.01	0.13	3	0
	Reticular tissue	1	6.5	1.96	8.6	2	100
	Thymic lymphoma	1	2.8	1.01	7.9	6	100
	Thyroid	1	0.05	0.03	0.08	2	0
	Uterine/vaginal	1	1.6	0.03	8.6	3	67
	Day 1	7	1.7	0.01	178	127	55
	Day 15	3	1.5	0.06	52	74	65
Chemicals with nonmutagenic mode of action							
Repeated		6	2.2	0.06	13	22	27
Lifetime		5	3.4	0.15	36	38	21

Table 9. Excess Relative Risk (ERR) estimates for cancer incidence from Life Span Study (Japanese survivors)[a]

Site	Average ERR at 1 Sv	
	<20[b]	>20[b]
Stomach	0.74	0.24
Colon	0.62	0.7
Liver	1.3	0.31
Lung	0.57	1.1
Bone and connective tissue	11	0.42
Skin	5.4	0.39
Breast	3.3	0.98
Urinary bladder	0.71	0.79
Leukemia	6.1	3.7

[a] Information extracted from tables in UNSCEAR, Annex I (2000).
[b] Age at exposure.

Table 10. Excess Relative Risk (ERR) estimates for incidence of thyroid cancer from Life Span Study[a]

Age at exposure	Average ERR at 1 Sv (No. cases)
0–9 yr	10.25 (24)
10–19 yr	4.5 (35)
20–29 yr	0.10 (18)
>30 yr	0.04 (55)

[a] Information extracted from tables in UNSCEAR, Annex I (2000).

Table 11. Coefficients for the Revised Methodology mortality risk model (from U.S. EPA, 1999)[a]

Cancer type	Risk model type[b]	Age group				
		0–9	10–19	20–29	30–39	40+
Male:						
Stomach	R	1.223	1.972	2.044	0.3024	0.2745
Colon	R	2.290	2.290	0.2787	0.4395	0.08881
Liver	R	0.9877	0.9877	0.9877	0.9877	0.9877
Lung	R	0.4480	0.4480	0.0435	0.1315	0.1680
Bone	A	0.09387	0.09387	0.09387	0.09387	0.09387
Skin	A	0.06597	0.06597	0.06597	0.06597	0.06597
Breast	R	0.0	0.0	0.0	0.0	0.0
Ovary	R	0.0	0.0	0.0	0.0	0.0
Bladder	R	1.037	1.037	1.037	1.037	1.037
Kidney	R	0.2938	0.2938	0.2938	0.2938	0.2938
Thyroid	A	0.1667	0.1667	0.1667	0.1667	0.1667
Leukemia	R	982.3	311.3	416.6	264.4	143.6
Female:						
Stomach	R	3.581	4.585	4.552	0.6309	0.5424
Colon	R	3.265	3.265	0.6183	0.8921	0.1921
Liver	R	0.9877	0.9877	0.9877	0.9877	0.9877
Lung	R	1.359	1.359	0.1620	0.4396	0.6047
Bone	A	0.09387	0.09387	0.09387	0.09387	0.09387
Skin	A	0.06597	0.06597	0.06597	0.06597	0.06597
Breast	R	0.7000	0.7000	0.3000	0.3000	0.1000
Ovary	R	0.7185	0.7185	0.7185	0.7185	0.7185
Bladder	R	1.049	1.049	1.049	1.049	1.049
Kidney	R	0.2938	0.2938	0.2938	0.2938	0.2938
Thyroid	A	0.3333	0.3333	0.1667	0.1667	0.1667
Leukemia	R	1,176	284.9	370.06	178.8	157.1

[a] The coefficients were derived using several models applied to data from A-bomb survivors and selected medical exposures.

[b] A = absolute risk with coefficient units of 10^{-4} $(Gy\ y)^{-1}$; R= relative risk with coefficient units of Gy^{-1}.

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Exhibit E

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Volume I: Human Health Evaluation Manual
(Part F, Supplemental Guidance for Inhalation Risk Assessment)

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LIST OF ACRONYMS

µg	Microgram
µm	Micrometer
ADAF	Age Dependent Adjustment Factor
AT	Averaging Time
ATSDR	Agency for Toxic Substances and Disease Registry
BMCL	Benchmark Concentration, Lower confidence limit
BMD	Benchmark Dose
BW	Body Weight
CA	Contaminant Concentration in Air
CERCLA	Comprehensive Environmental Response, Compensation, and Liability Act
CSF	Cancer Slope Factor
DAF	Dosimetric Adjustment Factor
ED	Exposure Duration
EC	Exposure Concentration
EF	Exposure Frequency
EPA	Environmental Protection Agency
ER	Extra-respiratory
ET	Exposure Time
ETh	Extrathoracic
F_r	Fractional Deposition in region r
F_{total}	Total particle deposition in respiratory tract
$H_{b/g\text{-}animal}$	Animal Blood:Gas Partition Coefficient
$H_{b/g\text{-}human}$	Human Blood:Gas Partition Coefficient
HEAST	Health Effects Assessment Summary Table
HEC	Human Equivalent Concentration
HI	Hazard Index
HQ	Hazard Quotient
ICRP	International Commission for Radiological Protection
IR	Inhalation Rate
IRIS	Integrated Risk Information System
IUR	Inhalation Unit Risk
kg	Kilogram
LEC_{10}	Lower limit on Effective Concentration, using a 10 percent response level
LOAEL	Lowest Observable Adverse Effect Level
ME	Microenvironment
MF	Modifying Factor
mg	Milligram
MOA	Mode of Action
MRL	Minimal Risk Level
MW	Molecular Weight
NCEA	National Center for Environmental Assessment
NOAEL	No Observable Adverse Effect Level
ORD	Office of Research and Development
OSRTI	Office of Superfund Remediation and Technology Innovation

LIST OF ACRONYMS (CONT.)

OSWER	Office of Solid Waste and Emergency Response
PBPK	Physiologically Based Pharmacokinetic
POD	Point of Departure
ppm	Parts Per Million
PPRTV	Provisional Peer Reviewed Toxicity Value
PRG	Preliminary Remediation Goal
PU	Pulmonary
Q-alv	Alveolar ventilation rate
QSAR	Quantitative Structure-Activity Relationship
RAGS	Risk Assessment Guidance for Superfund
RBC	Risk-Based Concentration
RfC	Reference Concentration
RfD	Reference Dose
RGDR	Regional Gas Dose Ratio
RDDR	Regional Deposited Dose Ratio
RME	Reasonable Maximum Exposure
SA	Surface Area
SSL	Soil Screening Level
STSC	Superfund Health Risk Technical Support Center
TB	Tracheobronchial
TOT	Total Respiratory System
UF	Uncertainty Factor
V_e	Minute Volume

1. INTRODUCTION

The Environmental Protection Agency's (EPA's) Superfund Program has updated its approach for determining risk from inhaled chemicals to be consistent with the inhalation dosimetry methodology described in *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry* (USEPA, 1994; hereafter, the *Inhalation Dosimetry Methodology*).[1] This document provides Superfund site risk assessors with guidance that should help more consistently address the *Inhalation Dosimetry Methodology*.

This document outlines recommended processes consisting of a series of steps as well as recommended equations for EPA Regions to consider when estimating inhalation exposure and risk at Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) sites. This guidance is intended to provide a recommended methodology for consistently addressing the inhalation pathway in risk assessments for Superfund sites.

Some of the statutory provisions described in this document contain legally binding requirements. However, this document does not substitute for those provisions or regulations, nor is it a regulation itself. Thus, it cannot impose legally binding requirements on EPA, States, or the regulated community, and may not apply to a particular situation based upon the circumstances. Any decisions regarding a particular remedy selection decision will be made based on the statute and regulations, and EPA decisionmakers retain the discretion to adopt approaches on a case-by-case basis that differ from this guidance where appropriate. EPA may change this guidance in the future.

1.1 Background

EPA's *Risk Assessment Guidance for Superfund (RAGS), Part A* (USEPA, 1989; hereafter, *RAGS, Part A*) outlined a previously recommended approach for conducting site-specific baseline risk assessments for inhaled contaminants.[2] According to the original RAGS approach, the inhalation exposure estimate was typically derived in terms of a chronic, daily "air intake" (mg/kg-day) using the following general approach. The intake of the chemical was estimated as a function of the concentration of the chemical in air (CA), inhalation rate (IR), body weight (BW), and the exposure scenario. Age-specific values for BW and IR were used when evaluating childhood exposures. Table 1 presents the *RAGS, Part A* equation for calculating intake for inhalation exposure. Inhalation toxicity values were "converted" into similar units for the risk quantification step. Cancer risk was estimated by multiplying the chronic daily intake of the chemical from the air by the "inhalation cancer slope factor" (CSF_i); the Hazard Quotient (HQ) for non-cancer effects was estimated by dividing the intake of the chemical by an "inhalation reference dose" (RfD_i).[3]

The approach outlined in *RAGS, Part A* was developed before EPA issued the *Inhalation Dosimetry Methodology*, which describes the Agency's refined recommended approach for interpreting

[1] The *Inhalation Dosimetry Methodology* can be found at the following web address: http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=71993.

[2] See sections 6.6.3, 7.2.3, 7.3.3, and 8.2 of *RAGS, Part A*.

[3] EPA defines an HQ in *RAGS, Part A* as: "The ratio of a single substance exposure level over a specified time period (e.g., subchronic) to a reference dose (RfD) for that substance derived from a similar exposure period" (USEPA, 1989).

inhalation toxicity studies in laboratory animals or studies of occupational exposures of humans to airborne chemicals. Under the *Inhalation Dosimetry Methodology*, the experimental exposures are typically extrapolated to a Human Equivalent Concentration (HEC), and a reference concentration (RfC) is typically calculated by dividing the HEC by uncertainty factors (UFs). As described in the Agency's *Guidelines for Cancer Risk Assessment* (USEPA, 2005a), the HEC developed in accordance with the *Inhalation Dosimetry Methodology* typically is also used in developing an inhalation unit risk (IUR) for cancer risk assessment (which may also be called an inhalation cancer slope factor).[4] The procedure that was used to calculate the published RfC or IUR is described in the Integrated Risk Information System (IRIS) profile or other toxicological reference document for a chemical.

TABLE 1
RAGS, PART A EQUATION DESCRIBING THE ESTIMATION OF INHALATION EXPOSURE

Equation	Location in RAGS, Part A
Intake (mg/kg-d) = CA x (IR/BW) x (ET x EF x ED)/AT	Exhibit 6-16, Page 6-44
Key: CA (mg/m^3) = contaminant concentration in air; IR (m^3/hr) = inhalation rate; BW (kg) = body weight; ET (hours/day) = exposure time; EF (days/year) = exposure frequency; ED (years) = exposure duration; and AT (days) = averaging time (period over which exposure is averaged).	

The Superfund Program has updated its inhalation risk paradigm to be compatible with the *Inhalation Dosimetry Methodology*, which represents the Agency's current methodology for inhalation dosimetry and derivation of inhalation toxicity values.[5] This document recommends that when estimating risk via inhalation, risk assessors should use the concentration of the chemical in air as the exposure metric (e.g., mg/m^3), rather than inhalation intake of a contaminant in air based on IR and BW (e.g., mg/kg-day).

1.2 Purpose and Scope

The intake equation described above (*RAGS, Part A*, Exhibit 6-16) is not consistent with the principles of EPA's *Inhalation Dosimetry Methodology* because the amount of the chemical that reaches the target site is not a simple function of IR and BW. Instead, the interaction of the inhaled contaminant with the respiratory tract is affected by factors such as species-specific relationships of exposure concentrations (ECs) to deposited/delivered doses and physiochemical characteristics of the inhaled contaminant. The *Inhalation Dosimetry Methodology* also considers the target site where the toxic effect occurs (e.g., the respiratory tract or a location in the body remote from the portal-of-entry) when applying dosimetric adjustments to experimental concentrations (USEPA, 1994). Therefore, this *RAGS, Part A* equation is not recommended for estimating exposures to inhaled contaminants.

[4] The phrase "inhalation cancer slope factor," as used in this guidance, refers generally to the risk per a measure of inhalation exposure. Inhalation exposure in cancer bioassays or occupational studies from which slope factors may be derived is most commonly expressed as an exposure concentration (e.g., µg agent/m^3 air). Please note that this differs from past use of the phrase "inhalation cancer slope factor" or "CSF_i" by the Superfund program to refer to a cancer slope expressed as an "inhalation intake" (e.g., *RAGS, Part A* (USEPA, 1989)).

[5] For additional information about the Superfund program's adoption of the *Inhalation Dosimetry Methodology*, please refer to the summary of a 2003 Superfund workshop on inhalation risk assessment: http://www.epa.gov/oswer/riskassessment/pdf/finalinhalationriskworkshop.pdf.

The purpose of this document is to provide a recommended approach for developing the information necessary to assist risk assessment and risk management decision-making at waste sites involving potential risks from inhalation exposures.[6, 7] This includes providing equations that may be used in conducting baseline risk assessments and in calculating risk-based concentrations (RBCs). It is intended that *RAGS, Part F* will replace those portions of *RAGS, Part A*, which addressed inhalation risk.

1.3 Effects on Other Office of Superfund Remediation and Technology Innovation Guidance

EPA recommends that the intake equation presented in *RAGS, Part A* (USEPA, 1989, Exhibit 6-16) should no longer be used when evaluating risk from the inhalation pathway. Implementation of a risk assessment approach consistent with the *Inhalation Dosimetry Methodology* will also affect the following guidance documents: *RAGS, Part B*, Section 3.3: Volatilization and Particulate Emission Factors (USEPA, 1991); and the Office of Solid Waste and Emergency Response's (OSWER's) *Draft Guidance for Evaluating the Vapor Intrusion to Indoor Air Pathway from Groundwater and Soils* (USEPA, 2002a; hereafter the *Vapor Intrusion Guidance*). EPA no longer recommends using the equations in Section 3.3 of *RAGS, Part B* nor the inhalation toxicity values generated using simple route-to-route extrapolation, such as those presented in the 2002 draft *Vapor Intrusion Guidance* and related documents.[8]

This guidance does not affect the equations pertaining to risk from inhaled chemicals in the *Soil Screening Guidance* (USEPA, 1996), Section 2.4, or the *Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites* (USEPA, 2002b), Sections 4.2.3, 5.3.2 and Appendix B, other than to clarify that the IURs and RfCs used in the equations are based on continuous exposure (24 hours per day). If the exposure scenario of interest is less than 24 hours per day, the scenario-specific exposure time (ET) in hours per day should be used in the equations and the averaging time should be in units of hours (see Equations 6 and 8 in this document). *RAGS, Part D* (USEPA, 2001) is also not affected by *RAGS, Part F*, as it includes sufficient flexibility to accommodate the revisions described in this guidance. In addition, the screening values presented on the "Regional Screening Levels for Chemical Contaminants at Superfund Sites" screening level/preliminary remediation goal table are consistent with *RAGS, Part F* (USEPA, 2008a).[9] Readers can contact EPA headquarters with questions about the compatibility of specific Superfund documents with *RAGS, Part F*.

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[6] Note that the assessment of risk from inhaled nanoparticles is outside the scope of this document.

[7] If a site contains asbestos contamination, risk assessors should contact EPA's Technical Review Workgroup for Metals and Asbestos for assistance.

[8] Related documents include the *Johnson and Ettinger (1991) Model for Subsurface Vapor Intrusion into Buildings* spreadsheet models (http://www.epa.gov/oswer/riskassessment/airmodel/johnson_ettinger.htm) and the accompanying *User's Guide for Evaluating Subsurface Vapor Intrusion into Buildings* (USEPA, 2004a).

[9] This table can be found on EPA Regions 3, 6, and 9 websites (http://www.epa.gov/reg3hwmd/risk/human/rb-concentration_table/index.htm; http://www.epa.gov/earth1r6/6pd/rcra_c/pd-n/screen.htm; and http://www.epa.gov/region09/waste/sfund/prg/index.html).

2. BACKGROUND ON DERIVATION OF INHALATION TOXICITY VALUES

For all exposure routes, there are generally two approaches for deriving toxicity values. One involves the derivation of a reference value (e.g., RfC or RfD), while the other involves derivation of a predictive cancer risk estimate (e.g., an oral or inhalation CSF, such as an IUR). For the inhalation route, both approaches rely on EPA's *Inhalation Dosimetry Methodology* for the extrapolation of experimental concentrations to HECs. This extrapolation is described in Section 2.1 and its subsections. The approaches for deriving a toxicity value from the HEC are described in Sections 2.2 and 2.3 and differ depending on the type of toxicity value (e.g., RfC, IUR). This information is provided for background purposes only. **The procedures outlined in Section 2 are typically performed by IRIS chemical managers or by inhalation toxicologists at the National Center for Environmental Assessment's (NCEA's) Superfund Health Risk Technical Support Center (STSC) rather than as part of a baseline risk assessment.**

2.1 Application of Inhalation Dosimetry

The *Inhalation Dosimetry Methodology* recognizes a hierarchy of approaches that can be used for determining the HEC that is used to derive the RfC or IUR. Generally, the preferred approach is to use physiologically-based pharmacokinetic (PBPK) models.[10] With sufficient data, a PBPK model is capable of calculating the amount of the chemical that reaches the target organ in an animal from any exposure scenario and then estimating what human exposure would result in this same amount of chemical reaching the target organ (i.e., the HEC). PBPK models can also be used to derive continuous ECs from human and animal studies with less-than-continuous exposures. Because constructing a valid PBPK model is an information-intensive process that typically requires substantial chemical-specific data, this approach has rarely been used (USEPA, 2004b); an example can be found in the IRIS file for vinyl chloride (USEPA, 2000a). In cases where a complete PBPK model is not available, an intermediate model relying on certain chemical-specific data may be used (USEPA, 1994).[11]

If the database to support the preferred approach is inadequate, an alternative approach, called the Default Chemical Category-Specific Method can be used. This method incorporates the use of limited or categorical chemical-specific and physiological information. The default method is discussed below, followed by the procedures outlined in the *Inhalation Dosimetry Methodology* for deriving the RfC and IUR as they apply to the interpretation of animal and human data.

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[10] EPA defines PBPK models in the IRIS glossary as a model that estimates the dose to a target tissue or organ by taking into account the rate of absorption into the body, distribution among target organs and tissues, metabolism, and excretion (USEPA, 2008b). For further information about PBPK modeling, please refer to *Approaches for the Application of Physiologically Based Pharmacokinetic Models and Supporting Data in Risk Assessment* (USEPA, 2006a).

[11] The *Inhalation Dosimetry Methodology* recognizes the existence of alternate approaches in addition to the two presented in this guidance. The PBPK approach is generally preferred. In the absence of such a model, alternate models may be more optimal than the default approach when default assumptions or parameters can be replaced by more detailed, biologically-motivated descriptions or actual data, respectively. For instance, a model may be considered more optimal if it incorporates chemical or species-specific information or if it accounts for mechanistic determinants. See Table 3-6 in the *Inhalation Dosimetry Methodology* for more details on the hierarchy of approaches (EPA, 1994, page 3-40).

2.1.1 Default Approach - Extrapolation from Experimental Animal Data

The default method involves a two-step procedure that uses limited or categorical chemical-specific and physiological information to calculate the HEC. First, the chosen point of departure (POD) from the experimental data for a chemical is adjusted to derive a concentration intended to represent an equivalent dose under conditions of continuous exposure (7 days a week, 24 hours a day).[12] In the second step, this concentration is then multiplied by a Dosimetric Adjustment Factor (DAF) to generate the HEC. Further details on each step are outlined below.

2.1.1.1 Duration Adjustment to Continuous Exposure

Most of the inhalation studies of laboratory animals used to derive RfCs and IURs involve an exposure regimen of four to six hours per day, five to seven days per week, for 13 weeks or more (equivalent to 10 percent or more of the lifetime of the animal). The POD concentration from an animal study is mathematically adjusted to reflect an equivalent dose under conditions of continuous exposure.[13] Adjustment of duration to a continuous exposure scenario is regularly applied as a default procedure to studies with repeated exposures but not to single-exposure inhalation toxicity studies in animals (USEPA, 1994). Operationally, this is accomplished by applying a *c* x *t* product (where "*c*" is concentration, and "*t*" is duration of exposure) for both the number of hours in a daily exposure period and the number of days per week that the exposure is experienced. For example, if exposure in a particular study was 6 hours per day, 5 days per week, the experimental exposure is multiplied by 6/24 x 5/7 to calculate an equivalent continuous exposure. The general equation provided in the *Inhalation Dosimetry Methodology* (USEPA, 1994, Equation 4-2) for calculating duration-adjusted exposure levels in mg/m^3 for experimental animals is presented below.

$NOAEL_{[ADJ]}$ = E x D x W **(Equation 1)**

Where:

$NOAEL_{[ADJ]}$ (mg/m^3) = the NOAEL or analogous exposure level obtained with an alternate approach (e.g., LOAEL, LEC_{10}), adjusted for duration of experimental regimen;
E (mg/m^3) = the NOAEL or analogous exposure level observed in the experimental study;
D (h/h) = number of hours exposed/24 hours; and
W (days/days) = number of days of exposure/7days.

Using the example above, the assumption is that the product of *c* x *t*, not concentration alone, is associated with the toxicity observed. This is roughly equivalent to implying that if an effect occurs from a chemical at an exposure of 6 hours per day at 40 parts per million (ppm), that same effect will

[12] Examples of PODs include the no-observed-adverse-effect level (NOAEL); the lowest-observed-adverse-effect level (LOAEL); Benchmark Concentration, Lower confidence limit (BMCL); and the Lower limit on an Effective Concentration using a 10 percent response level (LEC_{10}). For definitions of the various PODs, please refer to the IRIS glossary (http://www.epa.gov/ncea/iris/help_gloss.htm).

[13] Continuous exposure refers to 24 hours per day, 7 days per week.

occur at an exposure of 24 hours per day at 10 ppm.[14] Note that this adjustment always produces a lower concentration value than that administered to experimental animals. Thus, as stated in *A Review of the Reference Dose and Reference Concentration Processes* (hereafter, the *RfD/RfC Review*), application of this procedure results in an automatic margin of protectiveness for chemicals for which concentration alone may be the more appropriate dose metric, and it reflects the maximum dose for chemicals for which total or cumulative dose is the appropriate measure (USEPA, 2002c). If a different procedure is used to calculate the continuous exposure, it should be fully discussed in the relevant technical support document for the chemical (e.g., IRIS profile, Provisional Peer Reviewed Toxicity Values (PPRTVs) Assessment). For additional discussion, including the uncertainties associated with this approach, see Section 4.3.2 of the *Inhalation Dosimetry Methodology* and Section 4.4.2.1 of the *RfD/RfC Review* (USEPA, 2002c).

2.1.1.2 Dosimetric Adjustment to Human Equivalent Concentration

Typically, the adjusted POD concentration from the animal study is next converted to an HEC using the following equation (USEPA, 1994, Equation 4-3):

$$\mathbf{NOAEL_{[HEC]} = NOAEL_{[ADJ]} \times DAF} \qquad \textbf{(Equation 2)}$$

Where:

$NOAEL_{[HEC]}$ (mg/m^3) = the NOAEL or analogous exposure level obtained with an alternate approach, dosimetrically adjusted to an HEC;

$NOAEL_{[ADJ]}$ (mg/m^3) = the NOAEL or analogous exposure level obtained with an alternate approach, adjusted for duration of experimental regimen; and

DAF = Dosimetric Adjustment Factor for the specific site of effects (e.g., respiratory tract region or extra-respiratory).

The DAF is typically based on ratios of animal and human physiologic parameters. The specific DAF used depends on the nature of the contaminant (e.g., particle or gas) and the target site where the toxic effect occurs (e.g., respiratory tract or a location in the body remote from the portal-of-entry). For example, the DAF can be based on either the Regional Gas Dose Ratio (RGDR), for gases with respiratory effects, or the Regional Deposited Dose Ratio (RDDR) for particles.

Table 2 provides information on the site of effects for the different chemical types. It also lists the physiologic parameters considered when calculating the DAF for specific regions of the body.[15] In addition, the table provides references to the equations from the *Inhalation Dosimetry Methodology* used in deriving the DAFs. Figure 1 provides a schematic of the human respiratory tract, illustrating each of the different regions.

[14] This assumption is based on Haber's Law, which states that "the incidence and/or severity of an adverse health effect depends on the total exposure to a potentially toxic substance. Total exposure (*K*) is the concentration of the substance (*c*) times the duration time of exposure (*t*), (i.e., $c \times t = K$)" (Gaylor, 2000).

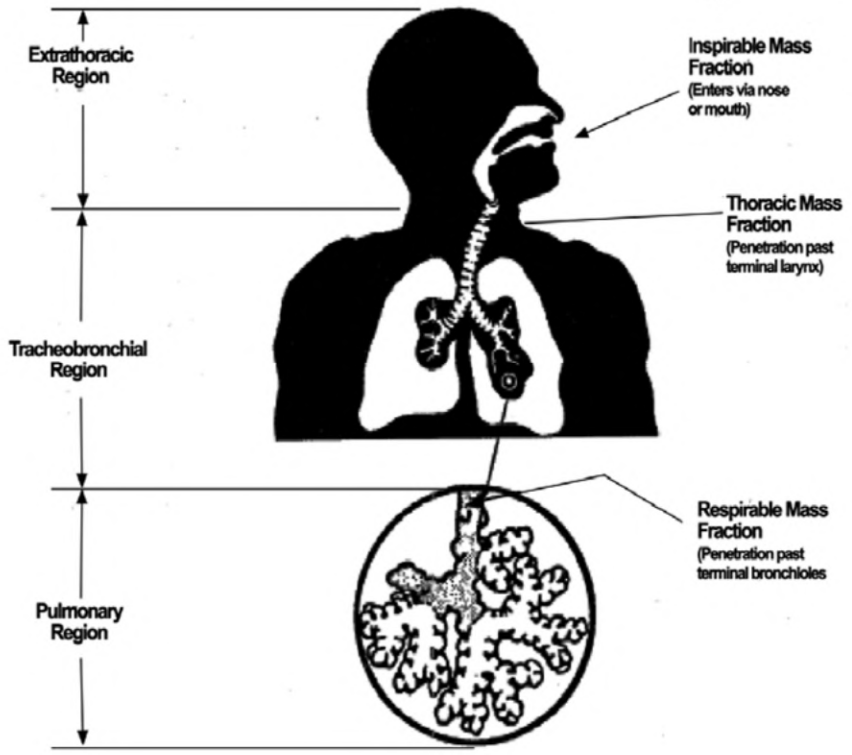
[15] The three main regions of the respiratory tract include the following: 1) Extrathoracic (includes nose, mouth, nasopharynx, oropharynx, laryngopharynx, and larynx); 2) Tracheobronchial (includes trachea, bronchi, and bronchioles); and 3) Pulmonary (includes respiratory bronchioles, alveolar ducts, alveolar sacs and the alveoli).

TABLE 2
CONTAMINANT PROPERTIES AND DOSIMETRIC ADJUSTMENT FACTORS[a]

Chemical Type	Site of Effects	Parameters Considered in Derivation of DAF for Regions of the Body[b]	DAF Equation Numbers in Inhalation Dosimetry Methodology[c]
Category 1 Gases (e.g., acrolein, hydrogen fluoride, chlorine)	Respiratory	-Minute volume (ETh, TB) -Surface area (ETh, TB, PU) -Mass transport coefficient (TB, PU) -Fraction of inhaled chemical penetrating the respiratory region (PU) -Alveolar ventilation rate (PU)	4-18 (ETh), 4-21 & 4-22 (TB), 4-28 (PU)
Category 2 Gases (e.g., acetonitrile, xylene, propanol, isoamyl alcohol)	Respiratory and Remote	-Mass transport coefficients (ETh, TB) -Blood:gas partition coefficient (ET, TB, ER) -Cardiac output (ETh, TB, ER) -Alveolar ventilation rate (PU) -Surface Area (PU) -Minute volume (ER)	4-18 (ETh), 4-21 & 4-22 (TB), 4-28 (PU), 4-48 (ER)[d,e]
Category 3 Gases (e.g., benzene, styrene)	Remote	Blood:gas partition coefficient (ER)	4-48[d]
Particles	Respiratory and Remote	-Minute volume (TOT, ER) -Surface area (TOT) -Fractional deposition of particle (TOT, ER) -Body weight (ER) -Inhaled concentration (ER)	4-14 (TOT), 4-15 (ER)

[a] Due to the complexities inherent in evaluating the health effects associated with exposure to gases, no definitive or comprehensive list of Category 1, 2, or 3 gases is available. Risk assessors should consult with an inhalation toxicologist in order to classify a specific gas as Category 1, 2, or 3, since there is overlap between the sites of effects and the parameters considered in deriving the DAF for different regions of the respiratory tract.
[b] Additional discussion of the terms used in this table can be found in the *Inhalation Dosimetry Methodology*.
[c] The *Inhalation Dosimetry Methodology* provides equations for deriving DAFs for the different contaminant categories. The equations listed in this table are the default equations for each specific region in the body.
[d] This refers to Equation 4-48 that is found on page 4-60 of the *Inhalation Dosimetry Methodology*.
[e] The equations presented for Category 2 gases in the *Inhalation Dosimetry Methodology* contain errors. Therefore, this table refers to the equations for Category 1 and 3 gases, which are expected to cover respiratory and remote effects from Category 2 gases.
Acronyms: ETh = Extrathoracic; TB = Tracheobronchial; PU = Pulmonary; ER = Extra-respiratory; TOT = Total respiratory system.

FIGURE 1
HUMAN RESPIRATORY TRACT



Source: EPA (1994), Figure 3-1, Page 3-5.

Category 1 gases are highly water-soluble and/or are rapidly irreversibly reactive in the respiratory tract (e.g., acrolein, hydrogen fluoride, chlorine). They do not significantly accumulate in the blood, and therefore their effects are usually exclusively respiratory (USEPA, 1994). The DAF for Category 1 gases consists of an RGDR and is based on the animal to human ratio of the minute volume (V_e) divided by the surface area (SA) of the region of the respiratory tract where the effect occurs.[16] See Appendix A, Sections 1, 2, and 3 of this guidance for examples of specific Category 1 DAF equations.

[16] For the purposes of this document, the V_e is defined as the total ventilation per minute and equals the product of the tidal volume (the air volume entering or leaving the lungs with a single breath) and the respiratory frequency.

Category 3 gases are relatively water-insoluble and are unreactive in the respiratory tract (e.g., benzene, styrene). Their toxicity is generally at sites remote to the respiratory tract (USEPA, 1994). The DAF for Category 3 gases is based on the ratio of the animal blood:gas partition coefficient ($H_{b/g\text{-}animal}$) and the human blood:gas partition coefficient ($H_{b/g\text{-}human}$). See Appendix A, Section 4 of this guidance for an example of a Category 3 DAF equation.

Category 2 gases are moderately water-soluble and may be rapidly reversibly reactive or moderately to slowly irreversibly reactive in respiratory tract tissue (e.g., acetonitrile, xylene, propanol, isoamyl alcohol). These gases have potential for significant accumulation in the blood, so they can exhibit both respiratory and remote toxicity (USEPA, 1994). The DAF for respiratory effects of Category 2 gases consists of an RGDR and is based on the animal to human ratio of the V_e and the SA of the region of the respiratory tract where the effect occurs, as for Category 1 gases. The DAF for extra-respiratory (ER) effects of a Category 2 gas is based on the ratio of the $H_{b/g\text{-}animal}$ and the $H_{b/g\text{-}human}$, as for Category 3 gases.

Particles also vary by solubility and reactivity. However, the default equations used to estimate the predicted regional deposition fractions for particles are based on non-soluble, non-hygroscopic particles (USEPA, 1994, Section 4.3.5.3). The DAF for a particle causing an effect in the respiratory tract is the $RDDR_r$. The $RDDR_r$ is based on the animal to human ratio of the V_e and the fractional deposition of the particle in that region (F_r), divided by the SA_r of the region where the effect occurs. This derivation, from the *Inhalation Dosimetry Methodology,* conservatively assumes that 100 percent of the deposited dose remains in the respiratory tract; clearance mechanisms are not considered. The DAF for a particle causing an ER effect, the $RDDR_{ER}$, is based on the animal to human ratio of the V_e and the total deposition of the particle in the entire respiratory tract (F_{total}), divided by BW (USEPA, 1994). The $RDDR_{ER}$ assumes that 100 percent of the deposited dose in the entire respiratory tract is available for uptake into the systemic circulation. See Appendix A, Section 5 for examples of specific particle DAF equations.

2.1.2 Default Approach - Extrapolation from Human Occupational Data

When human data are available to derive an RfC, duration adjustments are often required to account for differences in exposure scenarios (e.g., extrapolation from an 8 hour/day occupational exposure to a continuous chronic exposure). The default approach recommended by the *Inhalation Dosimetry Methodology* for adjusting the POD concentration (e.g., the no observable adverse effect level (NOAEL)) obtained from human study data is provided below in Equation 3 (USEPA, 1994, Equation 4-49).[17,18]

[17] If sufficient data are available, a PBPK model or intermediate approach using chemical-specific information may be employed in preference to the default method for extrapolating human occupational data to an HEC.

[18] EPA's IRIS glossary defines an adverse effect as the following: "A biochemical change, functional impairment, or pathologic lesion that affects the performance of the whole organism, or reduces an organism's ability to respond to an additional environmental challenge" (USEPA, 2008b).

$NOAEL_{[HEC]}$ = NOAEL x (VEho/VEh) x 5 days/7 days **(Equation 3)**

Where: $NOAEL_{[HEC]}$ (mg/m^3) = the NOAEL or analogous exposure level obtained with an alternate approach, dosimetrically adjusted to an ambient HEC;
NOAEL (mg/m^3) = occupational exposure level (time-weighted average over an 8-hour exposure period);
VEho = human occupational default minute volume over 8 hours (10 m^3); and
VEh = human ambient default minute volume over 24 hours (20 m^3).

2.2 Derivation of the Inhalation Unit Risk

The default approach for determining predictive cancer risk recommended by EPA's *Guidelines for Carcinogen Risk Assessment* (USEPA, 2005a; hereafter, *Cancer Guidelines*) is a linear extrapolation from exposures observed in the animal or human occupational study.[19] This approach involves drawing a straight line from the POD to the origin. The default linear extrapolation approach is generally considered to be conservatively protective of public health, including sensitive sub-populations (USEPA, 2005a). The slope of this line is commonly called the slope factor, and when the units are risk per $\mu g/m^3$, it is also called the IUR. EPA defines an IUR in the IRIS glossary as "the upper-bound excess lifetime cancer risk estimated to result from continuous exposure to an agent at a concentration of 1 $\mu g/m^3$ in air" (USEPA, 2008b). Equation 4 below presents a linear extrapolation from a POD of 10 percent response (LEC_{10}).[20]

$IUR = 0.1/LEC_{10[HEC]}$ **(Equation 4)**

Where: IUR $(\mu g/m^3)^{-1}$ = Inhalation Unit Risk; and
$LEC_{10[HEC]}$ ($\mu g/m^3$) = the lowest effective concentration using a 10 percent response level, dosimetrically adjusted to an HEC.

2.3 Derivation of the Reference Concentration

EPA defines an RfC in the IRIS glossary as "an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious effects during a lifetime" (USEPA, 2008b). The RfC is derived after a review of the health effects database for a chemical and identification of the most sensitive and relevant endpoint along with the principal study or studies demonstrating that endpoint. EPA Chemical Managers use UFs to account for recognized

[19] According to the *Cancer Guidelines*, "[a] nonlinear approach should be selected when there are sufficient data to ascertain the mode of action [MOA] and conclude that it is not linear at low doses and the agent does not demonstrate mutagenic or other activity consistent with linearity at low doses" (USEPA, 2005a, page 3-22). In addition, [l]inear extrapolation should be used when there are MOA data to indicate that the dose-response curve is expected to have a linear component below the POD" (USEPA, 2005a, page 3-21). This information will appear on the IRIS profile or other toxicological information source for a chemical. Chemicals with a mutagenic MOA are thought to pose a higher risk during early life. Procedures for assessing cancer risk from these chemicals are outlined in Section 5.1.

[20] The POD used in Equation 4 is an LEC_{10}, which is the lower 95 percent confidence limit on the concentration corresponding to a 10 percent response rate (i.e., the EC_{10}). Other PODs may be substituted for this value, which could be associated with alternative response levels (e.g., 1 percent, 5 percent).

uncertainties in the extrapolations from the experimental data conditions to an estimate appropriate to the assumed human scenario (USEPA, 1994). See Table 3 for a description of the standard UFs. The formula used for deriving the RfC from the HEC is provided below.

$RfC = NOAEL_{[HEC]}/(UF)$[1] **(Equation 5)**

Where: RfC (mg/m^3) = Reference Concentration
$NOAEL_{[HEC]}$ (mg/m^3) = The NOAEL or analogous exposure level obtained with an alternate approach, dosimetrically adjusted to an HEC; and
UF = Uncertainty factor(s) applied to account for the extrapolations required from the characteristics of the experimental regimen.

[1] Some toxicological information sources for RfCs will incorporate an additional factor to account for deficiencies in the available data set, called a modifying factor (MF). In 2002, however, EPA published the *RfD/RfC Review,* which recommended that the use of MFs be discontinued because their purpose is "sufficiently subsumed in the general database UF" (USEPA, 2002c, page xviii). Therefore, RfCs published subsequent to this document will not include MFs.

TABLE 3
THE USE OF UNCERTAINTY FACTORS IN DERIVING AN INHALATION REFERENCE CONCENTRATION

Standard UFs	Processes Considered in the UF Purview
H = Human to sensitive human: Extrapolation of valid experimental results from studies using prolonged exposure to average healthy humans. Intended to account for the variation in sensitivity among the members of the human population.	-Pharmacokinetics/Pharmacodynamics -Sensitivity[2] -Differences in body weight (age, obesity) -Concomitant exposures -Activity pattern -Does not account for idiosyncrasies
A = Animal to human: Extrapolation from valid results of long-term studies on laboratory animals when results of studies of human exposure are not available or are inadequate. Intended to account for the uncertainty in extrapolating laboratory animal data to the case of average healthy humans.	-Pharmacokinetics/Pharmacodynamics -Relevance of laboratory animal model -Species sensitivity
S = Subchronic to chronic: Extrapolation from less-than-chronic exposure results on laboratory animals or humans when there are no useful long-term human data. Intended to account for the uncertainty in extrapolating from less than chronic NOAELs to chronic NOAELs.	-Accumulation/Cumulative damage -Pharmacokinetics/ Pharmacodynamics -Severity of effect -Recovery -Duration of study -Consistency of effect with duration
L = LOAEL to NOAEL: Derivation from a LOAEL instead of a NOAEL. Intended to account for the uncertainty in extrapolating from LOAELs to NOAELs.	-Severity -Pharmacokinetics/Pharmacodynamics -Slope of dose-response curve -Trend, consistency of effect -Relationship of endpoints -Functional vs. histopathological evidence -Exposure uncertainties
D = Incomplete to complete data: Extrapolation from valid results in laboratory animals when the data are "incomplete." Intended to account for the inability of any single laboratory animal study to adequately address all possible adverse outcomes in humans.[1]	-Quality of critical study -Data gaps -Power of critical study/supporting studies -Exposure uncertainties

[1] The *RfD/RfC Review* indicates that this UF accounts for the potential for deriving an underprotective RfD/RfC as a result of an incomplete characterization of the chemical's toxicity or if the existing data suggest that a lower reference value might result if additional data were available (considering both the lacking and available data for particular organ systems as well as life stage) (USEPA, 2002c).
[2] The *RfD/RfC Review* also stresses that susceptible populations and life stages are accounted for with this UF (USEPA, 2002c).
Source: USEPA, 1994, Table 4-9, page 4-77.

3. CHARACTERIZING EXPOSURE

3.1 Introduction

This section describes an approach for characterizing exposure in a baseline risk assessment that is consistent with the *Inhalation Dosimetry Methodology*. The approach involves the estimation of exposure concentrations (ECs) for each receptor exposed to contaminants via inhalation in the risk assessment. ECs are time-weighted average concentrations derived from measured or modeled contaminant concentrations in air at a site, adjusted based on the characteristics of the exposure scenario being evaluated.[21,22]

Equations for estimating ECs are provided below. This document does not provide default input values for the exposure parameters referenced in these equations. EPA recommends the use of site-specific exposure values consistent with the exposure pathways and receptors at a site wherever practicable and appropriate. If a risk assessor opts to rely on default exposure input values, current Superfund-supported values may be found at the exposure assessment portion of the Superfund website: (http://www.epa.gov/oswer/riskassessment/superfund_hh_exposure.htm).

3.2 Estimating Exposure Concentrations for Assessing Cancer Risks

The estimation of an EC when assessing cancer risks characterized by an IUR involves the CA measured at an exposure point at a site as well as scenario-specific parameters, such as the exposure duration and frequency.[23] The EC typically takes the form of a CA that is time-weighted over the duration of exposure and incorporates information on activity patterns for the specific site or the use of professional judgment. The equation for estimating an EC for use with an IUR is presented below.

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[21] The default method for deriving inhalation toxicity values also involves calculating time-weighted ECs, as discussed in Sections 2.1.1.1 and 2.1.2.

[22] The ECs in this document are in units of $\mu g/m^3$. Inhalation toxicity values presented on IRIS are typically expressed in units of $\mu g/m^3$ or mg/m^3, which are mass units. Some regulatory contexts require the use of volumetric units such as ppm. The conversion from mass units to volumetric units depends on the molecular weight (MW) of the material as well as the ambient temperature and atmospheric pressure. To convert from ppm to mg/m^3, the following equation can be used: $\frac{ppm \times MW}{V} = mg/m^3$; where MW is the molecular weight of the gas and V is the volume of 1 gram molecular weight of the airborne contaminant. This is derived by the formula V = RT/P; where R is the ideal gas constant, T is the temperature in Kelvin (K = 273.16 + T°C) and P is the pressure in mm Hg. The value of R is 62.4 when T is in Kelvin, (K = 273.16 + T°C), the pressure is expressed in units of mm Hg and the volume is in liters. The value of R differs if the temperature is expressed degrees Fahrenheit (°F) or if other units of pressure are used (e.g., atmospheres, kilopascals).

[23] ECs are typically based on either estimated (i.e., modeled) or measured contaminant concentrations in air.

EC = (CA x ET x EF x ED)/AT **(Equation 6)**

Where: EC ($\mu g/m^3$) = exposure concentration;
CA ($\mu g/m^3$) = contaminant concentration in air;
ET (hours/day) = exposure time;
EF (days/year) = exposure frequency;
ED (years) = exposure duration; and
AT (lifetime in years x 365 days/year x 24 hours/day) = averaging time

3.3 Estimating Exposure Concentrations for Calculating Hazard Quotients

When estimating ECs for non-cancer or cancer hazards characterized by an HQ, risk assessors should match each exposure scenario at a site to the appropriate EC equation, based on the scenario duration and frequency of exposure.[24] Figure 2 presents a flowchart to assist risk assessors with this process and provides recommended equations that can be used to estimate the EC for each type of scenario.[25] As shown in Figure 2, the recommended process for estimating ECs to be used in calculating an HQ involves the following three steps: 1) assess the duration of the exposure scenario; 2) assess the exposure pattern of the exposure scenario; and 3) estimate the scenario-specific EC.

3.3.1 Step 1: Assess Duration

The first step in the recommended process of estimating an EC for use in calculating an HQ involves assessing the duration of the exposure scenario at a site. Step 1 in Figure 2 indicates that the risk assessor first should decide whether the duration of the exposure scenario is generally acute, subchronic, or chronic. Toxicologists have long been aware that effects from a single or short-term exposure can differ markedly from effects resulting from repeated exposures. The response by the exposed person depends upon factors such as whether the chemical accumulates in the body, whether it overwhelms the body's mechanisms of detoxification or elimination, or whether it produces irreversible effects (Eaton & Klaassen, 2001). Therefore, ideally, the chemical-specific elements of metabolism and kinetics, reversibility of effects, and recovery time should be considered as part of this recommended process when defining the duration of a site-specific exposure scenario.

[24] Traditionally, the HQ approach was limited to non-cancer hazard assessment. However, the HQ approach may also be appropriate for carcinogens with a non-linear mode of action. The 2005 *Cancer Guidelines* state the following on this subject: "For cases where the tumors arise through a nonlinear mode of action, an oral reference dose or an inhalation reference concentration, or both, should be developed in accordance with EPA's established practice for developing such values … this approach expands the past focus of such reference values (previously reserved for effects other than cancer) to include carcinogenic effects determined to have a nonlinear mode of action" (USEPA, 2005a; page 3-24).

[25] Figure 2 was developed for the evaluation of inhalation exposures. While the concepts presented in this flowchart may be useful for assessing other exposure routes (e.g., oral or dermal), these other routes are beyond the scope of this document, and therefore, are not explicitly considered. Caution should be used when using Figure 2 to evaluate other exposure routes, as considerations beyond those outlined in the flowchart may apply (e.g., time to reach steady state for dermal exposures).

To the extent possible, exposure durations (EDs) evaluated in a site-specific risk assessment should be consistent with the ED represented by the toxicity value. However, frequencies or durations of human exposures often are not as clearly defined as those in animal studies with controlled exposures, particularly for intermittent exposures. For example, the emission of some volatile chemicals into the ambient air may vary with temperature and season, providing fluctuating exposures for humans living near the source. Therefore, risk assessors should use best professional judgment to determine if the ED in a given scenario is reasonably similar to the duration associated with the toxicity value. Risk assessors should describe the uncertainties associated with their choice of toxicity value in the risk characterization section of the risk assessment (see Section 9.2.2 of this document). For situations where duration-appropriate toxicity values are not available, please follow the procedures outlined in Section 4.2 and Appendix C of this document.

The specific definition for each exposure duration category may vary depending on the source of the toxicity value being used. For Tier 1 toxicity values obtained from EPA's IRIS database, acute exposures are defined as lasting 24 hours or less; subchronic exposures are defined as repeated exposures by the oral, dermal, or inhalation route for more than 30 days, up to approximately 10 percent of the human lifespan; and chronic exposures are defined as repeated exposures for more than approximately 10 percent of the human lifespan (USEPA, 2008b).[26, 27]

After deciding which duration the exposure scenario most closely matches, risk assessors should then proceed to Step 2, following the path of the selected duration. Note that if an acute duration is selected, risk assessors should proceed directly to Step 3 to estimate an acute EC for each acute exposure period.

3.3.2 Step 2: Assess Exposure Pattern

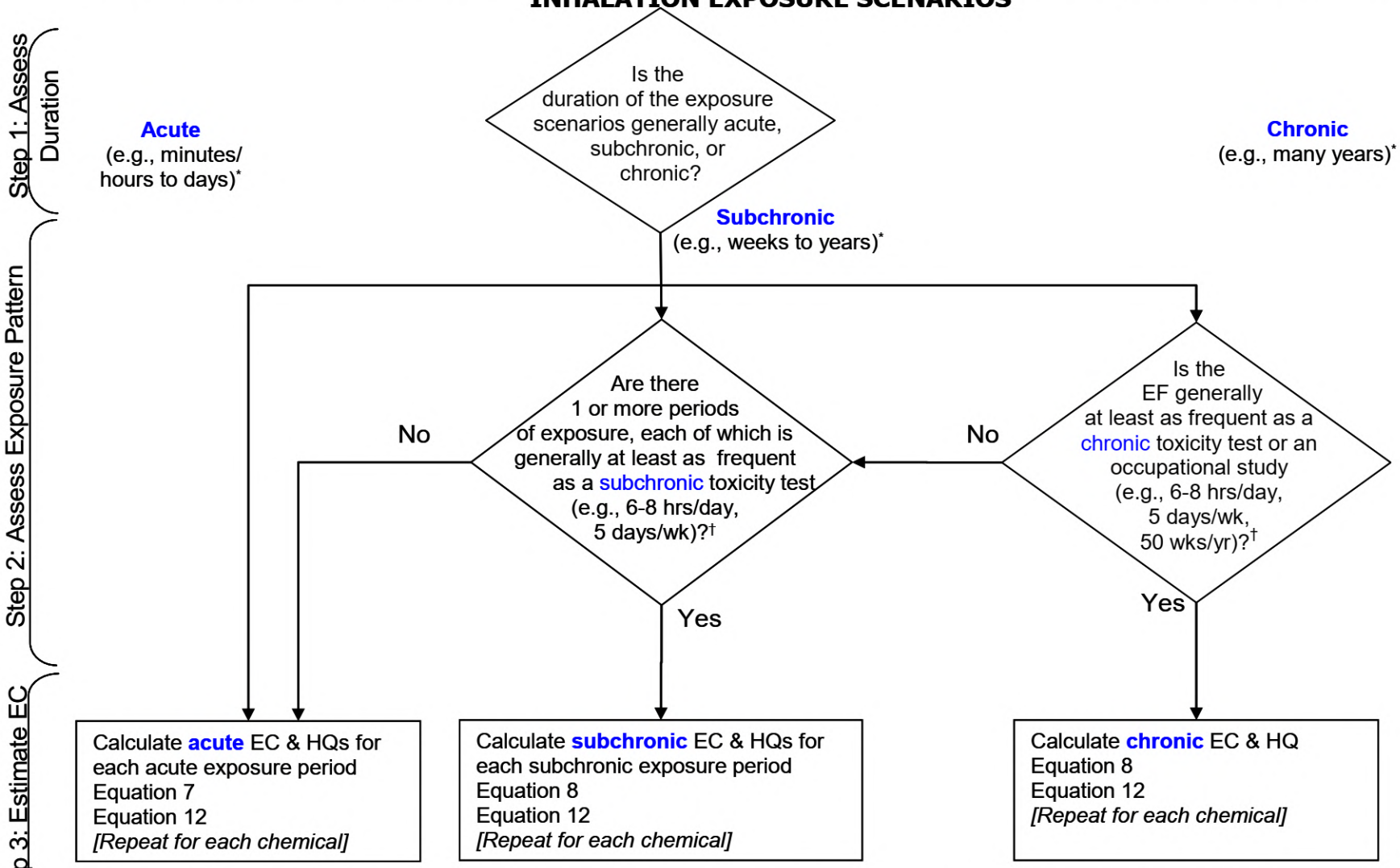
Step 2 of the recommended process for estimating an EC for use in a hazard quotient involves assessing the exposure pattern for each exposure scenario at a site. This entails comparing the exposure time and frequency at a site to that of a typical subchronic or chronic toxicity test.[28]

[26] Note that other sources of toxicity values may define exposures differently. For example, the Agency for Toxic Substances and Disease Registry (ATSDR) (which publishes Minimal Risk Levels (MRLs)) defines acute exposures as occurring from one to 14 days, intermediate exposures as greater than 14 to 364 days, and chronic exposures as 365 days or longer. However, the toxicity values are based on the same underlying toxicological concepts described in this section.

[27] Exposures with a duration lasting between 24 hours and 30 days should be treated as subchronic for the purposes of this document.

[28] Exposure regimens vary from study to study. Risk assessors should use best professional judgment to determine if the exposure pattern in a given scenario is reasonably similar to a typical regimen for a subchronic or chronic study.

FIGURE 2
RECOMMENDED PROCEDURE FOR DERIVING EXPOSURE CONCENTRATIONS AND HAZARD QUOTIENTS FOR INHALATION EXPOSURE SCENARIOS



* The specific definition for each duration category may vary depending on the source of the toxicity value being used. For Tier 1 toxicity values obtained from IRIS:
acute exposures are defined as those lasting 24 hours or less;
subchronic exposures are defined as repeated exposures for more than 30 days, up to approximately 10 percent of the life span in humans; and
chronic exposures are defined as repeated exposures for more than approximately 10 percent of the life span in humans (EPA, 2008b).
For the purposes of this document, short-term exposures, defined by the IRIS glossary as repeated exposures for more than 24 hours, up to 30 days, should be treated as subchronic.

† Exposure regimens vary from study to study. Risk assessors should use best professional judgment to determine if the exposure pattern in a given scenario is reasonably similar to a typical regimen for a chronic or subchronic study.

For exposure scenarios with a subchronic duration, risk assessors should follow the center path on the flowchart. Step 2 in this path asks whether there are one or more periods of exposure, each of which is generally as frequent as a subchronic toxicity test (e.g., 6-8 hours per day, 5 days per week). If the exposure scenario matches this description, risk assessors should proceed to Step 3 and estimate a subchronic EC for each subchronic exposure period. However, if the exposure pattern contains periods that are significantly shorter and/or involve significantly less frequent exposures than indicated in the flow chart, risk assessors should derive acute ECs for each of these exposure periods. If it is difficult to determine whether a specific exposure scenario is best modeled as a subchronic exposure or as a series of independent acute exposures, due to uncertainty in the time required to return to baseline following exposure, risk assessors may want to derive ECs using both approaches.

If the exposure scenario has a chronic duration, risk assessors should follow the right hand path on the flowchart. Step 2 in this path asks whether the exposure frequency (EF) is generally as frequent as a chronic animal toxicity test or a human occupational study (e.g., 6-8 hours per day, 5 days per week, for 50 weeks per year). If the exposure scenario matches this description, risk assessors should proceed to Step 3 and estimate a single chronic EC. However, if the scenario differs significantly from this pattern, risk assessors should proceed to the second question under the subchronic duration path and proceed as outlined above.

3.3.3 Step 3: Estimate Exposure Concentration

Step 3 of the recommended process involves estimating the EC for the specific exposure scenario based on the decisions made in Steps 1 and 2. For acute exposures, the EC is equal to the CA. Risk assessors can estimate an acute EC for each acute exposure period at a site using Equation 7. For longer-term exposures, risk assessors should take into consideration the exposure time, frequency, and duration for each receptor being evaluated as well as the period over which the exposure is averaged (i.e., the averaging time (AT)) to arrive at a time-weighted EC. If there are one or more exposure periods that are generally as frequent as a subchronic toxicity test, risk assessors should use Equation 8 to estimate a subchronic EC for each of these exposure periods. (Exposure periods with significantly less frequency should be treated as acute exposures.) If the exposure pattern is generally as frequent as a chronic toxicity test of an occupational study, risk assessors should use Equation 8 to estimate a single chronic EC for the duration of the exposure.

Acute Exposures

EC = CA **(Equation 7)**

Where: EC ($\mu g/m^3$) = exposure concentration;
CA ($\mu g/m^3$) = contaminant concentration in air;

Chronic or Subchronic Exposures

EC = (CA x ET x EF x ED)/AT **(Equation 8)**

Where:
EC ($\mu g/m^3$) = exposure concentration;
CA ($\mu g/m^3$) = contaminant concentration in air;
ET (hours/day) = exposure time;
EF (days/year) = exposure frequency;
ED (years) = exposure duration; and
AT (ED in years x 365 days/year x 24 hours/day) = averaging time

Note: If the duration of the exposure period is less than one year, the units in the above equation can be changed to the following: EF (days/week); ED (weeks/exposure period); and AT (hours/exposure period).

It is important to use the EC equation that most closely matches the exposure pattern and duration at a site. For instance, if the exposure pattern at a site consists of a series of short (e.g., 4-hour) periods of high exposure separated by several days of no exposure, the approach outlined above recommends estimating an acute EC for each acute exposure period. If the chronic EC equation (Equation 8) were to be used instead, the result would be an average EC value that may lead to an underestimate of risk since the inhaled concentrations could be higher than acute toxicity values during periods of exposure.

3.4 Estimating Exposure Concentrations in Multiple Microenvironments

When detailed information on the activity patterns of a receptor at a site is available, risk assessors can use these data to estimate the EC for either non-carcinogenic or carcinogenic effects. The activity pattern data describe how much time a receptor spends, on average, in different microenvironments (MEs), each of which may have a different contaminant concentration level.[29] By combining data on the contaminant concentration level in each ME and the activity pattern data, the risk assessor can calculate a time-weighted average EC for a receptor. Because activity patterns (and hence, MEs) can vary over a receptor's lifetime, EPA recommends that risk assessors pursuing the ME approach first calculate a time-weighted average EC for each exposure period characterized by a specific activity pattern (e.g., separate ECs for a school-aged child resident and a working adult resident). These exposure period-specific ECs can then be combined into a longer term or lifetime average EC by weighting the EC by the duration of each exposure period. The following sections further explain these two steps.

3.4.1 Using Microenvironments to Estimate an Average Exposure Concentration for a Specific Exposure Period

The ME approach can be used to estimate an average EC for a particular exposure period during which a receptor has a specified activity pattern. As a simplified example, a residential receptor may

[29] EPA defines a microenvironment in *Air Quality Criteria for Particulate Matter: Volume II* as a defined space that can be treated as a well-characterized, relatively homogeneous location with respect to pollutant concentration for a specified time period (e.g., rooms in homes, restaurants, schools, offices, inside vehicles, or outdoors) (USEPA, 2004b).

be exposed to a higher concentration of a contaminant in air in the bathroom for 30 minutes per day while showering, and exposed to a lower concentration in the rest of the house for the remaining 23.5 hours per day. In this case, risk assessors can use the CA value experienced in each ME weighted by the amount of time spent in each ME to estimate an average EC for the period of residency in that house using Equation 9.[30] This approach may also be used to address exposures to contaminants in outdoor and indoor environments at sites where both indoor and outdoor samples have been collected or where the vapor intrusion pathway has been characterized.

$$EC_j = \sum_{i=1}^{n} (CA_i \times ET_i \times EF_i) \times ED_j / AT_j \qquad \textbf{(Equation 9)}$$

Where:
EC_j ($\mu g/m^3$) = average exposure concentration for exposure period j;
CA_i ($\mu g/m^3$) = contaminant concentration in air in ME i;
ET_i (hours/day) = exposure time spent in ME i;
EF_i (days/year) = exposure frequency for ME i;
ED_j (years) = exposure duration for exposure period j; and
AT_j (hours) = averaging time = ED_j x 24 hours/day x 365 days/year.

3.4.2 Estimating an Average Exposure Concentration Across Multiple Exposure Periods

To derive an average EC for a receptor over multiple exposure periods, the average EC from each period (as calculated above in Equation 9) can be weighted by the fraction of the total exposure time that each period represents, using Equation 10. For example, when estimating cancer risks, the risk assessor may calculate a lifetime average EC where the weights of the individual exposure periods are the duration of the period, ED_j, divided by the total lifetime of the receptor. Alternatively, when estimating an HQ, risk assessors can use Equation 10 to calculate less-than-lifetime average ECs across multiple exposure periods. In that case, the AT will equal the sum of the individual EDs for all of the exposure periods.

$$EC_{LT} = \sum_{i=1}^{n} (EC_j \times ED_j) / AT \qquad \textbf{(Equation 10)}$$

Where:
EC_{LT} ($\mu g/m^3$) = long-term average exposure concentration;
EC_j ($\mu g/m^3$) = average exposure concentration of a contaminant in air for exposure period j;
ED_j (years) = duration of exposure period j; and
AT (years)[1] = averaging time.

[1] When evaluating cancer risk, the AT is equal to lifetime in years. When evaluating non-cancer hazard, the AT is equal to the sum of the EDs for each exposure period.

[30] If one or more MEs involve acute exposures, risk assessors should conduct a supplemental analysis comparing the CA for each of those MEs to a corresponding acute toxicity value to ensure that receptors are protected from potential acute health effects.

4. SELECTING APPROPRIATE TOXICITY VALUES

After characterizing the exposure scenarios and estimating ECs for each receptor at a site, the risk assessor should select appropriate inhalation toxicity values for each inhaled contaminant. For estimating cancer risks, this typically involves identifying and evaluating available published cancer potency estimates. For estimating HQs, this typically involves identifying and evaluating reference values that match the characterization of the exposure scenario from Figure 2 (i.e., acute, subchronic, or chronic reference values).

This section provides guidance for the selection of toxicity values appropriate for assessing risk under inhalation exposure scenarios. It describes sources for the most current inhalation data and provides guidance for proceeding when published inhalation toxicity data are not available.

4.1 Sources for Inhalation Toxicity Data

The OSWER Directive, *Human Health Toxicity Values in Superfund Risk Assessment* (USEPA, 2003), provides a recommended hierarchy of toxicological data sources to guide risk assessors when selecting appropriate toxicity values. This document sets out a recommended three-tiered framework for selecting human toxicity values. Tier 1 consists of EPA's IRIS, Tier 2 consists of EPA's PPRTVs, and Tier 3 includes other toxicity values as recommended by NCEA, such as the California EPA toxicity values, the Agency for Toxic Substances and Disease Registry's (ATSDR's) Minimal Risk Levels (MRLs), and Health Effects Assessment Summary Table (HEAST) toxicity values. Priority in Tier 3 should be given to sources that are the most current and those that are peer reviewed. Consultation with the Superfund Headquarters office is recommended regarding the use of Tier 3 values for Superfund response decisions when the contaminant appears to be a risk driver for the site.

The most up-to-date information on Superfund-supported cancer potency estimates and chronic and subchronic cancer and non-cancer reference values for inhaled contaminants are available on the Superfund risk assessment website (www.epa.gov/oswer/riskassessment/superfund_toxicity.htm). Superfund-recommended sources for acute non-cancer toxicity values can be found at www.epa.gov/oswer/riskassessment/superfund_acute.htm.[31]

In situations where the desired reference value (e.g., acute, subchronic, chronic) is not available, risk assessors may use a reference value based on the next longer duration of exposure as a conservative estimate that would be protective for a shorter-term ED (USEPA, 2002c). For example, if a risk assessor determines that an ED at a site is subchronic, but no subchronic toxicity value is available, a chronic RfC can be used to assess hazard.

EPA recommends that toxicity values published in Superfund-supported sources should generally be used in the risk equations presented in this guidance, without modification. This includes IURs on IRIS that were calculated from oral values using a default ventilation rate and BW (see Appendix B for a list of these chemicals). It is not generally appropriate to make adjustments to these values

[31] In selecting an acute toxicity value, risk assessors should consider the duration associated with their estimate of exposure (e.g., a 1-hour versus a 24-hour air sample). Use of a toxicity value specified for a longer duration than that of the exposure estimate may overestimate hazard, while the use of a shorter duration acute reference value may underestimate hazard.

based on IR and BW using the intake equation, because the amount of the chemical that reaches the target site through the inhalation pathway is not a simple function of these parameters (see Section 1.2). Use of the toxicity values listed in Appendix B should be noted in the uncertainty section of the risk assessment (see Section 9).

4.2 Recommended Procedures for Assessing Risk in the Absence of Inhalation Toxicity Values

The following section provides guidance on recommended procedures for situations where inhalation toxicity values are not available in any of the toxicity data sources described in Section 4.1.

If RfC and IUR values are not available for an inhaled contaminant, risk assessors should first contact NCEA's STSC for guidance.[32] Risk assessors working on Superfund sites can contact STSC to determine whether a provisional peer-reviewed toxicity value (PPRTV) exists for a contaminant; if not, the risk assessor, in cooperation with the appropriate EPA Regional office may request that STSC develop a PPRTV document or that STSC develop an inhalation toxicity value as a "consult". The latter would be specific to the site in question only. Additional information on STSC's current process for developing alternative toxicity values is described in Appendix C.

If STSC indicates that no quantitative toxicity information for the inhalation route is available, the risk assessor should conduct a qualitative evaluation of this exposure route. The risk assessor should discuss in the uncertainty section of the risk assessment report the implications of not quantitatively assessing risks due to inhalation exposures to chemicals lacking inhalation toxicity data. See the section on Risk Characterization (Section 9) in this guidance for more information.

Performing simple route-to-route extrapolation without the assistance of STSC is generally not appropriate because hazard may be misrepresented when data from one route are substituted for another without any consideration of the pharmacokinetic differences between the routes (USEPA, 1998). The following circumstances, outlined in the *Inhalation Dosimetry Methodology* (page 4-6), are specific examples of situations when route-to-route extrapolation from oral toxicity values might not be appropriate, even for use during screening:

- When groups of chemicals are expected to have different toxicity by the two routes – for example, metals, irritants, and sensitizers;
- When a first-pass effect by the respiratory tract is expected;
- When a first-pass effect by the liver is expected;
- When a respiratory tract effect is established, but dosimetry comparison cannot be clearly established between the two routes;
- When the respiratory tract was not adequately studied in the oral studies; and
- When short-term inhalation studies, dermal irritation, in vitro studies, or characteristics of the chemical indicate the potential for portal-of-entry effects at the respiratory tract, but studies themselves are not adequate for inhalation toxicity value development.

[32] All contact with STSC should be performed by an EPA regional risk assessor. States and other entities should first contact their EPA regional risk assessor with questions on inhalation toxicity values. Regional risk assessors can then contact STSC on their behalf.

The *Cancer Guidelines* (USEPA, 2005a) includes the following statement regarding route-to-route extrapolation:

> "When a qualitative extrapolation can be supported, quantitative extrapolation may still be problematic due to the absence of adequate data. The differences in biological processes among routes of exposure (oral, inhalation, dermal) can be great because of, for example, first-pass effects and different results from different exposure patterns. There is no generally applicable method for accounting for these differences in uptake processes in a quantitative route-to-route extrapolation of dose-response data in the absence of good data on the agent of interest. Therefore, route-to-route extrapolation of dose data relies on a case-by-case analysis of available data" (page 3-10).

5. ESTIMATING RISKS

This section provides updated equations recommended for estimating excess cancer risks and HQs from inhaled contaminants of concern at Superfund sites. Please see Section 8.2.1 of *RAGS, Part A* for further information about how to interpret calculated excess cancer risks and HQs.

5.1 Cancer Risks Characterized by an Inhalation Unit Risk

The excess cancer risk for a receptor exposed via the inhalation pathway can be estimated with the following equation:

Risk = IUR x EC **(Equation 11)**

Where: IUR $(\mu g/m^3)^{-1}$ = Inhalation Unit Risk; and
EC $(\mu g/m^3)$ = exposure concentration (See Equation 6).

When estimated ECs are above the POD used for the low dose extrapolation described in Section 2.3, a linear concentration-response relationship may not hold.[33] In such situations, the risk assessor should not use toxicity values developed through low dose extrapolation techniques. Instead, the risk assessor may report semi-quantitative risk estimates (e.g., risks are greater than 10^{-2}) or estimate risk using the original model underlying the toxicity value, which can be found in the technical support document for the value (e.g., IRIS profile, PPRTV Assessment).

When estimating cancer risks for children, risk assessors should be aware of chemicals that pose a higher risk of cancer when exposure occurs during early life. If evidence exists suggesting differences in risk across age groups for a chemical, this typically will be considered in the derivation of the toxicity value and described in the chemical's technical support document.

[33] Reviews of chemical-specific IRIS files indicate that the risk level corresponding to the concentration level above which the IUR should not be used often falls at or near 10^{-2}. However, this risk level varies by chemical and, therefore, risk assessors should refer to the toxicity value's technical support document for information on the concentration range for which the IUR was intended to be used.

Chemicals that have been determined to cause cancer by a mutagenic mode of action (MOA) are thought to pose a higher risk during early life. An EPA-recommended procedure exists for assessing risks from these chemicals. Figure 3 summarizes the recommendations of the *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* (USEPA, 2005b; hereafter *Supplemental Cancer Guidelines*) on how to adjust childhood risk calculations to account for chemicals with a mutagenic MOA for carcinogenicity. Please refer to the *Supplemental Cancer Guidelines* (USEPA, 2005b) for a list of chemicals with a mutagenic MOA that were used in the development of that document.

In addition, EPA's website for the "Handbook for Implementing the Supplemental Cancer Guidance at Waste and Cleanup Sites" contains an up-to-date list of chemicals that EPA has determined to have a mutagenic MOA (http://www.epa.gov/oswer/riskassessment/sghandbook/index.htm). As chemicals receive new assessments for mutagenicity, this information will appear in the IRIS profile or PPRTV assessment.

FIGURE 3
GUIDANCE ON ASSESSING RISK FROM EARLY-LIFE EXPOSURES FOR CHEMICALS ACTING BY A MUTAGENIC MODE OF ACTION FOR CARCINOGENICITY

If a chemical has been determined to cause cancer by a mutagenic MOA, it is possible that exposures to that chemical in early-life may result in higher lifetime cancer risks than a comparable duration adult exposure.

In risk assessments of exposure to chemicals for which a mutagenic MOA for carcinogenicity has been determined by EPA and a linear low-dose extrapolation performed, one of the following generally pertains:

1) If chemical-specific data on susceptibility from early-life exposures were available for derivation of CSFs, those slope factors are used for risk characterization, and Age Dependent Adjustment Factors (ADAFs) are not applied.
2) If chemical-specific data on susceptibility from early-life exposures were not available, the ADAFs are applied in calculating or estimating risks associated with early-life exposures (USEPA, 2005c).

If the latter case applies, the *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* (USEPA, 2005b) recommends the following default ADAFs be applied in risk assessments:

- 10-fold adjustment for exposures during the first 2 years of life;
- 3-fold adjustment for exposures from ages 2 to <16 years of age; and
- No adjustment for exposures after turning 16 years of age.

In such cases, Equation 11 can be altered to include the ADAFs in the following way:

$$Risk = (IUR \times EC_{<2} \times ADAF_{<2}) + (IUR \times EC_{2\text{-}16} \times ADAF_{2\text{-}16}) + (IUR \times EC_{>16})$$

Sources: USEPA, 2005b and USEPA, 2005c.
Note: All communications and factsheets pertaining to the implementation of the 2005 *Cancer Guidelines* can be found at www.epa.gov/osa/spc/cancer_guidelines.htm.

5.2 Hazard Quotients

The HQ for the inhalation pathway can be calculated with the following general equation:

HQ = EC/(Toxicity Value[1] x 1000 µg/mg) **(Equation 12)**

Where: HQ (unitless) = Hazard Quotient;
EC ($\mu g/m^3$) = exposure concentration (See Equations 7 or 8);
Toxicity Value (mg/m^3) = Inhalation toxicity value (e.g., RfC) that is appropriate for the exposure scenario (acute, subchronic, or chronic).

[1] Risk assessors should refer to the flowchart (Figure 2) to select an appropriate inhalation toxicity value for the exposure scenario at a site in order to calculate the HQ.

6. EXAMPLE EXPOSURE SCENARIOS

This section of the guidance includes examples of the types of exposure scenarios risk assessors may encounter when evaluating inhalation exposures at waste sites. Each scenario includes sample values for exposure parameters and reviews the process of estimating the EC and risks for cancer and other health effects. These examples are provided for illustrative purposes only and are not representative of every exposure scenario that could be encountered at a site. Furthermore, risk assessors should use site-specific values for exposure parameters if practicable when estimating ECs and risk levels or HQs. This would typically require some information on activity patterns for the specific site or the use of professional judgment. If default values are to be used for certain exposure parameters, please consult the Superfund website for up-to-date information on Superfund-recommended default exposure parameters.[34]

6.1 Residential Receptor

An example of a residential scenario could consist of inhalation exposure for up to 24 hours per day, up to 350 days per year for 6 to 30 years. When estimating cancer risk for this type of scenario, Equation 6 is recommended to calculate an EC and Equation 11 is recommended to estimate risk. For estimating hazard quotients for cancer or non-cancer effects, this scenario can be evaluated using the steps outlined in Figure 2. The duration of this scenario ranges from 6 to 30 years, which can be considered chronic (because it consists of repeated exposures for approximately 10 percent of a receptor's lifespan). The frequency of this scenario is generally as frequent as a chronic toxicity test and therefore Equation 8 is recommended to derive a chronic EC and Equation 12 with a chronic toxicity value is recommended to calculate an HQ. If information about multiple MEs is available, risk assessors should proceed according to Section 3.4 to estimate ECs to use in estimating cancer risks or HQs.

When assessing the risk under the residential scenario for children, the risk assessor should keep in mind that exposure parameters, specifically those related to activity patterns (e.g., exposure time, frequency, and duration) may be different for children and adults at the same site. For example, due

[34] http://www.epa.gov/oswer/riskassessment/superfund_hh_exposure.htm.

to outdoor play patterns, children may spend more time near the source of contamination than adults, and thus would have higher exposure time and/or exposure frequency values than adults living in the same location.[35] For indoor vapor intrusion from the subsurface, very young children might be more highly exposed due to substantial time spent indoors.

Beyond the consideration of activity patterns, MEs, and chemicals with a mutagenic MOA for carcinogenicity (as described in Section 5.1), no additional adjustments to account for specific child receptors should be made to the default values. Appendix A of this document is intended to illustrate that the use of default values sufficiently covers age-related variation in DAF or HEC values derived using the EPA *Inhalation Dosimetry Methodology's* default approach.

6.2 Commercial-Industrial/Occupational Receptor

An example of a commercial-industrial or occupational inhalation exposure scenario could be characterized by full-time workers (e.g., 8 hours per day, 5 days per week) in an indoor setting, such as an office building, exposed via vapor intrusion of subsurface contamination on a daily basis for 5 to 25 years. When estimating cancer risk for this type of scenario, Equation 6 is recommended to calculate an EC and Equation 11 is recommended to estimate risk. Following the flowchart in Figure 2, the duration and exposure pattern of this scenario would typically be considered chronic. Therefore, Equation 8 is recommended to derive a chronic EC and Equation 12 is recommended (with a chronic RfC) when calculating an HQ for cancer or non-cancer effects. If information about multiple MEs is available, risk assessors should proceed according to Section 3.4 when deriving ECs to use in estimating cancer risks or HQs. Exposure parameters should be adjusted to consider the exposure time, frequency and duration for this scenario, which may differ from a residential scenario. Risk assessors should also use appropriate exposure parameters for outdoor workers who, similar to children, may spend more time near a source of contamination than indoor workers.

6.3 Construction Worker

One example of a construction worker scenario could involve a long-term project (1-2 years) with workers exposed regularly to contaminant vapors and fugitive dust (8 hours per day, 5 days per week). When estimating cancer risk for this type of scenario, Equations 6 and 11 are recommended to calculate an EC and the risk estimate, respectively. Following the flowchart in Figure 2, the duration of this exposure scenario would typically be considered subchronic. In addition, this exposure is generally as frequent as a subchronic toxicity test. Therefore, Equation 8 is recommended to derive a subchronic EC, and Equation 12 is recommended for use with a subchronic toxicity value to calculate the HQ. If information about multiple MEs is available, risk assessors should proceed according to Section 3.4 when deriving ECs to use in estimating cancer risks or HQs.

6.4 Trespasser/Recreational Receptor

An example trespasser/recreational scenario could consist of an exposure of 1 to 2 hours per day, for 100 days per year or less. When estimating cancer risk for this type of scenario, Equations 6 and 11

[35] For additional information about early-lifestage age groups to consider when assessing children's exposure to environmental contaminants, please consult EPA's *Guidance on Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants* (EPA, 2005d).

are recommended to calculate an EC and the risk estimate, respectively. Following the steps in Figure 2 for cancer or non-cancer effects characterized by an RfC, each exposure period should be assessed separately because this exposure lasts only one to two hours each day for an average of two days per week. Therefore, Equation 7 is recommended to derive acute ECs for each exposure period. In addition, Equation 12 is recommended for use with an acute toxicity value to calculate HQs for each exposure period.

7. TARGET CONCENTRATIONS FOR SCREENING ANALYSIS OF INHALATION PATHWAYS

For purposes of this guidance, risk-based screening levels are values that may be compared to the contaminant concentration in air to help risk assessors identify potential contaminants of concern. Screening levels can also be calculated for comparison with samples from source media at a site, such as soil. Screening levels are generally not appropriate for use as clean-up levels; they are intended to aid in initial evaluation of contaminants and exposure pathways of concern prior to proceeding with a baseline risk assessment.[36] If contaminant concentrations in air exceed the risk-based screening levels appropriate for the receptor population of interest, risk assessors should gather site-specific information to determine the need for any remedial action. The following sections outline a recommended approach for calculating screening levels in air as well as source media.

7.1 Target Contaminant Concentrations in Air

The equations recommended for estimating ECs and risk (Equations 6 through 12) can be used to calculate target contaminant concentrations in air by following the four steps outlined below in Table 4.[37]

If air samples from a site are found to be below the target concentration, the risk assessor can generally conclude that this pathway does not pose an unacceptable level of risk from the contaminant. If the concentrations are found to exceed the screening levels, the risk assessor should evaluate the inhalation pathway further by gathering additional site-specific data on contaminant levels, site conditions, and receptor characteristics.

7.2 Screening Levels for Other Media

Inhalation risk-based screening levels may also be calculated for media other than air, including soils, tap water, soil gas, and ground water. The soil gas and ground water values may be derived specifically to address concerns about vapor intrusion from subsurface contamination into indoor spaces.

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[36] EPA regions, states, or other agencies may support unique screening levels for specific purposes that may differ from the method presented in this document. Generally, when using screening levels it is important that risk assessors understand the target risks, toxicity, and exposure assumptions as well as migration-attenuation assumptions on which they are based, and to apply them for their intended use.

[37] Target contaminant concentrations in air calculated according to the procedure outlined in this document are generally protective for direct inhalation exposures. This process should not be used to calculate concentrations in air to be protective of indirect exposures (e.g., ingestion of crops contaminated through air delivery or vapor phase transfer, ingestion of livestock or fish contaminated indirectly through air deposition or vapor phase transfer).

TABLE 4 RECOMMENDED PROCEDURE FOR CALCULATING RISK-BASED SCREENING CONCENTRATIONS FOR CONTAMINANTS IN AIR		
	Cancer Risk-Based	**Hazard-Based**[1]
Step 1: Select Target Levels	Select target cancer risk (e.g., 1 x 10^{-6}).	Select target HQ (e.g., 1).
Step 2: Identify Toxicity Value[2]	Identify inhalation cancer potency value (e.g., IUR). If none exists, proceed with hazard-based screening level calculation.	Identify inhalation reference value (e.g., RfC) to match exposure scenario (acute, subchronic, or chronic). If none exist, proceed with cancer screening level calculation.
Step 3: Calculate CA	Using target cancer risk from Step 1 along with the receptor- and scenario-specific exposure parameter values, calculate CA; the following equation is recommended: CA = (AT x Target Risk)/(IUR x ET x EF x ED)	Using target HQ from Step 1 along with the receptor- and scenario-specific exposure parameter values, calculate CA; the following equation is recommended: CA = (AT x Target HQ x RfC x 1000 µg/mg)/(ET x EF x ED)
Step 4: Select Screening Concentration	Select minimum of predicted cancer risk- and hazard-based values as screening concentrations.[3] Repeat for each receptor/scenario combination of interest.	

[1] Hazard-based screening concentrations are typically derived from reference values such as RfCs. These values may be available for non-cancer effects but may include cancer, if a nonlinear MOA is thought to operate for a chemical.
[2] If no inhalation toxicity value is available for a chemical, contact STSC for further direction on how to proceed.
[3] Screening levels estimated from the equations presented in Step 3 could yield concentrations that exceed the maximum possible vapor concentration for a chemical. In such cases, it may be useful to calculate the maximum possible vapor concentration of the pure contaminant at the temperature of interest, using the following formula: C_{max} = S x H x 10^3 L/m^3, where S = solubility at 25° C (or temperature of interest) and H (unitless) = Henry's Law Constant at 25° C (or temperature of interest). This equation is based on an established relationship (see, for example, Schwartzenbach et al. 1993), that allows the Henry's Law Constant to be estimated as the ratio of a compound's vapor pressure and aqueous solubility for compounds that are slightly to moderately soluble in water. When the dimensionless Henry's Law constant, H, is used, the relationship described above can be used to calculate the vapor concentration of a saturated solution of a given compound, assuming equilibrium between the vapor and aqueous phases.

7.2.1 Soil Screening Levels

When evaluating risk in a source medium, such as soil, it is typically possible to calculate screening levels for that medium that are expected to be protective of inhalation exposures based on the expected transfer of a contaminant from the source medium to the air. Soil Screening Levels (SSLs) can be described as "risk-based soil concentrations derived for individual chemicals of concern from standardized sets of equations. These equations combine EPA chemical toxicity data with parameters defined by assumed future land uses and exposure scenarios, including receptor characteristics and potential exposure pathways" (USEPA, 2002b). These SSLs may be used for screening analyses and may serve as the basis for the development of Preliminary Remediation Goals (PRGs). Refer to the *Soil Screening Guidance* (USEPA, 1996) and the *Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites* (USEPA, 2002b) for recommended equations that can be used to calculate SSLs for volatilization of chemicals from soil to air and for particulate emissions.

7.2.2 Tap Water Screening Values

Contaminated tap water may pose risk by the inhalation route if the contaminants present are volatile. Screening levels can be calculated for tap water that account for inhalation exposures resulting from the household use of water (e.g., showering, laundering, dishwashing). Risk assessors should consult their local EPA regional risk assessor for direction on how to calculate appropriate screening levels for tap water.

7.2.3 Soil Gas or Ground Water Screening Values for Vapor Intrusion

If there is concern at a site about the possibility of migration of vapor-forming chemicals from contaminated soil gas or ground water into the indoor air of overlying buildings ("vapor intrusion"), screening values can be calculated for these media. Risk assessors should first follow the procedure outlined in Section 7.1 and Table 4 to calculate a risk-based target concentration for the contaminant in air.

For the calculation of a soil gas screening-level concentration, the target air concentration is then divided by an assumed screening-level attenuation factor. The attenuation factor (the ratio of indoor air divided by subsurface source concentration) represents the factor by which subsurface vapor concentrations migrating into indoor air spaces are reduced due to a variety of attenuating mechanisms.

For the calculation of a ground water screening-level concentration, the target air concentration is divided by an assumed screening-level attenuation factor, and the resulting soil gas concentration is converted to a corresponding ground water concentration, assuming equilibrium between the aqueous and vapor phases at the water table.

Risk assessors should consult their local EPA regional risk assessor for direction on how to calculate appropriate screening levels for soil gas and ground water when vapor intrusion is an issue at a site.

8. DEVELOPING AGGREGATE AND CUMULATIVE RISK ESTIMATES

EPA's current approach to estimating cumulative risk or hazard at a site from multiple chemicals, set forth in *RAGS, Part A* (USEPA, 1989), is not affected by the *Inhalation Dosimetry Methodology* and therefore is not being updated at this time. In addition, the aggregation of risks and hazards across multiple exposure routes should remain unchanged. The recommended approaches for aggregating risk and hazard estimates are outlined below.

8.1 Estimating Cumulative Risks and Hazards Across Multiple Chemicals

The recommended method for estimating cumulative risk and hazard at a site from exposure to multiple chemicals is described in *RAGS, Part A*, Section 8.2.2. This method is based on the default approaches described in *Guidelines for the Health Risk Assessment of Chemical Mixtures* (USEPA, 1986). Additional information on this method was subsequently published in the *Supplementary Guidance for Conducting Health Risk Assessment of Chemical Mixtures* (USEPA, 2000b). The recommended methods to use with quantitative cancer risk estimates as well as with HQs are outlined below.

8.1.1 Cancer Risks

When evaluating predicted cancer risks from multiple contaminants, risk assessors should estimate the cancer risk for each substance and then sum these risks. This yields an estimate of total cancer risk, which represents the cumulative predicted cancer risk for the chemicals at a site.

Risk assessors should note, however, that this recommended method assumes "independence of action by the compounds involved (i.e., that there are no synergistic or antagonistic chemical interactions and that all chemicals produce the same effect, i.e., cancer)" (USEPA, 1989). In addition, this simple additive approach is generally most appropriate for total cancer risks less than 0.1. If these assumptions are incorrect, over- or under-estimation of actual multiple-substance risk could result (USEPA, 1989).

8.1.2 Hazard Quotients

When the evaluation involves multiple chemicals assessed via HQs, risk assessors typically first calculate the HQ for each substance, and then sum the individual HQ values. This generally yields an estimated hazard index (HI) for the multiple chemicals assessed via a hazard-based approach. Separate HIs should be calculated for each type of exposure period (i.e., chronic, subchronic, acute). If an HI is greater than 1, it is generally appropriate to derive separate HIs for each target organ of concern (for more information, see *RAGS, Part A*, page 8-14).[38] When multiple acute exposures are present at a site, risk assessors should evaluate each acute exposure event separately. Hazards from multiple chemicals generally should be summed only when the exposures to these chemicals occur simultaneously.[39]

8.2 Aggregating Risk and Hazard Quotients Across Exposure Routes

Guidance for combining the multi-chemical risk estimates and hazard quotients across exposure pathways is described in *RAGS, Part A*, Section 8.3 (USEPA, 1989). In order to determine whether risks or HIs should be combined across exposure pathways, risk assessors should first identify reasonable exposure pathway combinations. Then, risk assessors should examine whether it is likely that the same individuals would consistently face the reasonable maximum exposure (RME) by more than one pathway.

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[38] This recommended method assumes that "the dose for each individual component is at a level at which effects are not expected to occur, be observable, or be of concern; however, when the doses are combined, effects of concern may be expected or observed in response to the higher dose level of the mixture" (EPA, 2000b, page 12). Another assumption of the HI approach is that the compounds induce the same effect by the same mechanism of action. Therefore, "application of the HI equation to a number of compounds that are not expected to induce the same type of effects or that do not act by the same mechanism, although appropriate as a screening-level approach, could overestimate the potential for effects" (EPA, 1989, page 8-14). This is generally less of a concern if one to two substances are responsible for driving the HI above 1.

[39] In cases where a single chemical is present at a site and receptors are exposed through a series of acute exposure events, the highest single EC should be compared to an acute reference value of the appropriate duration to assess hazard.

The recommended approach for estimating excess cancer risk from exposure via multiple routes is to first estimate cancer risk from each exposure pathway and then sum across the multiple routes.[40]

For the effects assessed via a reference value, risk assessors should calculate the HI for each exposure pathway and sum across the multiple routes. Separate total HIs should be calculated for each type of exposure period (i.e., chronic, subchronic or acute). If the HI exceeds one, there may be concern for potential adverse effects and risk assessors should consider deriving separate HIs for each target organ of concern.

9. RISK CHARACTERIZATION

Risk characterization is the final, summarizing step in conducting a risk assessment. Generally, the purpose of the risk characterization section of a report is to:[41]

- Describe the key findings of the risk assessment in a transparent manner, including identifying hazard, characterizing the dose-response relationship, and describing receptor exposures;
- Identify and describe the scientific and policy assumptions used in the assessment;
- Characterize uncertainties in results; and
- Provide an overall conclusion about the risks present at a site (USEPA, 2000c).

A well-crafted risk characterization section puts risk calculations into context for risk managers so that they may effectively weigh and interpret risk assessment results (i.e., it is the interface between risk assessment and risk management). A few of the key issues and uncertainties involved in calculating risks from inhalation exposures are outlined below.

9.1 Highly Exposed or Susceptible Populations and Life Stages

EPA recommends that the risk characterization portion of the risk assessment explain any particular susceptibilities to inhaled toxicants or potential for increased inhalation exposures among the various receptor groups at a site.[42] We discuss below two possible examples, children and worker receptors, though this discussion could apply to other receptor characteristics as well (e.g., age, disease, gender, genetic characteristics).

9.1.1 Children

One population group that could potentially be more highly exposed to inhalation exposures at a site is children. As discussed in Section 6.2, exposure parameters related to activity patterns (e.g., exposure time, frequency, and duration) and MEs, may vary across age groups. For example, due to outdoor play patterns, children may spend more time near the source of contamination than adults,

[40] Note that this approach is generally most appropriate for total cancer risks of less than 0.1 (EPA, 1989).

[41] For specific information on the format of risk characterizations, refer to *Elements to Consider when Drafting EPA Risk Characterizations* (EPA, 1995c).

[42] EPA's IRIS glossary defines susceptibility as the following: "Increased likelihood of an adverse effect, often discussed in terms of relationship to a factor that can be used to describe a human subpopulation (e.g., life stage, demographic feature, or genetic characteristic)" (EPA, 2008b).

and thus would have higher exposure time and/or exposure frequency values than adults living in the same location. Therefore, it is important to carefully describe site-specific exposures to children, and assumptions made in risk calculations.[43]

If chemical-specific data on susceptibility to the toxic effects from early life exposures are available, these data are considered when developing toxicity values that specifically address differential toxicity to the young (e.g., vinyl chloride) (USEPA, 2005c). Toxicity values derived using the default approach from the *Inhalation Dosimetry Methodology* are developed for the human population as a whole, including sensitive subgroups. Therefore, as described in Section 6 of Appendix A, no quantitative adjustment of toxicity values derived using the default approach in the *Inhalation Dosimetry Methodology* is recommended for specific age groups to account for different ventilation rates or body weights of specific age groups.

When evaluating risk to carcinogenic chemicals with a demonstrated mutagenic MOA but which lack chemical-specific information on susceptibility from early life exposures, EPA recommends a quantitative adjustment of the toxicity value to account for early life susceptibility, as described in the *Supplemental Cancer Guidelines* (see USEPA, 2005b & 2005c; and Section 5.1 of this guidance for further information).

9.1.2 Workers

Workers could have increased exposure under certain occupational scenarios. Some outdoor workers might spend more time near a source of contamination in the course of their job and this should be reflected in adjustments to the exposure parameters (e.g., ET, Exposure Frequency (EF), and ED) describing the worker exposure scenario. Toxicity values derived using the *Inhalation Dosimetry Methodology* are developed for the human population as a whole, including sensitive populations and life stages. In the default *Inhalation Dosimetry Methodology* approach, typical variation in IRs between periods of high activity and rest is considered. However, if workers have especially high levels of exertion with correspondingly high ventilation rates, these workers could be at the upper end of the risk range, particularly if they are exposed to Category 1 gases, which have direct effects in the respiratory tract. This implication should be recognized in the risk characterization section.

9.2 Uncertainties in Inhalation Risk Assessment

This guidance recommends including an assessment of the key uncertainties that may significantly impact risk estimates for inhaled chemicals. This should ensure transparency, clarity, reasonableness and consistency in risk assessments, as recommended by EPA's *Policy for Risk Characterization* (USEPA, 1995a). Other sources of uncertainty may be present and other EPA documents provide guidance on characterizing uncertainty in risk the assessment process (USEPA, 1992, 1995a, 1995b, 1995c, 1997a, 1997b). Key uncertainties related to inhalation risk assessment, which is the focus of this section, include the development of ECs, choice of toxicity value, lack of quantitative toxicity information via inhalation, and the approach to estimating and aggregating risks. According to EPA's *Guidance for Risk Characterization*, the discussion of uncertainty "should reflect the type and complexity of the risk assessment, with the level of effort for analysis and discussion of uncertainty

[43] For additional information on children's health risk assessment, please consult *A Framework for Assessing Health Risks of Environmental Exposures to Children* (EPA, 2006b).

corresponding to the level of effort for the assessment" (USEPA, 1995b). Therefore, risk assessors should provide a qualitative and/or quantitative evaluation of key uncertainties pertaining to inhalation risk, and their impact on the outcome of the assessment, consistent with the level of effort of the specific risk assessment.

9.2.1 Development of Exposure Concentrations

As described in Section 3 of this guidance, with the exception of acute exposures, time-weighted averages are typically used to represent intermittent or variable inhalation exposures to receptors at a site. This recommended approach is consistent with the duration adjustment approach (based on Haber's Law) that is generally used in deriving the toxicity values (see Section 2.1.1.1 for further information). As mentioned in Section 3, when evaluating situations in which the exposure is long-term, yet there are short periods of significantly higher exposure, those periods should also be assessed using appropriate short-term toxicity values. This ensures that periods of much higher exposure can be appropriately assessed and not "diluted out" in the assessment of longer-term exposure.

When information on multiple MEs exists at a site, risk assessors may choose to estimate ECs as outlined in Section 3.4. However, this typically requires sufficient time-activity information of receptors at a site to accurately determine the time spent in each ME. Incomplete or low quality data on time-activity pattern may introduce uncertainty into the estimation of the ECs for MEs. Risk assessors should describe the quality and completeness of these data.

The recommended method for determining the CA at a site can potentially introduce uncertainty into the EC calculations. For instance, if contaminant concentrations in air are measured, risk assessors should consider uncertainties related to how well the set of air samples available at a site represents the duration and time period being assessed as well as measurement uncertainty related to the methods and equipment used. In addition, risk assessors should describe any potential confounding of indoor air samples by other sources of contaminants (e.g., household products). If contaminant concentrations in air are modeled, (e.g., by EPA's spreadsheet models for vapor intrusion) risk assessors should address model-related uncertainties and their potential impact on the estimate of contaminant concentrations in air. Considerations of particle size at the site versus particle size used to derive the toxicity value are also important.

9.2.2 Toxicity Assessment

Section 4.1 of this document indicates that some IURs on IRIS were developed through extrapolation from oral CSFs (see Appendix B of this document). The use of toxicity values derived through simple route-to-route extrapolation introduces additional uncertainty into risk calculations. Therefore, risk assessors should indicate when extrapolated IURs are used and should characterize the potential impact of the uncertainty associated with using these values, if known.

Section 4.2 and Appendix C of this guidance recommends contacting STSC to help identify appropriate toxicity values for conducting a risk assessment at Superfund sites in the absence of published inhalation toxicity values. If STSC is unable to recommend a toxicity value, risk assessors should acknowledge the resulting uncertainty in risk associated with the chemical(s) lacking inhalation toxicity data. If STSC provides risk assessors with a toxicity value based on a PBPK

model, model uncertainty should be discussed. In addition, if STSC provides risk assessors with one or more structurally analogous chemicals, risk assessors can use toxicity data for these chemicals to help characterize the potential magnitude of the inhalation risk associated with the chemical(s) lacking data. In this case, risk assessors should acknowledge the uncertainty associated with relying on toxicity data for analogous chemicals to characterize risk at the site.

Risk assessors should also acknowledge chemicals that lack duration-appropriate toxicity values and discuss the potential impacts of substituting alternative toxicity values for HQ calculations. For instance, if the ED is determined to be subchronic but no subchronic inhalation RfC or analogous toxicity value is available for that chemical, the risk assessor should address the uncertainty associated with calculating an HQ using a toxicity value for a different duration, such as chronic, or the impact of not quantifying those risks. In addition, if risk assessors use an acute toxicity value that does not match the duration of the acute exposure being assessed, the possibility of under or overestimating hazard should be discussed.

When conducting a screening-level risk assessment using screening values such as those described in Section 7, it is important to further evaluate and clearly describe the quality and uncertainties associated with the inhalation toxicity values used in the risk assessment if measured sample contaminant concentrations at a site exceed these screening values.

9.2.3 Estimating Cancer Risks

For high exposures, for example those within the range of epidemiological studies (usually those predicted to have risks greater than 10^{-2}), the IUR derived from the linear extrapolation below the range of observation is generally not appropriate for use (see Section 5.1 of this document for further information).[44] Risk assessors should provide specific information in the risk characterization describing how these high exposures were addressed in the risk assessment. For instance, if a risk assessor chose to provide a semi-quantitative approach (e.g., indicating that risks are above 10^{-2}), this should be indicated, along with a description of the uncertainties involved in not fully quantifying risk associated with exposure to this chemical. If a risk assessor chose to use the original model in the IRIS file or other technical background document, the risk characterization section should include a description of any uncertainties in the model used and could contain examples of the risks estimated.

9.2.4 Estimating Risk and Hazard from Multiple Chemicals and Exposure Pathways

Risk assessors should also describe uncertainties involved in aggregating risk and hazard across multiple chemicals and exposure pathways. For instance, the approaches described in Section 8 of this document are associated with several assumptions (e.g., independence of action and doses for individual compounds at levels not expected to be of concern). If these assumptions are not met, aggregation may not be appropriate. This should be fully described in the risk characterization section and any uncertainties involved in the lack of quantitative information should be indicated.

[44] Also refer to Section 8.2.1 of *RAGS, Part A* for further discussion of this topic (EPA, 1989, page 8-6).

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APPENDIX A

APPENDIX A

ANALYSIS OF DEFAULT APPROACH FOR HEC DERIVATION AS COMPARED TO POPULATION- AND LIFESTAGE-SPECIFIC CALCULATIONS

NOTE: The Agency's inhalation dosimetry methodology (USEPA, 1994; hereafter, "the *Inhalation Dosimetry Methodology"*) is a technical report that describes the derivation of human equivalent concentrations (HECs) from animal (or human) studies, as well as the other steps involved in developing a chronic Reference Concentration (RfC). This appendix is included to illustrate the HEC derivation using the *Inhalation Dosimetry Methodology*'s default approach (with the recommended default values for humans), and to also illustrate the impact of substituting alternate age- and activity-specific human values into the default calculations. The default approach is employed for chemicals for which more chemical-specific dosimetric and pharmacokinetic data are not available, thus precluding the use of more advanced models for deriving the HEC. The calculations in this appendix do not represent a refined or optimal model for assessing intra-human variability (e.g., age- and activity-specific risks), and are not intended to imply that risk assessors should deviate from the *Inhalation Dosimetry Methodology* by substituting alternate values into the default calculations. Age-specific data are limited. Because of these limitations, the calculations made for different ages and exposure groups in this appendix are not recommended for use in quantitative risk assessment (i.e., they are only for the purpose of illustration), but may be useful in discussions of uncertainty and variability associated with the default approach.

It is also noted that, as of this writing, the Agency is involved in a routine reevaluation of scientific advancements in the field, with consideration of the need for improvement to the *Inhalation Dosimetry Methodology*. Any revisions will consider current understanding of inhalation dosimetry and differences across and within species, as well as the Agency's risk assessment needs. In order to transparently and quantitatively address children's inhalation dosimetry and risk assessment, this guidance document will be updated (on-line) when Agency methodology updates are available that are specific to early life. Until that time, the 1994 *Inhalation Dosimetry Methodology* is the appropriate Agency methodology.

INTRODUCTION

This appendix consists of examples and discussions illustrating the current default chemical category-specific approach to inhalation dosimetry for the various categories of gases and particles as described in *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry* (USEPA, 1994; hereafter, the *Inhalation Dosimetry Methodology*). This default inhalation dosimetry approach is used to convert toxicological and epidemiological study data to an HEC that can then be used to derive chronic RfCs for the human population (inclusive of susceptible populations and life stages, such as children) and also in the development of Inhalation Unit Risks (IURs) (USEPA, 2005). The default approach does not rely on age- or activity-specific values for physiological parameters when calculating HECs; however the default approach has been designed by EPA to derive reference values that are protective across the entire population.

The appendix includes six sections. Sections 1 through 3 address Category 1 gases. These sections provide example calculations for Category 1 highly reactive, high water solubility gases that are typically absorbed in the upper airways, exhibiting adverse effects in the extrathoracic (ETh), tracheobronchial (TB), and pulmonary (PU) regions of the respiratory tract, respectively. These examples include comparisons of HEC calculations based on default parameters with those derived using age- and activity-specific parameters for the respiratory region affected. Section 4 addresses Category 3 low reactivity, limited water solubility gases that exhibit systemic effects outside the respiratory tract. Section 5 addresses changes in particle deposition in the respiratory tract across age groups. The conclusions are summarized in Section 6.

When reviewing the examples, please note the following:

- An RfC derived using the *Inhalation Dosimetry Methodology* is defined as "an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime" (USEPA, 2008).

- All examples in this appendix are based on the *Inhalation Dosimetry Methodology*. EPA is committed to periodically reviewing and updating the *Inhalation Dosimetry Methodology* to ensure that it reflects the current state of the science and that it yields toxicity values that sufficiently cover potential age- and activity-related variation in inhalation exposure. A review and update is currently underway.

- The examples in this appendix are all based on calculating HECs from a point of departure (POD) for non-cancer effects (e.g., a No Observed Adverse Effect Level (NOAEL), Lowest Observed Adverse Effect Level (LOAEL), or Benchmark Concentration, Lower confidence limit (BMCL)). These calculations could also be performed in an identical manner for carcinogens using a POD for cancer risk estimate derivation (e.g., a Lower limit on the Effective Concentration (LEC) value).

- The default animal and human values for minute volume (V_e) and surface area (SA) used in these examples were obtained from *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry* (USEPA, 1994).[45] The age- and activity-specific V_e values were obtained from the International Commission on Radiological Protection (ICRP) Publication 66, *Human Respiratory Tract Model for Radiological Protection* (ICRP, 1994).[46] Age-specific SA values used in Examples 1 and 2 were calculated using scaled estimates for the mass and thickness of respiratory region-specific target tissue from ICRP (1994); Values for Example 3 were calculated from an allometric scaling equation presented in a publication by Zeltner et al. (1987). EPA's Office of Research and Development (ORD) selected these data following review of the available physiological data for the age groups indicated in the examples.

- Chemical-specific data from the Integrated Risk Information System (IRIS) file for acrolein were used in the ETh example (Example 1). However, the other two examples, which focus on effects in the TB and PU regions, respectively, use hypothetical data for the POD because there are currently no chemicals on IRIS exhibiting Critical Effects (for RfC derivation) in those regions.[47] The conclusions of these two examples are unaffected by the use of hypothetical data because the results are driven by the values of parameters that are not chemical-specific (i.e., SA and V_e).

[45] The minute volume is the total ventilation per minute and equals the product of the tidal volume (the air volume entering or leaving the lungs with a single breath) and the respiratory frequency.

[46] For further information on inhalation rates in humans under different scenarios, refer to Chapter 5 of EPA's *Exposure Factors Handbook* (EPA, 1997).

[47] Hypothetical examples for the TB and PU regions were included in this appendix because currently no RfCs for gases on IRIS are calculated based on animal studies showing health effects occurring in these regions of the respiratory system

1. EXAMPLE 1: CATEGORY 1 GAS, EXTRATHORACIC EFFECTS, ACROLEIN

The Dosimetric Adjustment Factor (DAF) for a Category 1 gases, the Regional Gas Dose Ratio (RGDR), is based on the animal to human ratio of the V_e divided by the SA of the region of the respiratory tract where the effect occurs. For acrolein, the effect occurs in the ETh region. The DAF is typically calculated using the following equation (USEPA, 1994, Equation 4-18):

$$RGDR_{ETh} = \frac{\left(\frac{V_e}{SA_{ETh}}\right)_{animal}}{\left(\frac{V_e}{SA_{ETh}}\right)_{human}} = \frac{\frac{0.14\,L/min}{15\,cm^2}}{\frac{13.8\,L/min}{200\,cm^2}} = 0.14 \qquad \textbf{(Equation A-1)}$$

The default *Inhalation Dosimetry Methodology*-recommended values for the V_e and SA_{ETh} of the Wistar rat (the animal in the principal study for acrolein) are 0.14 L/min (0.20 m^3/day) and 15 cm^2, respectively (USEPA, 1994). EPA's default human values are 13.8 L/min (20 m^3/day) for V_e and 200 cm^2 for SA_{ETh} (USEPA, 1994). The RGDR for the ETh region ($RGDR_{ETh}$) was calculated using these values for the rat and the human as shown in Equation A-1. In the laboratory animal study on acrolein, the LOAEL adjusted for continuous exposure ($LOAEL_{[ADJ]}$) of 0.16 mg/m^3 (USEPA, 2003) is used as the point of departure. The $LOAEL_{[HEC]}$ is the $LOAEL_{[ADJ]}$ multiplied by the $RGDR_{ETh}$.

To illustrate any potential age- or activity-related variation in the $LOAEL_{[HEC]}$ that might result from using human parameter values other than the defaults, scaled estimates for the mass and thickness of ETh target tissue from ICRP (1994) at different ages are used to calculate the SA_{ETh} values in Table A-1. Age- and activity-related V_e reported in ICRP (1994) are based on daily time-budgeted reference values. Table A-1 shows little variation in the resultant $LOAEL_{[HEC]}$ across the groups in this example. The default procedure produces the lowest $LOAEL_{[HEC]}$ value in Table A-1 and is, therefore, sufficient to cover all of these groups.

TABLE A-1 COMPARISON OF THE HEC-DEFAULT (EPA, 1994) WITH EXAMPLE $LOAEL_{[HEC]}$ VALUES FOR HUMANS OF DIFFERENT AGES AND ACTIVITY PATTERNS FOR THE EXTRATHORACIC REGION					
	Total $V_{e\ (human)}$ (L/min)[a]	$SA_{ETh\ (human)}$ (cm^2)[b]	$(V_e/SA_{ETh})_{human}$ (L/min-cm^2)	$RGDR_{ETh}$	$LOAEL_{[HEC]}$ (mg/m^3)
Outdoor Worker, Male	17.5	470	0.037	0.25	0.04
Sedentary Worker, Male	15.4	470	0.033	0.28	0.04
Sedentary Worker, Female	12.6	407	0.031	0.30	0.05
15 Year-Old Male	14.0	439	0.032	0.29	0.05
15 Year-Old Female	10.9	397	0.027	0.35	0.06
10 Year-Old	10.6	293	0.036	0.26	0.04
5 Year-Old	6.1	198	0.031	0.30	0.05
1 Year-Old	3.6	97.1	0.037	0.25	0.04
3 Month-Old	2.0	65.8	0.030	0.31	0.05
HEC - Default	13.8	200	0.069	0.14	0.02
[a] These values are from the ICRP publication, Tables 8, 27, B.16a, B.16b and B.17 (ICRP, 1994). [b] These values are from the ICRP publication, Tables 1 and 5 (ICRP, 1994).					

2. EXAMPLE 2: CATEGORY 1 GAS, TRACHEOBRONCHIAL EFFECTS, HYPOTHETICAL CHEMICAL

The DAF for a Category 1 gas or vapor exhibiting effects in the TB region is based on the animal to human ratio of the V_e divided by the SA of the TB region for each species. The DAF is typically calculated using the following equation:

$$RGDR_{TB} = \frac{\left(\frac{V_e}{SA_{TB}}\right)_{animal}}{\left(\frac{V_e}{SA_{TB}}\right)_{human}} = \frac{\frac{0.14\ L/min}{22.5\ cm^2}}{\frac{13.8\ L/min}{3200\ cm^2}} = 1.4 \qquad \textbf{(Equation A-2)}^{48}$$

This example assumes that the hypothetical chemical has been tested on Wistar rats and therefore utilizes the EPA animal default values for that strain. The V_e value used is 0.14 L/min (0.20 m^3/day) and the default SA_{TB} is 22.5 cm^2 (USEPA, 1994). EPA's default human values are 13.8 L/min (20 m^3/day) for V_e and 3200 cm^2 for SA_{TB} (USEPA, 1994). The RGDR for the TB region ($RGDR_{TB}$) is calculated using these values for the rat and the human, as shown in Equation A-2. The example also assumes a NOAEL adjusted for continuous exposure ($NOAEL_{[ADJ]}$) of 0.16 mg/m^3 as the point of departure. The $NOAEL_{[HEC]}$ is the $NOAEL_{[ADJ]}$ multiplied by the $RGDR_{TB}$.

Table A-2 shows little variation across age and activity groups in the $NOAEL_{[HEC]}$. The variation from the default (less than a factor of 2) is less than the default value of 10 used for the uncertainty factor for intraspecies variability when deriving the RfC. Application of the normal procedure for

[48] This equation is the reduced, default version of Equation 4-19 of the *Inhalation Dosimetry Methodology*. Equation 4-19 is reduced to this form consistent with the derivation of the reduced form of the RGDR equation of extrathoracic effects described in section 4.3.6.1 and Appendix I of the *Inhalation Dosimetry Methodology*.

determining the RfC will accommodate the observed variation. In addition, RfCs and IURs are developed for chronic exposure and will generally involve an exposure for multiple years.

TABLE A-2
COMPARISON OF THE HEC-DEFAULT (EPA, 1994) WITH EXAMPLE $LOAEL_{[HEC]}$ VALUES FOR HUMANS OF DIFFERENT AGES AND ACTIVITY PATTERNS FOR THE TRACHEOBRONCHIAL REGION

	Total $V_{e\ (human)}$ (L/min)[a]	$SA_{TB\ (human)}$ (cm^2)[b]	$(V_e/SA_{TB})_{human}$ (L/min-cm^2)	$RGDR_{TB}$	$NOAEL_{[HEC]}$ (mg/m^3)
Outdoor Worker M	17.5	2660	0.0066	0.94	0.15
Sedentary Worker M	15.4	2660	0.0058	1.1	0.18
Sedentary Worker F	12.6	2640	0.0048	1.3	0.21
15 year M	14.0	2520	0.0056	1.1	0.18
15 year F	10.9	2250	0.0048	1.3	0.21
10 Year	10.6	1830	0.0058	1.1	0.18
5 Year	6.1	1340	0.0046	1.4	0.22
1 Year	3.6	857	0.0042	1.5	0.24
3 Months	2.0	712	0.0028	2.2	0.35
HEC-default	13.8	3200	0.0043	1.4	0.22

[a] These values are from the ICRP publication, Tables 8, 27, B.16a, B.16b and B.17 (ICRP, 1994).
[b] These values are from the ICRP publication, Tables 1 and 5 (ICRP, 1994).

3. EXAMPLE 3: CATEGORY 1 GAS, PULMONARY EFFECTS, HYPOTHETICAL CHEMICAL

The DAF for a Category 1 gas or vapor with an effect in the PU region is based on the animal to human ratio of the alveolar ventilation rate (Q-alv) divided by the SA of the PU region (SA_{PU}) for each species. The Q-alv is approximately equal to the V_e multiplied by 0.7. This adjustment accounts for the anatomic/physiologic deadspace in the PU region, making the Q-alv equivalent to the amount of inspired air available for gas exchange (West, 2000). The DAF for this region of the respiratory tract is typically calculated using the following equation:

$$RGDR_{PU} = \frac{\left(\frac{Q-alv}{SA_{PU}}\right)_{animal}}{\left(\frac{Q-alv}{SA_{PU}}\right)_{human}} = \frac{\frac{0.1\,L/min}{0.34\,m^2}}{\frac{9.7\,L/min}{54\,m^2}} = 1.6 \qquad \textbf{(Equation A-3)}^{49}$$

This example assumes that the hypothetical chemical has been tested on Wistar rats and therefore utilizes the EPA animal default values for that strain. The V_e valued used is 0.14 L/min (0.20 m^3/day), which when multiplied by 0.7, yields a Q-alv of 0.1 L/min. The example uses the EPA default rat SA_{PU} of 0.34 m^2 (USEPA, 1994). EPA's default human values are 13.8 L/min (20

[49] This equation is the reduced, default version of Equation 4-23 of the *Inhalation Dosimetry Methodology*. Equation 4-23 is reduced to this form consistent with the derivation of the reduced form of the RGDR equation of extrathoracic effects described in section 4.3.6.1 and Appendix I of the *Inhalation Dosimetry Methodology*.

m^3/day) for V_e (which yields a Q-alv of 9.7 L/min) and 54 m^2 for SA_{PU} (USEPA, 1994). The RGDR for the PU region ($RGDR_{PU}$) is calculated using these values for the rat and the human, as shown in Equation A-3. The example also assumes a $NOAEL_{[ADJ]}$ of 0.16 mg/m^3 as the point of departure. The $NOAEL_{[HEC]}$ is the $NOAEL_{[ADJ]}$ multiplied by the $RGDR_{PU}$.

Table A-3 below provides the Q-alv values for humans based on the daily time-budgeted V_e for different ages and activity levels from the ICRP publication (1994). SA data for the PU region in the ICRP publication are estimated using an allometric scaling model fitted to data from a morphometric analysis of SA_{PU} in a sample of seven children (ranging in age from 26 days to 5 years) and eight adults (Zeltner et al., 1987). ORD selected the Zeltner analysis for this example because these SA_{PU} data are based on empirical morphometric measurements of human lungs as opposed to scaled estimates determined from lung models (such as those done by Yu and Xu, 1987 or Yu and Yoon, 1991). In addition, the children and adult SA_{PU} values calculated in the Zeltner analysis are supported by several independent studies that measured SA_{PU} in children (Langston et al., 1984) or in adults using similar morphometric techniques (Crapo et al., 1982 & 1983; Stone et al., 1992; Mercer et al., 1994).

Table A-3 shows little variation in the resultant $NOAEL_{[HEC]}$ across the groups in this example. The default procedure produces the lowest $NOAEL_{[HEC]}$ value in Table A-3 and is, therefore, sufficient to cover all of these groups.

TABLE A-3

COMPARISON OF THE HEC-DEFAULT (EPA, 1994) WITH EXAMPLE $LOAEL_{[HEC]}$ VALUES FOR HUMANS OF DIFFERENT AGES AND ACTIVITY PATTERNS FOR THE PULMONARY REGION

	Total V_e (L/min)[a]	$Q\text{-}alv_{(human)}$ (L/min)[b]	$SA_{PU\ (human)}$ (m^2)	$(Q\text{-}alv/SA_{PU})_{human}$ (L/min-m^2)	$RGDR_{PU}$	$NOAEL_{HEC}$ (mg/m^3)
Outdoor Worker, Male	17.5	12	139	0.088	3.3	0.53
Sedentary Worker, Male	15.4	11	139	0.078	3.7	0.59
Sedentary Worker, Female	12.6	8.8	114	0.077	3.8	0.61
15 Year-Old Male	14.0	9.8	108	0.091	3.2	0.51
15 Year-Old Female	10.9	7.6	100	0.076	3.8	0.61
10 Year-Old	10.6	7.4	62.0	0.12	2.4	0.38
5 Year-Old	6.1	4.3	37.3	0.11	2.6	0.42
1 Year-Old	3.6	2.5	18.5	0.14	2.1	0.34
3 Month-Old	2.0	1.4	11.0	0.13	2.2	0.35
HEC-Default	13.8	9.7	54.0	0.18	1.6	0.26

[a] These values are from the ICRP publication, Tables 8, 27, B.16a, B.16b and B.17 (ICRP, 1994).
[b] These values are from Zeltner et al. (1987).

4. CATEGORY 3 GASES

The DAF for a Category 3 gas or vapor is based on the ratio of the animal blood:gas partition coefficient to the human blood:gas partition coefficient and is typically calculated using the following equation:

$$DAF = \frac{(H_{b/g})_{animal}}{(H_{b/g})_{human}} \qquad \textbf{(Equation A-4)}$$

The blood:gas partition coefficient is primarily determined by the solubility of the gas in an aqueous medium as well as the protein and lipid content of the blood. There is little reason to suspect that the blood:gas partition coefficient for a non-metabolized chemical will vary greatly across the human population. The limited data available indicate no difference in the blood:gas partition coefficient with age for methylene chloride in mice (Thomas et al., 1996), and for sevoflurane, isoflurane, and halothane in humans (Malviya and Lerman, 1990). Two studies examining the solubility of volatile anesthetics (isoflurane, enflurane, halothane, and methoxyflurane) in the blood and body tissues found higher blood:gas partition coefficients in adults compared with children (Lerman, et al., 1984 & 1986). Any variability in the blood:gas partition coefficient with age is expected to be less than the default value of 10 used for the uncertainty factor for intraspecies variability when deriving the RfC. Any variability in the blood:gas partition coefficient with age is also not expected to cause a large overestimate or underestimate in the calculated cancer risk.

Because of the limited data available, the *Inhalation Dosimetry Methodology* makes the science policy decision to use a value of one for the ratio of the partition coefficients when the animal to human ratio exceeds one or when the animal or human value is unknown. At this time, all chemicals on IRIS for which both human and animal data are available have an animal to human ratio of partition coefficient greater than 1.[50] Therefore, the default assumption of one is a conservative approach that is not likely to underestimate the chemical-specific DAF.

5. PARTICLE DEPOSITION ACROSS AGE GROUPS

The DAF for a particle causing an effect in the respiratory tract, the Regional Dose Deposition Ratio ($RDDR_r$), is based on the animal to human ratio of the V_e and the fractional deposition of the particle in that region (F_r), divided by the surface area of the region where the effect occurs (SA_r) (USEPA, 1994). Inherent in this derivation is the assumption that 100 percent of the deposited dose remains in the respiratory tract and any clearance mechanisms are not considered. The $RDDR_r$ is typically calculated using the following equation:

$$RDDR_r = \frac{\left(\frac{V_e}{SA_r} \times F_r\right)_{animal}}{\left(\frac{V_e}{SA_r} \times F_r\right)_{human}} \qquad \textbf{(Equation A-5)}$$

[50] While 1,4-dioxane has not yet been evaluated on IRIS, it provides an exception to this statement, in that the blood:gas partition coefficient is 2750 for mice, 1850 for rats, and 3650 for humans, yielding an animal to human ratio of 0.75 for mice and 0.51 for rats (Reitz et al., 1990).

The DAF for a particle causing an extra-respiratory (ER) effect, the $RDDR_{ER}$, is based on the animal to human ratio of the V_e and the total deposition of the particle in the entire respiratory tract (F_{total}), divided by body weight (BW) (USEPA, 1994). The $RDDR_{ER}$ assumes that 100 percent of the deposited dose in the entire respiratory tract is available for uptake into the systemic circulation. The following general equation can be used to estimate the $RDDR_{ER}$:

$$RDDR_{ER} = \frac{\left(\frac{V_e}{BW} \times F_{total}\right)_{animal}}{\left(\frac{V_e}{BW} \times F_{total}\right)_{human}} \qquad \textbf{(Equation A-6)}$$

The information on particle deposition in various age groups is quite limited. A discussion of the current state of the science can be found in the *Air Quality Criteria for Particulate Matter Volume II*, Section 6.2.3.2 (USEPA, 2004; hereafter, *PM Criteria Document*).

Experimental and modeling results are summarized in Table A-4. The results for experimental studies are mixed, some suggesting higher deposition in children and others finding no difference across age groups. Bennett and Zeman (1998) and Schiller-Scotland et al. (1994) found no difference between total deposition of particles in the respiratory tract of children (aged 7 to14 and 6 to12, respectively) and adults for 1 to 2 micrometer particles. Schiller-Scotland et al. did find two- to three-fold higher total particulate deposition in 6 to 12 year olds for particles of 2 to 3 micrometers in size. In addition, Bennett et al. (1997) found that deposition in the ETh region was 50 percent greater in children than adults. The *PM Criteria Document* concludes that "these...studies ...do not provide unequivocal evidence for significant differences in deposition between adults and children" (USEPA, 2004, page 6-29). The document notes, however, that children may have higher activity levels and higher associated minute ventilation per lung size, potentially causing a greater size-specific dose of particles to the lung.

Modeled results suggest a higher deposition of particles in the TB region of children when compared to adults, depending on the particle size (Xu and Yu (1986); Hofmann et al. (1989); Musante and Martonen (1999); Phalen and Oldham (2001); Asgharian et al. (2004); Jarabek et al. (2005); Ginsberg et al. (2005)). Mixed results again are found in modeling studies for total deposition and deposition in other respiratory regions. In general, where differences are observed in either experimental or modeled studies, variability in deposition between age groups has been reported to be most often in the range of 1- to 3-fold greater for children than for adults, but ranging from equivalency or less up to 7-fold greater.[51]

[51] A modeling analysis examining deposition fraction per unit area at various airway generations of the lung as a function of age for various particle sizes (ranging from 0.01 to 10 μm) reported comparisons between a 3-month old and 21-year old that ranged from equivalency up to a 14-fold difference in this metric for some specific airway generations (Asgharian et al., 2004).

TABLE A-4
PARTICLE DEPOSITION ACROSS AGE GROUPS

Study	Particle Size	Results
		Experimental Studies
Becquemin et al. (1991)	Various	Nasal deposition higher in adults (up to 1.8-fold higher at rest and up to 3.4-fold higher during exercise) than children – meaning that thoracic airways of children are less protected than those of adults.
Bennett et al. (1997)	4.5 µm	-ETh deposition of particles 50 percent greater in children (higher for younger ages). -No significant difference in total respiratory tract deposition.
Bennett and Zeman (1998)	1-2 µm	No difference between 7-14 year olds and adults in total deposition of particles in the respiratory tract.
Schiller-Scotland et al. (1994)	1-2 µm	No difference between 6-12 year olds and adults in total deposition of particles in the respiratory tract.
	2-3 µm	Two- to three-fold higher total deposition of particles in 6-12 year olds versus adults.
		Modeled Studies
Asgharian et al. (2004)	0.01-10 µm	-Up to 1.2-fold higher total deposition in 3 month olds compared to adults in the TB region. -Up to 1.5-fold higher total deposition in 8 year olds compared to adults in the alveolar region. Total deposition higher in adults than 3 and 23 month olds (up to 2-fold). -Estimates of deposition fraction per unit area at various airway generations of the lung and various particle sizes highest for 3 month olds compared to adults (up to 14-fold). Higher deposition also seen for 23 month olds (up to 5-fold) and 8 year olds (up to 3-fold) compared with adults. No difference in deposition in 14 year olds compared to adults.
Cheng et al. (1995)	0.0046-0.2 µm	Nasal casts of children's airways found increased deposition efficiency for ultrafine particles with decreasing age, suggesting that young children may receive a higher dose of ultrafine particles to the upper airways.
Ginsberg et al. (2005)	0.001-10 µm	-Higher deposition in 3 month olds compared with adults for coarse and fine particles in the upper TB (up to 2-fold) and PU (up to 4-fold) regions. -Higher deposition in adults in the lower TB region.
Hoffmann et al. (1989)	1-2 µm	-1.5- to 2-fold higher total deposition in the TB region for particles in resting 8 year olds versus adults. -40-50 percent lower total deposition of particles in 8 year olds under conditions of exercise.
Jarabek et al. (2005)	0.3-6 µm	-Retained mass in the TB region normalized to regional SA was compared across age groups. -Up to 2-fold lower deposition in 3 month olds compared to adults. -Up to 2-fold higher deposition in 3 year olds and 14 year olds compared to adults.
Musante and Martonen (1999)	0.25-5 µm	-Total deposition was generally higher in children (ages 7, 22, 48, and 98 months) than adults (e.g., total lung deposition in 48-month olds was 38 percent higher than adults for 1µm particles). -TB deposition monotonically decreased as a function of age (i.e., younger children had increased TB deposition). -PU deposition greatest in the 48 and 98-month children.
Musante and Martonen (2000)	2 µm	3-fold higher deposition of particles in the PU region for 7 month olds versus adults.
Oldham et al. (1997)	Various	Airway models of trachea and bronchial airways showed total deposition in children (ages 4 and 7) greater than adult (up to approximately 7-fold higher for 4 year olds compared to adults for 4.5 µm particles).
Phalen and Oldham (2001)	0.1-10 µm	-No difference in total deposition of particles in 2 year olds versus adults. -Somewhat higher (13-81 percent; depending on particle size) deposition of particles in the TB region. -Lower deposition of particles in the PU region.
Xu and Yu (1986)	Various	Increased total deposition (up to 1.5-fold higher) in children aged 6 months, 2 years, and 8 years compared with adults for particles of varying sizes.

6. CONCLUSIONS

The examples and discussions included in this appendix suggest that the *Inhalation Dosimetry Methodology's* default approaches for derivation of the HEC for Category 1 gases with effects in the ETh, TB, and PU regions and for Category 3 gases typically are sufficient to cover variation across human age- and activity-level groups. The process for deriving an RfC from the HEC includes applying an uncertainty factor (UF) to account for within-species variability, adding further protection. When deriving an IUR for a carcinogen, UFs are not used. However the procedures for estimating an IUR incorporate conservative assumptions that would likely accommodate the degree of variation observed in these examples.

Experimental and modeling results for particles suggest the potential for small differences in deposition of particles in the respiratory tract as a function of age. The assumption that 100 percent of the deposited dose is available for uptake into the systemic circulation (for remote acting toxicants), or for activity in the respiratory tract (for local toxicity) is likely to result in an overestimation of dose to the target tissue. Any small variation in deposition among age groups should be considered against the potential magnitude of such overestimation. These differences in calculated deposition are small relative to the default 10-fold UF that accounts for intra-species variability in the derivation of the RfC. In addition, RfCs and IURs are developed for chronic exposure and will generally involve an exposure for multiple years. No additional correction of the toxicity values for these age groups is needed when the RfC or IUR is used in a risk assessment. Calculations in these examples are based on empirical data from sources listed and referenced in ICRP Publication 66 (ICRP, 1994). While ORD selected the ICRP values as the best estimates for these examples, other published values for V_e and SA exist. The use of alternate values may change the $LOAEL_{[HEC]}$ calculated for the various populations and life stages and may show more or less variability in results across the age and activity groups. In addition, the examples for the TB and PU regions are based on a hypothetical chemical, since currently no RfCs for gases on IRIS are calculated based on animal studies showing health effects occurring in these regions of the respiratory system. Given the parameter values used in the default method for calculating the HEC, it is likely that the process would yield results sufficient to cover populations and life stages with varying activities and physiologic characteristics.

Note that the available data, albeit limited, generally support these conclusions. As recommended by the Reference Dose (RfD)/RfC Technical Panel (USEPA, 2002), EPA has been exploring issues involving dose to the young from inhalation exposures, both theoretically and experimentally as well as further considering the existing animal-to-human extrapolation procedures described in current methodologies (e.g., USEPA, 1994). This is especially important because of the significant developmental changes that occur in the lung from birth well into adolescence (Pinkerton and Joad, 2000). The review and updating of these methodologies will be based on the best available science.

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APPENDIX B

APPENDIX B

CHEMICALS ON IRIS WITH EXTRAPOLATED INHALATION UNIT RISKS

Table B-1 contains chemicals on the Environmental Protection Agency's (EPA's) Integrated Risk Information System (IRIS) with Inhalation Unit Risk (IUR) values calculated by extrapolation using the default ventilation rate and body weight from the oral Cancer Slope Factor (CSF). These chemicals cause tumors remote from the respiratory tract. Also listed is the year EPA verified the cancer assessment. The list was compiled in September 2008.

EPA recommends that extrapolated IURs should be used with risk Equations 6 and 11 in the main document without additional modification for calculation of cancer risk by the inhalation route of exposure. It is generally not appropriate to make adjustments based on ventilation rate and body weight using the intake equation, because the amount of the chemical that reaches the target site of the chemical through the inhalation pathway is not a simple function of the inhalation rate and body weight. Risk assessors should outline the uncertainties involved in using extrapolated IURs in the risk characterization section of the risk assessment.

TABLE B-1 CHEMICALS WITH EXTRAPOLATED INHALATION UNIT RISKS ON IRIS	
Chemical	**Year of Verification**
Acrylamide[1]	1988
Aldrin	1987
Aramite	1991
Azobenzene	1988
Bromoform	1989
Chlordane	1997
Chloroform[1]	1987
DDT	1987
1,2-Dichloroethane	1986
Dieldrin	1987
1,2-Diphenylhydrazine	1986
Heptachlor	1987
Heptachlor epoxide	1987
Hexachlorobenzene	1989
Hexachlorobutadiene[1]	1986
Alpha-hexachlorocyclohexane	1986
Beta-hexachlorocyclohexane	1986
Technical-hexachlorocyclohexane	1986
Hexachlorodibenzo-p-dioxin mixture	1987
Hexachloroethane	1986
N-nitroso-di-n-butylamine	1986
N-nitrosodiethylamine	1986
N-nitrosodimethylamine	1986
N-nitrosopyrrolidine	1986
Polychlorinated biphenyls	1996
1,1,2,2-Tetrachloroethane	1986
1,1,1,2-Tetrachloroethane	1988
Toxaphene	1987
1,1,2-Trichloroethane	1986
2,4,6-Trichlorophenol	1989
[1] Note that this chemical's IUR is currently under review.	

APPENDIX C

APPENDIX C

STSC's PROCESS FOR DERIVING ALTERNATIVE INHALATION TOXICITY VALUES

If Reference Concentration (RfC) and/or Inhalation Unit Risk (IUR) values for an inhaled contaminant are not available from the sources in the Environmental Protection Agency's (EPA's) Office of Solid Waste and Emergency Response (OSWER) hierarchy, risk assessors should first contact the National Center for Environmental Assessment's (NCEA's) Superfund Health Risk Technical Support Center (STSC) for guidance.[52] Risk assessors working on Superfund sites can contact STSC to determine whether a provisional peer-reviewed toxicity value (PPRTV) exists for a contaminant; if not, the risk assessor, in cooperation with the appropriate EPA Regional office may request that STSC develop a PPRTV document or that STSC develop an inhalation toxicity value as a "consult." The latter would be specific to the site in question only.

As a first choice, if human or whole animal studies exist providing a suitable No Observable Adverse Effect Level (NOAEL)/Lowest Observable Adverse Effect Level (LOAEL) or Point of Departure (POD) from a Benchmark Dose (BMD) analysis, this data normally will be used by STSC to develop an inhalation toxicity value. If, in addition, a suitable human inhalation physiologically based pharmacokinetic (PBPK) model exists that can be utilized to refine the dose metric to the target organ, then this information generally will be included in developing an inhalation toxicity value.

If no appropriate whole animal or human studies exist, but an appropriate peer reviewed human inhalation PBPK model exists that has been validated by experimental results, then STSC usually will attempt to derive an inhalation toxicity value from this model. If none exists, but a suitable PBPK animal inhalation models exists, STSC may attempt developing a human model and deriving an inhalation value.

PBPK modeling quantitatively describes the absorption/metabolism/distribution and elimination of the chemical from a point of entry (oral, inhalation, dermal) to the target organ(s). In some cases, an oral PBPK model can be extrapolated to the inhalation pathway, but care must be taken to consider direct pulmonary effects that may not be evident by oral dosing.

As a next approach, STSC typically will evaluate development of an inhalation toxicity value using a suitable surrogate chemical based on a quantitative structure-activity relationship (QSAR) model with structural selection criteria and solubility/toxicity considerations. STSC may evaluate possible surrogate chemicals based on several available structural models and provide a comparison. Selection of the appropriate surrogate may depend on the weight of evidence of these models.

[52] All contact with STSC should be performed by an EPA regional risk assessor. States and other entities should first contact their EPA regional risk assessor with questions on inhalation toxicity values. Regional risk assessors can then contact STSC on their behalf.

If STSC uses any of the methods for developing toxicity values other than from human or whole animal data, the value normally will be presented as a "screening" value with the caveat that it should not be used as a risk driver for a site without consultation with the STSC. The uncertainties associated with using toxicity values derived through PBPK modeling or QSAR, or with using a surrogate value should be described in the risk characterization portion of the risk assessment (see Section 9). Risk assessors are discouraged from performing simplistic route-to-route extrapolations from oral data using default assumptions about Inhalation Rate (IR) and body weight (BW).[53]

[53] If STSC indicates that no quantitative toxicity information for the inhalation route is available, the risk assessor should conduct a qualitative evaluation of this exposure route. The risk assessor should discuss in the uncertainty section of the risk assessment report the implications of not quantitatively assessing risks due to inhalation exposures to chemicals lacking inhalation toxicity data. See the section on Risk Characterization (Section 9) in the main text of this guidance for more information.

Exhibit F

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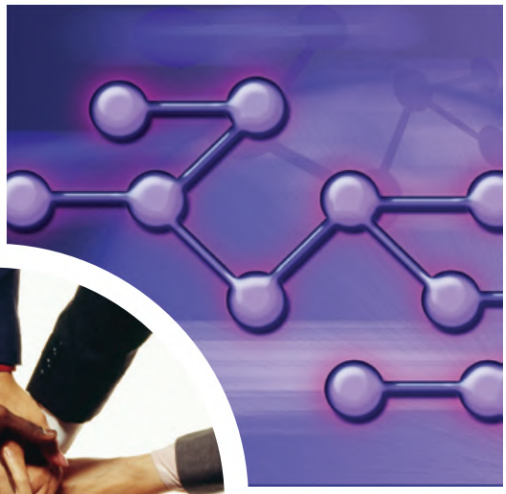
Interim Guidance on

Human Health Risk Assessment for Short-Term Exposure to Carcinogens at Contaminated Sites











Federal Contaminated Sites Risk Assessment in Canada

Canada

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FEDERAL CONTAMINATED SITES RISK ASSESSMENT IN CANADA

Interim Guidance on

Human Health Risk Assessment for Short-Term Exposure to Carcinogens at Contaminated Sites

2013
Prepared by:
Contaminated Sites Division
Safe Environments Directorate

TR 3664

REC 6468

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PREFACE

The Federal Contaminated Sites Action Plan (FCSAP) is a program of the Government of Canada designed to achieve improved and continuing federal environmental stewardship as it relates to contaminated sites located on federally owned or operated properties. Guidance documents on human health risk assessment (HHRA) prepared by the Contaminated Sites Division of Health Canada in support of the FCSAP are available on our website and may also be obtained by contacting the Contaminated Sites Division at *cs-sc@hc-sc.gc.ca*.

This interim guidance document provides additional direction for custodial departments with respect to amortization of short-term exposure to carcinogens at contaminated sites. It is of particular importance at remote sites or sites that are accessed infrequently. The guidance is intended to be advisory in nature and will be updated periodically on the basis of revisions to current expertise, applicable standards and recommendations received from stakeholders. Readers are advised to consult with Health Canada, Contaminated Sites Division, to confirm that they are using the most recent version available on the Health Canada website and that the use of HHRAs is reflective of current and best practices. This document is not to be considered a substitute for the guidance of a qualified professional practitioner.

Work and opinions from various consultants, academics and governmental agencies were used to create this guidance. In particular, Angela Li-Muller, Margaret Yole, Norm Healey and Sanya Petrovic of Health Canada are recognized for their contribution.

Health Canada requests that any questions, comments, criticisms, suggested additions or revisions to the document be directed to the following: Contaminated Sites Division, Safe Environments Directorate, Health Canada, 269 Laurier Avenue West, 4th floor, Address Locator: 4904A, Ottawa, ON K1A 0K9. Email: *cs-sc@hc-sc.gc.ca*.

See also: *www.hc-sc.gc.ca/ewh-semt/contamsite/index-eng.php*.

ABBREVIATIONS AND ACRONYMS

A-D	Armitage-Doll
ADAF	age-dependent adjustment factors
AF	absorption factor
ASF	age sensitivity factor
BHT	butylated hydroxytoluene
BW	body weight
C	concentration
CalEPA	California Environmental Protection Agency
CSD	Contaminated Site Division
DES	diethylstibesterol
DMBA	dimethylbenzanthracene
DNA	deoxyribonucleic acid
DQRA	detailed quantitative risk assessment
ED	exposure duration
ED_{01}	maximum likelihood estimate of the dose corresponding to a 1% additional cancer risk
ER	exposure rate
FCSAP	Federal Contaminated Sites Action Plan
HC	Health Canada
HHRA	human health risk assessment
ILCR	incremental lifetime cancer risk
IR	intake rate
LADD	lifetime average daily dose
LMS	linearized multistage
LOAEL	lowest observed adverse effect level
MVK	Moolgavkar-Venzon-Knudson
NOAEL	no observed adverse effect level
PAHs	polycyclic aromatic hydrocarbons
PBBs	polybrominated biphenyls
PBPK	physiologically based pharmacokinetic
PQRA	preliminary quantitative risk assessment
SF	slope factor
TC	tolerable concentration
TDI	tolerable daily intake
TRV	toxicological reference value
UR	unit risk
US EPA	United States Environmental Protection Agency

EXECUTIVE SUMMARY

This document provides guidance for application at federal contaminated sites funded under the Federal Contaminated Sites Action Plan (FCSAP). It is considered to be interim and is based on an assessment of the current scientific literature. The document does not represent the opinion of Health Canada outside the application of federal contaminated sites funded under the FCSAP.

The current approach to evaluating health risks associated with human exposure to carcinogens at contaminated sites focuses on incremental lifetime cancer risks. The approach to cancer risk assessment varies according to the mode of action at the tumour site in question. Unless there is evidence to support a threshold mode of action, the current approach assumes a linear dose-response relationship at low doses (i.e. non-threshold). The incremental lifetime cancer risk (ILCR) is calculated as a product of the lifetime daily dose (or concentration) and the toxicological reference value (TRV), expressed as cancer slope factor (or inhalation unit risk).

A threshold approach can be applied when there are sufficient data to ascertain the mode of action at the tumour site in question and to conclude that the dose-response relationship is not linear at low doses. For these carcinogenic effects, the TRVs are expressed as tolerable daily intakes (TDIs) or concentrations (TCs), the intakes or concentrations to which it is believed that a person can be exposed daily over a lifetime without deleterious effects. Human exposure is compared with these TRVs, where appropriate, to determine health risks.

Characterization of human cancer risks usually makes use of TRVs that have been derived from epidemiological or toxicological studies with comparable exposure patterns. TRVs for carcinogens are often based on the results of animal studies in which the animals were exposed on a daily basis throughout their adult lifespan. Exposures at contaminated sites may mirror these exposure patterns, but in some circumstances exposures may occur over a period of time much shorter than the lifetime of the exposed individual. In a short-term exposure scenario, short-term exceedance (or excursion) above chronic average daily exposure could occur as a result of variation in intake rates or daily fluctuation in chemical concentrations in environmental media. As a result, the health risks of short-term exposure often need to be addressed.

For contaminated site risk assessments, the current practice of characterizing ILCR associated with less-than-lifetime exposures to carcinogens that act via a non-threshold mode of action involves averaging the short period of exposure over a lifetime to calculate the lifetime average daily dose (LADD). Several issues regarding this practice of averaging the exposure have been raised:

- There is a potential for underestimating cancer risks with the practice of time-averaging of exposures (LADD).
- Variability in sensitivity among different lifestages may not be fully considered.

In addition, depending on the magnitude of exposure, carcinogenic agents may elicit other, chronic and short-term non-cancer health effects as a result of short-term exposures. At present, these effects are often not evaluated.

The Contaminated Sites Division (CSD) will continue to review information related to risk assessments for carcinogenic agents, including short-term exposure and dose averaging.

Cancer Risk Assessment: Non-Threshold Carcinogenic Effects

A literature review was conducted to evaluate whether averaging short-term exposure over a lifetime would be adequate to estimate cancer risk using cancer slope factors derived from chronic animal studies. Both theoretical studies using mathematical models of carcinogenesis and empirical studies involving exposure during discrete age windows suggest that exposures in early lifestages are usually associated with a higher risk of carcinogens acting through a mutagenic mode of action. It was concluded that application of age-dependent adjustment factors to the cancer slope factor with exposure averaged over a lifetime can provide a generally conservative estimate of lifetime cancer risks. As an interim measure, the United States Environmental Protection Agency (EPA) approach has been adopted as a default recommendation for contaminated site risk assessments.

The ILCR can be estimated by summing the risk from each discrete exposure period. For non-threshold carcinogens acting through a mutagenic mode of action, it is recommended that age-dependent adjustment factors (ADAFs) be applied to the cancer slope factor (or inhalation unit risk) with exposure averaged over a lifetime to account for the sensitivity of the age-specific exposure period. We have developed default ADAFs by adjusting the US EPA's ADAFs to be consistent with the age groups recommended by CSD. These default factors can be applied when age-specific cancer slope factors (or inhalation unit risks) or chemical-specific data are not available.

When exposure periods do not match the CSD's age groupings, CSD recommends that the US EPA's ADAFs be applied. For example, if exposure occurs only between 7 months and less than 2 years of age, the adjustment factor of 10 applies. Likewise, if exposure occurs only between 12 and < 16 years of age, the ADAF of 3 applies. When chemical-specific data are available for a susceptible lifestage, these data can be used directly to evaluate risks for the chemical and the lifestage on a case-by-case basis.

Recommended interim adjusted age-dependent adjustment factors (ADAFs) for cancer risk assessment at contaminated sites for carcinogenic effects via a mutagenic mode of action

Lifestage	Age	Adjusted age-dependent adjustment factor (ADAF)[a]
Infant	0–6 months	10
Toddler	7 months–4 years	5[b]
Child	5–11 years	3
Teenager	12–19 years	2[c]
Adult	20+	1

[a] US EPA (2005 a, b), except as noted.

[b] $ADAF_{7\ mo-4\ yr} = (ADAF_{0-<2} * D_{7\ mo-1} / D_{7\ mo-4}) + (ADAF_{2-4} * D_{2-4} / D_{7\ mo-4}) = 10 * 1.5/4.5 + 3 * 3/4.5 = 5$, and D_i = exposure duration in years

[c] $ADAF_{12-19} = (ADAF_{12-<16} * D_{12-15} / D_{12-19}) + (ADAF_{16+} * D_{16-19} / D_{12-19}) = 3 * 4/8 + 1 * 4/8 = 2$, and D_i = exposure duration in years

When the mode of action is unknown or the burden of proof for a threshold mode of action has not been met, CSD recommends a non-threshold approach to cancer risk estimation. If chemical-specific data are available on quantitative differences between early lifestages and adults, an analysis of the differences could be used to adjust risk estimates for early life exposures. Otherwise, CSD does not recommend extending the default age-dependent potency adjustment factors to these carcinogenic effects. This position would be analogous to recommending a default ADAF of 1 for all lifestages.

Cancer Risk Assessment: Threshold Carcinogenic Effects

At this time, the CSD does not recommend a default age-specific adjustment for carcinogenic effects determined to have a non-linear dose-response relationship (i.e. threshold) at low doses. Adjustment can be made on a chemical-specific basis if supported by experimental data. These substances would be included in an HHRA using a TDI (or a TC in the case of inhalation exposure).

The CSD recommends that dose averaging for short-term exposure for these types of carcinogenic effects be performed in the same way as for substances with threshold non-carcinogenic effects. It is important that dose averaging should not underestimate the potential for threshold carcinogenic effects. Without a sound basis for doing so (i.e. it cannot be a default assumption), the human health risk assessor should not simply mathematically spread out a short-term dose over a longer period and conclude that the short-term dose is toxicologically equivalent to a lower dose over the long period. Instead, exposure should be averaged over the total actual exposure period and compared with the appropriate TRV. A scientific rationale is required to support any proposed amortization (dose averaging beyond actual exposure period) to ensure that short-term risks are not underestimated. This analysis needs to be done on a chemical-specific basis.

Assessment of Potential Non-Cancer Health Effects from Short-Term Exposure

For short-term exposure, carcinogenic agents may elicit other, chronic and short-term non-cancer health effects, depending on the magnitude of exposure. Short-term effects can be evaluated for potential critical receptors/lifestages[1] using short-term TRVs where available (either from other regulatory agencies or derived from literature values as per the Health Canada, 2010, detailed quantitative risk assessment [DQRA] guidance) and when applicable to the exposure scenarios. If short-term TRVs are not available, such evaluation can be conducted on the basis of relevant dose-response information from toxicity studies. It is also important to consider whether the short-term exposure might elicit early biological key events that might progress to health effects at a later date.

[1] Including relevant receptors/lifestages with the highest exposure and receptors/lifestages associated with specific sensitivity to the toxicity of the contaminants.

1.0 INTRODUCTION

1.1 Current Cancer Risk Assessment Approach

Health Canada's Contaminated Sites Division (CSD) has a current risk assessment approach for carcinogenic effects that assumes a linear dose-response relationship at low doses (non-threshold) unless there are adequate data to ascertain a mode of action that is consistent with a non-linear dose-response relationship at low doses (i.e. threshold). This approach is particularly relevant for agents that are mutagenic[2] and DNA reactive. The incremental lifetime cancer risk is calculated as a product of the lifetime daily dose and cancer slope factor.

A threshold approach can be applied when there are sufficient data to ascertain the mode of action at the tumour site in question and to conclude that the dose-response relationship is not linear at low doses. Such a carcinogenic agent usually has not been shown to demonstrate mutagenic or other properties consistent with linearity at low doses. Endocrine disruption, cell proliferation, cytotoxicity and receptor-binding are some examples of a non-linear mode of action. For these carcinogenic effects, the CSD risk assessment approach assumes a non-linear dose-response relationship at low doses. The toxicological reference value (TRV) is derived by applying an uncertainty factor to a benchmark dose or benchmark concentration (if available)—a NOAEL (no observed adverse effect level) or a LOAEL (lowest observed adverse effect level)—as appropriate to establish a tolerable daily intake (TDI) or concentration (TC), i.e. the intake or concentration to which it is believed that a person can be exposed daily over a lifetime without deleterious effects.

In many cases, non-carcinogenic effects rather than carcinogenicity may be the main determinant of health risk from long-term exposure to the threshold carcinogenic agent. For example, the developmental effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin occur at lower exposure levels than those required for carcinogenicity and have been used to establish the TRV.

1.2 Issues Related to Less-Than-Lifetime Exposure to Carcinogens at Contaminated Sites

Short-term exposure to carcinogens at contaminated sites may be associated with activities that occur over a relatively short period of time, such as seasonal activities like camping, occasional visits to a remote site and certain occupational activities, e.g. construction and underground service installation. As a result, short-term health risks need to be addressed.

The significance of exposure to contaminants is best characterized by comparison with TRVs derived from epidemiological or toxicological studies with comparable exposure patterns (i.e. short-term exposure compared with TRVs derived from a short-term study). Otherwise, significant uncertainty could be introduced into risk characterization.

TRVs for carcinogens are often based on the results of animal studies in which the animals were exposed on a daily basis throughout their adult lifespan. Exposures to human receptors at a contaminated site may mirror this pattern of exposure, but more often exposure occurs for only a portion of the lifetime or may be intermittent. Exposures at a contaminated site may occur during childhood or in utero, lifestages not represented in standard cancer bioassays.

The current practice of characterizing incremental lifetime cancer risks (ILCR) associated with less-than-lifetime exposures to non-threshold carcinogens involves averaging the short period of exposure over a lifetime to calculate the lifetime average daily dose (LADD). The following issues related to dose averaging (sometimes referred to as dose amortization) have been raised when exposures occur over a short time frame:

1. There is a potential for underestimating cancer risks with the calculation of a LADD associated with a short exposure period.
2. The possibility of acute/subchronic non-cancer effects due to elevated exposures has not been considered and may be relevant when the exposure is elevated above the LADD over a subchronic period. For example, the physiological response will be different following a large short-term exposure as compared with the same exposure averaged over a longer period.
3. Variability in sensitivity among different lifestages may not have been fully considered. For example, the prenatal and neonatal periods, childhood, adolescence, and peri-menopausal and senior lifestages, as well as genetic predisposition, are currently not included in standard adult animal bioassays for deriving estimates of cancer potency.

This document provides a background discussion on each of these issues and presents interim guidance and supporting rationales.

[2] A carcinogen acts via a mutagenic mode of action if the carcinogen or its metabolite is DNA-reactive or has the ability to bind to the DNA. Mutagenicity is "the induction of permanent, transmissible changes in the amount, chemical properties or structures of the genetic material. In most cases, mutation involves changes in DNA structure that either have no effect or cause harm" (USEPA, 2005b; Schoeny, 2011).

1.3 Practice of Dose Averaging

Dose averaging refers to the practice of time averaging a short period of exposure or several intermittent short-duration exposure(s) over a longer duration. This practice is also referred to as exposure amortization. It assumes toxicity to be linearly proportional to the magnitude and duration of exposure. For example, it assumes an exposure of 365 µg/kg bw-day for 1 day, 36.5 µg/kg bw-day for 10 days and 1 µg/kg bw-day for 365 days to be toxicologically equivalent, which could be untrue. The risk for the shorter-term exposure could be underestimated. With this practice, daily exposures that exceed the maximum chronic acceptable daily dose (either a TDI or a risk-specific dose) may be incorrectly considered acceptable because they occur for only a short period of time. In the case of threshold carcinogens, this practice raises questions about the magnitude by which the TDI can be exceeded and for what duration before unacceptable chronic health risks (including carcinogenicity) are possible or expected. For non-threshold carcinogens, the practice raises the question of whether a high dose over a short period results in the same lifetime cancer risk as the same total dose over a lifetime. Also at issue is whether the short-term exposure could elicit adverse acute/subchronic non-carcinogenic health effects.

The answers to these questions, in part, depend on the following:

- when (at what lifestage) the excess exposure is expected to occur;
- whether there are any specific sensitivities associated with that lifestage; and
- whether these sensitivities have been accounted for (perhaps through application of uncertainty factors) in the TRV.

2.0 DOSE AVERAGING FOR NON-THRESHOLD CARCINOGENIC EFFECTS

The current practice of characterizing incremental cancer risks associated with less-than-lifetime exposures involves averaging the short period of exposure over a lifetime to calculate the LADD. This practice assumes that the overall incremental cancer risk is a function of the total dose received and is independent of the exposure pattern: a high dose of a carcinogen received over a short period is assumed to be equivalent to the corresponding total dose spread over a lifetime (US EPA, 1986). However, this practice is not based on firm scientific evidence or principles (Hrudey, 1998), and the US EPA (1986) has acknowledged that the approach is fraught with uncertainty; it recommends that risk assessments include a qualitative discussion of the uncertainty of this assumption.

Various groups of scientists have expressed concern that the LADD approach could underestimate cancer risk (Kodell et al., 1987, Chen et al., 1988; Murdoch et al., 1992; US EPA, 2005a; Halmes et al., 2000); the summary of some of these studies is presented in Table 2. In addition, the age at which short-term exposure occurs could influence cancer risk, as different lifestages may vary in susceptibility (Drew et al., 1983; Crump and Howe, 1984; Ginsberg, 2003; US EPA, 2005a, 2005b; Hattis et al., 2004, 2005).

The uncertainty of the practice was identified as an issue "under review" in Health Canada's (2004) guidance on Human Health Preliminary Quantitative Risk Assessment for contaminated sites. Since that publication, Health Canada's CSD has commissioned a series of contractor reports from consulting and academic experts (Brand, 2004; GlobalTox International Consultants, 2005; Wilson Scientific Consulting Inc., 2006; Orr, 2007; Al-Zoughool and Krewski, 2008) to aid in the decision-making on this issue.

Table 2.1 Summary of modelling studies that compare cancer risks from short-term exposure with those from lifetime-equivalent exposure (extent of under/overestimation reported quantitatively for short-term adult exposure only)

Reference	Study type	Qualitative assessment	Range of most likely predicted LADD underestimate to overestimate of risk	Maximum predicted underestimate (overestimate) of risk
Murdoch et al., 1992	Theoretical modelling for 30-day exposures of astronauts aged 25 to 45 to hypothetical carcinogens inside the space station. Both A-D[a] multistage and MVK[b] models were used.	LADD may underestimate or overestimate risks.	–2 to +6 fold (A-D multistage model); –2 to +7 fold (MVK model)	–2 (+33) fold (A-D multistage model); –1.4 (+63) fold (MVK model)
Kodell et al., 1987	The A-D multistage model was used to model intermittent exposure to a hypothetical carcinogen starting at age 0, 10, 20 and 50 for 1, 10 and 20 years. The ratio of excess risk for intermittent dosing relative to predicted excess risk based on LADD was calculated.	LADD underestimates risk maximally when the number of cancer stages is assumed to be 6, the 1st stage is dose-dependent and exposure occurs during years 1–10 of life.	–3 to +14 fold	–3 (> $+10^5$) fold
Chen et al., 1988	The MVK model was used to calculate the ratio of excess risk for short-term exposure to a hypothetical carcinogen to predicted excess risk associated with underlying assumptions of LADD, with various input parameters, including duration of exposure and start time of exposure.	LADD underestimates risk maximally with early-stage carcinogen and exposure early in life.	–2 to +13 fold (initiator); –4.5 to +13 fold (completer); –9 to +9 fold (promoter)	–2 (> +100) fold (initiator); –5 (> +25) fold (completer); –77 (+100) fold (promoter)

[a] Armitage-Doll

[b] Moolgavkar-Venzon-Knudson

2.1 Dose Averaging for Less-Than-Lifetime Adult-Only Exposures

The issue of dose averaging can be confounded by the potential for varied susceptibility among different lifestages. The TRV developed from studies involving adult-only exposure (e.g. occupational studies) may be inadequate to account for earlier sensitive lifestages, especially when short-duration, high-magnitude exposure is experienced during these sensitive time windows. For this reason, less-than-lifetime exposure occurring only during the adult lifestage is addressed first. In this case, the only issue leading to the potential underestimate of health risk is assumed to be the mathematical manipulation of the level of exposure. For example, daily occupational exposures occurring 5 days per week for 48–52 weeks per year are amortized to the equivalent daily dose over 7 days per week for 52 weeks per year (resulting in a lower calculated daily exposure). Amortization of this magnitude is common, as TRVs are often derived from epidemiological studies based in occupational environments. Similarly, animals are dosed 5 days per week in some toxicity studies.

Two general lines of inquiry have been explored to determine the extent to which time averaging may over or underestimate cancer risks in adult-only exposures:

1. Evidence from animal bioassays or epidemiological studies in which the cancer risks estimated from short-term exposures are compared with those derived from adult lifetime exposures.
2. Comparison of the cancer risk estimates from short-term exposures with those derived for lifetime exposures at the LADD-equivalent dose using generally accepted mathematical models of carcinogenesis.

2.1.1 Dose Averaging Implications from Adult Animal Bioassays

Standard carcinogenicity bioassays involve near-lifetime exposures; however, exposures of very limited duration may also result in tumour formation. A literature review by Calabrese and Blain (1999) found 426 chemicals from a broad range of chemical classes that could induce cancer after a single administration in a large number of animal models. Most of these chemicals, if not all, were found to be genotoxic. Thirty nine percent caused more tumours, 22% caused fewer tumours, and the remaining 39% showed similar tumourigenic responses when the carcinogen was administered as a single dose as compared with the same dose fractionated over a lifetime. However, Calabrese and Blain (1999) and others (Ginsberg, 2003) did not consider varied lifestage susceptibility when analyzing the available data, which involved a single exposure at different lifestages (i.e. fetal, neonatal).

Stop-exposure studies (summarized in Table 2.2) illustrate the influence of exposure schedule and duration on cancer risk. Exposures were stopped after only a portion of the animal's lifespan, and the animals were observed long enough to measure tumour development.

Table 2.2 Summary of studies comparing cancer risks from short-term (adult-only) exposure with those from lifetime-equivalent exposure (with same total dose)[a]

Reference	Study type	Qualitative assessment	Range of most likely predicted LADD underestimate to overestimate of risk	Maximum predicted underestimate (overestimate) of risk
	Animal experiments			
Halmes et al., 2000	Animal stop-exposure—data from 11 National Toxicology Program studies (adult animals—male rats or mice). Cancer potency was estimated using 2-year continuous bioassay data with or without inclusion of stop-exposure data.	Tumour responses in the stop-exposure experiment were underpredicted by continuous exposure data at 34/59 tumour sites for 6/11 chemicals, and overpredicted at 2/59 tumour sites for 2/11 chemicals. Prediction was accurate for 26/59 tumour sites for 9/11 chemicals.	Undefined	Undefined
		Inclusion of stop-exposure data in ED_{01}[b] estimation (as compared with using continuous bioassay data alone) led to a decrease for 63% of the chemical/tumour/site combinations and an increase for 17% of the chemical/site combinations, mostly within one order of magnitude. 15% (of all tumour sites examined) showed a greater than 10-fold decrease (greater risk or potency) in ED_{01}, implying a higher risk with shorter exposure.	Undefined	Undefined
		The "equivalent averaging times"[c] for the stop-exposures were generally longer than the actual exposure durations but less than 104 weeks for 12 of the 14 dose groups for which this comparison was made. The median "equivalent averaging time" for all the groups was 62 weeks, indicating that averaging stop-exposure duration over a lifetime (LADD) would underestimate the risk by a median factor of 2.	–5 to +2 fold	–5 (+2) fold

Table 2.2 – cont'd ➜

Reference	Study type	Qualitative assessment	Range of most likely predicted LADD underestimate to overestimate of risk	Maximum predicted underestimate (overestimate) of risk
Drew et al., 1983	Animals exposed to constant concentrations of vinyl chloride (adult animals—rats, 2 strains of mice, hamsters) by inhalation. Animal age at the start of exposure and exposure duration were varied among different exposure groups.	For most of the animal species studied, exposure from months 2–8 of life produced higher tumour frequency than exposure at later lifestages for the same duration (8–14, 14–20 or 20–26 months of age), possibly because animals died before a potential tumour could be expressed in the latter groups.	Undefined	Undefined
Hattis et al., 2004	Animals—rats and mice exposed to four types of ionizing radiation at different stages of life	On the basis of a total of 138 group tumour incidence observations, dosage delivered to older animals (6–12 or 19–21 months old) appeared to be 3 fold less effective than a similar dosage delivered to young adult animals (3–3.5 months), suggesting greater sensitivity during early adulthood.	Undefined	Undefined
	Epidemiological studies			
Hauptmann et al., 2000	Case-control study of lung cancer and smoking in adults (4300 cases). The effect of smoking pattern on lung cancer risk was examined using a linear model taking into consideration that different exposure periods vary in their contribution to the overall cancer risk.	The number of cigarettes smoked within 5–15 years prior to patient interview strongly determined lung cancer risk; the number smoked more than 20 years earlier contributed minimally to risk. The pattern corresponds to an observed decrease in risk corresponding to the time since smoking cessation. Authors concluded that use of cumulative or average dose may not be appropriate for estimating lung cancer risk.	Undefined	Undefined
Hauptmann et al., 2002	Pooled data from two German case-control studies (2652 cases) on asbestos and lung cancer were assessed in terms of various exposure metrics.	The results suggested that cancer risk increased for 5–15 years after exposure and then declined. Other studies have indicated a 20–40 year latency period for asbestos-induced lung cancer. Dose averaging over a lifetime would underestimate the risk for people whose remaining lifespan is greater than the latency period and would overestimate the risk for people whose remaining lifespan is shorter than the latency period.	Undefined	Undefined

Table 2.2 – cont'd ➜

Reference	Study type	Qualitative assessment	Range of most likely predicted LADD underestimate to overestimate of risk	Maximum predicted underestimate (overestimate) of risk
Elwood et al., 1985; Elwood, 1992	Histories of exposure to sun of 595 patients with malignant melanoma in Western Canada were examined in a case-control study.	Significant increase in risk was correlated with summer vacation and recreational activities with intense sun exposure. A moderate amount of total occupational exposure (likely from intermittent seasonal exposure) increased the risk; further increased exposure (> 200 whole body equivalent hours of exposure per season associated with long continuous exposure) had no effect or resulted in decreased risk (for men). At the same total sun exposure, the relative risk of melanoma from short-term intermittent recreational exposure exceeded long-term occupational exposure by up to 2 fold.	+1 to –2 fold	–2(+1)

[a] Adapted from Tables 4.5-1 and 4.5-2 in Orr (2007); edited to exclude studies in which juvenile exposures were compared with adult exposures.

[b] ED_{01} is the maximum likelihood estimate of the dose corresponding to a 1% additional cancer risk.

[c] Equivalent averaging time is the length of time over which stop-exposure doses have to be averaged so that the observed response falls exactly on the fitted dose-response curve developed from the continuous exposure (i.e. 104 weeks) data.

Halmes et al. (2000) evaluated cancer data from 12 similar United States National Toxicology Program animal bioassays in which both chronic lifetime and stop-exposure dosing protocols (using male rats except for 1,3-butadiene, to which male mice were exposed) were followed. The Weibull Model was fitted first to the chronic data only and then to the combined chronic and stop-exposure data adjusted to average lifetime exposure. Tumours developed following exposure to 11 chemicals (acting through different modes of action), some at multiple sites, totalling 59 chemical/site combinations. The same response rate was observed for 44% of the chemical/tumour site combinations. However, for 46% of the chemical/tumour site combinations, the response rate was higher in the stop-exposure groups than the chronic lifetime exposure groups. About 5% showed a lower response in the stop-exposure groups than the chronic lifetime exposure groups. Therefore, the assumption of equivalent cancer risk at equivalent total doses (i.e. that the product of concentration and time is constant independent of the exposure pattern) was incorrect at least half of the time. Combining stop-exposure and continuous exposure data in ED_{01}[3] estimation showed varied effect. Inclusion of responses from the stop-exposure groups led to a decrease in the ED_{01} (greater risk or potency) for 63% of the chemical/tumour/site combinations and an increase in the ED_{01} (lesser risk or potency) for 17% of the chemical/site combinations, mostly within one order of magnitude. While the overall change was less than 2-fold (in either direction) for 36% of the tumour sites examined, approximately 15% (of all tumour sites examined) showed a greater than 10-fold decrease (greater risk or potency) in ED_{01}, implying a higher risk with shorter exposure. The largest reduction was 102-fold for lymphomas following 1,3-butadiene exposure.

Halmes et al. (2000) also evaluated dose averaging by determining the "equivalent averaging time". Equivalent averaging time is the length of time over which stop-exposure doses have to be averaged so that the observed response falls exactly on the fitted dose-response curve developed from the continuous exposure (i.e. 104 weeks) data. This method of evaluation has a direct implication for cancer risk assessment. The stop-exposure studies exposed animals for varying durations that ranged from 13 weeks to 66 weeks. For most endpoints, the "equivalent averaging times" were generally longer than the actual exposure durations but less than 104 weeks for 12 of the 14 dose groups for which this comparison was made. The median "equivalent averaging time" for all the groups was 62 weeks, indicating that averaging the stop-exposure dose over a lifetime (i.e. LADD) would underestimate cancer risk by a median factor of 2 (ranging from an overestimation of 2-fold to an underestimation of 5-fold).

In addition to duration-related variability (i.e. short-term versus long-term exposures), carcinogenic sensitivity may not be constant throughout the adult period. On the basis of their analysis of animal (rats and mice) experimental data involving four different types of ionizing radiation, Hattis et al. (2004) demonstrated that the dosage delivered to older animals (6–12 months or 19–21 months old) appeared to be several-fold less effective than a similar dosage delivered to young adults (3–3.5 months old), suggesting greater sensitivity for exposures in early adulthood.

In summary, experimental data with animals suggest that averaging short-term exposure over a lifetime results in uncertainties and may overestimate or underestimate the risk when exposure occurs during adulthood. The level of underestimation or overestimation is generally within an order of magnitude for the substances studied. However, many carcinogens found at contaminated sites have not been studied in this manner.

2.1.2 Dose Averaging Implications from Adult Exposures in Epidemiological Studies

The available epidemiological data on the effect of exposure patterns on cancer risks (summarized in Table 2.2) are limited, lung and skin cancer being the most frequently studied.

A review (Wilson Scientific Consulting Inc., 2006) of the literature on cancer risk from smoking indicates a general scientific consensus that cancer risk decreases for individuals who quit smoking when compared with those who continue to smoke, the extent of the reduction lessening as the age of quitting increases. The review concluded that an appreciable amount of cancer risk is removed 10 years after smoking cessation. However, although smoking reduction may also lead to reduced lung cancer risk, the conclusion did not consider the intensity of smoking or the age of the smoker. Smoking is a unique activity that involves inhaling a high dose of a mixture of carcinogenic and non-carcinogenic chemicals, which include irritants and pharmacologically active levels of nicotine. The effects of both psychological and physical addiction as well as other socioeconomic factors may not have been accounted for in the analyses. Therefore, the exposure–risk relationship observed for smoking may not be applicable to carcinogens and exposures typical of contaminated sites. In addition, the available analysis of the smoking data lacks a quantitative comparison of the cancer risks predicted by LADD and alternative approaches with the observed cancer risks as a function of smoking intensity (dose) and duration.

Hauptmann et al. (2002) investigated lung cancer risk associated with occupational exposure to asbestos in two German case-control studies. The data suggest that an individual's lung cancer risk increased for 5–15 years after exposure and then declined. The risk declined to about one-half after more than 20 years from the final exposure. When individual risks were modelled and compared, the risk was higher and peaked earlier at high exposure rates as

[3] Maximum likelihood estimate of the dose corresponding to a 1% additional cancer risk.

compared with lower exposure rates (5 fiber-yrs/yr for 5 years versus 0.5 fiber-yrs/yr over 50 years). The result suggests that dose averaging over a lifetime would underestimate the risk, especially for people whose remaining lifespan is longer than the latency period. On the other hand, the risk would be overestimated for people whose remaining lifespan is shorter than the latency period.

Case control studies of the incidence of melanoma or basal cell carcinoma involving patients 20–79 years of age with a recent diagnosis in Western Canada (Elwood et al., 1985) found an individual's total dose alone did not determine cancer risk, as the intensity of exposure also played a role. Activities that likely involved more intense sun exposure (vacation and recreation) conferred a greater level of risk (by up to 2-fold) than if the same dose had been achieved by predominantly occupational exposure. A moderate amount of occupational sun exposure (likely from intermittent seasonal exposure) increased the risk, but further increase in exposure (typical of chronic occupational exposure) either had no effect or resulted in decreased risk (for men) (Elwood, 1992). Other major studies showed a similar pattern following intermittent exposures, although results from the northern hemisphere studies are more definitive than from Australian studies (Kricker et al., 1995), partly because the total dose received in Australia is so much greater (Elwood, 1992).

The limited human data associated with short-term or intermittent exposure support the notion that averaging short-duration or intermittent exposure over a longer time period may not be appropriate for predicting cancer risk.

2.1.3 Theoretical Cancer Modelling Studies of Less-Than-Lifetime Exposure

Mathematical models of cancer, such as the A-D multistage model and MVK model (the latter model is also known as the two stage birth-death-mutation model), are generally compatible with the current understanding of the mechanism of carcinogenesis. The A-D multistage model assumes cancer to be the end result of a normal cell going through a finite number (e.g. k) of irreversible independent transitions (stages) that must take place in a specific order (Armitage, 1985; Al-Zoughool and Krewski, 2008). The MVK model assumes that the clonal expansion of cancer involves two discrete phases: initiation (due to genetic damage) and malignant conversion with progression (Al-Zoughool and Krewski, 2008). Although these models have not been validated (United Kingdom Department of Health, 2004), they have been used to describe the age-dependent rate of cancer formation and to explore the extent to which the LADD approach could over or underestimate cancer risk resulting from less-than-lifetime exposure scenarios (Kodell et al., 1987; Murdoch and Krewski, 1988; Chen et al., 1988; Murdoch et al., 1992, Al-Zoughool and Krewski, 2008). These analyses may provide insight into the upper bound estimate of the level of over or underestimation of the risk.

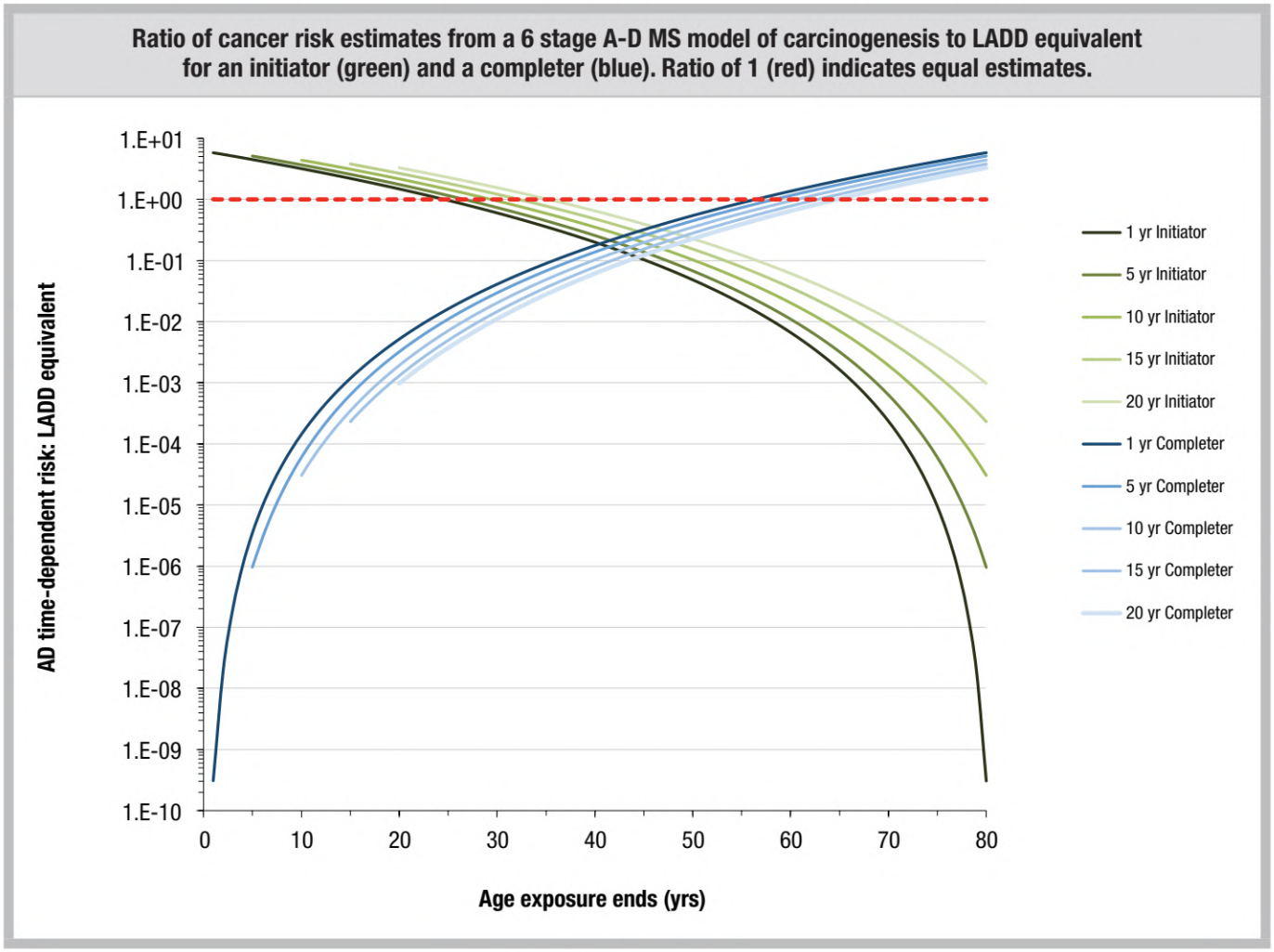
Using the A-D multistage time-to-tumour model, a number of publications (Murdoch et al., 1992; Al-Zoughool and Krewski, 2008; Kodell et al., 1987) have demonstrated the propensity of LADD to over or underestimate cancer risk under certain exposure scenarios. The theoretical upper bound of underestimation by the LADD approach was also estimated. The consensus is that the LADD approach can over or underestimate cancer risks for less-than-lifetime exposures depending on the exposure. The greatest extent of underestimation was postulated for two general scenarios: short-term exposures in early life to initiators (carcinogens that increase the rate of the first stage of carcinogenesis) and short-term exposures late in life to completers (carcinogens that increase the rate of the last stage of carcinogenesis, Chen et al., 1988). In both cases, LADD can underestimate cancer risk by up to a factor of 6. When short-duration exposure occurs in an adult's mid-life period, the extent of underestimation is less than 2- to 3-fold. Depending on the mode of action, cancer risk from short-term exposure may also be overestimated by up to several orders of magnitude.

The relationships between the prevalence and magnitude of potential under and overestimates of cancer risk using the LADD approach are illustrated in Figure 2.1. This figure compares the relative risk estimates generated using a 6-stage A-D multistage model (to estimate cancer risks for time-dependent exposure patterns) with those calculated using an "equivalent" LADD (a time-weighted average dose assuming constant lifetime exposure). The value of 1 on the Y axis represents equivalent risk estimates. Values greater than 1 represent cases in which LADD underestimates cancer risks relative to the time-dependent risk model, and values smaller than 1 represent cases in which LADD overestimates those risks. The figure illustrates that, except for the specific cases discussed above, the LADD is more likely to overestimate cancer risk, and the magnitude of potential overestimation is much greater than the magnitude of underestimation.

It is important to note that the difference in cancer risk estimates between the models is dependent on the number of stages considered in the A-D multistage model, which stage is affected and the age at first exposure. Figure 2.1 illustrates a comparison using the 6-stage A-D multistage model and an assumption that only one stage (i.e. first or last stage) is dose-related. The difference between the models in cancer risk estimates will be smaller if one uses a lower number of cancer stages in the A-D multistage model. The modelled cancer risk estimates become approximately equivalent with a 2-stage A-D model (assuming carcinogenesis has only two stages).

The results from the MVK model generally parallel those from the A-D multistage model exercises (Chen et al., 1988; Murdoch et al., 1992). The model predicts LADD may over or underestimate cancer risks depending on the cell growth rate, time of first exposure, duration of exposure and the type of carcinogen. The maximum underestimate of risk reported by Chen et al. (1988) using the LADD approach would occur with early-life, shorter exposures to an initiator (maximum 7-fold underestimate) or with longer duration, late-life exposures to a completer (maximum 4.5-fold underestimate). When exposure takes place during mid-life, the degree to which LADD can underpredict cancer risk (up to 2-fold) for initiators using the MVK model is generally quite comparable with the A-D multistage model prediction (Chen et al., 1988; Murdoch et al., 1992).

Figure 2.1 Relative cancer risk estimates for various ages and durations of adult exposure calculated using a 6-stage Armitage-Doll multistage (MS) model for estimating cancer risks for time-dependent exposure patterns versus lifetime average daily dose (LADD). Only one stage was assumed to be dose-related in the modelling, the first stage for "initiators" and the last (or kth) stage for "completers". A value of 1 on the Y axis (indicated by the red horizontal dotted line) represents equivalent risk estimates. Values greater than 1 represent cases in which LADD underestimates cancer risks, and values smaller than 1 represent cases in which LADD overestimates risks.



2.1.4 Summary for Dose Averaging for Less-Than-Lifetime Adult Exposure

Evidence from animal experiments, epidemiological studies and theoretical modelling studies supports the conclusion that exposure pattern has an effect on lifetime cancer risk. Averaging less-than-lifetime exposure over a lifetime using LADD may underestimate or overestimate cancer risks, depending on the timing of exposure and the mode of action of the carcinogen. The degree of underestimation seems generally to be confined to within an order of magnitude and is approximately 2-fold for short exposure during all but the very late stages of adulthood. Theoretical modelling predicts up to a 6-fold underestimation of risk for exposure to a completer only late in life; however, most chemicals act through multiple mechanisms, and few exclusive completers have been identified. The original multistage A-D model assumes that cancer incidence increases with age at a constant rate. The review by Al-Zoughool and Krewski (2008) indicates that this assumption does not apply to the incidence of prostate and breast cancers, which increase until age 40 and 50 and decline thereafter; the incidence of most cancer types declines after the age of 80. The multistage model may therefore overestimate cancer rates in the elderly, and LADD may not underpredict cancer risk from less-than-lifetime exposure to (theoretical) completers late in life as much as the model suggests.

Overall, the limited evidence currently available suggests dose averaging over a lifetime (LADD) overestimates as frequently as it underestimates cancer risk for short-term exposure. However, for adult exposures to mutagenic carcinogens (e.g. initiators), the underestimation of cancer risk is insignificant in most cases. Adjustment to correct for underestimation of cancer risk resulting from using the LADD approach for less-than-lifetime exposures in adults is therefore not recommended (i.e. the status quo is maintained).

2.2 Dose Averaging for Less-Than-Lifetime Early-Life Exposure

Cancer slope factors are generally derived from adult human epidemiological studies or standard chronic adult rodent bioassays. The US EPA (2005a) conducted a comprehensive review of cancer risk associated with early-life exposure to determine whether specific age-dependent adjustments of adult cancer slope factors were needed when assessing cancer risk from early-life exposure.

The review found limited cancer epidemiological data involving childhood exposure to radiation and chemotherapeutic agents. A review of available animal studies (Barton et al., 2005; Chhabra et al., 1993; Peto et al., 1984; Vesselinovitch et al., 1979) indicated that early-life exposures (i.e. perinatal) usually resulted in a higher tumour incidence later in life than standard adult-only exposures.

These findings are consistent with the current understanding of biological processes involved in carcinogenesis and are supported by other reviews (McConnell, 1992; Miller et al., 2002; US EPA, 1996), which found the following:

- Tumours usually occur at the same sites following either perinatal or adult exposure.
- Perinatal exposure followed by adult exposure usually increases the percentage of treated animals bearing tumour or reduces the latency period before tumours are observed as compared with adult-only exposures.

The US EPA (2005a) identified several factors that may contribute to increased susceptibility to carcinogens in early life:

- Differences in the capacity to metabolize and clear chemicals at different ages can result in larger or smaller internal doses of the active agent(s), either increasing or decreasing risk (Ginsberg et al., 2002; Renwick, 1998).
- More frequent cell division during development can result in enhanced fixation of mutations because of the reduced time available for repair of DNA lesions, and clonal expansion of mutant cells results in a larger population of mutants (Slikker et al., 2004).
- Some embryonic cells, such as brain cells, lack key DNA repair enzymes.
- Some components of the immune system are not fully functional during development (Holladay and Smialowicz, 2000; Holsapple et al., 2003).
- Hormonal systems operate at different levels during different lifestages (Anderson et al., 2000).
- Induction of developmental abnormalities can result in a predisposition to carcinogenic effects later in life (Anderson et al., 2000; Birnbaum and Fenton, 2003; Fenton and Davis, 2002).
- While tumour promotion processes can be very dependent upon the duration of promotion, initiation processes can occur in relatively brief periods.
- Most tumours take extended periods to develop, which means that damage occurring earlier in life is more likely to result in tumours before death than would exposures that occur later in life.

The US EPA (2005a) compared the cancer potencies from early-life exposure with the cancer potencies from adult exposure in repeated (continuous) dosing studies taken from the published literature. Studies included in the analysis involved a) exposure of animals either only during the juvenile or adult period and followed through adulthood to assess tumour incidence; or b) exposure of animals beginning either in the juvenile or adult period, but once begun continuing through life. Cancer potencies were estimated by fitting the one-hit model, or a restricted form of the Weibull model, to the data for each age group. The analysis for the six carcinogens

(benzidine, diethylnitrosamine, 3-methylcholanthrene, safrole, urethane and vinyl chloride) with a mutagenic mode of action is most informative. The results indicate that the early lifestages can be, but are not always, much more susceptible to cancer development than when exposure occurs in the adult lifestage. The ratio of tumour incidence from early life to adult exposure varies by chemical, sex and species with the weighted geometric mean ratio estimated at 10.4.

The US EPA (2005a) performed a similar analysis of acute dosing studies (which generally compared a single exposure during the juvenile period with identical or similar exposure in adult animals). The results[4] supported the concept that early-lifestage exposure to carcinogenic chemicals with a mutagenic mode of action leads to increased tumour incidence when compared with adult exposure of a similar dose and duration.

On the basis of the analysis involving repeated (continuous) dosing studies, the US EPA (2005a) recommended adjusting the adult cancer slope factor by a factor of 10 for exposures to mutagenic carcinogens occurring during the first 2 years of life. Pharmacokinetic and pharmacodynamic differences between children and adults are greatest during the first 2 years of life (World Health Organization, 2006), which corresponds to the period of birth to weaning in laboratory rodents (Hattis, 2005; WHO, 2006).

The US EPA (2005a) considered the available data insufficient to calculate a specific adjustment factor for the period from 2 through 15 years of age, which represents middle adolescence and follows the period of rapid developmental changes during puberty. The US EPA therefore selected a 3-fold adjustment as it is the geometric mean between the 10-fold adjustment for the first 2 years of life and a unity adjustment for adult exposure. The US EPA recommends that these default age-dependent adjustment factors be applied only when chemical-specific data on early-life exposure are absent.

Although the limited data for carcinogens with a non-mutagenic mode of action (e.g. hormonally mediated) suggest increased susceptibility when exposure occurs perinatally, the US EPA (2005a) considered the data inadequate to derive a generic adjustment of cancer response. More research is needed, particularly because it was observed that tumours arising from hormonally active chemicals appeared to involve different sites when exposure occurred during early life versus adulthood.

The California Environmental Protection Agency (CalEPA, 2009) released its findings on a similar study it undertook to address age-related cancer. This study compared cancer potencies (estimated by applying the linearized multistage [LMS] model to the dose-response data from animal experiments) from early-life exposures (exposed during the prenatal, postnatal or juvenile period) with exposure at an older age, preferably during adulthood. CalEPA used the full distribution of the cancer slope to derive the ratios of cancer potencies from early-life to adult exposures with adjustment for time to manifest tumour (i.e. to account for the longer available time the young animals had from exposure to tumour development). Each chemical was represented by a single distribution based on cancer potencies estimated from one or more studies and from all tumour sites.

The medians of the postnatal age sensitivity factor (ASF), estimated from data on 18 carcinogens (55 distributions), and the juvenile ASF, estimated from data on 5 carcinogens (7 distributions), were reported as 13.5 and 4.5 respectively. Because of the limited database and the broad distributions of results for different chemicals, CalEPA found no basis for specifying a default ASF with greater than half-log precision (i.e. values of 1, 3, 10, 30, etc). Further, rodents are born at a stage of maturity that approximates that of a third-trimester human foetus. Therefore, in the absence of chemical-specific data, CalEPA recommended applying a default ASF of 10 for the third trimester to age 2 years (totalling 2.25 years) and a factor of 3 for ages 2 through 15 years to account for potential higher sensitivity during early lifestages. While the same values were selected by US EPA (2005a) to be applied only to carcinogens with a mutagenic mode of action, CalEPA will apply these factors to all carcinogens. CalEPA (2009) included in its analysis three non-genotoxic carcinogens and found evidence that early life is a susceptible time for a carcinogen thought to act through a non-mutagenic mode of action, e.g. diethylstilbestrol (DES). CalEPA's rationale for not restricting ASF to chemicals acting via a mutagenic mode of action includes the potential problems of defining "mutagenic mode of action" when applied narrowly and the possibility of carcinogens with multiple modes of action that dominate at different lifestages (CalEPA, 2009).

2.3 Dose Averaging for Prenatal Exposure (Transplacental Carcinogenesis)

A number of agents are suspected to be transplacental carcinogens, i.e. in utero exposure to these agents leads to cancer development later in life, involving either a mutagenic or a non-mutagenic mode of action. Most data are from animal studies, such as those involving DES, genistein, tamoxifen, polycyclic aromatic hydrocarbons (PAHs), polybrominated biphenyls, polychlorinated dibenzo-p-dioxins (dioxin; reviewed in Birnbaum and Fenton, 2003), arsenic (Waalkes et al., 2004) and nitrosamines (Mohr et al., 1983). In humans, only radiation and DES have been shown to cause cancer following in utero exposures (Anderson et al., 2000; Barton et al., 2005; and Birnbaum and Fenton, 2003). Other chemicals suspected to be transplacental carcinogens

[4] Based on acute dosing carcinogenic data for eight chemicals with a mutagenic mode of action: benzo[a]pyrene, dibenzanthracene, diethylnitrosamine, dimethylbenzanthracene, dimethylnitrosamine, ethylnitrosourea, methylnitrosourea, urethane.

on the basis of human data include aflatoxin B1 and the hormones used for assisted reproduction (in vitro fertilization). These substances are not typically found at federal contaminated sites; moreover, for many substances that are found at contaminated sites, the data on transplacental carcinogenesis are available only from animal studies.

Some chemicals may be acting as initiators following in utero exposures or prezygotic exposure of the male parent, with cancer formed only upon subsequent postnatal promotion and/or additional exposures (i.e. in utero exposure creates altered susceptibility to cancer later in life). This effect has been seen experimentally with various chemicals, including dioxin/dimethylbenzantracene (DMBA; Brown et al., 1998), 3-methylcholanthrene/butylated hydroxytoluene (Gressani et al., 1999), genistein or atrazine/DMBA (Hilakivi-Clarke et al., 1999; Fenton and Davis, 2002) and N-methyl-N-nitrosourea or PAHs/phenobarbital (Diwan et al., 1989). In utero initiation/postnatal promotion has been demonstrated in humans only for DES and radiation (Yamasaki et al., 1992).

The prenatal to adult cancer potency ratio has not been considered in the US EPA (2005a) supplemental guidance. The CalEPA (2009) has conducted a probabilistic analysis of the prenatal to adult potency ratio. The prenatal age window showed an increased sensitivity to the majority of the 14 carcinogens (22 potency ratio distributions) analyzed. The median of the prenatal ASF distribution was 2.9. However, because of the limited database and the considerable variability in available data, no recommendation on a default adjustment factor was proposed for prenatal exposures in the first and second trimesters. As rodents are born at a stage of maturation similar to that of a third-trimester human foetus, the trimester is included in the default ASF of 10 proposed for up to 2 years of age (i.e. total duration of 2.25 years). No other major regulatory agency has a default position for adjustment of risk calculations for prenatal exposures. While CalEPA (2009) illustrated how an ASF of 10 can be applied when the daily exposure (mg/kg-d) is known, the agency has not provided sample risk calculations for human exposure from known environmental concentrations.

Physiologically based pharmacokinetic (PBPK) modeling of transplacental transfer could theoretically better define the magnitude of increased susceptibility in the foetus. However, validated PBPK models are unlikely to become available in the near future, as the necessary data for modelling and reliable markers of foetal exposure are lacking, and the models themselves require further refinement (Anderson et al., 2000). Efforts to advance knowledge on issues such as the temporal profile and gene polymorphism in enzymes involved in carcinogen activation/detoxification and DNA repair enzymes in the foetus would facilitate development of better PBPK models. More work with animal models is needed to identify transplacental carcinogens and their mechanism of action, including interaction with target genes.

2.4 Dose Averaging for Less-Than-Lifetime Exposure during Puberty

Mutagenic carcinogens are generally more effective in rapidly dividing tissues. The higher rates of cell division provide more opportunities for carcinogens to interact with DNA and less time for DNA repair prior to cell division, which results in increased probability of initiation activity. During puberty, there is dramatic growth in reproductive and other related organs, including some parts of the brain, potentially making them more susceptible to mutagenic carcinogens acting at those sites.

Changes in physiological and biological processes during puberty could also alter susceptibility to the effects of some non-mutagenic carcinogens (e.g. endocrine-disrupting chemicals). On the basis of its analysis of the limited available data, the US EPA Science Advisory Board (US EPA, 2004) concluded that altered sensitivity to the development of cancer may occur when exposure takes place during puberty as compared with other exposure time windows.

3.0 PROPOSED INTERIM MEASURE FOR HUMAN HEALTH RISK ASSESSMENT FOR LESS-THAN-LIFETIME EXPOSURE TO CANCER-CAUSING AGENTS AT CONTAMINATED SITES

The CSD provides this interim guidance with regard to HHRA of carcinogenic agents, including short-term exposure and dose averaging. Risk assessments submitted to CSD should provide a rationale taking into consideration the mode of action at the tumour site in question.

3.1 Assessment of Cancer Risk for Non-Threshold Carcinogenic Effects

3.1.1 Carcinogenic Effects Acting Through a Mutagenic Mode of Action

The US EPA (2005 a, b) provides one of the most comprehensive analyses of the available data related to increased sensitivity when exposure to a carcinogen with a mutagenic mode of action occurs at early lifestages. As an interim measure, CSD has adapted the US EPA approach for contaminated site risk assessments.

The US EPA's default adjustment factor of 10 is supported by LMS modelling studies (Al-Zoughool and Krewski, 2008) indicating that a default factor of 6 should be applied to LADD-based cancer risk estimates for mutagens (i.e. to account for potential increased effectiveness of early-life exposure to an initiator). An additional factor of 1.6 may be applied to slope factors derived from rodent bioassays in which exposure begins in early adulthood (6–8 weeks of age), to give a total adjustment of 10 (6×1.6). This additional factor (1.6) is needed to account for the neonatal/infant period (i.e. from birth to 6–8 weeks of age).

This cancer risk assessment approach takes into account the varying sensitivity of different lifestages to cancer effects. The ILCR is estimated by summing the risk from each discrete exposure period. For non-threshold carcinogens acting through a mutagenic mode of action, it is recommended that ADAFs be applied to the cancer slope factor (or inhalation unit risk) with exposure averaged over a lifetime, to account for the sensitivity of the age-dependent exposure period. This approach can be illustrated by the equations below.

ILCR from oral exposure can be estimated using the following equation:

$$ILCR = \sum_i (LADD_i * SF_i)$$

$$= \sum_i (LADD_i * SF * ADAF_i)$$

Where:
$LADD_i$ = dose received during lifestage i averaged over a lifetime
SF_i = age-specific slope factor
SF = adult cancer slope factor (per mg/kg-d)
$ADAF_i$ = age-dependent adjustment factors for lifestage i

For exposure by inhalation, the following equation applies:

$$ILCR = \sum_i (C_{ai} * TR_i * UR * ADAF_i)$$

Where:
C_{ai} = concentration in air during lifestage i (mg/m^3)
TR_i = fraction of time exposed (yr/80 yr)
UR = adult cancer unit risk ($per\ mg/m^3$)
$ADAF_i$ = age-dependent adjustment factors for lifestage i

LADD is defined by the following equation:

LADD (mg/kg-d) = [ER * ED]/Lifetime or

LADD (mg/kg-d) = [C * IR * AF * ED] / [BW* Lifetime]

Where: ER = exposure rate (mg/kg-d)
C = chemical concentration in the media (mg/m^3 or mg/kg)
IR = intake rate of medium (m^3/day or kg/day)
AF = medium-specific absorption factor
ED = exposure duration (days)
BW = body weight (kg)
Lifetime = days in a lifetime = 365 d/yr * 80 yr

$LADD_i$ is defined as the dose received during lifestage i averaged over a lifetime and can be represented by the following equation:

$LADD_i$ (mg/kg-d) = [C_i * IR_i * AF * ED_i] / [BW_i * Lifetime]

Where: C_i = chemical concentration in the media a person is exposed to during lifestagei (mg/m^3/ or mg/kg)
IR_i = intake rate of medium during $lifestage_i$ (m^3/day or kg/day)
AF = medium-specific absorption factor
ED_i = exposure duration during $lifestage_i$ (days)
BW_i = body weight during $lifestage_i$ (kg)
Lifetime = days in a lifetime = 365 d/yr * 80 yr

The US EPA's ADAFs have been adjusted to fit the age groups presented in the PQRA (Health Canada, 2004). Table 3.1 summarizes the default adjusted ADAFs that CSD recommends for contaminated site risk assessments of non-threshold carcinogens with a mutagenic mode of action. These default factors can be applied when age-specific cancer slope factors, age-specific inhalation unit risks or chemical-specific data are not available. In scenarios where exposure periods do not match the CSD's age groups, CSD recommends that the US EPA's ADAFs be applied. For example, if exposure occurs only between 7 months and less than 2 years of age, the adjustment factor of 10 would apply. Likewise, if exposure occurs only between 12 and < 16 years of age, the ADAF of 3 would apply. Worked examples are illustrated in Section 4.

When age-specific cancer slope factors, age-specific inhalation unit risks or chemical-specific data are available for a susceptible lifestage, it is preferable to use these data directly to evaluate risks for the chemical and the lifestage on a case-by-case basis. In these cases, such as vinyl chloride, application of default ADAFs would not be appropriate. The US EPA recommends twice the adult inhalation unit risk to be applied for estimating incremental cancer risk from continuous exposure to vinyl chloride from birth.

For intermittent exposures, the total cancer risk will be the sum of each discrete exposure with lifestage-specific potency and exposure averaged over a lifetime.

Table 3.1 Recommended interim adjusted age-dependent adjustment factors (ADAFs) for cancer risk assessment at contaminated sites for carcinogenic effects via a mutagenic mode of action

Lifestage	Age	Adjusted age-dependent adjustment factor (ADAF)[a]
Infant	0–6 months	10
Toddler	7 months–4 years	5[b]
Child	5–11 years	3
Teenager	12–19 years	2[c]
Adult	20+	1

[a] US EPA (2005 a, b), except as noted.

[b] $ADAF_{7\ mo–4\ yr}$ = ($ADAF_{0–<2}$ * D7 mo-1 / $D_{7\ mo–4}$) + ($ADAF_{2–4}$ * $D_{2–4}$ / $D_{7\ mo–4}$) = 10 * 1.5/4.5 + 3 * 3/4.5 = 5, and D_i = exposure duration in years

[c] $ADAF_{12–19}$ = ($ADAF_{12–<16}$ * $D_{12–15}$ / $D_{12–19}$) + ($ADAF_{16+}$ * $D_{16–19}$ / $D_{12–19}$) = 3 * 4/8 + 1 * 4/8 = 2, and D_i = exposure duration in years

The prenatal period (in utero) may be a sensitive window of exposure for some cancers, and an ADAF of 3 (or 2) may not be sufficient to address increased sensitivity during puberty, but further study is needed to delineate more accurately the magnitude of increased sensitivity. CSD will continue to evaluate the issue as new research data become available and as other regulatory agencies consider this issue. In the interim, CSD recommends addressing the risks associated with mutagenic carcinogen exposure during these lifestages on a case-by-case basis.

To date, among the carcinogens for which CSD provides TRV values, the US EPA (2009, 2011a) has identified carcinogenic PAHs, trichloroethylene and vinyl chloride as acting through a mutagenic mode of action. After a toxicological review, the US EPA (2010) proposed that chromium (VI) is "likely carcinogenic to humans" via the oral route of exposure and hypothesized a mutagenic mode of action for its carcinogenicity. This US EPA report is currently undergoing review (US EPA, 2011b).

3.1.2 Carcinogenic Effects Acting Through an Unknown Mode of Action

For carcinogenic effects with an unknown mode of action or for which the burden of proof for a threshold mode of action has not been met, CSD recommends treating the effect as non-threshold. The mathematical equations used to estimate cancer risk for mutagenic carcinogens can be applied in these situations. If chemical-specific data are available on quantitative differences between early lifestages and adults, an analysis of the differences could be used to adjust risk estimates for early life exposures. Otherwise, CSD does not recommend extending the default age-dependent potency adjustment factors to these carcinogenic effects. This position would be analogous to recommending a default ADAF of 1 for all lifestages.

The non-threshold approach for carcinogenicity risk assessment arises initially from the mechanistic, one-hit model, which assumes that only one-hit is required for the cell to be altered. The role of the body's defence mechanism (e.g. repair, apoptosis), which has an influence on the health outcome, is not considered. CSD considers the use of the linear low-dose extrapolation approach (without further adjustment) to be sufficiently conservative and to provide adequate public health protection for carcinogenic effects with a mode of action that is not mutagenic.

3.2 Assessment of Health Risk from Threshold Carcinogens

The CSD does not recommend a default age-specific adjustment for carcinogenic effects found to have a non-linear dose-response relationship (i.e. threshold) at low doses at this time. An adjustment can be made on a chemical-specific basis if supported by experimental data. These substances would be included in an HHRA using a TDI (or a TC in the case of inhalation exposure).

The CSD recommends that dose averaging for short-term exposure for these types of carcinogenic effects be performed in the same way as for other substances with threshold effects. It is important that dose averaging does not underestimate the potential for threshold carcinogenic effects. Without a sound basis for doing so (i.e. it cannot be a default assumption), the human health risk assessor should not simply mathematically spread out a short-term dose over a long period and conclude that the short-term dose is toxicologically equivalent to a lower dose over the long period. In short, CSD recommends that the exposure be averaged over the total actual exposure period and compared with the appropriate TRV. A scientific rationale is required to support any proposed amortization (dose averaging beyond actual exposure period) to ensure that short-term risks are not underestimated. This analysis needs to be done on a chemical-specific basis.

3.3 Assessment of Health Risk from Non-Cancer Health Effects

For short-term exposure, carcinogenic agents may elicit other chronic and short-term non-cancer health effects, depending on the magnitude of exposure. Short-term effects can be evaluated for potential critical receptors/lifestages[5] using short-term TRVs where available (either from other regulatory agencies or derived from literature values, as per Health Canada, 2010, guidance) and applicable to the exposure scenarios. If short-term TRVs are not available, such evaluation can be conducted according to relevant dose-response information from toxicity studies. It is also important to consider whether the short-term exposure might elicit early biological key events that might progress to health effects at a later date. In many cases, both the short-term and chronic non-carcinogenic effects, rather than carcinogenicity, may be the main determinant of the risk from short-term exposure. For example, keratosis rather than carcinogenicity could drive a risk assessment for exposure to high levels of arsenic in soil (e.g. 100 mg/kg) in a less-than-lifetime exposure scenario.

[5] Including relevant receptors/lifestages with the highest exposure and receptors/lifestages associated with specific sensitivity to the toxicity of the contaminants

4.0 WORKED EXAMPLES

4.1 Assessment of Lifetime Risk Associated with Exposure to a Carcinogen with a Mutagenic Mode of Action

When assessing cancer risk, it is important to consider both the difference in exposure and the increased susceptibility for early lifestages. ADAFs in dose-response (i.e. slope factors) need to be combined with age-specific exposure estimation.

The following examples illustrate how to integrate potential lifestage differences in exposure and susceptibility in risk estimation for both lifetime and less-than-lifetime exposure during a specific period in life. The examples consider risk from oral exposure. Risks associated with inhalation exposure to mutagenic carcinogens can be calculated in a similar manner by applying the appropriate ADAFs with the corresponding inhalation unit risk estimates using appropriate estimates of exposure concentrations.

These calculations assume that the available slope factor does not specifically consider early-life exposure. In the case of carcinogens for which age-specific (and in particular early-life) slope factors are available, these factors should be used instead of adjusting the adult slope factor.

4.1.1 Example 1: Exposure Occurs Over a Lifetime

Consider a scenario of exposure to a hypothetical carcinogen with a mutagenic mode of action present in drinking water. The oral slope factor derived from a typical animal study (i.e. in which dosing begins after puberty) is estimated to be 2 $(mg/kg\text{-}d)^{-1}$. The absorption factor of the carcinogen from drinking water is 1. The carcinogen is present in drinking water at 0.001 mg/L.

To calculate lifetime risk for a population with average life expectancy of 80 years, sum the risk associated with each of the time periods, applying recommended ADAFs to the relevant time periods:

- risk for the infant—first 6 months of life (where ADAF = 10),
- risk for toddler—6 months through 4 years of life (ADAF = 5),
- risk for child—ages 5 through 11 (ADAF = 3),
- risk for teenager—ages 12 through 19 (ADAF = 2) and
- risk for adult—ages 20 to 80 (ADAF = 1)

Thus, the ILCR equals the sum of the various age groups:

- Risk for infant
  = slope factor × ADAF x $LADD_{0–6\ mo}$
  = 2 $(mg/kg\text{-}d)^{-1}$ × 10 × [(0.001 mg/L × 0.3 L/d / 8.2 kg) × 0.5 yr/80yr]
  = 5 x 10^{-6}
- Risk for toddler
  = slope factor × ADAF × $LADD_{7\ mo–4}$
  = 2 $(mg/kg\text{-}d)^{-1}$ × 5 × [(0.001 mg/L × 0.6 L/d / 16.5 kg) × 4.5 yr/80yr]
  = 2 × 10^{-5}
- Risk for children
  = slope factor × ADAF × $LADD_{5–11}$
  = 2 $(mg/kg\text{-}d)^{-1}$ × 3 × [(0.001 mg/L × 0.8 L/d / 32.9 kg) × 7 yr/80yr]
  = 1 × 10^{-5}
- Risk for teenager
  = slope factor × ADAF × $LADD_{12–19}$
  = 2 $(mg/kg\text{-}d)^{-1}$ × 2 × [(0.001 mg/L × 1 L/d / 59.7 kg) × 8 yr/80yr]
  = 8 × 10^{-6}
- Risk for adult
  = slope factor × ADAF × $LADD_{20+}$
  = 2 $(mg/kg\text{-}d)^{-1}$ x 1 × [(0.001 mg/L × 1.5 L/d / 70.7 kg) × 60 yr/80yr]
  = 3 × 10^{-5}

Total ILCR
= 5 × 10^{-6} + 2 × 10^{-5} + 1 × 10^{-5} + 8 × 10^{-6} + 3 × 10^{-5}
= 7 × 10^{-5}

4.1.2 Example 2: Exposure Occurs at Less Than 2 Years of Age

Consider a scenario in which exposure to the same hypothetical carcinogen only takes place for a limited period of time, e.g. in a family that lives near a source of contamination for a short time and then moves away. The exposure may occur with a child aged from 1 to less than 2 years of age. It is important to consider lifestage-specific differences in exposure. The carcinogen has an oral cancer slope factor of 2 $(mg/kg\text{-}d)^{-1}$ derived from a typical animal study, and the concentration in drinking water is 0.001 mg/L.

As this exposure period does not match CSD age groupings, the US EPA's ADAF applies[6].

Risk = slope factor × ADAF × $LADD_{1-<2}$
Risk = 2 $(mg/kg\text{-}d)^{-1}$ × 10 × 0.001 mg/L × 0.6 L/d/16.5 kg × 1 yr/80 yrs
= 9 × 10^{-6}

Thus, the incremental lifetime cancer risk from 1 year of exposure to a carcinogen with a mutagenic mode of action assuming initial exposure at 1 year of age is estimated at 9 × 10^{-6}.

[6] Please note that when the exposure period matches a CSD age grouping, CSD recommends that its ADAFs be used.

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Exhibit G

Technical Support Document for Cancer Potency Factors:

Methodologies for derivation, listing of available values, and adjustments to allow for early life stage exposures.

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Office of Environmental Health Hazard Assessment

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EXECUTIVE SUMMARY

The Air Toxics "Hot Spots" Information and Assessment Act (AB 2588, Connelly) was enacted in September 1987. Under this Act, stationary sources of air pollution are required to report the types and quantities of certain substances their facilities routinely release into the air. The goals of the Air Toxics "Hot Spots" Act are to collect emission data, identify facilities having localized impacts, ascertain health risks posed by those facilities, notify nearby residents of significant risks and reduce emissions from significant sources.

The Technical Support Document for Cancer Potency Factors (TSD) contains cancer unit risks and potency factors for 107 of the 201 carcinogenic substances or groups of substances for which emissions must be quantified in the Air Toxics Hot Spots program. These unit risks are used in the cancer risk assessment of facility emissions.

The purpose of this revision to the TSD is to provide updated calculation procedures used to derive the estimated unit risk and cancer potency factors, and to describe the procedures used to consider the increased susceptibility of infants and children compared to adults to carcinogens. This updates cancer risk assessment methods originally laid out in the California Department of Health Services' Guidelines for Chemical Carcinogen Risk Assessment (CDHS, 1985), and more recently summarized in the previous Hot Spots technical support document Part II (OEHHA, 2005a). Summaries of cancer potency factors and the underlying data are provided in Appendices A and B, which are subject to ongoing updates but were not changed as part of the revision process which created this TSD.

The procedures used to consider the increased susceptibility to carcinogens of infants and children as compared to adults include the use of age-specific weighting factors in calculating cancer risks from exposures of infants, children and adolescents, to reflect their anticipated special sensitivity to carcinogens

This document is one part of the Air Toxics Hot Spots Program Risk Assessment Guidelines. The other documents originally included in the Guidelines are Part I: Technical Support Document for the Determination of Acute Toxicity Reference Exposure Levels for Airborne Toxicants; Part III: Technical Support Document for Determination of Noncancer Chronic Reference Exposure Levels; Part IV: Technical Support Document for Exposure Assessment and Stochastic Analysis; Part V: Air Toxic Hot Spots Program Risk Assessment Guidelines. As a part of the same revision process which led to production of this revised TSD on cancer potencies, the original TSDs for Acute and Chronic Reference Exposure Levels have been replaced with a new unified TSD for Acute, 8-hour and Chronic Reference Exposure Levels.

The major changes to the TSD include the following:

- Based on the OEHHA analysis of the potency by lifestage at exposure, OEHHA proposes weighting cancer risk by a factor of 10 for exposures that occur from the third trimester of pregnancy to 2 years of age, and by a factor of 3 for exposures that occur from 2 years through 15 years of age. We intend to apply this weighting factor to all carcinogens,

regardless of purported mechanism of action, unless chemical-specific data exist to the contrary. In cases where there are adequate data for a specific carcinogen of potency by age, we would use the data to make any adjustments to risk.

- OEHHA proposes to use the Benchmark Dose method to compute potency factors rather than the more traditional linearized multistage model (LMS), although the LMS will still be used in some instances. The BMDL model essentially uses an empirical fit to the data (usually best with the multistage model), and then extrapolates with a straight line from the 95% lower confidence limit of the BMD (BMDL) to zero. This method is simpler and does not assume any underlying theoretical mechanisms at the low dose range. The BMDL method results in estimates of potency very similar to those obtained using the LMS method.

- OEHHA will use scaling based on body weight to the ¾ power, rather than to the ⅔ power.

- OEHHA's evaluations of the carcinogenicity of chemicals generally follow the guidelines laid out by IARC for identification and classification of potential human carcinogens, which are described in detail in the most recent revision of the *Preamble* to the IARC monographs series (IARC, 2006).

PREFACE

The Air Toxics "Hot Spots" Information and Assessment Act (AB 2588, Connelly) was enacted in September 1987. Under this Act, stationary sources are required to report the types and quantities of certain substances their facilities routinely release into the air. The goals of the Air Toxics "Hot Spots" Act are to collect emission data, identify facilities having localized impacts, ascertain health risks posed by those facilities, notify nearby residents of significant risks and reduce emissions from significant sources.

The Technical Support Document for Cancer Potency Factors (TSD) contains cancer unit risks and potency factors for 107 of the 201 carcinogenic substances or groups of substances for which emissions must be quantified in the Air Toxics Hot Spots program. These unit risks are used in risk assessment of facility emissions. The TSD provides updated calculation procedures used to derive the estimated unit risk and cancer potency factors, and procedures to consider early-life susceptibility to carcinogens. Summaries of cancer potency factors and the underlying data are provided in Appendices A and B.

In this document, OEHHA is responding to the requirements of the 1999 Children's Environmental Health Protection Act (SB25, Escutia) by revising the procedures for derivation and application of cancer potency factors to take account of general or chemical-specific information which suggests that children may be especially susceptible to certain carcinogens (OEHHA, 2001a). The revised cancer potency derivation procedures described will not be used to impose any overall revisions of the existing cancer potencies, although they do reflect updated methods of derivation. However, individual cancer potency values will be reviewed as part of the ongoing re-evaluation of health values mandated by SB 25, and revised values will be listed in updated versions of the appendices to this document as necessary. The revisions also include the use of weighting factors in calculating cancer risks from exposures of infants, children and adolescents, to reflect their anticipated special sensitivity to carcinogens. Similar legal mandates to update risk assessment methodology and cancer potencies apply to the OEHHA program for development of Public Health Goals (PHGs) for chemicals in drinking water, and Proposition 65 No Significant Risk Levels (NSRLs). The NSRLs may also be revised to reflect concerns for children's health. Revising these numbers will require the originating program to reconsider the value in an open public process. For example, OEHHA would need to release any revised potency factors for public comment and review by the Scientific Review Panel on Toxic Air Contaminants (SRP) prior to adoption under the TAC program. The procedures for outside parties to request reevaluation of cancer potency values by the programs which originated those values are listed in Appendix G.

Appendices A and B provide previously adopted Cal/EPA values which were included in the previous version of the TSD for Cancer Potency Factors (OEHHA, 2005a). Cal/EPA values were developed under the Toxic Air Contaminant (TAC) program, the PHG program, the Proposition 65 program, or in some cases specifically for the Air Toxics Hot Spots program. All the Cal/EPA values are submitted for public comments and external peer review prior to adoption by the program of origin. In the future, new values developed by the Toxic Air Contaminants or Hot Spots programs or other suitable sources will be added as these are approved.

Some U.S. EPA IRIS cancer unit risk values were adopted under the previous versions of these guidelines, and these values will continue to be used unless and until revised by Cal/EPA. U.S. EPA has recently revised its cancer risk assessment guidelines (U.S. EPA, 2005a). Some of the recommended changes in methodology could result in slightly different potency values compared to those calculated by the previous methodology, although in practice a number of the recommendations (for example, the use of ¾ power of the body weight ratio rather than ⅔ power for interspecies scaling) have been available in draft versions of the revised policy for some time and appear in many more recent assessments. U.S. EPA has stated that cancer potency values listed in IRIS will not be revisited solely for the purpose of incorporating changes in cancer potency value calculation methods contained in the revised cancer risk assessment guidelines. U.S. EPA has also issued supplementary guidelines on assessing cancer risk from early-life exposure (U.S. EPA, 2005b).

OEHHA uses a toxic equivalency factor procedure for dioxin-like compounds, including polychlorinated dibenzo-*p*-dioxins, dibenzofurans and polychlorinated biphenyls (PCBs). The Toxicity Equivalency Factor scheme (TEF_{WHO-97}) developed by the World Health Organization/European Center for Environmental Health (WHO-ECEH) is used for determining cancer unit risk and potency values for these chemicals where individual congener emissions are available (Appendix C).

This document is one part of the Air Toxics Hot Spots Program Risk Assessment Guidelines. The other documents originally included in the Guidelines are Part I: Technical Support Document for the Determination of Acute Toxicity Reference Exposure Levels for Airborne Toxicants; Part III: Technical Support Document for Determination of Noncancer Chronic Reference Exposure Levels; Part IV: Technical Support Document for Exposure Assessment and Stochastic Analysis; Part V: Air Toxic Hot Spots Program Risk Assessment Guidelines. As a part of the same revision process which led to production of this revised TSD on cancer potencies, the original TSDs for Acute and Chronic Reference Exposure Levels have been replaced with a new unified TSD for Acute, 8-hour and Chronic Reference Exposure Levels.

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APPENDICES

Appendix A. A lookup table containing unit risk and cancer potency values.

Appendix B. Chemical-specific summaries of the information used to derive unit risk and cancer potency values.

Appendix C. A description of the use of toxicity equivalency factors for determining unit risk and cancer potency factors for polychlorinated dibenzo-*p*-dioxins, dibenzofurans and dioxin-like polychlorinated biphenyls.

Appendix D. A listing of Toxic Air Contaminants identified by the California Air Resources Board.

Appendix E. Descriptions of the International Agency for Research on Cancer (IARC) and U.S. Environmental Protection Agency (U.S. EPA) carcinogen classifications.

Appendix F. An asbestos quantity conversion factor for calculating asbestos concentrations expressed as 100 fibers/m^3 from asbestos concentrations expressed as $\mu g/m^3$.

Appendix G. Procedures for revisiting or delisting cancer potency factors by the program of origin.

Appendix H. Exposure routes and studies used to derive cancer unit risks and slope factors.

Appendix I. "Assessing susceptibility from early-life exposure to carcinogens": Barton *et al.*, 2005 (from *Environmental Health Perspectives)*.

Appendix J. "In Utero and Early Life Susceptibility to Carcinogens: The Derivation of Age-at-Exposure Sensitivity Measures" – conducted by OEHHA's Reproductive and Cancer Hazard Assessment Branch.

INTRODUCTION

The Technical Support Document (TSD) for Describing Available Cancer Potency Factors provides technical information support for the Air Toxics Hot Spots Program Risk Assessment Guidelines. The TSD consists of 12 sections:

1. The TSD introduction.

2. A description of the methodologies used to derive the unit risk and cancer potency values listed in the lookup table.

3. A lookup table containing unit risk and cancer potency values. (Appendix A)

4. Chemical-specific summaries of the information used to derive unit risk and cancer potency values. (Appendix B).

5. A description of the use of toxicity equivalency factors for determining unit risk and cancer potency factors for polychlorinated dibenzo-*p*-dioxins, dibenzofurans and dioxin-like polychlorinated biphenyls (Appendix C).

6. A listing of Toxic Air Contaminants identified by the California Air Resources Board (Appendix D).

7. Descriptions of the International Agency for Research on Cancer (IARC) and U.S. Environmental Protection Agency (U.S. EPA) carcinogen classifications (Appendix E).

8. An asbestos quantity conversion factor for calculating asbestos concentrations expressed as 100 fibers/m^3 from asbestos concentrations expressed as $\mu g/m^3$ (Appendix F).

9. Procedures for revisiting or delisting cancer potency factors by the program of origin (Appendix G).

10. Exposure routes and studies used to derive cancer unit risks and slope factors (Appendix H).

11. "Assessing susceptibility from early-life exposure to carcinogens": Barton *et al*., 2005 (from *Environmental Health Perspectives)* (Appendix I).

12. "In Utero and Early Life Susceptibility to Carcinogens: The Derivation of Age-at-Exposure Sensitivity Measures" – conducted by OEHHA's Reproductive and Cancer Hazard Assessment Branch (Appendix J)

SELECTION OF CANCER POTENCY VALUES

The Office of Environmental Health Hazard Assessment (OEHHA) has developed a number of cancer potencies for use in the Toxic Air Contaminants and Air Toxics Hot Spots programs. This document also provides summaries of cancer potency factors which were originally developed for other California Environmental Protection Agency (Cal/EPA) programs, or by the U.S. EPA. These were reviewed for accuracy, reliance on up-to-date data and methodology, and applicability in the context of the Air Toxics Hot Spots program. Values found appropriate were adopted after public and peer review rather than devoting the resources necessary for a full *de novo* assessment. Thus, cancer potency values (CPF) included in the Technical Support Document (TSD) for Cancer Potency Factors were from the following sources:

1. Toxic Air Contaminant documents

2. Standard Proposition 65 documents

3. U.S.EPA Integrated Risk Information Systems (Office of Health and Environmental Assessment, U.S.EPA)

4. Expedited Proposition 65 documents

5. Other OEHHA assessments , for example for the drinking water program.

All the cancer potency value sources used generally follow the recommendations of the National Research Council on cancer risk assessment (NRC, 1983, 1994). All Cal/EPA program documents undergo a process of public comment and scientific peer review prior to adoption, although the procedures used vary according to the program. The publication procedure for Toxic Air Contaminant documents includes a public comment period and review by the Scientific Review Panel on Toxic Air Contaminants (SRP) before identification of a Toxic Air Contaminant by the Air Resources Board of the California Environmental Protection Agency (Cal/EPA). Furthermore, a petition procedure is available to initiate TAC document review and revision if appropriate because of new toxicity data. Documents developed for the Air Toxics Hot Spots program similarly undergo public comment and peer review by the SRP before adoption by the Director of OEHHA. The standard Proposition 65 document adoption procedure includes a public comment and external peer review by the Proposition 65 Carcinogen Identification Committee. The expedited Proposition 65 document adoption procedure included a public comment period. Risk assessments prepared for development of Public Health Goals (PHGs) for chemicals in drinking water are subject to two public comment periods before the final versions and responses to comments are published on the OEHHA Web site. PHG documents may also receive external peer review. Documents from U.S. EPA's Integrated Risk Information System (IRIS) receive external peer review and are posted on the Internet for public viewing during the external peer review period, and any public comments submitted are considered by the originating office. Additionally, public comment may be solicited during the document posting period. Future preference for use of developed cancer potency factors/unit risks will be done on a case by case basis. Preference will be given to those assessments most relevant to inhalation exposures of the California population, to the most recent derivations using the latest data sets and scientific methodology, and to those having undergone the most open and extensive peer review process.

CANCER RISK ASSESSMENT METHODOLOGIES

This section describes in general the methodologies used to derive the cancer unit risk and potency factors listed in this document. As noted in the Preface to this document, no new cancer unit risks or potency factors were developed for this document. All of the values contained here were previously developed in documents by Cal/EPA or U.S. EPA. Following the recommendations of the National Academy of Sciences (NRC, 1983), Cal/EPA and U.S. EPA have both used formalized cancer risk assessment guidelines, the original versions of which (California Department of Health Services, 1985; U.S. EPA, 1986) were published some time ago. Both these guidelines followed similar methodologies.

In the twenty years since these original guidelines were published there have been a number of advances in the methodology of cancer risk assessment. There have additionally been considerable advances in the quantity of data available not only from animal carcinogenesis bioassays and epidemiological studies, but also from mechanistic studies of carcinogenesis and related phenomena. Some of these advances have been incorporated into newer risk assessments by both agencies on a more or less *ad hoc* basis. There has also been an ongoing effort to provide updated risk assessment guidance documents. In 1995, U.S. EPA released for public comment the "Proposed and Interim Guidelines for Carcinogen Risk Assessment", which was the first of several drafts released for public comment. Many risk assessments appearing since then have used elements of the recommendations contained in that document, in spite of its draft status. A final version of the U.S. EPA's revised cancer risk assessment guidelines has now been released (U.S. EPA, 2005a). Although these new guidelines incorporate a number of substantial changes from their predecessors (U.S. EPA, 1986; 1995), U.S. EPA has stated that cancer potency values listed in IRIS will not be revisited solely for the purpose of incorporating changes in cancer potency value calculation methods.

Cal/EPA has not produced a revised cancer risk assessment guideline document to replace the original version (DHS, 1985). Rather, Cal/EPA has relied on incorporating new data and methodologies as these became available, and described the methods used on a case by case basis in the individual risk assessment documents where these went beyond the original guidance. However, this revision of the TSD for cancer potencies provides a convenient opportunity to summarize the current status of the methodology used by OEHHA for the air toxics programs, and also to highlight points of similarity to, and difference from, the recommendations of U.S. EPA (2005a).

In this document, OEHHA intends to follow the recommendations of the NRC (1994) in describing a set of clear and consistent principles for choosing and departing from default cancer risk assessment options. NRC identified a number of objectives that should be taken into account when considering principles for choosing and departing from default options. These include, "protecting the public health, ensuring scientific validity, minimizing serious errors in estimating risks, maximizing incentives for research, creating an orderly and predictable process, and fostering openness and trustworthiness". The OEHHA cancer risk methodologies discussed in this document are intended to generally meet those objectives cited above.

Hazard Identification

This section will describe: 1) how weight of evidence evaluations are used in hazard evaluation; 2) guidelines for inferring causality of effect; 3) the use of human and animal carcinogenicity data, as well as supporting evidence (*e.g.,* genetic toxicity and mechanistic data); 4) examples of carcinogen identification schemes.

Evaluation of Weight of Evidence

In evaluating the range of evidence on the toxicity and carcinogenicity of a compound, mixture or other agent, a "weight-of-evidence" approach is generally used to describe the body of evidence on whether or not exposure to the agent causes a particular effect. Under this approach, the number and quality of toxicological and epidemiological studies, as well as the consistency of study results and other sources of data on biological plausibility, are considered. Diverse and sometimes conflicting data need to be evaluated with respect to possible explanations of differing results. Consideration of methodological issues in the review of the toxicological and epidemiological literature is important in evaluating associations between exposure to an agent and animal or human health effects. This aspect of the evaluation process has received particular emphasis with respect to epidemiological data, where concerns as to the statistical and biological significance and reliability of the data and the impacts of confounding and misclassification are pressing. Such concerns are also relevant to some extent in the interpretation of animal bioassay data and mechanistic studies. Although the test animals, laboratory environment and characterization of the test agent are usually much better controlled than the equivalent parameters in an epidemiological study, the small sample size can be problematic. In addition, there are uncertainties associated with extrapolation of biological responses from test animal species to humans.

Criteria for Causality

There has been extensive discussion over the last two centuries on causal inference. This has particularly related to epidemiological data, but is also relevant to interpretation of animal studies. Most epidemiologists utilize causal inference guidelines based on those proposed by Bradford Hill (1971). OEHHA has relied on these and on recommendations by IARC (2006), the Institute of Medicine (2004), the Surgeon General's Reports on Smoking (U.S. DHHS, 2004) and standard epidemiologic texts (*e.g.,* Lilienfeld and Lilienfeld, 1980; Rothman and Greenland, 1998). The criteria for determination of causality used by OEHHA have been laid out in various risk assessment documents. The summary below is adapted from the Health Effects section of the document prepared to support the identification of environmental tobacco smoke (ETS) as a Toxic Air Contaminant (OEHHA, 2005b).

1. *Strength of Association*. A statistically significant strong association, which is easier to detect if there is a high relative risk, between a factor and a disease is often viewed as an important criterion for inferring causality because, all other things being equal, a strong and statistically significant association makes alternative explanations for the disease less likely. However, as discussed in Rothman and Greenland (1998), the fact that a relative risk is small in magnitude does not exclude a casual association between the risk factor and the outcome in question. Since it is more difficult to detect (*i.e.*, reach statistical

significance) a small magnitude risk, it is just as likely to indicate causality as a larger magnitude risk.

When assessing all evidence, it is important to consider the strength of the study design (particularly controlling for confounding variables, obtaining an unbiased sample, measurement error) and the level of statistical significance (*i.e.*, the ability to exclude a Type I [false positive] error). The power of the study to detect biologically meaningful effects (*i.e.*, the risk of a Type II [false negative] error) is important in considering studies that do not reach traditional (*i.e.*, $P < 0.05$) statistical significance, particularly if the biological endpoint is serious. If the outcome is serious and the study small (*i.e.*, low power), a larger P value (*e.g.*, $P < 0.10$) may be adequate evidence for identifying an effect.

There are a number of examples of statistically significant, small magnitude associations that are widely accepted as causal, such as causal links between air pollution and cardiovascular/pulmonary mortality and between second-hand smoke exposure and various cancers and heart disease. From a public health perspective, even a small magnitude increase in risk for a common disease can mean large numbers of people affected by the health outcome when exposure is frequent and widespread, as measured by the population attributable risk or attributable fraction. Small magnitude of association must not be confused with statistical significance, which is much more important.

2. *Consistency of Association.* If several investigations find an association between a factor and a disease across a range of populations, geographic locations, times, and under different circumstances, then the factor is more likely to be causal. Consistency argues against hypotheses that the association is caused by some other factor(s) that varies across studies. Unmeasured confounding is an unlikely explanation when the effect is observed consistently across a number of studies in different populations.

   Associations that are replicated in several studies of the same design or using different epidemiological approaches or considering different sources of exposure and in a number of geographical regions are more likely to represent a causal relationship than isolated observations from single studies (IARC, 2006). If there are inconsistent results among investigations, possible reasons are sought, such as adequacy of sample size or control group, methods used to assess exposure, or range in levels of exposure. The results of studies judged to be rigorous are emphasized over those of studies judged to be methodologically less rigorous. For example, studies with the best exposure assessment are more informative for assessing the association between ETS and breast cancer than studies with limited exposure assessment, all else being equal.

3. *Temporality.* Temporality means that the factor associated with causing the disease occurs in time prior to development of the disease. The adverse health effect should occur at a time following exposure that is consistent with the nature of the effect. For example, respiratory irritation immediately following exposure to an irritant vapor is temporally consistent, whereas irritation noted only years later may not be. On the other hand, tumors, noted immediately following exposure, might be temporally inconsistent with a causal relationship, but tumors arising after a latency period of months (in rodents) or years (in rodents or humans) would be temporally consistent.

4. *Coherence and Biological Plausibility.* A causal interpretation cannot conflict with what is known about the biology of the disease. The availability of experimental data or mechanistic theories consistent with epidemiological observations strengthens conclusions of causation. For example, the presence of known carcinogens in tobacco smoke supports the concept that exposure to tobacco smoke could cause increased cancer risk. Similarly, if the mechanism of action for a toxicant is consistent with development of a specific disease, then coherence and biological plausibility can be invoked. It should be noted that our understanding of the biology of disease, and therefore biological plausibility, changes in light of new information which is constantly emerging from molecular biology (including epigenetics), and from new clinical and epidemiological investigations revealing effects influenced by genetic polymorphisms, pre-existing disease, and so forth.

5. *Dose-Response.* A basic tenet of toxicology is that increasing exposure or dose generally increases the response to the toxicant. While dose-response curves vary in shape and are not necessarily always monotonic, an increased gradient of response with increased exposure makes it difficult to argue that the factor is not associated with the disease. To argue otherwise necessitates that an unknown factor varies consistently with the dose of the substance and the response under question. While increased risk with increasing levels of exposure is considered to be a strong indication of causality, absence of a graded response does not exclude a causal relationship (IARC, 2006).

   The dose-response curves for specific toxic effects may be non-monotonic. Under appropriate circumstances, where the dose response shows saturation, the effect of exposures could be nearly maximal, with any additional exposure having little or no effect. In some instances, a response is seen strongly in susceptible subpopulations, and the dose-response is masked by mixing susceptible and non-susceptible individuals in a sample. Further, there are examples of U-shaped or inverted U-shaped dose-response curves, (*e.g.*, for endocrine disrupters) (Almstrup et al., 2002; Lehmann et al., 2004). Finally, timing of exposure during development may mask an overall increase in risk with increasing dose.

6. *Specificity.* Specificity is generally interpreted to mean that a single cause is associated with a single effect. It may be useful for determining which microorganism is responsible for a particular disease, or associating a single carcinogenic chemical with a rare and characteristic tumor (*e.g.*, liver angiosarcoma and vinyl chloride, or mesothelioma and asbestos). However, the concept of specificity is not helpful when studying diseases that are multifactorial, or toxic substances that contain a number of individual constituents, each of which may have several effects and/or target sites.

7. *Experimental evidence.* While experiments are often conducted over a short period of time or under artificial conditions (compared to real-life exposures), experiments offer the opportunity to collect data under highly controlled conditions that allow strong causal conclusions to be drawn. Experimental data that are consistent with epidemiological results strongly support conclusions of causality. There are also "natural experiments" that can be studied with epidemiological methods, such as when exposure of a human population to a substance declines or ceases; if the effect attributed to that exposure decreases, then there is evidence of causality. One example of this is the drop in heart disease death and lung cancer risk after smoking cessation.

It should be noted that the causal criteria are guidelines for judging whether a causal association exists between a factor and a disease, rather than hard-and-fast rules. Lilienfeld and Lilienfeld (1980) note that "*In medicine and public health, it would appear reasonable to adopt a pragmatic concept of causality. A causal relationship would be recognized to exist whenever evidence indicates that the factors form part of the complex of circumstances that increases the probability of the occurrence of disease and that a diminution of one or more of these factors decreases the frequency of that disease. After all, the reason for determining the etiological factors of a disease is to apply this knowledge to prevent the disease.*" Rothman and Greenland (2005) discuss the complexities of causation and the use of rules and deductive methods in causal inference. They also concur with Bradford Hill and others that a determination of causality is a pragmatic conclusion rather than an absolute verdict, and advocate that these criteria should be seen as "*deductive tests of causal hypotheses".*

Data Sources

Human studies: epidemiology, ecological studies and case reports

The aim of a risk assessment for the California Air Toxics programs is to determine potential impact on human health. Ideally therefore, the hazard identification would rely on studies in humans to demonstrate the nature and extent of the hazard. However, apart from clinical trials of drugs, experimental studies of toxic effects in human subjects are rarely undertaken or justifiable. Pharmacokinetic studies using doses below the threshold for any toxic effect have been undertaken for various environmental and occupational agents, but are not usually regarded as appropriate for suspected carcinogens.

The human data on carcinogens available to the risk assessor therefore mostly consist of epidemiological studies of existing occupational or environmental exposures. It is easier to draw reliable inferences in situations where both the exposures and the population are substantial and well-defined, and accessible to direct measurement rather than recall. Thus, many important findings of carcinogenicity to humans are based on analysis of occupational exposures. Problems in interpretation of occupational epidemiological data include simultaneous exposure to several different known or suspected carcinogens, imprecise quantification of exposures and confounding exposures such as active or passive tobacco smoking. The historical database of occupational data has a bias towards healthy white adult males. Thus, the hazard analysis of these studies may not accurately characterize effects on women, infants, children or the elderly, or on members of minority ethnic groups. Nevertheless, the analysis of occupational epidemiological studies, including meta-analyses, has proved an important source for unequivocal identification of human carcinogens.

Epidemiological evidence may also be obtained where a substantial segment of a general population is exposed to the material of interest in air, drinking water or food sources. Rigorous cohort and case-control studies may sometimes be possible, in which exposed individuals are identified, their exposure and morbidity or mortality evaluated, and compared to less exposed but otherwise similar controls. More often at least the initial investigation is a cross-sectional study, where prevalence of exposures and outcomes is compared in relatively unexposed and exposed populations. Such studies are hypothesis-generating, but are important sources of information

nevertheless, and can often also justify more costly and labor-intensive follow-up cohort and/or case-control studies.

The clinical medical literature contains many case reports where a particular health outcome is reported along with unusual exposures that might have contributed to its occurrence. These reports typically describe a single patient or a small group, and have no statistical significance. They are nevertheless useful as indications of possible associations that deserve follow-up using epidemiological methods, and as supporting evidence, addressing the plausibility of associations measured in larger studies.

Animal studies

Although the observation of human disease in an exposed population can provide definitive hazard identification, adequate data of this type are not always available. More often, risk estimates have to be based on studies in experimental animals, and extrapolation of these results to predict human toxicity. The animals used are mostly rodents, typically the common laboratory strains of rat and mouse.

Rats and mice have many similarities to humans. Physiology and biochemistry are similar for all mammals, especially at the fundamental levels of xenobiotic metabolism, DNA replication and DNA repair that are of concern in identifying carcinogens. However, there are also several important differences between rodents and humans. Rodents, with a short life span, have differences in cell growth regulation compared to longer-lived species such as the human. For instance, whereas laboratory investigations have suggested that mutations in two regulatory genes (*e.g.,* H-ras and p-53) are sometimes sufficient to convert a rodent cell to a tumorigenic state, many human cancers observed clinically have seven or eight such mutations. In addition, cultured normal human cells have a very stable karyotype, whereas cultured rodent cells facilely undergo tetraploidization and then aneuploidization in cell culture. Further, cultured human cells senesce and rarely undergo spontaneous immortalization (frequency is 10^{-7} or less), whereas cultured rodent cells facilely undergo immortalization at frequencies on the order of 10^{-3}. The use of genomics to study chemical carcinogenesis is relatively new, but the differences at present appear to be a matter of degree rather than kind.

Differences in regulation of cell division are another likely reason for variation between species in the site of action of a carcinogen, or its potency at a particular site. A finding of carcinogenesis in the mouse liver, for instance, is a reasonably good indicator of potential for carcinogenesis at some site in the human, but not usually in human liver (Huff, 1999). The mouse liver (and to a lesser extent that of the rat) is a common site of spontaneous tumors. It is also relatively sensitive to chemical carcinogenesis. The human liver is apparently more resistant to carcinogenesis; human liver tumors are unusual except when associated with additional predisposing disease, such as hepatitis B or alcoholic cirrhosis, or exposure to aflatoxin B1, or simultaneous exposure to hepatitis B virus and aflatoxin B1. Conversely, other tumor sites are more sensitive in the human than in experimental animals. Interspecies variation in site and sensitivity to carcinogenesis may also arise from differences in pharmacokinetics and metabolism, especially for carcinogens where metabolic activation or detoxification is important. This variability may cause important differences in sensitivity between individuals in a diverse population such as humans. Variability

between individuals in both susceptibility and pharmacokinetics or metabolism is probably less in experimental animal strains that are bred for genetic homogeneity.

Animal carcinogenesis studies are often designed to maximize the chances of detecting a positive effect, and do not necessarily mimic realistic human exposure scenarios. Thus extrapolation from an experimentally accessible route to that of interest for a risk assessment may be necessary. Even for studies by realistic routes such as oral or inhalation, doses may be large compared to those commonly encountered in the environment, in order to counter the limitation in statistical power caused by the relatively small size of an animal experiment. Whereas the exposed population of an epidemiological study might number in the thousands, a typical animal study might have fifty individuals per exposure group. With this group size any phenomenon with an incidence of less than about 5% is likely to be undetectable. Statistically significant results may be obtained even with groups as small as ten animals per dose group, when incidence of a tumor that is rare in the controls approached 100% in a treated group. The consensus experimental design for animal carcinogenesis studies, which has evolved over the last 50 years of investigation, is represented by the protocol used by the U.S. National Toxicology Program (NTP) for studies using oral routes (diet, gavage or drinking water) or inhalation. These carcinogenesis bioassays usually involve both sexes of an experimental species, and most often two species. NTP has standardized the use of the C57BlxC3H F_1 hybrid mouse, and the Fischer 344 rat as the standard test species, although NTP has announced plans to substitute use of the Wistar Han rat for the Fischer 344 rat. There is now an extensive database of background tumor incidences, normal physiology, biochemistry, histology and anatomy for these strains, which aids in the interpretation of pathological changes observed in experiments. Nevertheless, there is enough variation in background rates of common tumors that the use of concurrent controls is essential for hazard identification or dose-response assessment. "Historical control" data are mainly used to reveal anomalous outcomes in the concurrent controls. The fact that a significantly elevated incidence of a tumor relative to the concurrent control group is within the range of historical controls at that site for the test sex and strain is not necessarily grounds for dismissing the biological significance of the finding.

Groups of fifty animals of each sex and species are used, with control groups, and several dose groups, the highest receiving the maximum tolerated dose (MTD). Recent study designs have emphasized the desirability of at least three dose levels covering a decade with "logarithmic" spacing (*i.e.* MTD, 1/2 MTD or 1/3 MTD, and 1/10 MTD). This extended design is aimed at providing better dose-response information, and may contribute important additional information, such as mechanistic insights, for the hazard identification phase.

Supporting evidence: genetic toxicity, mechanistic studies

Investigators have developed additional data sources that can support or modify the conclusions of animal carcinogenesis bioassays, and provide information on mechanisms of action of agents suspected of being carcinogenic based on epidemiological studies or animal bioassays.

Genetic damage in exposed organisms includes both gene mutations (point or frameshift), and larger scale effects such as deletions, gene amplification, sister-chromatid exchanges, translocations and loss or duplication of segments or whole chromosomes. These genetic effects of chemical exposures are deleterious in their own right. In addition, since carcinogenesis results from somatic mutations and similar genetic alterations, agents that cause genetic damage generally

have carcinogenic potential. Conversely, many known carcinogens are also known to be genotoxic, although there is also a significant class of carcinogens that are not directly genotoxic according to the usual tests. These latter agents presumably work by some other mechanism, such as methylation of tumor suppressor genes or demethylation of cellular proto-oncogenes, although recent genetic studies have shown that even tumors induced by these agents may show mutations, deletions or amplification of growth regulatory genes.

Experimental procedures to demonstrate and measure genetic toxicity may involve exposure of intact animals, and examination of genetic changes in, for example, bone marrow cells (or cells descended from these, *e.g.,* the micronucleus test, which detects remnants of chromosomal fragments in immature erythrocytes), mutations in flies (*Drosophila)*, or appearance of color spots in the coat of mice. However, many tests have employed single celled organisms or mammalian cells in culture. The best known of these tests is the *Salmonella* reverse mutation assay, popularly known as the Ames test after its inventor. This is representative of a larger class of tests for mutagenic activity in prokaryotic organisms (bacteria), which necessarily only look at gene-level mutations. Similar tests in eukaryotic microorganisms (yeasts, *Aspergillus*) and cultured mammalian cells also detect chromosomal effects. Many tests using microorganisms *in vitro* involve addition of activating enzymes (*e.g.,* liver postmitochondrial supernatant – "S9") to mimic the metabolism of promutagenic chemicals *in vivo*. Another type of test examines the induction in mammalian cells of morphological transformation or anchorage-independent growth. These two chemically induced, *in vitro* changes are considered two of the many changes that fibroblastic cells must undergo on their route to neoplastic transformation (tumorigenicity). These various genetic tests contribute different information, which may be used to amplify and confirm conclusions drawn from human studies or animal bioassays, or to draw conclusions in the absence of epidemiological or bioassay data. In the latter case they have also been used in prioritizing agents for further evaluation by means of bioassays.

Carcinogen Identification Schemes

Some regulatory programs, such as California's Safe Drinking Water and Toxics Enforcement Act ("Proposition 65") and various activities of the U.S. EPA, require that explicit lists of substances having the potential to act as human carcinogens be maintained. Other such lists are developed by non-regulatory research organizations, such as the U.S. National Toxicology Program and the International Agency for Research on Cancer (IARC), an international program of the World Health Organization. The California air toxics programs do not have any statutory requirement to "identify" carcinogens. The requirement instead is to identify hazardous substances as Toxic Air Contaminants, and to determine whether or not a threshold concentration, below which no adverse effects are expected, is likely to exist:

> ***HEALTH AND SAFETY CODE, Division 26 (Air Resources), § 39660.***
>
> *(2) The evaluation shall also contain an estimate of the levels of exposure that may cause or contribute to adverse health effects. If it can be established that a threshold of adverse health effects exists, the estimate shall include both of the following factors:*
>
> *(A) The exposure level below which no adverse health effects are anticipated.*

> *(B) An ample margin of safety that accounts for the variable effects that heterogeneous human populations exposed to the substance under evaluation may experience, the uncertainties associated with the applicability of the data to human beings, and the completeness and quality of the information available on potential human exposure to the substance. In cases in which there is no threshold of significant adverse health effects, the office shall determine the range of risk to humans resulting from current or anticipated exposure to the substance.*

In practice however this requirement amounts to the need to establish whether or not a substance is carcinogenic. Any such effects are clearly harmful. Whereas the great majority of non-cancer health effects of chemicals are regarded as having a threshold, the default assumption for carcinogens is that there is no threshold (as described below). OEHHA follows the guidelines laid out by IARC for identification and classification of potential human carcinogens, which are described in detail in the most recent revision of the *Preamble* to the IARC monographs series (IARC, 2006). The IARC Monograph series provides evaluations of the carcinogenicity of individual substances or commonly occurring mixtures. The evaluation guidelines used are similar to those used by other scientific or regulatory authorities, including U.S.EPA.

The data inputs to hazard identification for carcinogens are human epidemiological studies, animal bioassays, along with supporting evidence such as mechanistic and genotoxicity data and structure-activity comparisons. IARC also assembles data on the structure and identity of the agent. The list of agents considered includes specific chemicals and also complex mixtures, occupational and lifestyle factors, physical and biological agents, and other potentially carcinogenic exposures.

IARC evaluations determine the quality of evidence for both animal and human evidence as falling into one of four categories: sufficient evidence of carcinogenicity, limited evidence of carcinogenicity, inadequate evidence of carcinogenicity and evidence suggesting lack of carcinogenicity. Stringent requirements for data quality are imposed. In view of their crucial importance, these definitions are quoted directly from the *Preamble* (IARC 2006):

> **"(a) Carcinogenicity in humans**
>
> ***Sufficient evidence of carcinogenicity:*** The Working Group considers that a causal relationship has been established between exposure to the agent and human cancer. That is, a positive relationship has been observed between the exposure and cancer in studies in which chance, bias and confounding could be ruled out with reasonable confidence. A statement that there is *sufficient evidence* is followed by a separate sentence that identifies the target organ(s) or tissue(s) where an increased risk of cancer was observed in humans. Identification of a specific target organ or tissue does not preclude the possibility that the agent may cause cancer at other sites.
>
> ***Limited evidence of carcinogenicity*:** A positive association has been observed between exposure to the agent and cancer for which a causal interpretation is considered by the Working Group to be credible, but chance, bias or confounding could not be ruled out with reasonable confidence.
>
> ***Inadequate evidence of carcinogenicity:*** The available studies are of insufficient quality, consistency or statistical power to permit a conclusion regarding the presence or absence

of a causal association between exposure and cancer, or no data on cancer in humans are available.

Evidence suggesting lack of carcinogenicity: There are several adequate studies covering the full range of levels of exposure that humans are known to encounter, which are mutually consistent in not showing a positive association between exposure to the agent and any studied cancer at any observed level of exposure. The results from these studies alone or combined should have narrow confidence intervals with an upper limit close to the null value (*e.g.,* a relative risk of 1.0). Bias and confounding should be ruled out with reasonable confidence, and the studies should have an adequate length of follow-up. A conclusion of *evidence suggesting lack of carcinogenicity* is inevitably limited to the cancer sites, conditions and levels of exposure, and length of observation covered by the available studies. In addition, the possibility of a very small risk at the levels of exposure studied can never be excluded.

(b) Carcinogenicity in experimental animals

Carcinogenicity in experimental animals can be evaluated using conventional bioassays, bioassays that employ genetically modified animals, and other in-vivo bioassays that focus on one or more of the critical stages of carcinogenesis. In the absence of data from conventional long-term bioassays or from assays with neoplasia as the end-point, consistently positive results in several models that address several stages in the multistage process of carcinogenesis should be considered in evaluating the degree of evidence of carcinogenicity in experimental animals.

The evidence relevant to carcinogenicity in experimental animals is classified into one of the following categories:

***Sufficient evidence of carcinogenicity*:** The Working Group considers that a causal relationship has been established between the agent and an increased incidence of malignant neoplasms or of an appropriate combination of benign and malignant neoplasms in (a) two or more species of animals or (b) two or more independent studies in one species carried out at different times or in different laboratories or under different protocols. An increased incidence of tumours in both sexes of a single species in a well-conducted study, ideally conducted under Good Laboratory Practices, can also provide *sufficient evidence*.

A single study in one species and sex might be considered to provide *sufficient evidence of carcinogenicity* when malignant neoplasms occur to an unusual degree with regard to incidence, site, type of tumour or age at onset, or when there are strong findings of tumours at multiple sites.

***Limited evidence of carcinogenicity*:** The data suggest a carcinogenic effect but are limited for making a definitive evaluation because, *e.g.,* (a) the evidence of carcinogenicity is restricted to a single experiment; (b) there are unresolved questions regarding the adequacy of the design, conduct or interpretation of the studies; (c) the agent increases the incidence only of benign neoplasms or lesions of uncertain neoplastic potential; or (d) the evidence of carcinogenicity is restricted to studies that demonstrate only promoting activity in a narrow range of tissues or organs.

***Inadequate evidence of carcinogenicity*:** The studies cannot be interpreted as showing either the presence or absence of a carcinogenic effect because of major qualitative or quantitative limitations, or no data on cancer in experimental animals are available.

***Evidence suggesting lack of carcinogenicity*:** Adequate studies involving at least two species are available which show that, within the limits of the tests used, the agent is not carcinogenic. A conclusion of *evidence suggesting lack of carcinogenicity* is inevitably limited to the species, tumour sites, age at exposure, and conditions and levels of exposure studied."

IARC utilizes the evaluations of animal and human data, along with supporting evidence including genotoxicity, structure-activity relationships, and identified mechanisms, to reach an overall evaluation of the potential for carcinogenicity in humans. The revised *Preamble* (IARC, 2006) includes a description of the data evaluation criteria for this supporting evidence, and indications as to the situations where the availability of supporting evidence may be used to modify the overall conclusion from that which would be reached on the basis of bioassay and/or epidemiological evidence alone. The overall evaluation is expressed as a numerical grouping, the categories of which are described below, as before by directly quoting IARC (2006):

"Group 1: The agent is *carcinogenic to humans*.

This category is used when there is *sufficient evidence of carcinogenicity* in humans. Exceptionally, an agent may be placed in this category when evidence of carcinogenicity in humans is less than *sufficient* but there is *sufficient evidence of carcinogenicity* in experimental animals and strong evidence in exposed humans that the agent acts through a relevant mechanism of carcinogenicity.

Group 2.

This category includes agents for which, at one extreme, the degree of evidence of carcinogenicity in humans is almost *sufficient*, as well as those for which, at the other extreme, there are no human data but for which there is evidence of carcinogenicity in experimental animals. Agents are assigned to either Group 2A (*probably carcinogenic to humans*) or Group 2B (*possibly carcinogenic to humans*) on the basis of epidemiological and experimental evidence of carcinogenicity and mechanistic and other relevant data. The terms *probably carcinogenic* and *possibly carcinogenic* have no quantitative significance and are used simply as descriptors of different levels of evidence of human carcinogenicity, with *probably carcinogenic* signifying a higher level of evidence than *possibly carcinogenic*.

Group 2A: The agent is *probably carcinogenic to humans*.

This category is used when there is *limited evidence of carcinogenicity* in humans and *sufficient evidence of carcinogenicity* in experimental animals. In some cases, an agent may be classified in this category when there is *inadequate evidence of carcinogenicity* in humans and *sufficient evidence of carcinogenicity* in experimental animals and strong evidence that the carcinogenesis is mediated by a mechanism that also operates in humans. Exceptionally, an agent may be classified in this category solely on the basis of *limited*

evidence of carcinogenicity in humans. An agent may be assigned to this category if it clearly belongs, based on mechanistic considerations, to a class of agents for which one or more members have been classified in Group 1 or Group 2A.

Group 2B: The agent is *possibly carcinogenic to humans*.

This category is used for agents for which there is *limited evidence of carcinogenicity* in humans and less than *sufficient evidence of carcinogenicity* in experimental animals. It may also be used when there is *inadequate evidence of carcinogenicity* in humans but there is *sufficient evidence of carcinogenicity* in experimental animals. In some instances, an agent for which there is *inadequate evidence of carcinogenicity* in humans and less than *sufficient evidence of carcinogenicity* in experimental animals together with supporting evidence from mechanistic and other relevant data may be placed in this group. An agent may be classified in this category solely on the basis of strong evidence from mechanistic and other relevant data.

Group 3: The agent is *not classifiable as to its carcinogenicity to humans.*

This category is used most commonly for agents for which the evidence of carcinogenicity is *inadequate* in humans and *inadequate* or *limited* in experimental animals.

Exceptionally, agents for which the evidence of carcinogenicity is *inadequate* in humans but *sufficient* in experimental animals may be placed in this category when there is strong evidence that the mechanism of carcinogenicity in experimental animals does not operate in humans.

Agents that do not fall into any other group are also placed in this category.

An evaluation in Group 3 is not a determination of non-carcinogenicity or overall safety. It often means that further research is needed, especially when exposures are widespread or the cancer data are consistent with differing interpretations.

Group 4: The agent is *probably not carcinogenic to humans*.

This category is used for agents for which there is *evidence suggesting lack of carcinogenicity* in humans and in experimental animals. In some instances, agents for which there is *inadequate evidence of carcinogenicity* in humans but *evidence suggesting lack of carcinogenicity* in experimental animals, consistently and strongly supported by a broad range of mechanistic and other relevant data, may be classified in this group."

The IARC hazard evaluation system provides a detailed and generally accepted scheme to classify the strength of evidence as to the possible human carcinogenicity of chemicals and other agents. This includes careful consideration of mechanistic data and other supporting evidence, the evaluation of which is also important to inform selection of models or defaults used in dose response assessment, as is described below. The extended consideration of supporting evidence is in fact the primary difference between more recent versions of the guidance from IARC, and also by other organizations including U.S. EPA, and the original versions of that guidance. In fact, the basic criteria for hazard identification based on bioassay and epidemiological data have not

changed substantially in other respects from earlier guidance documents, including that originally published by California (DHS, 1985). Although as noted earlier the California Air Toxics programs do not categorize identified carcinogens, it has generally been the practice to regard any agent with an IARC overall classification in Group 1 or Group 2 as a known or potential human carcinogen. This implies the selection of various policy-based default options, including absence of a threshold in the dose-response curve, unless specific data are available to indicate otherwise. The same basic identification criteria are used by OEHHA scientific staff to determine the appropriate treatment of agents not evaluated by IARC, or for which newer data or revised interpretations suggest that an earlier IARC determination is no longer appropriate.

U.S. EPA has also proposed a scheme for carcinogen hazard identification and strength of evidence classification in their recently finalized Guidelines for Carcinogen Risk Assessment (U.S. EPA, 2005). These principally differ from the IARC guidance in recommending a more extensive narrative description rather than simply a numerical identifier for the identified level of evidence, and also to some degree in the weight accorded to various types of supporting evidence. However, for most purposes they may be regarded as broadly equivalent to the scheme used by IARC, and OEHHA has chosen to cite the IARC (2006) *Preamble* as representing the most up-to-date and generally accepted guidance on this issue.

Dose Response Assessment

The dose-response phase of a cancer risk assessment aims to characterize the relationship between an applied dose of a carcinogen and the risk of tumor appearance in a human. This is usually expressed as a cancer slope factor ["potency" – in units of reciprocal dose - usually $(mg/kg\text{-}body\ weight.day)^{-1}$ or "unit risk" – reciprocal air concentration – usually $(\mu g/m^3)^{-1}$] for the lifetime tumor risk associated with lifetime continuous exposure to the carcinogen at low doses. Cancer potency factors may also be referred to as "cancer slope factors". (As will be described later, additional algorithms may need to be applied to determine risk for specific age groups, or at higher doses where toxicokinetic factors have significant effect.) The basic methodologies recommended in this document are similar to those described by U.S. EPA (2005a) in their Carcinogen Risk Assessment Guidelines. This document therefore refers to U.S. EPA (2005a) for explanation of detailed procedures, and will provide only a brief summary except in cases where OEHHA recommendations are different from or more explicit than those of U.S. EPA.

The following descriptions of methods for dose response assessment, and considerations in their application, apply in principle to the analysis of both animal and human (epidemiological) cancer incidence data. Indeed, the original formulation of the multistage model (Armitage and Doll, 1954) described below was developed based on human cancer incidence. Nevertheless, the number and quality of human cancer incidence datasets are limited. The more complex analyses have usually only been possible for animal experimental data, where the interindividual variability and the exposure conditions can be both measured and controlled. Most commonly, epidemiological studies have necessarily used a form of multivariate analysis to separate the effects of several different variables relating to exposure, demographics and behaviors (*e.g.,* smoking). In these analyses it is usually assumed that the effect measure(s) vary linearly with the exposure: any more complex variance assumptions might exceed the power of the data to determine the required model parameters. However, there are exceptions, especially for occupational studies where the critical exposure is measured as a continuous variable (rather than

just categorical) and where the effect of this exposure is substantial relative to other confounding factors. For example, OEHHA (1998) used a multistage model dealing with both exposure intensity and duration in the analysis of cancer incidence in railroad workers exposure to diesel exhaust (Garshick et al., 1988)

Interspecies Extrapolation

The procedures used to extrapolate low-dose human cancer risk from epidemiological or animal carcinogenicity data are generally health-protective in that they determine an upper confidence bound on the risk experienced by an exposed population. As statistical estimates they cannot be regarded as definite predictions of the risk faced by any one specific individual, who might for a variety of reasons, including individual exposure and susceptibility, experience a risk different from the estimate. The risk assessment procedures used aim to include the majority of variability in the general human population within the confidence bounds of the estimate, although the possibility that some individuals might experience either lower or even no risk, or a considerably higher risk, cannot be excluded. Additionally, differences may exist between the characteristics of the general public and those of studied populations. For example, healthy workers, the subject of most epidemiological studies, are often found to have lower rates of morbidity and mortality than the general population (Wen et al., 1983; Monson, 1986; Rothman and Greenland, 1998). Most human data are derived from studies of largely male adult workers and risk estimates cannot take into account specific physiological factors of women, children, and older populations that may affect the potency of a carcinogen, including early age-at-exposure.

Dose-response assessment based on environmental epidemiological studies may involve evaluation of health impacts at exposure levels within the range of those measured in the study population. However, more usually the source data are studies of occupationally exposed humans or of animals, in which case the exposures in the study are likely to be much higher than those of concern for risk assessments relating to community or ambient exposures. Further, even when extrapolation from animal species to humans is not required, the general population to which the URF is applied may differ in characteristics relative to the occupational population studied. It is therefore necessary to extrapolate from the available data to the population and exposure range of concern, which is done by using a dose-response model derived from the source data. The models used fall into three main classes: mechanistically based models, empirical models and (where data are lacking to support a true data-based model) default assumptions. The factors affecting the dose-response relationships for carcinogenesis may also be divided into those relating to absorption, distribution, metabolism and excretion on the one hand (*i.e.* toxicokinetics), and those relating to the underlying dose-response characteristics of carcinogenesis at the tissue or cellular level (*i.e.* toxicodynamics). In this sense the problem of dose response assessment for carcinogens is similar to that for non-cancer toxic effects. The toxicokinetic models used may in fact be similar for both situations, but the toxicodynamic models are generally different.

Intraspecies Extrapolation and Inter-individual Variability

In estimating the impact of a particular level of exposure to a carcinogen on a target human population, it is necessary to consider the range of susceptibility in the target population. In the present case this is typically defined as the general population of the State of California, including of course women (some of whom are pregnant), infants and children, the elderly, the sick, and

those with genetic polymorphisms or acquired differences which affect their susceptibility to carcinogens. In general it has been assumed that the upper-bound risk estimates obtained from the standard toxicodynamic models described below are sufficiently health-protective to cover the intrinsic variability of the adult human target population, in spite of the fact that these models do not explicitly address this type of variability, except in the few cases where an estimate is based on epidemiological data from a large and unselected study group (U.S. EPA, 2005a). However, various analyses (Drew et al., 1983; Barton et al., 2005; Appendix J) have suggested that this assumption is inadequate to cover the expected variability within a human population that includes infants and children. Accordingly both U.S. EPA (2005b) and this document now offer guidance on the use of age-specific adjustment factors to allow for the potentially greater sensitivity of infants and children to chemical carcinogenesis.

The ability to accommodate human variability with regard to the toxicokinetic factors affecting susceptibility to carcinogens varies with the level of detail used in the particular assessment. If the generic interspecies extrapolation approach based on body weight is used without any explicit toxicokinetic model, then the assumption is made, as in the case of toxicodynamic variability, that the overall health-protective assumptions made are sufficient to cover the toxicokinetic variability. On the other hand if explicit models such as those referenced in the following paragraph are used, this variability may be more explicitly accommodated by using parameter values which are taken as point estimates from measured distributions of population values, or by using Monte Carlo techniques to include those distributions in the model (Bois et al., 1996; OEHHA, 1992; 2001b).

Toxicokinetic Models

Considerable literature exists showing the importance of understanding the toxicokinetics of carcinogens in understanding their mechanism of action, sites of impact and dose-response relationships. U.S. EPA (2005) in Section 3.1 refers to the importance of identifying an appropriate dose metric for the dose-response analysis. Early cancer risk assessments typically used applied dose as the dose metric, which is adequate in simple cases provided appropriate correction factors are applied for interspecies extrapolation. However, it is often observed that the uptake, metabolism and elimination of the carcinogenic substance (and/or a procarcinogen and metabolites) is non-linear, especially at the higher doses employed in experimental animal studies (Hoel *et al*., 1983, Gaylor *et al*., 1994). Extrapolation to lower doses where such relationships tend to linearity (Hattis, 1990) is aided by the use of toxicokinetic models. These may be relatively simple compartment models, or sophisticated "physiologically based pharmacokinetic (PBPK) models" which to a greater or lesser degree model the actual biochemical and physiological events of toxicokinetic importance. Applications of both types of model may be found in various risk assessment documents prepared for the Toxic Air Contaminants program (and other OEHHA risk assessments). Since the details vary widely according to the nature of the chemical and the availability of appropriate kinetic data these general guidelines will defer to those examples rather than attempt a fuller exposition here. Further analysis of the use of toxicokinetic modeling in extrapolation from animals to humans, and in accounting for interindividual variability among adult humans, infants and children is presented in the Air Toxics Hot Spots *Technical Support Document for the Derivation of Noncancer Reference Exposure Levels* (OEHHA, 2008). Although this refers to the use of toxicokinetic modeling in non-cancer risk assessment, the primary considerations are similar for cancer risk assessment.

Toxicodynamic Models

An early use of mechanistic analysis to support risk assessment was the development of the Armitage-Doll multistage model of dose-response for carcinogenesis. The multistage model was initially developed on theoretical grounds, and by examination of epidemiological and animal data on time to tumor incidence. Subsequent discovery of the molecular biology of proto-oncogenes has provided a basis for explaining the model in terms of actual biological events and systems (Barrett and Wiseman, 1987). This model was developed by Crump and others into the "linearized multistage model", which has been extensively used for carcinogen risk assessment. It leads to a number of partially verifiable predictions, including linearity of the dose-response relationship at low doses, which is observed for many genotoxic carcinogens. It also predicts the form of the dose-response relationship at higher doses, which generally follow a polynomial form (subject to sampling and background corrections) except where other identifiable factors such as pharmacokinetics intervene.

It has been argued that the simple linearized form of the multistage model has limitations as a description of carcinogenic mechanisms, which detract from its usefulness and generality. Cell proliferation is known to be important in the progression of cancer. It may actually be the primary mechanism of action for a few carcinogens, as opposed to the direct modification of DNA by the carcinogen or a metabolite which is assumed to cause the mutational event at each stage in the original multistage description. A cell proliferation model has been developed (Moolgavkar and Knudson, 1981), which retains the concept of an initiating mutational event (in most cases caused by interaction of the chemical with DNA, although it could also be a spontaneous mutation) as in the original multistage model, but also considers proliferation, death or terminal differentiation of both normal and initiated cells. This model is thought to better describe the biological events in carcinogenesis. However, it has not been used extensively in risk assessment because it requires many parameters that are difficult to define and measure (such as proliferation and death rates for various classes of cell). If these cannot be accurately determined, the model has too many free parameters and is not helpful in defining extrapolated values for risk assessment purposes. This highlights a general problem in using mechanistic models in carcinogen risk assessment, which is that the carcinogenesis data themselves are generally insufficient to define fully the dose response curve shape at low doses or provide much mechanistic information. The analysis is therefore supplemented with policy-based assumptions (such as the expectation of linearity at low doses) and, wherever possible, additional experimental measurements relating to the mechanism of action, in order to make meaningful prediction of risk from environmental exposures to humans.

Because of the difficulties in validating simplified mechanistic models such as the basic multistage model, and the additional difficulty of parameter estimation with more complex mechanistic models, the new U.S. EPA guidelines (U.S. EPA, 2005a) and some recent California risk assessments have chosen instead to use a less overtly mechanistic approach. This approach combines benchmark dose methodology (described below) with an explicit choice of the method for low-dose extrapolation, either assuming low-dose linearity or, for certain carcinogens where data indicate that this is appropriate, a "margin of exposure" or safety/uncertainty factor based approach. This benchmark method is now normally recommended for carcinogen dose response analysis, and the results generally differ little from those derived by the linearized multistage model. Although the linearized multistage method is no longer recommended as the default approach for cancer potency estimation it remains a plausible alternative in many cases, and still

has useful applications, such as for time-to-tumor analyses for which benchmark methods are not yet widely available. Additionally, a considerable number of existing cancer potencies in Appendices A and B, and used in the Air Toxics Hot Spots program were derived by this method. Many of these would not be significantly different if calculated by the benchmark approach, and are unlikely to be replaced soon by newly calculated values. The linearized multistage method will therefore also be briefly described here.

Benchmark Dose Methodologies

The use of benchmark dose methodology has been explored by various investigators [including Gaylor et al. (1998); van Landingham et al. (2001) and Crump (1984, 1995, 2002)] as a tool for dose response extrapolation. This has been recommended in regulatory guidelines for both carcinogenic (U.S. EPA, 2005a) and non-carcinogenic (U.S. EPA, 1995) endpoints. The basic approach is to fit an arbitrary function to the observed incidence data, and to select a "point of departure" (POD) (benchmark dose) *within the range of the observed data.* From this a low dose risk estimate or assumed safe level may be obtained by extrapolation, using an assumed function (usually linear) or by application of uncertainty factors. The critical issue here is that no assumptions are made about the nature of the underlying process in fitting the data. The assumptions about the shape of the dose response curve (linear, threshold, etc.) are explicitly confined to the second step of the estimation process, and are chosen on the basis of policy, mechanistic evidence or other supporting considerations. The benchmark chosen is a point at the low end of the observable dose-response curve. Usually a dose at which the incidence of the tumor is 10% is chosen for animal studies, although lower effect levels may be appropriate for large epidemiological data sets. Because real experimental data include variability in the response of individual subjects, and measurement errors, likelihood methodology is applied in fitting the data. A lower confidence bound (usually 95%) of the effective dose (LED_{10}), rather than its maximum likelihood estimate (MLE), is used as the point of departure. This properly reflects the uncertainty in the estimate, taking a cautious interpretation of highly variable or error-prone data. It also reflects the instability of MLE values from complex curve-fitting routines, which has been recognized as a problem also with the linearized multistage model.

For cancer dose-response estimation using the benchmark dose method, either animal bioassay data or epidemiological data provide a suitable basis. In the absence of a pharmacokinetic model (which could provide tissue-specific dose metrics), the potency would ordinarily be based on the time-weighted average exposure during the exposure or dosing period. The model used to fit the data can be chosen from a range of available alternative quantal models, depending on which provides the best fit to the data in the observable range. In practice, the multistage polynomial fit developed for the linearized multistage model works well for most tumor data sets. Here it is being used merely as a mathematical curve-fitting tool, where the model well fits the data set, without making assumptions about its validity as a biological model of carcinogenesis.

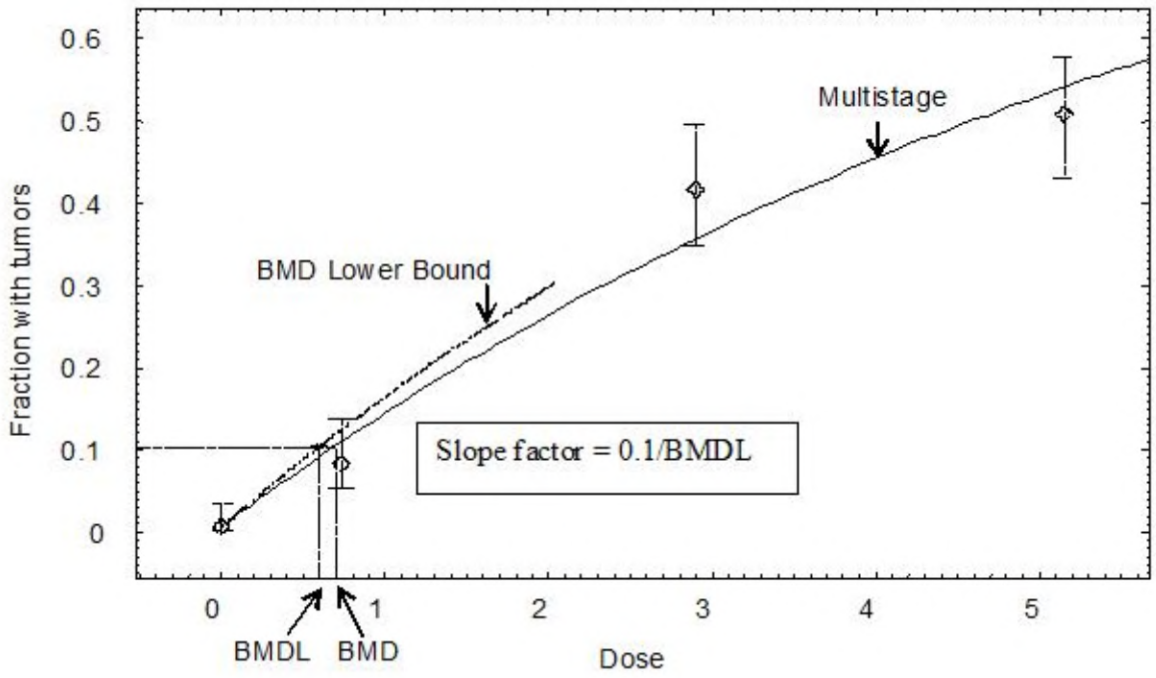
Suitable polynomial fits and estimates of the benchmark may be obtained using U.S. EPA's BMDS software. The benchmark often used is the 95% lower confidence bound on the dose producing 10% tumor incidence. However, if data are available which include a significant dose-response at less than 10% tumor incidence, then that lower benchmark should be used (*e.g.,* LED_{05} or LED_{01}). Other software such as Tox_Risk, which was used for the linearized multistage model, has been

used successfully, although the earlier GLOBAL program and its relatives are less suitable as curve-fitting tools for benchmark dose analysis.

Since it is usually assumed in cancer risk estimation that the low-dose response relationship is linear, risk estimates and a potency value (slope factor) may be obtained by linear extrapolation from an appropriate benchmark dose. The potency is the slope of that line ($0.1/LED_{10}$). The low dose linearity assumption is a general default for any carcinogen, and it is unlikely to be altered for genotoxic carcinogens.

A calculation using the benchmark dose approach (using a polynomial model with exponents restricted to zero or positive values), and linear extrapolation from the LED_{10} to obtain a potency estimate is shown in Figure 1 (the figure was generated by the U.S. EPA's BMDS program). This is based on tumor incidence data from an actual experiment with vinyl bromide in rats (Benya *et al*., 1982), with metabolized dose calculated by means of a pharmacokinetic model (Salmon *et al.,* 1992). The value of q_1* obtained by this calculation would then be corrected for the duration of the experiment if it had lasted for less than the standard rat lifetime, and for bodyweight and route-specific pharmacokinetic factors as described below. This is in addition to the correction for exposure duration that would be necessary if the study had not lasted for 105 weeks, and the interspecies correction, both of which are described below.

Figure 1. Benchmark dose calculation for tumor data in rats exposed to vinyl bromide



From Salmon *et al*. (1992), based on data from Benya *et al*. (1982)

Linearized Multistage Model

Quantal Analyses

A "multistage" polynomial (U.S. EPA, 1986, 2005a; Anderson *et al.*, 1983), based on the mechanistic insights of the original Armitage and Doll model of cancer induction and progression, has been used extensively by U.S. EPA, OEHHA and other risk assessors to model the dose response for lifetime risk of cancer. It usually is used for analysis of animal bioassay data, although related approaches have occasionally been used with epidemiological data. In mathematical terms, the probability of dying with a tumor (P) induced by an average daily dose (d) is:

$$P(d) = 1 - \exp[-(q_0 + q_1 d + q_2 d^2 + \ldots + q_i d^i)]$$

with constraints

$$q_i \geq 0 \text{ for all } i.$$

Equivalently, $$A(d) = 1 - \exp\left[- (q_1 d + q_2 d^2 + \cdots + q_k d^k)\right],$$

where $$A(d) = \frac{P(d) - P(0)}{1 - P(0)}$$ is the extra risk over background at dose d.

The q_i model parameters are constants that can be estimated by fitting the polynomial to the data from the bioassay, *i.e.* the number of tumor bearing animals (as a fraction of the total at risk) at each dose level, including the controls. The fit is optimized using likelihood methodology, assuming that the deviations from expected values follow a χ^2 distribution, with the number of degrees of freedom (and hence the maximum number of terms allowed in the polynomial) determined by the number of points in the data set. All the coefficients of the terms are constrained to be zero or positive, so the curve is required to be straight or upward curving, with no maxima, minima or other points of inflection. In addition to the maximum likelihood estimates of the parameters, the upper 95% confidence limits on these parameters are calculated.

The parameter q_0 represents the background lifetime incidence of the tumor. The 95% upper confidence limit of the slope factor q_1 (q_1^*), is termed the cancer potency. The maximum likelihood estimate (MLE) of q_1 is not usually regarded as a reliable estimate for several reasons. First, it fails to reflect the uncertainty and variability in the data which affect the value of the estimate. This is an important issue for protection of public health, which is emphasized by current regulatory guidelines. Secondly, due to the variable order of the polynomial and the effect of some terms being zero as opposed to having a small but finite value, the MLE is unstable, and may show large and unpredictable changes in response to very slight changes in the input data. It may also erratically have a zero value, even when the data imply a significant positive dose-response relationship. The MLE is not a measure of central tendency for this estimate distribution (which is always asymmetrical and often multi-peaked). For small doses, the cancer potency is the ratio of excess lifetime cancer risk to the average daily dose received. Details of the estimation procedure are given in Crump (1981) and Crump, Guess, and Deal (1977). Several software programs are available to perform the necessary calculations, including U.S. EPA's BMDS, Tox_Risk and the earlier GLOBAL programs by Crump and colleagues, and Mstage, written by Crouch (1987).

When dose is expressed in units of mg/kg-d, the potency is given in units of $(\text{mg/kg-d})^{-1}$. Likewise, when the model input is in units of concentration ($\mu g/m^3$, ppb), the potency is given in units of $\mu g/m^3)^{-1}$ pr $(\text{ppb})^{-1}$. As in the case of potencies obtained by the benchmark approach, the experiment-based potency value needs to be corrected for less-than lifetime or intermittent exposure, and extrapolated from the test species to humans. Risk calculations using potency value estimated using the linearized multistage model predict the cancer risk at low doses only, with the higher order terms of the fitted polynomial being ignored since their contribution is negligible at low doses.

Selection of Site and Tumor Type

In developing cancer potency estimates from animal data, standard practice has been to use dose-response data for the most sensitive tumor site as the basis of the estimate (CDHS, 1985). Where tumors of more than one histological type (*e.g.,* adenomas and carcinomas) are observed at a single

site, the combined incidence, *i.e.* proportion of animals affected with at least one tumor of any of the relevant types, is used for dose-response assessment. The same rules for combining tumor types are generally applied in determining statistical significance for carcinogen identification (IARC, 2006). Tumor types considered to represent different stages of progression following initiation of a common original normal cell type are combined, whereas tumor types having different cellular origins are generally not combined by this procedure. Other considerations that may influence choice of site for dose response estimation include the quality of the data (especially, the statistical impact of a high or variable rate of a particular tumor type and site in control animals), and biological relevance to humans. However, it is an important principle that, just as for the hazard identification phase, concordance of site or tumor type between animal models and human health effects may occur but is not assumed or required.

Carcinogens Inducing Tumors at Multiple Sites

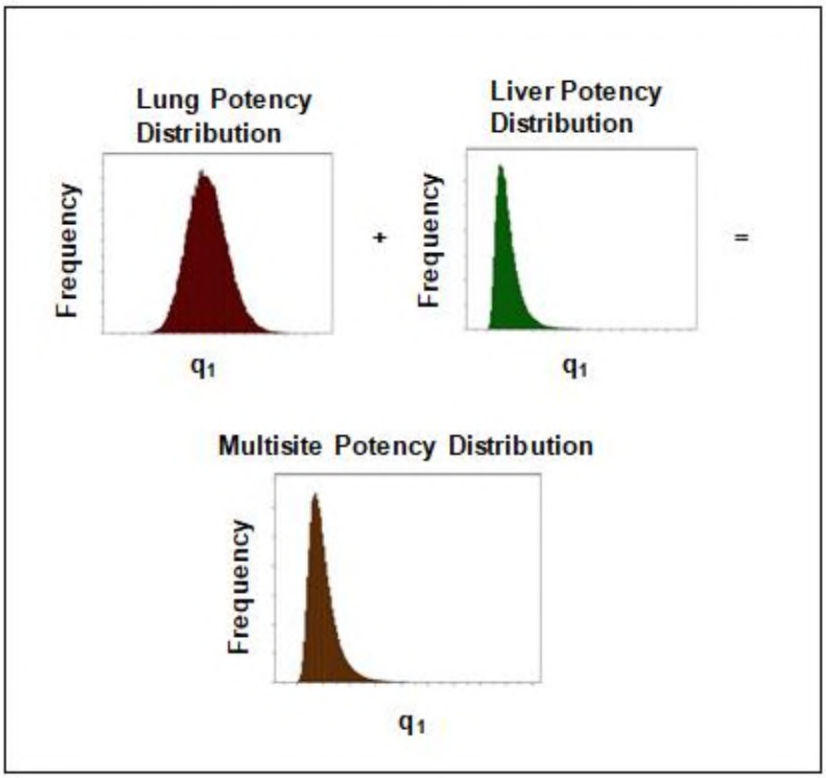
For most carcinogens, the selection of the most sensitive site in the animal studies is recognized as providing a risk estimate which is appropriate to protect human health. However, for chemicals that induce tumors at multiple sites, the single-site approach may underestimate the true carcinogenic potential. For example, the overall assessment of cancer risk from cigarette smoking (U.S. DHHS, 1982) or ionizing radiation (NRC, 1990) is not based on risk at one site, such as lung cancer. Instead, total cancer risk is estimated from all the sites at which agent-induced tumors are observed (lung, bladder, leukemia, etc), combined.

For carcinogens that induce tumors at multiple sites and/or with different cell types in a particular species and sex, OEHHA derives the animal cancer potency by probabilistically summing the potencies from the different sites and/or cell types. Using the combined potency distribution takes into account the multisite tumorigenicity and provides a basis for estimating the cumulative risk of all treatment-related tumors.

The linear term (q_1) of either the multistage model or the multistage-in-dose, Weibull-in-time model is first estimated based on the dose-response data for each of the treatment-related tumor sites. Statistical distributions, rather than point estimates, are generated at each site by tracing the profile likelihood of the linear term (q_1) (Zeise et al., 1991). The distributions of q_1 for each of the treatment-related sites are then statistically summed using a Monte Carlo approach and assuming independence (Figure 2). The sum is created by adding the linear term for each tumor site, according to its distribution, through random sampling. The upper 95 percent confidence limit on the summed distribution is taken as the multisite animal cancer potency estimate (McDonald et al., 2003, McDonald and Komulainen, 2005).

OEHHA has applied this approach in several recent dose-response analyses, including that for naphthalene presented in Appendix B of this document.

Figure 2. Addition of potency distributions for multi-site cancer potency derivations.



Early-Lifestage Cancer Potency Adjustments

In recent years, there have been growing concerns regarding the exposure of children to environmental chemicals, including the possibility that they may be more susceptible than adults to injury caused by those chemicals. The California Legislature passed the Children's Environmental Health Protection Act (Senate Bill 25, Escutia; Chapter 731, Statutes of 1999; "SB 25") to help address these concerns. Under SB25, OEHHA is mandated to consider infants and children specifically, where data permit, in evaluating the health effects of Toxic Air Contaminants (TACs).

The development of cancer is one of the adverse health effects that may occur in children as a result of exposure to environmental chemicals. The document "Prioritization of Toxic Air Contaminants under the Children's Environmental Health Protection Act" (OEHHA, 2001a) noted that risks of cancer from exposures to carcinogens occurring from conception through puberty can be different than those from exposures occurring in adulthood. Exposure to a carcinogen early in life may result in a greater lifetime risk of cancer for several reasons:

1. Cancer is a multistage process and the occurrence of the first stages in childhood increases the chance that the entire process will be completed, and a cancer produced, within an individual's lifetime.
2. Tissues undergoing rapid growth and development may be especially vulnerable to carcinogenic agents. During periods of increased cell proliferation there is rapid turnover of DNA, and more opportunity for misrepair of damage (*e.g.*, DNA breaks, crosslinks, adducts) or alterations to result in permanent changes to the DNA (*e.g.*, mutations, altered DNA methylation) that may ultimately lead to cancer.
3. During early development, a greater proportion of the body's cells are relatively undifferentiated stem cells, and as such represent a large target population of somatic cells capable of passing along permanent changes to the DNA during future cell divisions.
4. There may be greater sensitivity to hormonal carcinogens early in life since the development of many organ systems is under hormonal control (*e.g.*, male and female reproductive systems, thyroid control of CNS development).
5. Other factors that may play a role in increased cancer risk from exposures during critical developmental periods include differences in immunological activity, intestinal absorption, biliary and kidney excretion, blood and fat distribution, and expression of enzyme systems that activate or detoxify carcinogens.

Data in humans and animals for a variety of carcinogens suggest that exposures to such carcinogens early in life may result in a greater lifetime risk of cancer compared to exposures later in life. Examples of this effect in humans are carcinogenicity due to ionizing radiation, diethylstilbestrol (DES), chemotherapeutic agents, and tobacco smoke.
Ionizing radiation exposure carries an increased risk of cancer when exposures occur early in life compared to adult exposures for a number of tumor types. Children exposed to ionizing radiation (diagnostic X-rays) *in utero* demonstrate a larger excess of leukemia cases than children exposed to ionizing radiation postnatally (NRC, 1990). Exposure to radioisotopes (^{131}I, ^{137}Cs, ^{134}Cs, ^{90}Sr) as a consequence of the 1986 Chernobyl nuclear accident resulted in an elevated thyroid cancer

incidence in children but not adults (Moysich, 2002). Treatment of children for Hodgkin's lymphoma with both chemotherapeutic agents and irradiation has been shown to increase the risk of secondary tumors (Swerdlow et al., 2000; Franklin et al., 2006). Age at irradiation in Hodgkin's disease patients treated with radiotherapy strongly influenced the risk of developing breast cancer. The relative risk (RR) of developing breast cancer was 136 for women treated before 15 years of age, 19 for women 15-24 years of age, and 7 for those 24-29 years of age. In women above 30 years of age, the risk was not increased (Hancock *et al*., 1993).

DES was administered to pregnant women in the 1940s-1960s for the purpose of preventing pregnancy loss. In 1970, Herbst and Scully described 7 cases of vaginal adenocarcinoma (6 cases of the clear-cell type) in women aged 15-22 years. This type of cancer is extremely rare in that age range. A follow-up epidemiological study included an additional case, and noted the fact that the mothers of 7 of the 8 patients had been treated with DES during their pregnancy (Herbst *et al*., 1971). Reports by other investigators confirmed the association between maternal use of DES during pregnancy and the development of vaginal adenocarcinoma in their female offspring (Preston-Martin, 1989). It was observed that *in utero* DES exposure resulted in female genital tract morphological changes which correlated with both dose and duration of exposure, and those changes were not related to the maternal conditions which were the reason for the DES administration. Additionally, the risk of occurrence of those morphological changes declined with increasing gestational age at first exposure (O'Brien *et al*., 1979; Preston-Martin, 1989). In contrast, vaginal adenocarcinoma incidence did not increase in the exposed mothers themselves, indicating an increased early-life susceptibility to the carcinogenic effects of DES.

There is evidence in the epidemiological literature indicating that exposure to tobacco smoke during puberty may increase risk of breast cancer later in life, particularly among women who are NAT2 slow deacetylators (Marcus *et al*., 2000; Morabia *et al*., 2000; Lash and Aschengrau, 1999). Wiencke *et al*. (1999) report that early age at initiation of smoking is associated with a higher level of DNA adducts in lung tissue of former-smokers with lung cancer.

It has also been observed by Smith *et al*. (2006) that human *in utero* or early childhood exposure to arsenic in drinking water results in significantly increased lung cancer incidences during adult life.

Data from animal studies provide additional examples of increased sensitivity to early life (typically postnatal and juvenile) exposures. These effects span a range of target tissues, including the liver (vinyl chloride, safrole), brain (methylnitrosourea), reproductive tract (DES, tamoxifen), and lung (urethane) (OEHHA, 2001a).

In the following sections we summarize two efforts to evaluate quantitatively the effect of lifestage at exposure on carcinogenic response in experimental animal studies. The first section provides a description of OEHHA's analysis of data on the effect of age at exposure on carcinogenic potency. (Details of this analysis are in Appendix J.) The second section describes U.S. EPA's work in this area. (We also provide the published paper in Appendix I that presents the U.S. EPA analyses.) Both analyses used extant data available in the published literature. U.S. EPA used their analysis to modify the procedures they have used to estimate cancer risk by weighting risk by specific factors for childhood exposures. The weighting factors are a policy choice supported by U.S. EPA's data analysis. The results of OEHHA's analysis, summarized below and described in detail

in Appendix J, support the decision to modify policy to weight risk when exposure occurs during childhood.

OEHHA Analysis of the Effect of Age at Exposure on Cancer Potency

The analysis of animal cancer studies which include early life exposure by the Reproductive and Cancer Hazard Assessment Branch (RCHAB) of OEHHA also supports the application of lifestage-specific cancer potency factor adjustments. This analysis is provided in detail as Appendix J of this document.

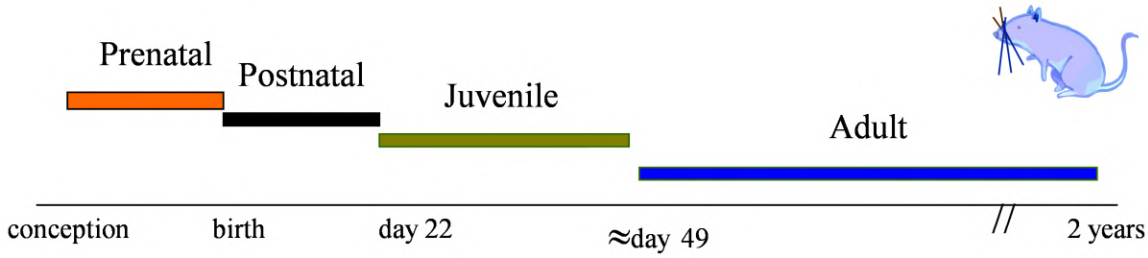
Early-in-life susceptibility to carcinogens has long been recognized by the scientific community and clinicians as a public health concern. Numerous scientific publications and symposia have addressed this issue over the years and the scientific literature contains a number of human clinical findings and epidemiological studies of early life cancer susceptibility. While there are many indications of increased human cancer susceptibility in early life, the magnitude of the impact has been difficult to gauge. Until recently risk assessment procedures have not in general addressed the issue. As described in the next section, in 2005 the U.S. EPA adopted an approach to weight carcinogens by age at exposure if they act via a mutagenic mode of action. The California legislature in 2000 directed OEHHA to assess methodologies used in addressing early-in-life risk, compile animal data to evaluate those methods, and develop methods to adequately address carcinogenic exposures to the fetus, infants, and children (Children's Environmental Health Initiative [AB 2872, Shelly]; California Health and Safety Code [HSC] section 901 [a] through [e]).

OEHHA assessed cancer risk assessment methodologies, and found that the existing risk assessment approaches did not adequately address the possibility that risk from early-in-life and adult exposures may differ. OEHHA further concluded that there was a need to address early-in-life cancer risk, and undertook studies to develop methods for doing so. Age-related cancer susceptibility data were identified from published animal cancer bioassays in which these issues were addressed. Two types of studies with early-in-life exposures were compiled. The first type are "multi-lifestage exposure studies." These studies have at least two groups exposed during different lifestages: One dose group is exposed to a chemical only during one of the following lifestages (Figure 3):

- prenatal (from conception to birth),
- postnatal (from birth to weaning),
- juvenile (from weaning to sexual maturity).

The second dose group is exposed for some period of time at an older age, preferably during the adult lifestage, that is, after sexual maturity. This group served as the reference group. In some cases where there was no adult exposure group, animals exposed as juveniles served as the reference group. Multi-lifestage exposure studies are available for many chemicals, enabling the exploration of patterns in early-life susceptibility across chemicals.

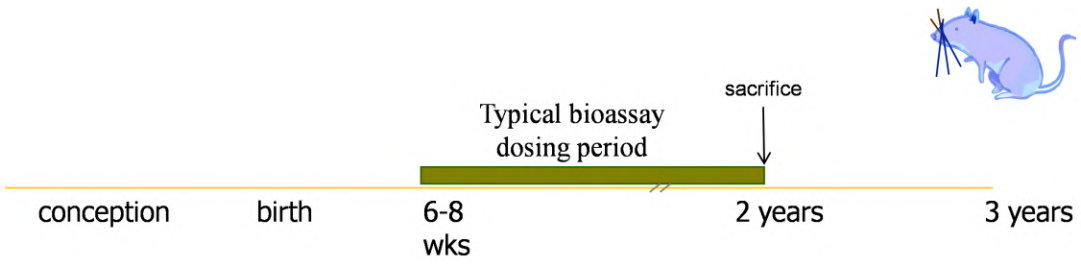
Figure 3. Definition of Rodent Lifestage Adopted in the OEHHA Analyses



OEHHA also conducted "chemical-specific case studies" of early-life sensitivity for two carcinogens, ethyl-N-nitrosoamine (DEN) and N-ethyl-N-nitrosourea (ENU) that combine data from a number of studies. These "chemical-specific case studies" were conducted to explore the feasibility of analyzing chemical-specific data on age susceptibility from single-lifestage exposure experiments. For these chemicals, OEHHA compiled from the literature a second type of study, "single-lifestage exposure experiments." In these experiments dose groups were exposed only during a particular lifestage and, unlike the "multi-lifestage exposure studies," there was no requirement that the same study also include groups exposed during a different lifestage. Thus, single-lifestage exposure experiments were identified as being either prenatal, postnatal, juvenile, or adult exposure studies. For each of the two chemicals, there were many prenatal studies conducted that were compiled, analyzed, and grouped together. Postnatal studies from different publications were similarly compiled, analyzed and grouped together, as were juvenile studies. Adult studies were not available for either DEN or ENU, thus for both chemicals juvenile exposure studies served as the referent for prenatal studies, and for postnatal studies.

Typical cancer bioassays such as those conducted in rats and mice by NTP involve exposing animals starting at six to eight weeks of age, which is the time at which these animals reach sexual maturity (late teenagers relative to humans). The experiments are run for two years, ending when the animal is in late middle age. Thus, early and very late life exposures are not included in the typical rodent bioassay (see Figure 4). If the NTP bioassay is used as a basis for estimating cancer potency, the potency and resulting risk estimates may be too low. Thus OEHHA focused on finding studies that evaluated early in life exposures.

Figure 4. Dosing Period for Typical Rodent Bioassays.



Since bioassays examining the effect of age at exposure on carcinogenesis were conducted by various investigators for different purposes, there is a great deal of variation across studies in terms of dose selection, duration of exposure, number of animals, and length of study duration. To be included in the compilation of studies with early life exposure, a study or an experimental group in a study had to meet minimum requirements.

The criteria for study inclusion are as follows:

- Treated groups were exposed to a single chemical carcinogen or a single carcinogenic chemical mixture.
- Study groups were not compromised by severe treatment-related non-cancer toxicity.
- Overall the duration of exposure period plus observation period exceeded 40 weeks, unless animals died of tumor.
- For included dose groups, the study must report age at dosing, age at sacrifice, and site-specific tumor incidence.
- Each lifestage exposure treatment group has an appropriate concurrent control group, or, for rare tumors only, an appropriate historical control.
- The studies were on mammals.
- Each treatment and control group consists of at least ten animals, unless the conduct and design of the study was well done in all other aspects (*e.g.*, the length of the study was sufficiently long to observe treatment-related tumors) and tumor incidence was high in treated groups and very low in controls.
- Site specific tumor data were reported, not only total number of tumor bearing animals.
- The test compound was administered in the diet, water, via gavage, or by intraperitoneal (i.p.), intravenous (i.v.), or subcutaneous (s.c.) injection. For dermal and subcutaneous injection studies, distal tumor findings are utilized (for dermal, other than skin tumors; for injection, non-injection site tumors).

- While studies designed to histopathologically examine tumors at multiple sites were preferred, studies that examined only a select set of organ/tissue sites were not excluded if the sites examined were known with confidence to be the only target tissues for the chemical and lifestage in question in that particular strain of animal.

Different approaches were taken to identify animal cancer studies that included groups of animals exposed during early life stages. First, MEDLINE and TOXLINE (National Library of Medicine) databases were searched using combinations of various key words for cancer (*e.g.*, tumor(s), neoplasm(s), cancer, neoplasia, cancerous, neoplasms-chemically induced) and for early-life exposure (*e.g.*, age, age-at-exposure, development (al), prenatal, *in utero*, gestation (al), postnatal, neonatal, juvenile, weaning, weanling, adolescent, adolescence, young). Second, the extensive compilation of bioassays in the *Survey of Compounds which have been Tested for Carcinogenic Activity*, was reviewed. This survey, formerly maintained by the National Cancer Institute as Public Health Service Publication Number 149, or PHS 149, is now available from a private source electronically as CancerChem, 2000. Third, from bibliographies from relevant published papers additional studies were identified. Finally the Single Dose Database developed by Calabrese and Blain (1999) was obtained and utilized to identify additional publications that appeared to contain potentially useful data. All of these publications were evaluated to determine if the study dosed separate groups of animals early in life and at or near adulthood. A total of 145 publications, providing data on 84 chemicals, were identified as meeting the criteria for study inclusion. A subset of these met the criteria for inclusion in the multi-lifestage exposure analysis.

Finally, for the OEHHA multi-lifestage analyses, we define "experiment" as a study component consisting of a control group as well as a treated group(s) exposed during the same lifestage (*i.e.*, prenatal, postnatal, juvenile or adult), and using the same experimental protocol (*e.g.*, route of exposure, strain, species, laboratory). Thus, by our definition one publication may report multiple experiments.

In the OEHHA analysis, data from studies on 23 unique carcinogens, 20 of which are considered to act via primarily genotoxic modes of action, were analyzed. Of these 20 carcinogens, 15 are thought to require metabolic activation to the ultimate carcinogenic species (Table 1). Fourteen carcinogens, including one thought to act via primarily nongenotoxic modes of action, were included in the prenatal multi-lifestage exposure studies. Eighteen carcinogens, including two thought to act via primarily nongenotoxic modes of action, were included in the postnatal multi-lifestage exposure studies. Five carcinogens were included in the juvenile multi-lifestage exposure studies. The case study chemicals, DEN and ENU, are both genotoxic. ENU is a direct acting alkylating agent, while DEN requires metabolic activation.

Table 1. Carcinogens for which studies with multi-lifestage exposures in animal studies are available

Genotoxic carcinogens requiring metabolic activation
Benzidine Benzo[a]pyrene Dibutylnitrosamine Diethylnitrosamine (DEN) 7,12-Dimethylbenz[a]anthracene (DMBA) Dimethylnitrosamine (DMN) Di-n-propylnitrosamine (DPN) 1 -Ethyl-nitrosobiuret 2-Hydroxypropylnitrosamine 3-Hydroxyxanthine 3-Methylcholanthrene (3-MC) 4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) Safrole Urethane Vinyl chloride
Genotoxic carcinogens not requiring metabolic activation
Butylnitrosourea 1,2-Dimethylhydrazine Ethylnitrosourea (ENU) Methylnitrosourea (MNU) ß-Propiolactone
Nongenotoxic carcinogens
1,1-Bis(p-chlorophenol)-2,2,2-trichloroethane (DDT) Diethylstilbestrol (DES) 2,3,7,8-Tetrachlorodibenzodioxin (TCDD)

Cancer Potency Estimation

Statistical methods were developed and used to analyze the data and derive measures of early-life susceptibility. These are described in detail in Appendix J. In brief, a cancer potency (the slope of the dose response curve) was developed for each of the experiments selected using the linearized multistage model. This model was chosen because of widespread use in risk assessment, and its flexibility in being able to fit many different data sets needed to evaluate the effect of lifestage-at-exposure on cancer potency. The dose metric used for the potency analyses is cumulative dose normalized to body weight. The cancer potency is thus expressed as the increase in tumor probability with increasing cumulative dose in units of mg/kg body weight.

To take into account uncertainty in potency estimation, cancer potencies are depicted by a statistical distribution, rather than by a single, fixed value, using methods described in Appendix J. While these methods have typically been used to obtain and report the 95th percentile of the cancer slope parameter for cancer risk assessment purposes, here OEHHA utilized the full distribution of the cancer slope parameter to derive measures of early-life susceptibility to carcinogens. This was done to systematically take into account uncertainty in the analysis.

For experiments where treatment related tumors were observed at multiple sites or at the same site but arising from different cell types, slopes from these sites were statistically combined by summing across the potency distributions (assuming independence across the sites that were observed) to create an overall multisite cancer potency. It is not uncommon that a carcinogen causes more than one type of cancer or causes tumors at different sites depending on lifestage at exposure. For example, in humans tobacco smoke causes cancers of the lung, bladder, and certain other organs. This multi-site carcinogenicity is frequently observed in animal experiments as well. In order to account for this, all treatment-related tumors that were observed in a given lifestage were taken into account in estimating cancer potency from that particular experiment.

Addressing Early-Age Sensitivity in Estimating Cancer Risk: Age Sensitivity Factors

Inherent Sensitivity of Lifestages – Lifestage Potency Ratios

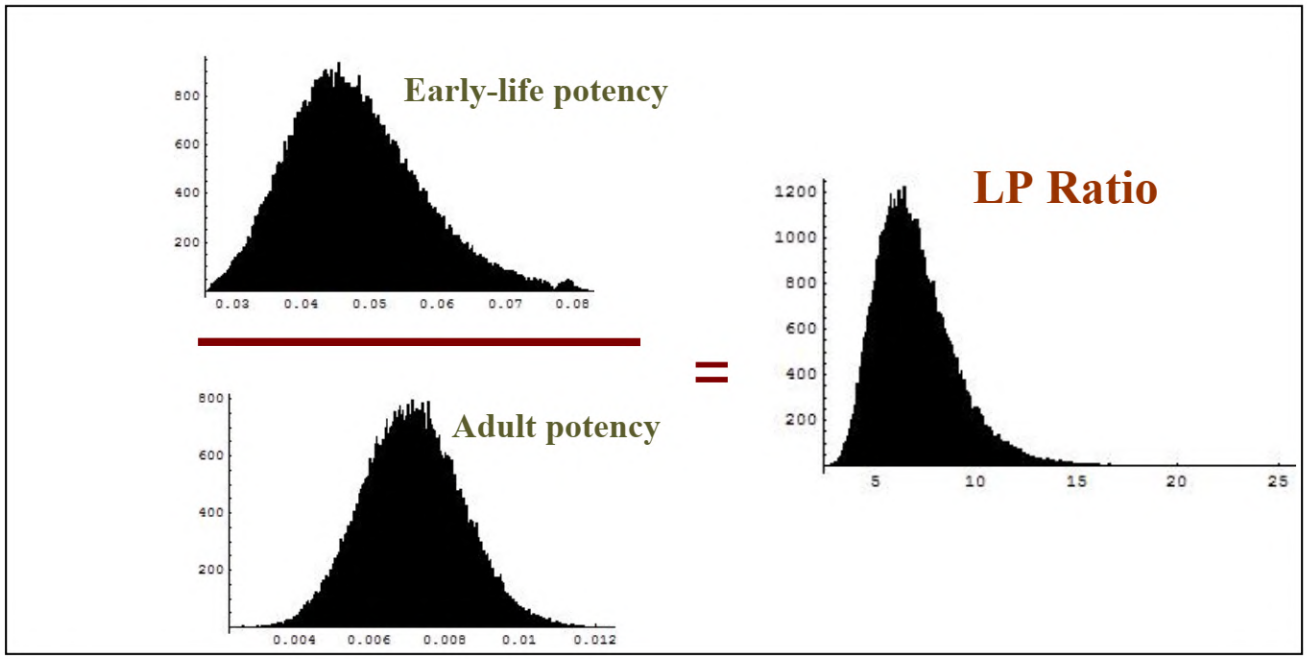
For this analysis, OEHHA calculates the ratio of cancer potency derived from an early lifestage exposure experiment(s) to that derived from an experiment(s) conducted in adult animals. OEHHA used the potency distributions for the individual lifestage exposures, rather than a point estimate, to derive the ratios. The lifestage cancer potency ratio is then described as a distribution and one can select specific percentiles from the distribution to better understand and bound the uncertainty (Figure 5). Of particular importance is the location of the ratio distribution in relation to the reference value of 1.0, which would mean no difference in risk from exposures at early versus adult lifestages. A lifestage cancer potency ratio distribution that primarily lies above the value of 1.0 indicates early life exposures to a carcinogen result in a stronger tumor response relative to adult exposure. Conversely, a lifestage cancer potency ratio distribution that mainly lies below the value of 1.0 indicates early life exposure to a carcinogen results in a weaker tumor response relative to adult exposure.

A lifestage potency (LP) ratio distribution was derived for each multi-lifestage study, resulting in 22 prenatal ratio distributions representing 14 unique carcinogens, 55 postnatal LP ratio distributions representing 18 unique carcinogens, and seven juvenile LP ratio distributions representing five unique carcinogens. The LP ratio distributions for a given early lifestage were combined into a single "LP ratio mixture distribution," in order to show the range of susceptibilities of that lifestage to the carcinogens studied.

LP ratio mixture distributions for a given early lifestage were developed by (1) obtaining a single LP ratio distribution for each chemical (when a chemical is represented by more than one study) and then (2) equally sampling across all chemicals. When a chemical is represented by more than one study, then the LP ratio distributions from all studies of that chemical were combined by equally sampling from each LP ratio distribution via Monte Carlo methods to obtain a single LP ratio distribution for that chemical. (Appendix J describes this in more detail, as well as a

sensitivity analysis that included two alternative sampling methods.) Once each chemical is represented by a single LP ratio distribution, then the LP ratio mixture distribution for each early lifestage (prenatal, postnatal, and juvenile) is obtained by equally sampling across all of the chemicals via Monte Carlo methods.

Figure 5. Lifestage Potency Ratio (LPR) distribution.

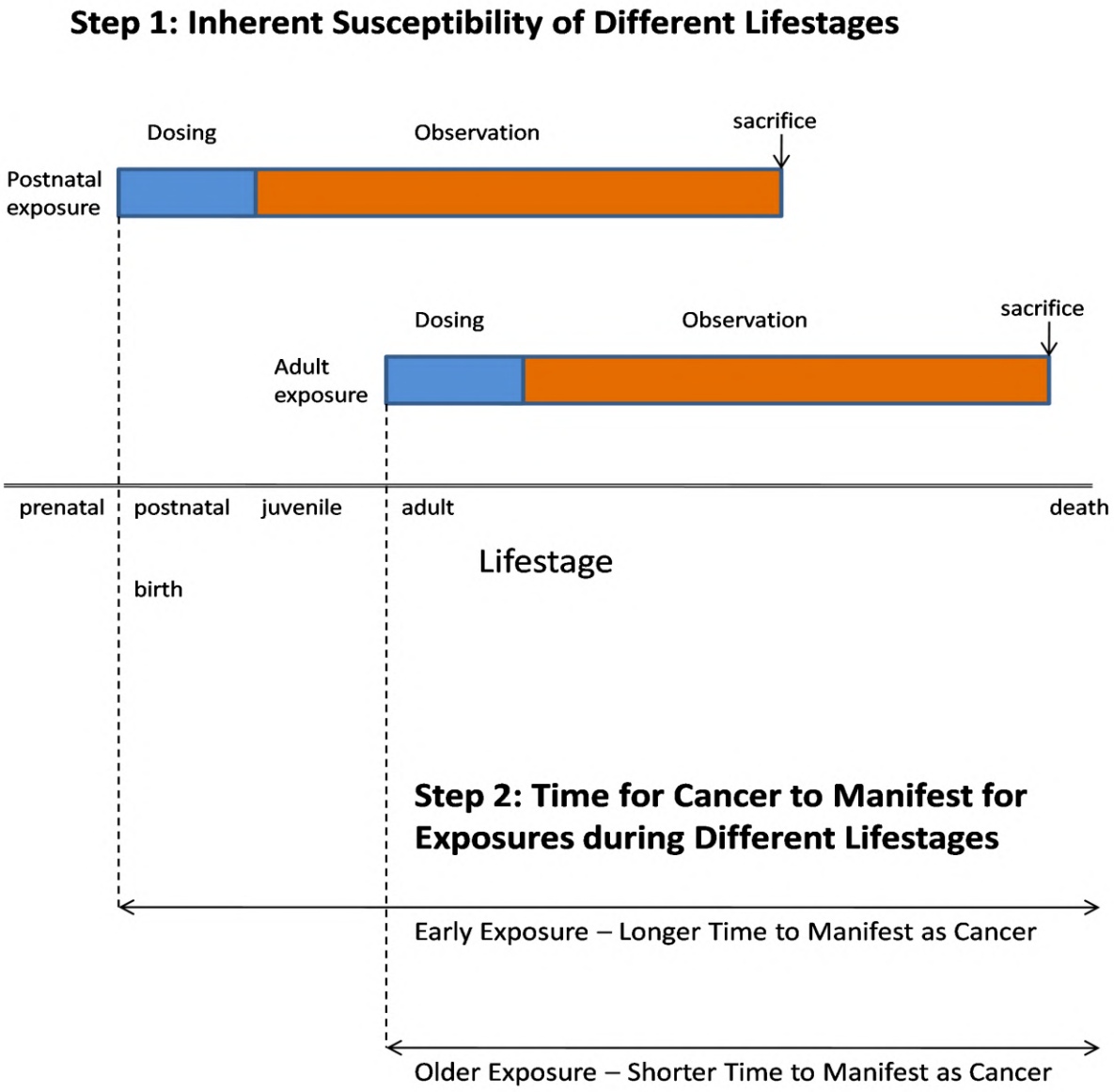


Effect of Longer Time Period for Cancer to Manifest

The LP ratios described above characterize the inherent susceptibility of early lifestages to carcinogen exposure, by comparing potencies for individuals followed for similar periods of time and similarly exposed, but exposed during different lifestages. Age-specific adjustments to the cancer potency must also take into account the longer period of time that carcinogen exposure to the young has to manifest as cancer. Empirical data from studies of both humans and animals demonstrate that, for many cancers, cancer risk increases with age, or time since first exposure. While some cancers have been seen to increase by as much as the sixth power of age, a general approach taken for example by the National Toxicology Program in analyzing tumor incidences in its chronic bioassays is to assume that cancer risk increases by the third power of age. Thus, consistent with the approach used by the NTP in analyzing rodent cancer bioassay data, the longer period of time that exposed young have to develop tumors is addressed by taking into account time-of-dosing. This was done by multiplying the LP ratio by a time-of-dosing factor, to yield an age sensitivity factor (ASF). Specifically, the prenatal LP ratio is multiplied by a factor of 3.0, the postnatal LP ratio is multiplied by a factor of 2.9, and the juvenile LP ratio is multiplied by 2.7. Thus, ASFs were developed for each experiment, by first calculating the LP ratio to address inherent susceptibility of early lifestages relative to adults, and then accounting for the effect of years available to manifest a tumor following carcinogen exposure. (see Figure 6). Note that we

are not using the term "sensitivity" in the immunologic sense (*e.g.*, sensitization), but rather are using the term more generically.

Figure 6. Issues addressed by the Age-Sensitivity Factor (ASF)



Application of this approach for risk associated with lifetime exposures would include an ASF of less than 1 for exposures during the latter part of adult life for carcinogens that act on early stages. Therefore, the addition of this adjustment to the younger lifestages but not to the later part of the adult period could overestimate the risk of whole-life exposures. On the other hand, the 70 year "lifetime" used in estimating lifetime cancer risk does not reflect the longer lifespan of the U.S. population. Further, as noted above, the animal bioassays on which potency was based typically exclude pre-weaning dosing and sacrifice animals during their late middle-age. Use of cancer potencies calculated from standard assays can therefore underestimate lifetime cancer risk. The ASF calculated for carcinogens includes both inherent sensitivity of developing animals and the available time since exposure to develop cancer.

Results of OEHHA Analysis

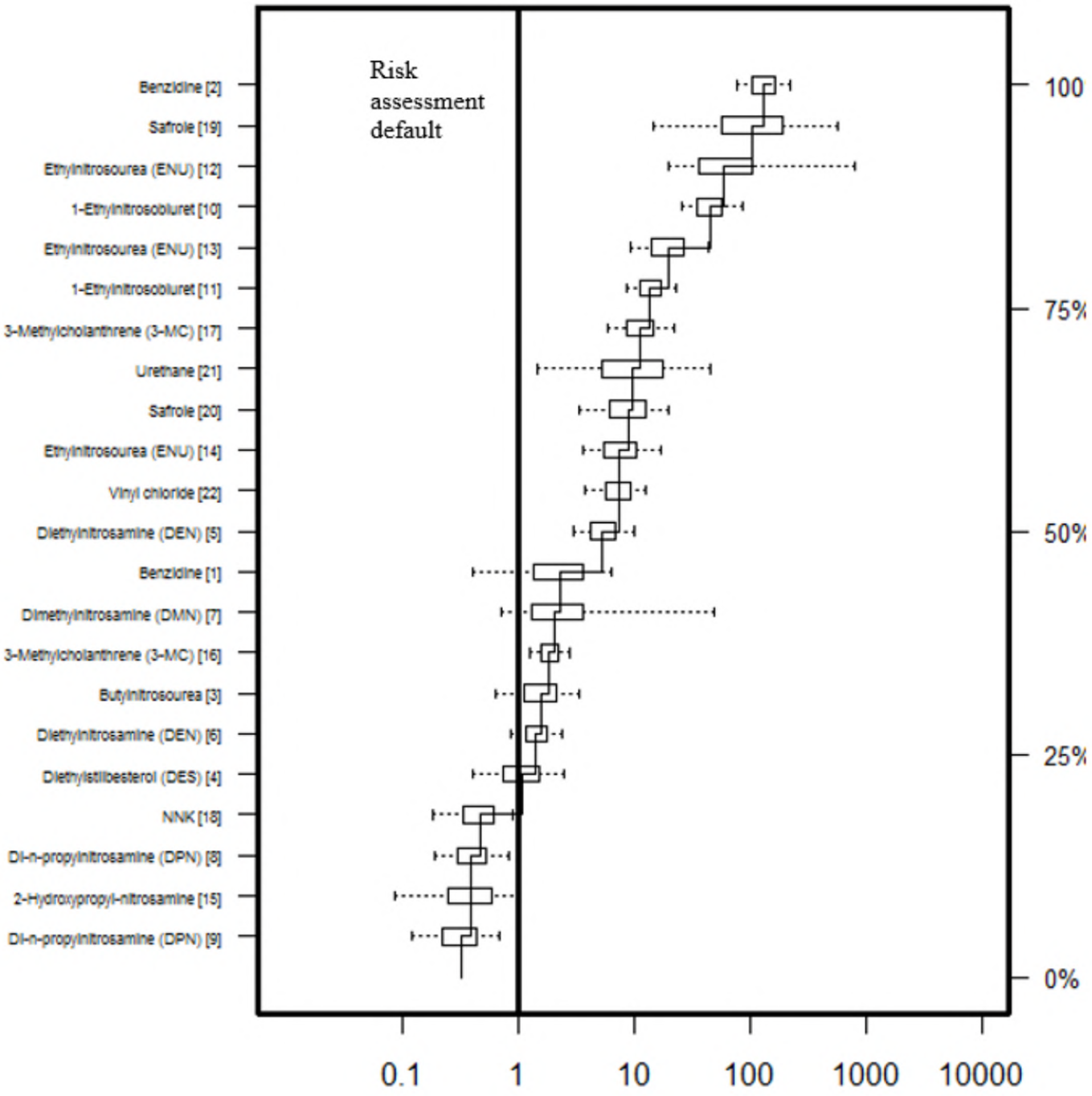
The analyses indicate that both the prenatal and postnatal lifestages can be, but are not always, much more susceptible to developing cancer than the adult lifestage. The analyses also indicated that the ASFs for these age windows vary by chemical, gender and species.

Regarding prenatal lifestage exposure, few cases were indicative of equal inherent adult and prenatal susceptibility, with an LP ratio of unity. The LP ratio distribution was roughly bimodal, with LP ratios for several studies significantly greater than unity and several others significantly less than unity. Figure 7 below shows the ASFs from each of the prenatal multi-lifestage exposure studies, displayed as a cumulative frequency profile. The median of the prenatal ASF mixture distribution was 2.9 (see also Table 6 in Appendix J),

The modality in the prenatal LP ratio distribution was reflected in the DEN and ENU case studies, with results for DEN suggesting inherently less sensitivity than older animals from exposure *in utero*, and for ENU just the opposite. For the DEN and ENU case studies, the referent groups were juvenile rather than adult animals, and the results may have underestimated the LP ratio and ASF, to the extent that some of the apparent sensitivity for DEN and ENU in the prenatal period carries through to the juvenile period. ENU is a direct acting carcinogen that does not require metabolic activation, whereas DEN can not be metabolized to any significant extent by fetal tissues until relatively late in gestation. This may explain the lower fetal susceptibility of DEN. However, prenatal metabolic status is not the sole determinant of prenatal susceptibility; *e.g.*, benzidine and safrole require metabolic activation and exhibit greater susceptibility from prenatal exposure.

The median of the postnatal ASF mixture distribution was 13.5 (see Table 7 in Appendix J). Figure 8 below shows the ASFs from each of the postnatal multi-lifestage exposure studies, displayed as a cumulative frequency profile. Thus, for the chemicals studied, there was generally greater susceptibility to carcinogens during the early postnatal compared to the adult period, particularly when the ASF accounts for the longer period cancer has to manifest when exposure occurs early in life. The DEN and ENU case studies also exhibited substantial extra susceptibility during the postnatal period. To summarize, for most of the carcinogens studied here, rodents are inherently more sensitive in the postnatal period, as indicated by Figure 8.

Figure 7. Prenatal ASF Cumulative Frequency Profile

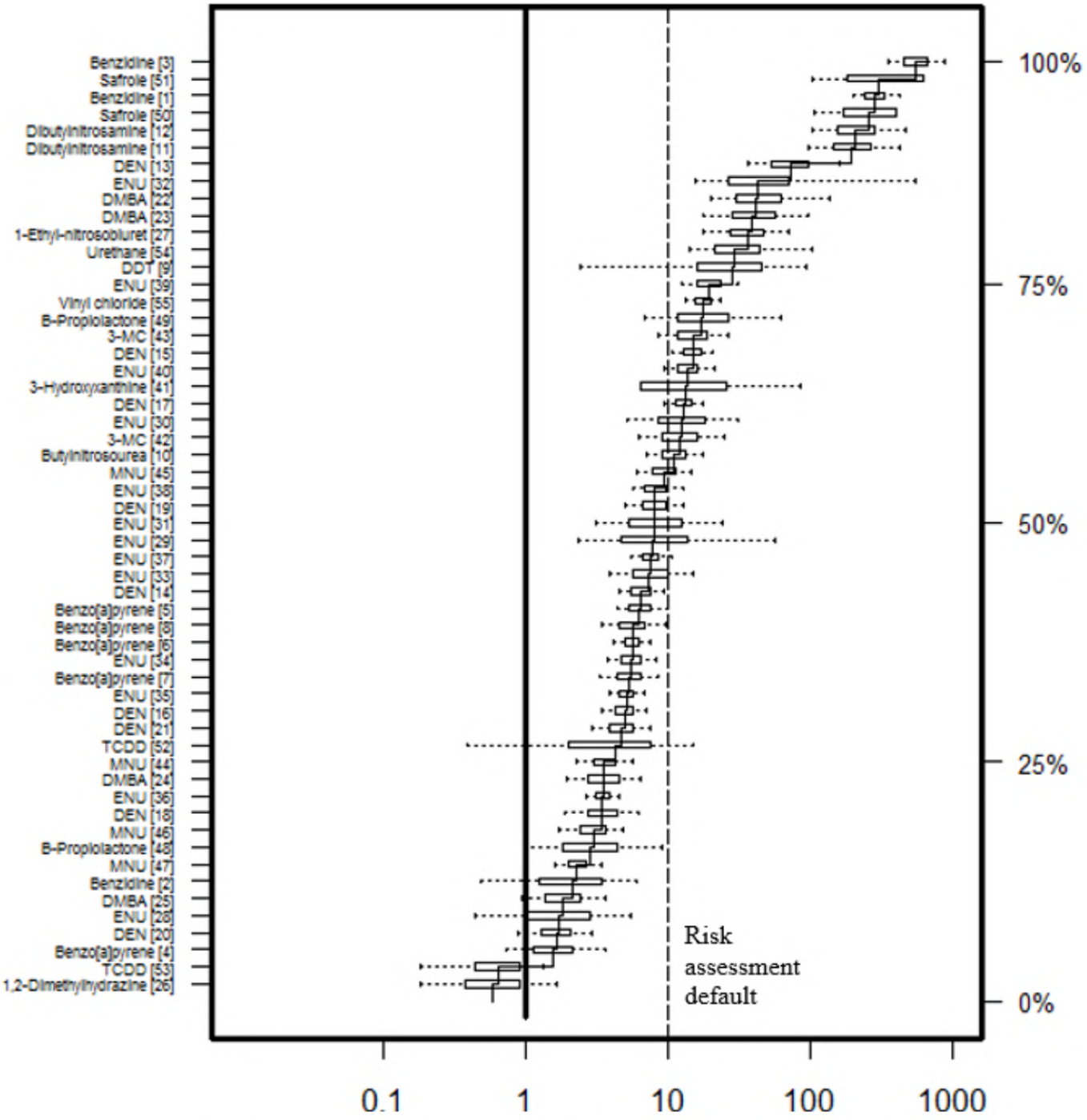


The median of the prenatal ASF mixture distribution was 2.9 (see also Table 6 in Appendix J). References are given in the legend on the next page

Figure 7 Legend (References as in Appendix J)

1. Vesselinovitch *et al.* (1979a), mouse, B6C3F$_1$, F, day -9 to 0
2. Ibid, M, day -9 to 0
3. Zeller *et al.* (1978), rat, Sprague Dawley, M/F day -2
4. Turusov *et al.* (1992), mouse, CBA, F, day -2
5. Mohr et al. (1975), hamster, Syrian Golden, day -15 to -1
6. Mohr *et al.* (1995), hamster, Syrian Golden, F, day -3
7. Althoff *et al.* (1977), hamster, Syrian Golden, M/F, day -9 to -3
8. Ibid, day -9 to -3
9. Althoff and Grandjean (1979), hamster, Syrian Golden, F, day -9 to -3
10. Druckrey and Landschutz (1971), rat, BD IX, M/F, day -10
11. Ibid, day -3
12. Naito *et al.* (1981), rat, Wistar, day -9
13. Ibid, day -9
14. Tomatis *et al.* (1977), rat, BDVi, F, day -5
15. Althoff and Grandjean (1979), hamster, Syrian Golden, M/F, day -9 to -3
16. Tomatis *et al.* (1971), mouse, CF-1, F day -4 to -1
17. Turusov *et a*l. (1973), mouse, CF-1, F, day -2
18. Anderson *et al.* (1989), mouse, C3H & B6C3 F$_1$,M/F day -8 to -4
19. Vesselnovitch *et al.* (1979a), mouse, B6C3 F$_1$, M, day -9 to -3
20. Vesselnovitch *et al.* (1979b), mouse, B6C3 F$_1$, F day -9 to -3
21. Choudari Kommineni *et al.* (1970), rat, MRC, M/F, day -4
22. Maltoni *et al.* (1981), rat, Sprague Dawley, M/F day -13 to -7

Figure 8. Postnatal ASF Cumulative Frequency Profile



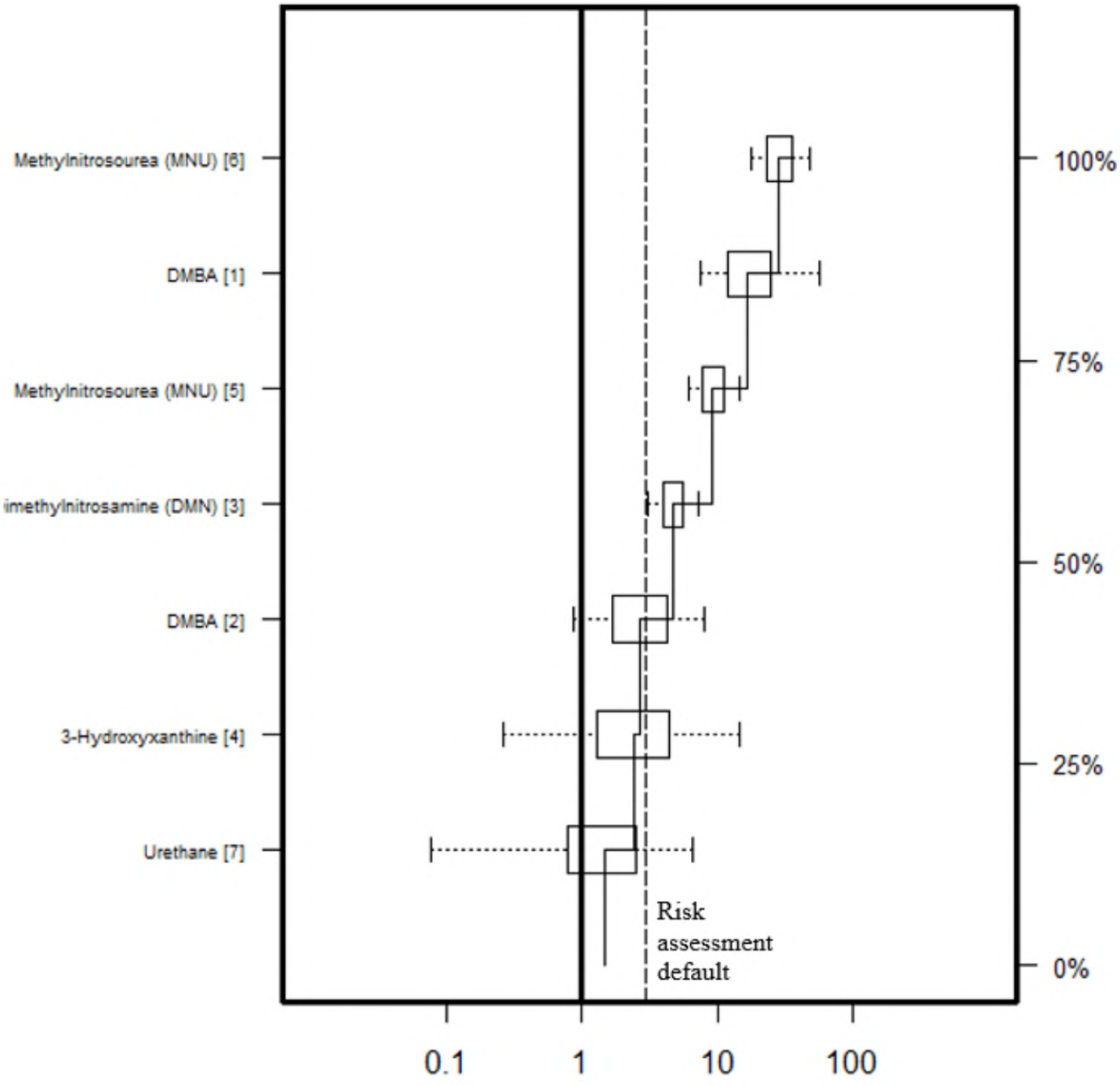
The median of the postnatal ASF mixture distribution is 13.5. The dotted line represents the default ASF for weighting risk for carcinogen exposures to humans between the third trimester and 2 years of age (see next section). References are given in the legend on the next page.

Figure 8 Legend (References as in Appendix J)

1 Vesselinovitch *et al.* (1975b), mouse, B6C3F$_1$, M, day 7-27
2 Vesselinovitch *et al.* (1979), mouse, B6C3F$_1$, F, day 1-21
3 Ibid, M, day 1-21
4 Truhaut *et al.* (1966), mouse, swiss, M/F, day 1
5 Vesselinovitch *et al.* (1975a), mouse, B6C3F$_1$, F, day 1
6 Ibid, M, day 1
7 Ibid, C3A F$_1$, F, day 1
8 Ibid, M, day 1
9 Vesselinovitch *et al.* (1979a), mouse, B6C3F$_1$, M, day 1-28
10 Zeller *et al.* (1978), rat, Sprague Dawley, M/F, day 2
11 Wood *et al.* (1970), mouse, IF x C57, F, day 1-15
12 Ibid, M, day 1-15
13 Rao and Vesselinovitch (1973), mouse, B6C3F$_1$, M, day 15
14 Vesselinovitch *et al.* (1984), mouse, B6C3F$_1$, F, day 1
15 Ibid, M, day 1
16 Ibid, F, day 15
17 Ibid, M, day 15
18 Ibid, C3A F$_1$, F, day 1
19 Ibid, M, day 1
20 Ibid, F, day 15
21 Ibid, M, day 15
22 Meranze *et al.* (1969), rat, Fels-Wistar, F, day 10
23 Ibid, M, day 10
24 Walters (1966), mouse, BALB/c, F, day 17
25 Ibid, M, day 17
26 Martin *et al.* (1974), rat, BDIX, M/F, day 10
27 Druckrey and Landschutz (1971), rat, BDIX, M/F, day 10
28 Naito *et al.* (1985), gerbil, mongolian, F, day 1
29 Ibid, M, day 1
30 Bosch (1977), rat, WAG, F, day 8
31 Ibid, M, day 8
32 Naito *et al.* (1981), rat, Wistar, F, day 7
33 Ibid, M, day 7
34 Vesselinovitch *et al.* (1974), mouse, B6C3F$_1$, F, day 1
35 Ibid, M, day 1
36 Ibid, F, day 15
37 Ibid, M, day 15
38 Ibid, C3A F$_1$, F, day 1
39 Ibid, M, day 1
40 Ibid, M, day 15
41 Anderson *et al.* (1978), rat, Wistar, F, day 9
42 Klein (1959), mouse, A/He, F, day 8-31
43 Ibid, M, day 8-31
44 Terracini and Testa (1970), mouse, B6C3F$_1$, F, day 1
45 Ibid, M, day 1
46 Terracini *et al.* (1976), mouse, C3Hf/Dp, F, day 1
47 Ibid, M, day 1
48 Chernozemski and Warwick (1970), mouse, B6A F$_1$, F, day 9
49 Ibid, M, day 9
50 Vesselinovitch *et al.* (1979a), mouse, B6C3F$_1$, M, day 1-21
51 Vesselinovitch *et al.* (1979b), mouse, B6C3F$_1$, M, day 1-21
52 Della Porta *et al.* (1987), mouse, B6C3F$_1$, F, day 10-45
53 Ibid, M, day 10-45
54 Choudari Kommineni *et al.* (1970), rat, MRC, M/F, day 1-17
55 Maltoni *et al.* (1981), rat, Sprague Dawley, M/F, day 1-35

There were only five chemicals and seven studies, two of which were not independent, available to examine susceptibility in the juvenile period. The juvenile LP ratios indicated significantly greater susceptibility in this period for three independent studies, with the remaining studies consistent with equal inherent susceptibility to adult animals (see Figure 16 in Appendix J). Figure 9 below shows the ASFs from each of the juvenile multi-lifestage exposure studies, displayed as a cumulative frequency profile. The median of the juvenile ASF mixture distribution was 4.5 (see Table 8 in Appendix J).

Figure 9. Juvenile ASF Cumulative Frequency Profile



The median of the juvenile ASF mixture distribution is 4.5. The dotted line represents the default value for weighting risk for carcinogen exposures between 2 and 15 years of age (see next section).

Figure 9 Legend (References as in Appendix J)

1. Meranze *et al.* (1969), rat, Fels-Wistar, F, day 45
2. Ibid, M, day 45
3. Noronha and Goodall (1984), rat, CRL/CDF, M, day 46
4. Anderson *et al.* (1978), rat, Wistar, F, day 28
5. Grubbs *et al.* (1983), rat, Sprague Dawley, F, day 50-57; adult comparison group dosed on days 80-87
6. Ibid, F, day 50-57; adult comparison group dosed on days 140-147
7. Choudari Kommineni *et al.* (1970), rat, MRC, M/F, day 28-43

The studies that comprise the set of multi-lifestage exposure studies available for these analyses were not homogeneous. That is, they do not represent observations from the same distribution. Sensitivity analyses were conducted to test the robustness of the findings to different procedures for analyzing data and combining results. Of the methods used to combine the LC ratio distributions for underlying studies within each lifestage, the method of equally weighting studies within a chemical appeared to best represent the available data.

In calculating the ASF, to take into account the longer period of time for early carcinogen exposures to result in tumors, the hazard function was assumed to increase with the third power of age. This assumption is standard and has been borne out by a number of observations (Bailer and Portier, 1988). If the true rate of increase with age is greater than that, then the use of these ASFs may result in underestimates of the true sensitivity of these early life stages.

As the multi-lifestage exposure and case studies show, there appears to be considerable variability in age-at-exposure related susceptibility across carcinogens. There is also variability in age-at-exposure related susceptibility among studies of the same carcinogen. The sources of variability evident in the analyzed studies include timing of exposure within a given age window, and gender, strain, and species differences in tumor response. The set of studies identified and analyzed was not sufficiently robust to fully describe the variability quantitatively. This variability raises concerns that selection of the median (the 50th percentile) estimates may considerably underestimate effects for certain agents or population groups. Relatively large variability in humans in response to carcinogens is expected to be common (Finkel, 1995). On the other hand, the numbers of carcinogens represented in the available data are limited and may not be representative of the population of carcinogens to which we are exposed (*e.g.*, greater than 500 on the Proposition 65 list alone). Thus, the size of the weighting factors used to weight risk by age at exposure is a policy decision.

Several of the carcinogens studied induced tumors at multiple sites in the same experiment, and at different sites, depending upon the lifestage during which exposure occurred. For these cases the combined multisite potency distribution referred to above was the basis for the lifestage comparison. This approach differs from other researchers investigating early vs. late in life differences who focused on tumor site-specific measures of carcinogenic activity (*e.g.*, Barton *et al.*, 2005; Hattis *et al.*, 2004, 2005). OEHHA believes that use of combined multisite potency distributions provides a more complete approach for considering age specific differences in carcinogenic activity. However, the observation that early life is generally a period of increased

susceptibility was similarly found using the tumor site-specific approach by these other researchers.

One limitation of the approach was the focus on lifestages, without attempting to describe changes in susceptibility that occur within a lifestage. Timing of carcinogen exposure within a given age window can affect the cancer outcome. For example, experiments with 1-ethyl-1-nitroso-biuret in prenatal and adult rats showed a three-fold difference in activity between groups exposed on prenatal day -10 versus prenatal day -3. In a second example, female rats exposed early in the adult period were more than three times as sensitive to the breast cancer effects of MNU as females exposed six weeks later. In general, the adult comparison groups in the multi-lifestage exposure studies were fairly young. The extent to which this may result in an overall bias of the results presented here is unclear. Also, for several cases, juvenile animals were used as the later life exposure group. In these cases the ASFs are likely underestimates of the relative sensitivity of the prenatal and postnatal lifestages, compared to that of the adult lifestage.

Excluded from the analysis were early in life studies in which the period of exposure for a specific exposure group crossed multiple lifestages. An example of results from studies of this type is provided by mouse studies for two non-genotoxic carcinogens, diphenylhydantoin (Chhabra *et al*., 1993a) and polybrominated biphenyls (PBBs) (Chhabra *et al*., 1993b), in which exposures began prior to conception, and continued throughout the prenatal, postnatal, and post-weaning period, up to the age of eight weeks. The data demonstrate an increased sensitivity of the early life period. Some studies that crossed multiple lifestages were included in the analyses of Barton *et al*. (2005) (Appendix I), which are consistent with the general conclusions discussed above.

Selection of Default Age-Sensitivity Factors (ASF)

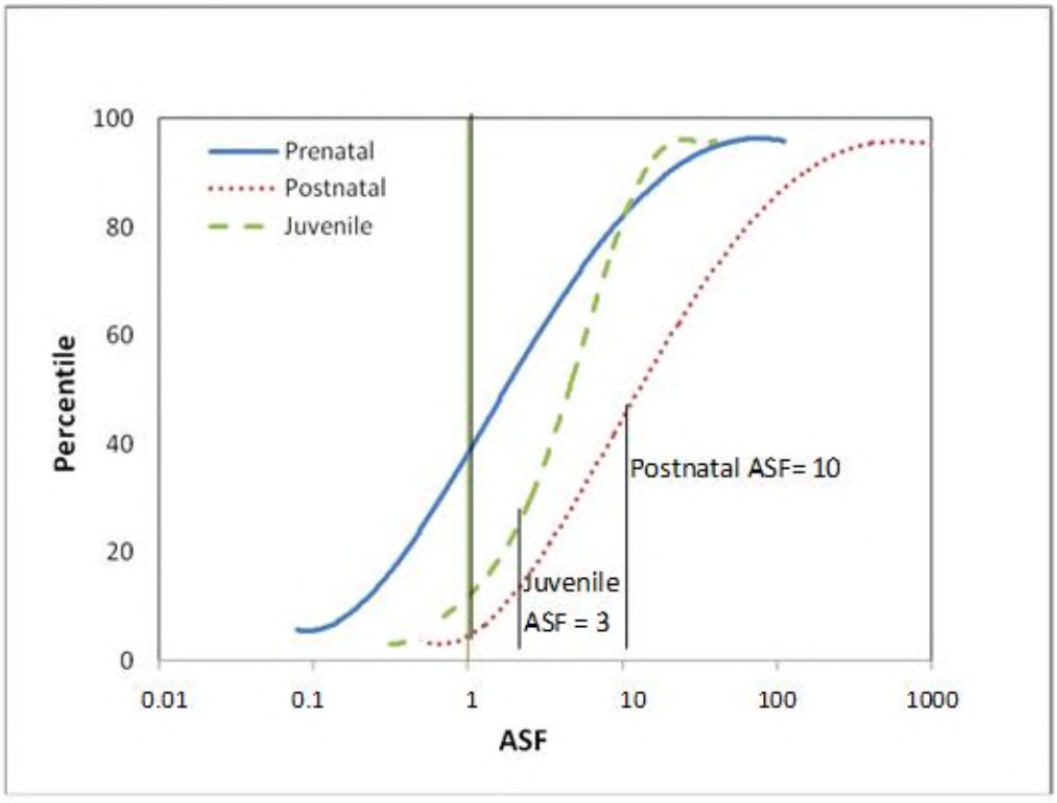
Selection of appropriate values to use to weight exposures that occur early in life using default ASFs for prenatal, postnatal and juvenile exposures is complicated by the limited database of chemicals and studies available for analysis, and the broad distribution of results for different chemicals as is shown in Figure 7, Figure 8, and Figure 9 (see also Appendix J). In view of the variability thus shown, and the considerable uncertainty in applying conclusions from this relatively small set of chemicals to the much larger number of chemicals of concern, it is probably unreasonable to specify a default ASF with greater than half-log precision (*i.e.* values of 1, 3, 10, 30 etc.). Further, rodents are born at a stage of maturity that approximates a third trimester human. Therefore, in the absence of chemical-specific data, OEHHA proposes to apply a default ASF of 10 for the third trimester to age 2 years, and a factor of 3 for ages 2 through 15 years to account for potential increased sensitivity to carcinogens during childhood. A factor of 10 falls just below the median estimate of the ASF for postnatal studies. This is also the value selected by U.S. EPA; while it is consistent with the OEHHA analysis, it may underestimate risk for some chemicals. The broad distribution of observed chemical-specific sensitivity ratios clearly indicates that there are some chemicals for which the sensitivity ratio is much larger than 10. Further research is needed to develop criteria for identifying these cases. Similarly, a factor of 3 for juvenile exposures is consistent with the range of estimates derived from the multi-lifestage exposure studies, and falls close to the median juvenile ASF estimate. It is acknowledged that there are few data available on which to base an estimate for the juvenile period. A factor of 3 adjusts for the longer time available for cancer to manifest, but may not fully account for some inherent differences in susceptibility to cancer, for example the observed susceptibility of breast tissue of

pubescent girls exposed to radiation. For specific carcinogens where data indicate enhanced sensitivity during lifestages other than the immediate postnatal and juvenile periods, or demonstrate ASFs different from the default ASFs, the chemical-specific data should be used in order to adequately protect public health.

The ASFs will be applied to all carcinogens, regardless of the theorized mode of action. While U.S. EPA currently intends to apply weighting factors only to those carcinogens with "a mutagenic mode of action" (U.S.EPA, 2005), OEHHA notes that there is evidence that early life is a susceptible time for carcinogens that are thought to act via non-mutagenic mode of action (DES is a prime example). Defining a mutagenic mode of action may be problematic if approached narrowly (ERG, 2008). Further, carcinogens may have multiple modes of action and one mode may predominate over other modes at different lifestages. The complexity of carcinogenesis argues against restricting the ASF to chemicals acting via a mutagenic mode of action.

Figure 10 provides a visual comparison of the ASF mixture distributions for the three early-life stages, prenatal, postnatal, and juvenile. In this figure, which is in log space, the policy choice of an ASF of 10 for exposures during the third trimester to age 2 years and 3 for the period of life from 2 to 15 years of age are indicated as vertical lines. It is apparent from this figure that weighting risk from exposures to carcinogens early in life is well-supported.

Figure 10. Prenatal, Postnatal, and Juvenile ASF Mixture Distributions and relation to default ASFs



OEHHA recognizes the limitations in the data and analyses presented, as discussed above. However, the analyses do provide some guidance on the extent to which risk may be over or underestimated by current approaches. While there is a great deal of variability across chemicals in the prenatal ASFs, the data indicate that the potency associated with prenatal carcinogen exposure is not zero. A factor of 3 is close to the median ASF, while a factor of 10 falls roughly at the 70th percentile of the prenatal ASF estimate. An ASF could be applied as a default when calculating lifetime cancer risk in humans arising from carcinogen exposures that occur *in utero*. In view of the considerable variability in the data for different carcinogens and the limited database available for analysis, OEHHA is not proposing the application of a specific factor to cancer potency estimates for prenatal exposures in the first and second trimesters as a default position in these Guidelines. However, given that the rodent is born at a stage of maturation similar to a third trimester fetus, it is reasonable to include the third trimester in the 10X potency weighting proposed up to age 2 years. The applicability of a cancer potency adjustment factor for first and second trimester prenatal exposure will be evaluated on a case-by-case basis, and may be used as evidence develops that supports such use. The consideration of prenatal exposures, including application of an appropriate susceptibility factor, would not make a large difference for risk estimates based on continuous lifetime exposures, due to the relatively short duration of gestation. However, risk estimates for short-term or intermittent exposures would be slightly increased by inclusion of the risks to the fetus during the prenatal period. Thus, risk may be underestimated when the first and second trimesters are excluded from the analysis.

Age Bins for Application of ASFs

The choice of human ages to which the ASFs apply is based on toxicodynamic and toxicokinetic considerations. Important toxicodynamic factors related to susceptibility to carcinogens include the rate of cellular proliferation and differentiation, which is quite high during organ maturation. In addition, toxicokinetic differences by age are important, due to impacts on detoxification and clearance of carcinogens (see following section). OEHHA's analysis of the influence of age-at-exposure on carcinogenesis broke the experimental rodent data into age bins that we termed "lifestages" including prenatal, "postnatal" (birth to weaning, about day 21) and "juvenile" (weaning to sexual maturation, or about day 22 to about day 49). Experiments were placed into the lifestage bins if exposure occurred at some time during the experimental rodent age bin.

There is no simple way to compare the rodent age groups used in the OEHHA analysis of available data to equivalent age groups in humans. Complicating factors include variations in organ system structural and functional maturation both within and between species. Further, the rodent age bins were chosen by gross indicators of development namely birth, weaning and sexual maturation, not on the basis of known susceptibility to carcinogenesis. Thus, critical factors relating to carcinogen susceptibility by age are the focus of the choice of human age bins to which the ASFs of 10 and 3 apply, rather than an attempt at exact correlation of rodent lifestage bin with human age.

The investigations used by OEHHA to evaluate the relationship between age at exposure and cancer potency were not conducted by standardized protocol. Further, the windows of susceptibility are quite varied by chemical and organ system, even within the lifestages defined in the OEHHA analysis. This complicates choosing a default ASF and the human age bin to which it applies. Examples from animal studies provided in Appendix J include the chemical diethylnitrosamine (DEN). The cancer potency varied over several orders of magnitude depending

on when during gestation and postnatal life the exposure occurred. A three-fold difference in potency between exposure on prenatal day -3 and prenatal day -10 is noted for 1-ethyl-1-nitrosobiuret in rats. There are also human examples of extensive variation of potency by age at exposure, including radiation, DES, and chemotherapeutic agents. The diversity of responses to different agents obviously underscores uncertainty in the choice of age bins to apply the default ASFs. However, the ASFs are a ***default*** to use when you have no chemical-specific data on influence of age-at-exposure on potency in order to protect public health. There will always be specific chemical examples where the ASF for either the third trimester-<2 yrs or 2-<16 yrs age bin is quite a bit larger or quite a bit smaller than the default.

In the following sections, we discuss our logic in proposing age bins of third trimester to age 2 years, and 2 to age <16 years to which the ASFs of 10 and 3 apply, respectively, and indicate the impact on risk estimates of these age bins.

Toxicokinetic Factors Relevant to Age Bins

Choice of the age-bins to which the default ASFs are applied is based on our understanding of the two primary drivers of age-related sensitivity to carcinogens, namely age-related toxicokinetic factors and toxicodynamic factors. In the case of toxicokinetics, the largest postnatal differences in xenobiotic metabolic capability occur between infants and adults. As noted in OEHHA (2001) and reviewed in detail elsewhere (*e.g.*, Cresteil et al., 1998; Ginsberg et al., 2004), hepatic drug metabolism by the cytochrome P-450 family of enzymes and the Phase II conjugating enzymes undergoes a maturation process during the first few years of life. The hepatic cytochrome P-450 enzymes exist in fetal isoforms at birth, and progressively change to adult isoforms at a relatively early stage of postnatal development. Thus, in humans the metabolic capability towards prototypical substrates develops over the first year of life towards adult levels. Similarly, the largest differences in metabolic capability of Phase II enzymes (conjugation of xenobiotic metabolites prior to excretion) tend to be between infants and adults. Other factors such as renal capability also are most different between neonates and adults. Thus, the first 2 years of life would encompass the increased sensitivity of early life stages due to toxicokinetic differences between early life and adulthood.

Ontogeny of Cytochrome P-450 Enzymes in Humans.

Cresteil (1998) describes three groups of neonatal cytochrome P-450: Cyp3A7 and Cyp4A1 present in fetal liver and active on endogenous substrates; an early neonatal group including Cyp2D6 and 2E1 which surge within hours of birth; and a later developing group, Cyp3A4, Cyp2Cs, and Cyp1A2. Total Cyp 3A protein, a major cytochrome P-450 enzyme responsible for biotransformation of many xenobiotics, is relatively constant in neonates and adults. However, Cyp3A7 is the primary fetal form (Hakkola et al., 1998), while Cyp3A4 is the primary adult hepatic form of the 3A series. At one month Cyp3A4 activity is about one-third of that in the adult liver (Lacroix et al., 1997; Hakkola et al., 1998). Allegaert *et al*. (2007) stated that Cyp3A4 (testosterone-6ß-hydroxylase) activity equaled or exceeded adult activity after 1 year of age. Cyp2E1, which metabolizes benzene, trichloroethylene and toluene, among others, increases gradually postnatally, reaching about one-third of adult levels by one year of age and attains adult levels by 10 years of age (Vieira et al., 1996; Cresteil, 1998). Cyp1A2, and Cyp2C9 and 2C19, the most abundant Cyp2 enzymes in adult human liver, appear in the weeks after birth, and reach

30% to 50% of adult levels at about 1 year of age (Treluyer et al., 1997; Hines and McCarver, 2002). Cyp1A1 is expressed in fetal liver where it can activate such xenobiotics as benzo[a]pyrene and aflatoxin B1 (Shimada et al., 1996), but is less important in adult liver (Hakkola et al., 1998).

Ontogeny of Cytochrome P-450 Enzymes in Rodents.

Hart et al. (2009) report developmental profiles of a number of cytochrome P-450 enzymes (measured as levels of mRNA transcripts of the specific genes) in mice. They identified three groups of isoforms. Group 1 (Cyp3A16 in both sexes; Cyp3A41b in males) appeared rapidly after birth but declined to essentially zero at 15-20 days, which is the period of weaning in mice. A second group (Cyp2E1, Cyp3A11 and Cyp4A10 in both sexes; Cyp3A41b in females) also increased rapidly after birth, but reached a stable maximal level by postnatal day 5. The third group (Cyp1A2, Cyp2A4, Cyp2B10, Cyp2C29, Cyp2D22, Cyp2F2, Cyp3A13 and Cyp3A25) were expressed only at low levels until days 10 to 15, but reached high stable levels by day 20.

ElBarbry et al. (2007) examined the developmental profiles of two toxicologically significant cytochrome P-450 enzymes, Cyp1A2 and Cyp2E1 in rats. mRNA transcripts of these genes were very low postnatally, but thereafter increased to reach a peak at or shortly after weaning (postnatal day 21 - 28 for rats). Immunoreactive Cyp1A2 and Cyp2E1 proteins were first detectable at postnatal day 3 and reached 50% of adult levels at weaning and adult levels at puberty. Differences in profiles between gene expression as mRNA and appearance of specific proteins as determined by immunoassay may reflect changes in the relative importance of transcription and translation control processes at various phases in development. Enzyme activities characteristic of Cyp1A2 and Cyp2E1 were found to parallel gene expression levels (ElBarbry et al., 2007) rather than immunodetectable protein levels, so there may also be issues of cross-reactivity between these two isoenzymes and others for which gene expression was not measured in these experiments.

In summary, the gene expression data in rats and mice show differences in details, but broadly resemble one another in that the main changes occur in the early postnatal period, with the major adjustments completed at or around the time of weaning, although the adult pattern may not be completely established until puberty. There do not appear to be substantive data for experimental species other than rats and mice, although the situation in humans appears similar in general outline and one may conclude that this pattern or some variant of it is characteristic of mammalian species in general.

Ontogeny of Phase II Enzymes

Phase II conjugating enzymes are generally less active in the neonate than the adult (Milsap and Jusko, 1994). Hence, there is concern that detoxification and elimination of chemicals is slower in infants. In humans, expression of some of the UGT enzymes matures to adult levels in two months after birth, although glucuronidation of some drugs by the UGT1A subfamily does not reach adult levels until puberty (Levy et al., 1975; Snodgrass, 1992; McCarver and Hines, 2002). Reduced glucuronidation in neonates slows the clearance of *N*-hydroxyarylamines, phenol, and benzene metabolites. Acetylation by the N-acetyltransferases and sulfation by sulfotransferases are generally somewhat comparable to adult levels, although it varies by tissue and by specific sulfotransferase (McCarver and Hines, 2002). Human glutathione sulfotransferase (GST) is present as a fetal isoform which decreases postnatally, while GST-alpha and GST-mu increase

over the first few years of life to adult levels (McCarver and Hines, 2002). Epoxide hydrolase, important in detoxifying reactive epoxide metabolites, is present in neonatal liver although at much reduced activity relative to adults (McCarver and Hines, 2002).

Clearances of Drugs in Infants and Children vs. Adults

Several investigators have evaluated age-related drug disposition (Renwick, 1998; Renwick et al., 2000; Ginsberg et al., 2002; Hattis et al., 2003). Renwick et al. (2000) noted higher internal doses in neonates and young infants versus adults for seven drugs that are substrates for glucuronidation, one with substrate specificity for CYP1A2, and four with substrate specificity for CYP3A4 metabolism. Ginsberg et al (2002) evaluated toxicokinetic information on 45 drugs in children and adults metabolized by different cytochrome P-450 pathways, by Phase II conjugations, or eliminated unchanged by the kidney. These authors noted half-lives 3-9-fold longer in infants than those in adults. It was also shown that the bulk of the elevated child/adult half-life ratios occurred primarily in the 0 to 6 month age range, and that for some compounds the clearance is actually higher in the 6 month to 2 year age grouping. In evaluating the interindividual variability by age, Hattis et al (2003) note that the largest interindividual variability occurs in the youngest children, apparently due to variability in development of critical metabolism and elimination pathways. Anderson and Holford (2008) noted that a comparison of three early-life drug clearance models (surface area, allometric ¾ power and per kilogram scaling) all demonstrated an increase in clearance over the first year of life due to the maturation of metabolic capacity.

Renal elimination depends on maturity of processes related to tubular reabsorption and secretion, and glomerular filtration rates. At birth, the glomerular filtration rate (GFR) is low (2-4 ml/min), increases in the first few days (8-20 ml/min) and slowly increases to adult values in 8-12 month old infants (Plunkett et al., 1992; Kearns et al, 2003).

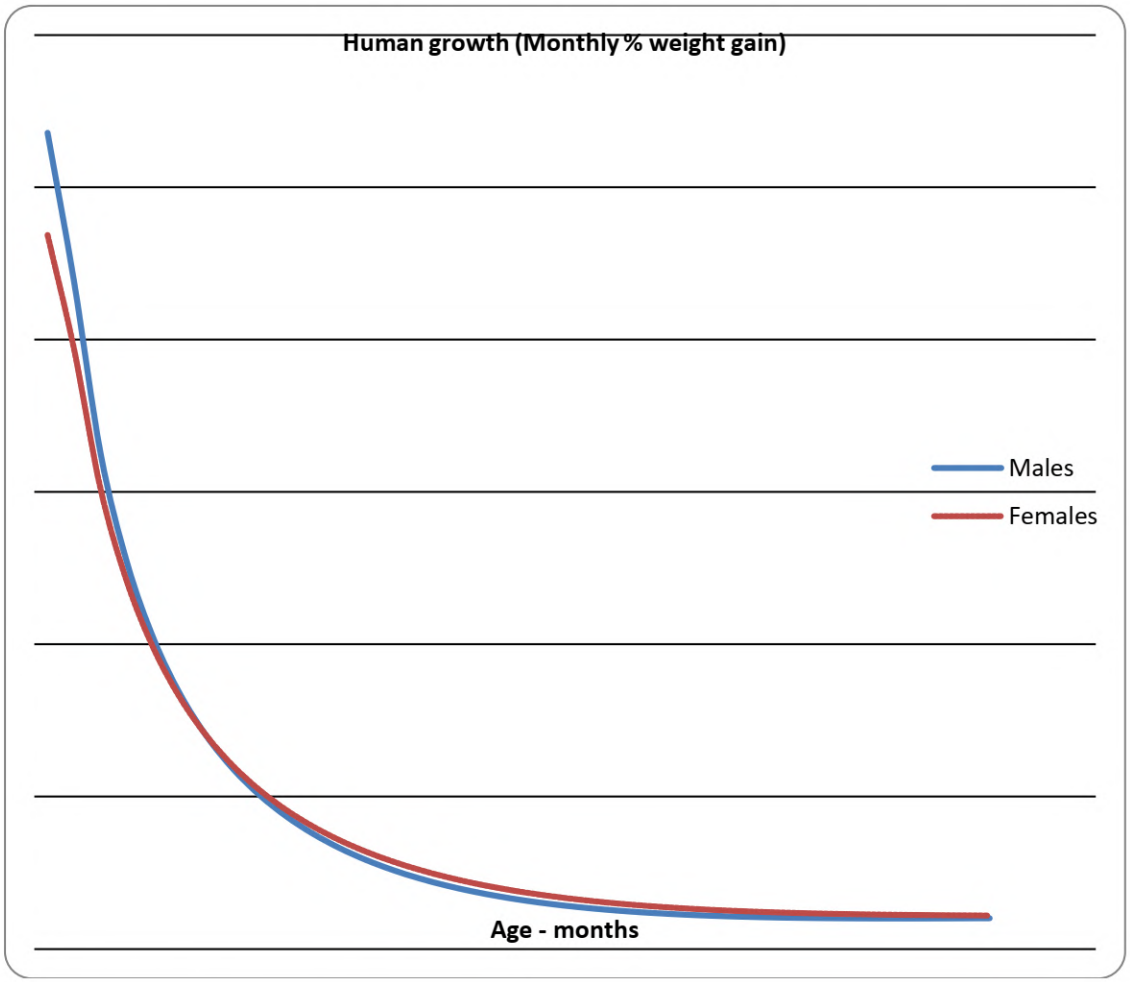
Newborn and young animals have less capacity to excrete chemicals into the bile than do adult animals. A number of chemicals are excreted more slowly via bile in neonates than adult rats, including ouabain, the glucuronide conjugate of sulfobromophthalein (Klaassen, 1973), and methyl mercury (Ballatori and Clarkson, 1982), resulting in a longer half-life in neonates.

Toxicodynamic Factors Relevant to Age Bins

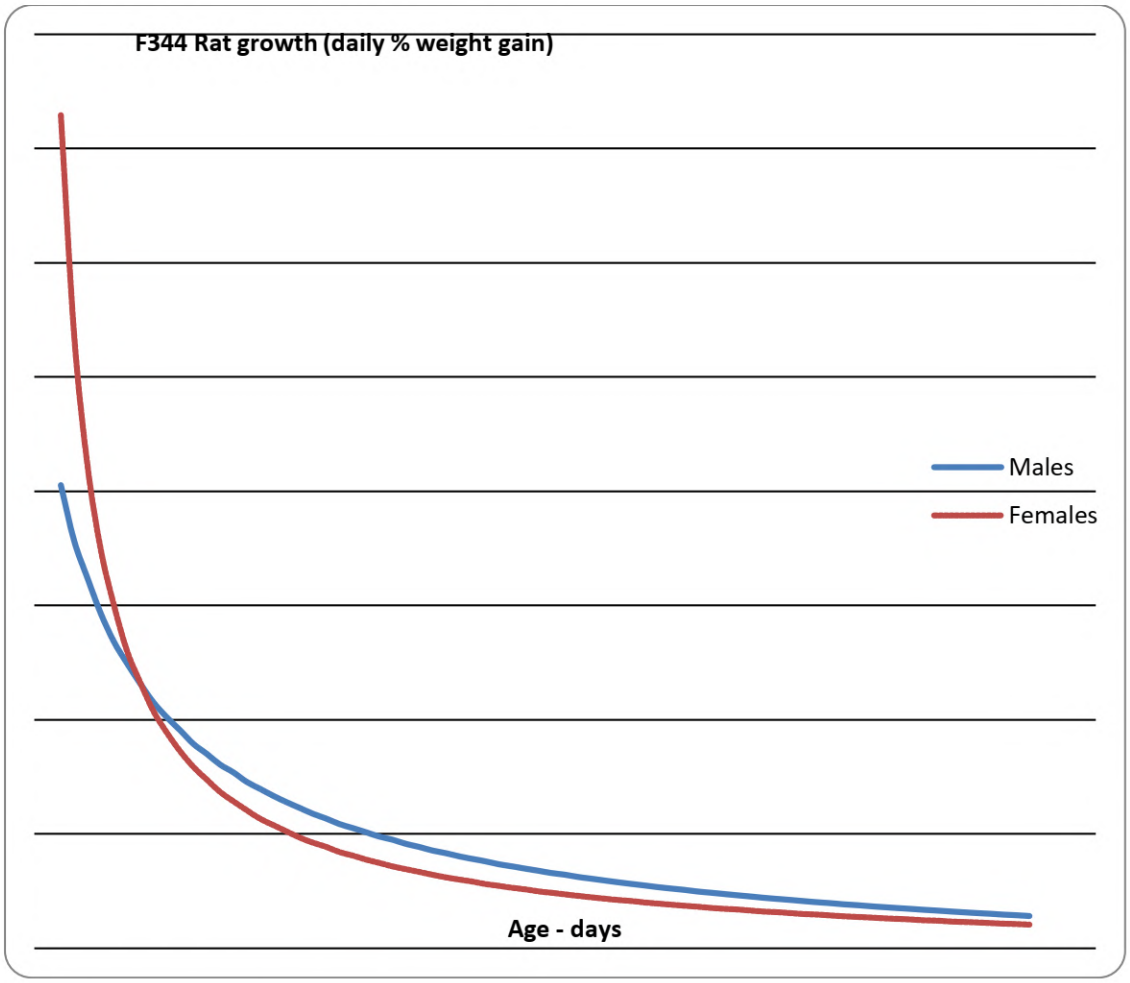
Important as the developmental changes in toxicokinetics are in determining sensitivity to carcinogens and other toxicants, it is likely that the toxicodynamic differences, *i.e.* intrinsic differences in susceptibility to carcinogenesis at the tissue or cellular level, are even more influential. Changes in cell division rates and differentiation, which are thought to be important toxicodynamic determinants of susceptibility to carcinogenesis, peak in the first 2 years of life for most major organ systems. Cell division continues to accommodate growth throughout childhood and adolescence, extending in some cases even into the young adult period in both humans and experimental animals. Adolescence is an important period for organ cell division and differentiation for the mammary gland and reproductive organs.

As noted above, one of the key factors influencing susceptibility to carcinogenesis is believed to be cell division rate, which acts both by forcing error-prone repair which fixes DNA damage as mutated gene sequences (McLean et al, 1982) and by promoting expansion of mutated clones

(Moolgavkar and Knudson, 1981). Actual cell division rates as a function of age are hard to determine for practical and (in the human case) ethical reasons. However, growth curves expressed as the proportional increment in body weight with time may be regarded as a reasonable although not perfect surrogate since for most tissues of the body cell size does not change markedly during growth. Both humans and rodents show remarkably high growth rates in infancy, which then drop steeply to a lower but still significant rate during childhood. A growth spurt at the beginning of adolescence is noticeable in its absolute magnitude, especially in males, but does not approach the proportional growth rate seen in infancy. The time intervals proposed to reflect the period of highest sensitivity to carcinogenesis (up to about 21 days in rodents, up to 24 months in humans) encompass the period of highest growth rate and thus it is assumed the highest cell division rates, as show in the following charts:



Data from CDC NHANES 2000:
http://www.cdc.gov/nchs/about/major/nhanes/growthcharts/datafiles.htm



Data from Tables A3 and A4 of Appendix J

Cell division rates in adult rodents and humans are harder to relate to growth curves since at least some tissues retain active cell division as part of their ongoing functionality and repair. In humans growth in body weight slows to essentially zero at the end of adolescence (and any later increments represent tissue specific changes such as increase in muscle or adipose tissue mass rather than overall growth). On the other hand, rodents continue to increase in body size (at a modest rate compared to that seen in earlier lifestages) throughout the adult period. However, it appears reasonable to conclude from the body weight data that an essentially adult pattern of overall cell division is established by the late adolescent period (age six weeks in rodents; 16 years in humans). However, increased cell division and cell differentiation are seen in the reproductive system and its accessories during puberty.

Organ Development

The age intervals chosen for the ASFs are generally supported by human organ system development data. Examples of supporting data are available for the lung, brain, immune system and liver. Zeltner and Burri (1987) stated that postnatal lung development consists of an alveolar stage, which lasts to about 1-1.5 years of age, and a stage of microvascular maturation, which exists from the first months after birth to the age of 2-3 years. Pinkerton and Joad (2006) describe

alveolar proliferation as occurring most prominently in the 0-2 year age range, with alveolar expansion continuing in the 2-8 year age range. Ballinoti et al. (2008) demonstrated that addition of alveoli rather than expansion is a major mode of lung growth in infants and toddlers by measuring a constant carbon monoxide diffusion capacity to lung volume from 3 through 23 months of age. Kajekar (2007) also considered the 0-2 age range to be the primary period of alveolar development, although there is continued cellular proliferation resulting in lung growth and expansion up to approximately 18 years of age.

Rice and Barone (2000) note that most of the cell proliferation phase of human radial glia and neuronal growth is finished by 2 years of age, based on evidence in Bayer et al. (1993). They note further that numerous studies have shown actively proliferating brain regions are more susceptible to anti-mitotic agents than the same structures after active proliferation ceases. Peak brain growth as a percentage of body weight occurs at birth and around post-natal day (PND) 7-8 in humans and rats, respectively (Watson *et al.*, 2006). De Graaf-Peters and Hadders-Algra (2006) reviewed the ontogeny of the human central nervous system and found that a large amount of axon and dendrite sprouting and synapse formation and the major part of telencephalic myelination take place during the first year after birth. While the brain continues to remodel itself throughout life, cellular proliferation in the whole brain peaks by about one year of age and is relatively complete by age 2. Development of the blood-brain barrier (BBB) appears to continue in humans until approximately 6 months of age. Rat BBB functionality is essentially complete by approximately two weeks after birth (Watson *et al.*, 2006).

The immune system development occurs in stages, primarily prenatally in primates and both pre- and post-natally in rodents (Dietert et al., 2000). Formation and expansion of hematopoetic stem cells is followed by expansion of lineage-specific stem cells, colonization of bone marrow and thymus, and maturation of cells to immunocompetence. In the primate, this is largely complete by 1 to 2 years of age (Holsapple et al., 2003), although establishment of immune memory develops throughout childhood and beyond. In the rodent, maturation to immunocompetence occurs postnatally from birth to about 30 days of age. In terms of carcinogenesis, perhaps one of the more important immune cells is the NK cell, thought to be responsible for immune surveillance and killing of circulating transformed cells. Based on immunohistochemistry, the principal cell lines including NK cells are present at gestation day 100 in the monkey and are at about 60% of adult values at birth (Holladay and Smialowicz, 2000).

As noted above, renal and hepatic clearance are both lower in humans at birth than in adults. Nephrogenesis is complete by 35 weeks gestation in humans and before birth in the mouse (but after birth in the rat). The ability to concentrate urine and the development of acid-base equilibrium appear in the first few months after birth (Zoetis and Hurtt, 2003). Renal clearance of drugs, a function of a number of processes in the kidney, appears to be comparable to adults within the first few months of life (Hattis et al., 2003; Ginsberg et al., 2002), while glomerular filtration, which rises rapidly over the first few postnatal months, is at adult values by two years of age (Zoetis and Hurtt, 2003). While complete anatomic maturity of the human liver is noted by 5 years of age (Walthall et al, 2005), liver function also appears to mature within the first year of life as seen by drug clearance studies cited above.

Critical Windows of Susceptibility to Carcinogens

It has been shown that there are critical windows during development both pre-and postnatally where enhanced susceptibility to carcinogenesis occurs (Anderson et al, 2000). Some of these observations relate to factors affecting the incidence of cancers in childhood, resulting from prenatal or preconception mutational events. For example, prenatal exposure to ionizing radiation and DES can result in leukemia and vaginal carcinoma, respectively, in childhood. Although obviously a source of great concern, these cancers appearing during childhood are relatively rare compared to cancers appearing later in life. Thus the concern in risk assessment for early in life exposures is to address the lifetime cancer incidence as a result of these exposures, including both cancers appearing during childhood and those appearing later.

OEHHA (see Appendix J) and other investigators (U.S. EPA, 2005; Barton et al, 2005; Hattis et al., 2004) have examined the available rodent data on sensitivity to carcinogenic exposures early in life. All these investigators found substantial increases in sensitivity to carcinogens in animal studies where exposures to young animals were compared to similar exposures to adults. Hattis et al. (2004) reported maximum likelihood estimates for the ratio of carcinogenic potency during the period from birth to weaning to the adult potency of between 8.7 and 10.5, whereas Barton et al (2005) reported a weighted geometric mean of 10.4 for the ratio of juvenile (less than 6-8 weeks) to adult potency in rodents. However, the number of experiments which provide information of this type, and the carcinogenic agents which have been studied, are relatively limited. Hattis examined several different datasets and study designs, but these covered only 13 different chemicals, while the mean value reported by Barton et al. was based on only six of the 18 chemicals which they examined. OEHHA's analysis included data in rodents on 23 chemicals, and found median potency ratios of 13.5 for the postnatal period (birth to day 22) and 4.5 for the juvenile period (postnatal days 22 to ~49) relative to adults (day ~49 to 2 years). These potency ratios include the adjustment for time to manifest tumor (*e.g.*, age to the power of three), unlike the earlier investigations. All these investigations identified variations in the observed lifetime potency ratio depending on the type of experimental design, the sex of the animals, the time of exposure and especially between chemicals. Nevertheless these analyses, although falling far short of a comprehensive evaluation of the age dependence of carcinogenic potency for all the chemicals of interest, do show a consistent overall trend of increasing potency for exposures early in life, especially soon after birth.

An evaluation of cancer induction by ionizing radiation also provides support for the concept of enhanced sensitivity to carcinogenesis at younger ages. Various studies of this phenomenon have been undertaken in animal models, but the important point for the present discussion is that epidemiological data exist which indicate age-dependent sensitivity in humans (U.S. EPA, 1994; 1999). The most extensive data set showing age-dependent effects is that for Japanese survivors of the atomic bomb explosions at Hiroshima and Nagasaki. Analysis of these data shows linear increases in tumor incidence at a number of sites with increasing radiation dose and younger age at exposure. There are other data suggesting humans are more susceptible to chemical carcinogens when exposure occurs in childhood. These data exist for tobacco smoke (Marcus et al., 2000; Wiencke et al., 1999) and chemotherapy and radiation (Mauch et al., 1996; Swerdlow et al., 2000; Franklin et al., 2006).

Proposed Age Bins for Application of Default Age Sensitivity Factors

In developing a default science-based risk assessment policy to address this general conclusion, one key variable to define is the age interval or intervals over which age-dependent sensitivity factors should be applied. Different investigators have considered different age ranges, but in general the more sensitive period has at least been defined as including the time from birth up to mid-adolescence when the major phases of growth and hormonal change are complete. It is also recognized that, apart from the dramatic prenatal developmental events, the earliest postnatal stages represent the greatest differences in physiology and biochemistry from the adult. This reflects the immaturity of many organ systems, extremely rapid growth, and the incomplete maturation of various metabolic capabilities. As noted earlier, the rodent age bins in OEHHA's analysis were based on gross developmental milestones (birth, weaning, sexual maturity). OEHHA's analysis of studies that included exposure sometime between birth and weaning indicated this period as having the highest sensitivity to carcinogenesis. The data for the later juvenile period (postnatal days 22 to ~ 49) are somewhat sparse, covering only three carcinogens and only one where there are corresponding data for both postnatal and juvenile lifestages. However, it appears based on the overall range of potency ratios observed for the juvenile period that sensitivity to many carcinogens is elevated in this period also, but to a lesser extent than during the first 22 days. [Hattis et al. (2005) and Barton et al. (2005) report analyses for exposures at any time during the juvenile period, i.e. up to 6-8 weeks, and do not separate by additional age bins].

Weaning is not such an obvious or consistently timed transition for humans, being subject to a wide range of cultural and economic variables. However, it is generally considered that the human infant period encompasses the first two years of life. This period includes the most rapid periods of cellular division and differentiation for the major organ systems (excluding the breast and reproductive organs). Although there is linear growth between 2 and 8 years of age, the organ development is largely although not entirely complete.

Thus, considering both the development of major organ systems and the associated differences in toxicodynamic and toxicokinetic factors, OEHHA initially proposed to apply the postnatal ASF derived from rodent studies (birth to 21 days) to the human age intervals of birth - < 2 years. Similarly, OEHHA chose to apply the "juvenile" ASF derived from rodent studies (22 - ~49 days) to the human ages 2 - < 16 years. This timetable was also selected by U.S. EPA (2005) in their supplemental guidance for assessing early-life susceptibility to carcinogens. They describe their choice of critical periods as follows:

> "The adjustments described below reflect the potential for early-life exposure to make a greater contribution to cancers appearing later in life. The 10-fold adjustment represents an approximation of the weighted geometric mean tumor incidence ratio from juvenile or adult exposures in the repeated dosing studies (see Table 8). This adjustment is applied for the first 2 years of life, when toxicokinetic and toxicodynamic differences between children and adults are greatest (Ginsberg et al., 2002; Renwick, 1998). Toxicokinetic differences from adults, which are greatest at birth, resolve by approximately 6 months to 1 year, while higher growth rates extend for longer periods. The 3-fold adjustment represents an intermediate level of adjustment that is applied after 2 years of age through <16 years of age. This upper age limit represents middle adolescence following the period of rapid developmental changes in puberty and the conclusion of growth in body height in

NHANES data (Hattis et al., 2005). Efforts to map the approximate start of mouse and rat bioassays (i.e., 60 days) to equivalent ages in humans ranged from 10.6 to 15.1 years (Hattis et al., 2005)."

There is general agreement that rodents are born at a maturational stage approximately equivalent to a third trimester human fetus. Thus, there is good rationale to include the third trimester of pregnancy in the age bin for application of the ASF of 10. Therefore, OEHHA is applying the ASF of 10 for exposures during the third trimester of pregnancy to age 2. The default ASF values used by OEHHA are summarized in Table 2.

While there is strong evidence that growth and therefore cell proliferation rates and cell differentiation are extremely high prior to age 2, and lower (although still elevated relative to the adult) thereafter, there is still residual uncertainty with respect to the cut point for application of the ASFs of 10 and 3. Thus, another possible approach would be to move the cut point for the application of the ASF of 10 to a later age to account for this uncertainty. We present the effect on risk estimates of varying cut points in Table 3 and Table 4.

Table 2. Default Age Sensitivity Factors to be used to estimate cancer risks to infants and children

R (third trimester to age 2yrs)	10
R (age 2 to age 16 yrs)	3
R (age 16 to 70 yrs)	1

Application of ASFs in Risk Assessment

The effect of using the proposed default ASFs in calculating cancer risk over a 70 year lifetime, and for a 9 year exposure common in the Hot Spots program risk assessments is demonstrated in Table 3 and Table 4 below. Ignoring for the moment the increased exposures to carcinogens that children experience, the effect of the weighting factors is to increase the lifetime cancer risk by about 2. For risks from shorter exposures, such as the commonly used 9 year exposure scenario, OEHHA proposes to evaluate risk from exposures starting at the third trimester in the surrounding general population. The weighting factors in this case increase the risk to a larger extent. Depending on the exposure scenario, the use of age-specific distributions for uptake rates for air, food and water would also increase the risk estimates significantly independent of any application of ASFs. This is because the uptake rates for all these media per unit of body weight are higher in children and, especially, infants.

Assessing risks to short-term exposures to carcinogens involves additional uncertainties. The cancer potency factors are generally based on long-term exposures. However, in reality, the local air districts in California are frequently assessing risk from short term activities related to construction, mitigation of contaminated soils, and so forth. OEHHA recommends that when assessing such shorter term projects, the districts assume a minimum of 2 years of exposure and apply the slope factors and the 10 fold ASF to such assessments. Exposure durations longer than 2 years would use the method for the remaining years as noted above.

Table 3. Example of default ASF use for a lifetime exposure (not adjusted for age-specific exposure)

Carcinogen Potency = 1 $(mg/kg\text{-}d)^{-1}$
Exposure = 0.0001 mg/kg-d
No consideration of differences of exposure

No adjustment: Lifetime Risk = potency × dose	Risk
70 year Lifetime risk = 1 × 0.0001	**1.0×10^{-4}**

With proposed default ASF of 10 for third trimester to age 2, and 3 for ages 2 to 16 years: LR = Σ (potency x dose x ASF x fraction of lifetime)	ASF	Duration	Risk
R (third trimester to age 2yrs)	10	2.25/70	0.321×10^{-4}
R (age 2 to age 16 yrs)	3	14/70	0.600×10^{-4}
R (age 16 to 70 yrs)	1	54/70	0.771×10^{-4}
70 year Lifetime Risk			**1.7×10^{-4}**

For comparison, if ASF of 10 were applied to age 5, and ASF of 3 for the ages 5 to 16 years: LR = Σ (potency x dose x ASF x fraction of lifetime)	ASF	Duration	Risk
R (birth to age 5)	10	5.25/70	0.750×10^{-4}
R (age 5 to 16 yrs)	3	11/70	0.471×10^{-4}
R (age 16 to 70 yrs)	1	54/70	0.771×10^{-4}
70 year Lifetime Risk			**2.0×10^{-4}**

Table 4. Example of default ASF use for a 9-year exposure

Carcinogen Potency = 1 $(mg/kg\text{-}d)^{-1}$
Exposure = 0.0001 mg/kg-d
No consideration of differences of exposure

No adjustment: Total Risk = potency × dose x fraction of lifetime		Duration	Risk
9-year Total Risk		9/70	**0.13×10^{-4}**
With default ASF of 10 for third trimester to age 2 and 3 thereafter: LR = Σ (potency x dose x ASF x fraction of lifetime)	ASF	Duration	Risk
R (third trimester to age 2yrs)	10	2.25/70	0.321×10^{-4}
R (age 2 to 9 yrs)	3	7/70	0.300×10^{-4}
9 year Total Risk			**0.62×10^{-4}**
For comparison, if ASF of 10 applied to age 5, and ASF of 3 thereafter: LR = Σ (potency x dose x ASF x fraction of lifetime)	ASF	Duration	Risk
R (birth to age 5 yrs)	10	5/70	0.750×10^{-4}
R (age 5 to 9 yrs)	3	4/70	0.171×10^{-4}
9 year Total Risk			**0.92×10^{-4}**

Special Consideration of Puberty

In addition to the general concerns over increased sensitivity to carcinogenesis during infancy and childhood, there are specific concerns for exposure during the period when hormonal and developmental changes associated with puberty are in process, especially for carcinogens with hormonal modes of action or with impacts on the reproductive system and its accessory organs. At puberty, there is increased development of breast and reproductive organs that clearly involves rapid cellular division and differentiation. Thus, for carcinogens that induce mammary and reproductive organ cancers, puberty represents a time of increased sensitivity. As noted in the section on Selection of Default Age-Sensitivity Factors (page 50), if the risk assessor is evaluating a chemical with the potential for more than usually enhanced potency during this period, such as those which induce mammary or reproductive organ tumors (*e.g.*, a polycyclic aromatic hydrocarbon), then the risk assessment may use a larger ASF to calculate risk from exposure during puberty. OEHHA may recommend chemical-specific ASFs for puberty to the local air quality management districts for use in the Air Toxics Hot Spots program.

U.S.EPA Analysis of the Effect of Age at Exposure on Cancer Potency

U.S. EPA addressed the potential for increased susceptibility to cancer caused by environmental chemicals when the exposure occurs during an early lifestage in "Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens" (U.S. EPA, 2005b) (referred to henceforth as the Supplemental Guidance). This document is intended to be a companion to the revised "Guidelines for Carcinogen Risk Assessment" (U.S. EPA, 2005a). We present a summary of their analysis, which supports the policy decision to weight cancer potency and therefore risk by age-at-exposure. As previously noted, there are several methodological differences between the U.S. EPA analysis and the OEHHA analysis. Of note, in the OEHHA analysis all treatment-related tumors that were observed in a given lifestage exposure experiment were taken into account in estimating cancer potency. Thus in comparing cancer potencies associated with early life vs. adult exposure, OEHHA compared the total cancer risk associated with exposure during a given lifestage, rather than comparing the risk for cancers at one single site in each lifestage, as the U.S. EPA did. In addition, the age groupings are somewhat different in the U.S. EPA analysis from those used by OEHHA in their analysis (described above). For example, prenatal (*in utero*) exposures were not part of the analysis performed by U.S. EPA, and that Agency's analyses did not distinguish between postnatal and juvenile exposures.

U.S. EPA oral exposure cancer risk methodology relies on estimation of the lifetime average daily dose, which can account for exposure factor differences between adults and children (*e.g.*, eating habits and body weight). However, early lifestage susceptibility differences have not been taken into consideration when cancer potency factors were calculated. The Supplemental Guidance document focused on studies that define the potential duration and degree of increased susceptibility that may arise from early-life exposures. An analysis of those studies including a detailed description of the procedures used was published in Barton *et al.* (2005) (included as Appendix I). The criteria used to decide if a study could be included in the quantitative analysis are as follows (excerpted from U.S. EPA, 2005b):

1. Exposure groups at different post-natal ages in the same study or same laboratory, if not concurrent (to control for a large number of potential cross-laboratory experimental variables including pathological examinations),
2. Same strain/species (to eliminate strain-specific responses confounding age-dependent responses),
3. Approximately the same dose within the limits of diets and drinking water intakes that obviously can vary with age (to eliminate dose-dependent responses confounding age-dependent responses),
4. Similar latency period following exposures of different ages (to control for confounding latency period for tumor expression with age-dependent responses), arising from sacrifice at >1 year for all groups exposed at different ages, where early-life exposure can occur up to about 7 weeks. Variations of around 10 to 20% in latency period are acceptable,
5. Postnatal exposure for juvenile rats and mice at ages younger than the standard 6 to 8 week start for bioassays; prenatal (*in utero*) exposures are not part of the current analysis. Studies that have postnatal exposure were included (without adjustment) even if they also involved prenatal exposure,

6. "Adult" rats and mice exposure beginning at approximately 6 to 8 weeks old or older, *i.e.* comparable to the age at initiation of a standard cancer bioassay (McConnell, 1992). Studies with animals only at young ages do not provide appropriate comparisons to evaluate age-dependency of response (*e.g.*, the many neonatal mouse cancer studies). Studies in other species were used as supporting evidence, because they are relatively rare and the determination of the appropriate comparison ages across species is not simple, and
7. Number of affected animals and total number of animals examined are available or reasonably reconstructed for control, young, and adult groups (i.e., studies reporting only percent response or not including a control group would be excluded unless a reasonable estimate of historical background for the strain was obtainable).

Cancer potencies were estimated from a one-hit model (a restricted form of the Weibull time-to-tumor model), which estimates cumulative incidence for tumor onset. U.S. EPA (2005b) compared the estimated ratio of the cancer potency from early-life exposure to the estimated cancer potency from adult exposure. The general form of the equation for the tumor incidence at a particular dose, [P(dose)] is:

$$P(dose) = 1-[1-P(0)]\exp(-\text{cancer potency}*\text{dose})$$

where P(0) is the incidence of the tumor in controls. The ratio of juvenile to adult cancer potencies at a single site were calculated by fitting this model to the data for each age group. The model fit depended upon the design of the experiment that generated the data. Studies evaluated by U.S. EPA had two basic design types: experiments in which animals were exposed either as juveniles or as adults (with either a single or multiple dose in each period), and experiments in which exposure began either in the juvenile or in the adult period, but once started, continued through life.

The model equations for the first study type are:

$$P_A = P_0 + (1-P_0)\,(1-e^{-m_A \delta_A})$$

$$P_J = P_0 + (1-P_0)\,(1-e^{-m_A e^{\lambda} \delta_J})$$

where A and J refer to the adult and juvenile period, respectively, λ is the natural logarithm of the juvenile:adult cancer potency ratio, P_0 is the fraction of control animals with the particular tumor type being modeled, P_x is the fraction of animals exposed in age period x with the tumor, m_A is the cancer potency, and δ_x is the duration or number of exposures during age period x.

The goal of the model is to determine λ, which is the logarithm of the estimated ratio of juvenile to adult cancer potencies. This serves as a measure of potential susceptibility for early-life exposure.

For the second study type, the model equations take into account that exposures that were initiated in the juvenile period continue through the adult period. The model equations for the fraction of animals exposed only as adults with tumors in this design are the same as in the first study type, but the fraction of animals whose first exposure occurred in the juvenile period is:

$$P_J = P_0 + (1-P_0)\,(1-e^{-m_A\, e^{\lambda\,(\delta_J - \delta_A)} - m_A\,\delta_A})$$

δ_J includes the duration of exposure during the juvenile period and the subsequent adult period.

Parameters in these models were estimated using Bayesian methods and all inferences about the ratios were based on the marginal posterior distribution of λ. A complete description of these procedures (including the potential effect of alternative Bayesian priors that were examined) was published in Barton *et al.* (2005) (Appendix I). This method produced a posterior mean ratio of the early-life to adult cancer potency, which is an estimate of the potential susceptibility of early-life exposure to carcinogens. Ratios of greater or less than one indicate greater or less susceptibility from early-life exposure, respectively.

U.S. EPA reviewed several hundred studies reporting information on 67 chemicals or complex mixtures that are carcinogenic via perinatal exposure. Eighteen chemicals were identified which had animal study designs involving early-life and adult exposures in the same experiment. Of those 18 chemicals, there were overlapping subsets of 11 chemicals involving repeated exposures during early postnatal and adult lifestages and 8 chemicals using acute exposures (usually single doses) at different ages. Those chemicals are listed in Table 5.

Table 5 Chemicals having animal cancer study data available with early-life and adult exposures in the same experiment.

Chemical	Study Type
Amitrole	repeat dosing
Benzidine	repeat dosing
Benzo[a]pyrene (BaP)	acute exposure
Dibenzanthracene (DBA)	acute exposure
Dichlorodiphenyltrichloroethane (DDT)	lifetime exposure, repeat dosing
Dieldrin	lifetime exposure, repeat dosing
Diethylnitrosamine (DEN)	acute exposure, lifetime exposure
Dimethylbenz[a]anthracene (DMBA)	acute exposure
Dimethylnitrosamine (DMN)	acute exposure
Diphenylhydantoin, 5,5-(DPH)	lifetime exposure, repeat dosing
Ethylnitrosourea (ENU)	acute exposure
Ethylene thiourea (ETU)	lifetime exposure, repeat dosing
3-Methylcholanthrene (3-MC)	repeat dosing
Methylnitrosourea (NMU)	acute exposure
Polybrominated biphenyls (PBBs)	lifetime exposure, repeat dosing
Safrole	lifetime exposure, repeat dosing
Urethane	acute exposure, lifetime exposure
Vinyl chloride (VC)	repeat dosing

U.S. EPA calculated the difference in susceptibility between early-life and adult exposure as the estimated ratio of cancer potency at specific sites from early-life exposure over the cancer potency from adult exposure for each of the studies that were determined qualitatively to have appropriate study designs and adequate data. The results were grouped into four categories: 1) mutagenic chemicals administered by a chronic dosing regimen to adults and repeated dosing in the early postnatal period (benzidine, diethylnitrosamine, 3-methylcholanthrene, safrole, urethane and vinyl chloride); 2) chemicals without positive mutagenicity data administered by a chronic dosing regimen to adults and repeated dosing in the early postnatal period (amitrole, dichlorodiphenyltrichloroethane (DDT), dieldrin, ethylene thiourea, diphenylhydantoin, polybrominated biphenyls); 3) mutagenic chemicals administered by an acute dosing regimen (benzo[*a*]pyrene, dibenzanthracene, diethylnitrosamine, dimethylbenzanthracene, dimethyl-nitrosamine, ethylnitrosourea, methylnitrosourea and urethane); 4) chemicals with or without positive mutagenicity data with chronic adult dosing and repeated early postnatal dosing.

The acute dosing animal cancer studies were considered qualitatively useful by U.S. EPA because they involve identical exposures with defined doses and time periods demonstrating that differential tumor incidences arise exclusively from age-dependent susceptibility. However, they

were not used to derive a quantitative cancer potency factor age adjustment, primarily because most of the studies used subcutaneous or intraperitoneal injection as a route of exposure. These methods have not been considered quantitatively relevant routes of environmental exposure for human cancer risk assessment by U.S. EPA, for reasons including the fact that these routes of exposure are expected to have a partial or complete absence of first pass metabolism which could affect potency estimates. Additionally, U.S. EPA decided that cancer potency estimates are usually derived from chronic exposures, and therefore, any adjustment to those potencies should be from similar exposures.

The repeated dosing studies with mutagenic chemicals using exposures during early postnatal and adult lifestages were used to develop a quantitative cancer potency factor age adjustment. Studies with repeated early postnatal exposure were included in the analysis even if they also involved earlier maternal and/or prenatal exposure, while studies addressing only prenatal exposure were not used in the analysis. The weighted geometric mean susceptibility ratio (juvenile to adult) for repeated and lifetime exposures in this case was 10.4 (range 0.12 – 111, 42% of ratios greater than 1).

USEPA suggests the use of age-dependent-adjustment factors (ADAF) for chemicals acting through a mutagenic mode of action., based on the results of the preceding analysis, which concluded that cancer risks generally are higher from early-life exposure than from similar exposure doses and durations later in life:

1. For exposures before 2 years of age (i.e., spanning a 2-year time interval from the first day of birth until a child's second birthday), a 10-fold ADAF.

2. For exposures between 2 and <16 years of age (i.e., spanning a 14-year time interval from a child's second birthday until their sixteenth birthday), a 3-fold ADAF.

3. For exposures after turning 16 years of age, no adjustment (ADAF=1).

The ADAF of 10 used for the 0 – 2 years of age range is approximately the weighted geometric mean cancer potency ratio from juvenile versus adult exposures in the repeated dosing studies. U.S. EPA considered this period to display the greatest toxicokinetic and toxicodynamic differences between children and adults. Data were not available to calculate a specific dose-response adjustment factor for the 2 to <16-year age range, so EPA selected an ADAF of 3 because it was half the logarithmic scale difference between the 10-fold adjustment for the first two years of life and no adjustment (*i.e.*, 1-fold) for adult exposure. The ADAF of 3 represents an intermediate level of adjustment applied after 2 years of age through <16 years of age. The upper age limit (16 years of age) reflects the end of puberty and the attainment of a final body height. U.S. EPA recognizes that the use of a weighted geometric mean of the available study data to develop an ADAF for cancer potencies may either overestimate or underestimate the actual early-life cancer potency for specific chemicals, and therefore emphasizes in the Supplemental Guidance that chemical-specific data should be used in preference to these default adjustment factors whenever such data are available.

U.S. EPA is recommending the ADAFs described above only for mutagenic carcinogens, because the data for non-mutagenic carcinogens were considered to be too limited and the modes of action

too diverse to use this as a category for which a general default adjustment factor approach can be applied. OEHHA considers this approach to be insufficiently health protective. There is no obvious reason to suppose that the toxicokinetics of non-mutagens would be systematically different from those of mutagens. It would also be inappropriate to assume by default that non-mutagenic carcinogens are assumed to need a toxicodynamic correction factor of 1. Most if not all of the factors that make individuals exposed to carcinogens during an early-lifestage potentially more susceptible than those individuals exposed during adulthood also apply to non-mutagenic carcinogen exposures (*e.g.*, rapid growth and development of target tissues, potentially greater sensitivity to hormonal carcinogens, differences in metabolism). It should also be noted that carcinogens that do not cause gene mutations may still be genotoxic by virtue of causing chromosomal damage. Additionally, many carcinogens do not have adequate data available for deciding on a specific mode of action, or do not necessarily have a single mode of action. For these reasons, OEHHA will apply the default cancer potency factor age adjustments described above to all carcinogens unless data are available which allow for the development of chemical-specific cancer potency factor age adjustments. In those cases, an agent-specific model of age dependence (based on observational or experimental data) might be used, or alternative (larger or smaller) adjustment factors and age ranges may be applied where understanding of the mechanism of action and target tissues makes this appropriate.

Other Source Documents for Cancer Risk Assessment Guidance

As noted previously, the cancer potencies and unit risks tabulated in this technical support document have been developed by various programs over a number of years. The methods used therefore necessarily varied according to the date of the assessment and the program responsible. The following section summarizes the sources and procedures most commonly applied, and their historical context where this is apposite.

United States Environmental Protection Agency (U.S. EPA)

The U.S. EPA was one of the first regulatory agencies to develop and apply cancer risk assessment methodology. Their guidance documents and technical publications have been influential for many programs, including the California Air Toxics (Toxic Air Contaminants and Hot Spots) programs.

Guidelines for Carcinogen Risk Assessment (U.S. EPA, 1986)

Prior to the more recent guidelines updating project which, after nearly ten years of internal and public review drafts culminated in the 2005 final revision (see below), U.S. EPA carcinogen risk assessment procedures were generally as described in Anderson *et al*. (1983) and "Guidelines for Carcinogen Risk Assessment" (U.S. EPA, 1986). These methods, which are outlined below, were used to calculate the Integrated Risk Information System (IRIS) cancer potency values, some of which are cited in this document. U.S. EPA has always indicated that cancer risk estimates based on adequate human epidemiologic data are preferred if available over estimates based on animal data. Although the newer guidelines offer alternative methods for dose-response analysis of animal bioassays, and updated consideration of specific topics such as lifestage-related differences in sensitivity, and mechanism of action for some types of carcinogen, the underlying principles and many of the specific procedures developed in these original guidelines are still applicable and in use.

U.S. EPA Calculation of Carcinogenic Potency Based on Animal Data

In extrapolating low-dose human cancer risk from animal carcinogenicity data, it is generally assumed that most agents that cause cancer also damage DNA, and that the quantal type of biological response characteristic of mutagenesis is associated with a linear non-threshold dose-response relationship. U.S. EPA stated that the risk assessments made with this model should be regarded as conservative, representing the most plausible upper limit for the risk. The mathematical expression used by U.S. EPA in the 1986 guidelines to describe the linear non-threshold dose-response relationship at low doses is the linearized multistage procedure developed by Crump (1980). This model is capable of fitting almost any monotonically increasing dose-response data, and incorporates a procedure for estimating the largest possible linear slope at low extrapolated doses that is consistent with the data at all experimental dose levels. A description of the linearized multistage procedure has been provided above (page 29). U.S. EPA used an updated version (GLOBAL86, Howe *et al*., 1986) of the computer program GLOBAL79 developed by Crump and Watson (1979) to calculate the point estimate and the 95% upper confidence limit of the extra risk $A(d)$.

U.S. EPA separated tumor incidence data according to organ sites or tumor types. The incidence of benign and malignant tumors was combined whenever scientifically defensible. U.S. EPA considered this incidence combination scientifically defensible unless the benign tumors are not considered to have the potential to progress to the associated malignancies of the same histogenic origin. The primary comparison in carcinogenicity evaluation is tumor response in dosed animals as compared to contemporary matched control animals. However, U.S. EPA stated that historical control data could be used along with concurrent control data in the evaluation of carcinogenic responses, and notes that for the evaluation of rare tumors, even small tumor responses may be significant compared to historical data. If several data sets (dose and tumor incidence) are available (different animal species, strains, sexes, exposure levels, exposure routes) for a particular chemical, the data set used in the model was the set where the incidence is statistically significantly higher than the control for at least one test dose level and/or where the tumor incidence rate shows a statistically significant trend with respect to dose level. The data set generating the highest lifetime cancer risk estimate (q_1^*) was chosen where appropriate. An example of an inappropriate data set would be a set which generates an artifactually high risk estimate because of a very small number of animals used. If there are 2 or more data sets of comparable size for a particular chemical that are identical with respect to species, strain, sex and tumor sites, the geometric mean of q_1^* estimated from each of those data sets was used for risk estimation. U.S. EPA assumed that mg/surface area/day is an equivalent dose between species. Surface area was further assumed to be proportional to the 2/3 power of the weight of the animal in question. Equivalent dose was therefore computed using the following relationship:

$$d = \frac{l_e * m}{L_e * W^{2/3}}$$

where L_e = experimental duration, l_e = exposure duration, m = average dose (mg/day) and W = average animal weight. Default average body weights for humans, rats and mice are 70, 0.35 and 0.03 kg, respectively.

Exposure data expressed as ppm in the diet were generally converted to mg/day using the relationship m = ppm * F * r, where ppm is parts per million of the chemical in the diet, F is the weight of the food consumed per day in kg, and r is the absorption fraction (assumed to be 1 in the absence of data indicating otherwise). The weight of food consumed, calories required, and animal surface area were generally all considered to be proportional to the 2/3 power of the animal weight, so:

$$m \propto \text{ppm} * W^{2/3} * r, \text{ or } \quad \frac{m}{r W^{2/3}} \propto \text{ppm}$$

The relationship could lead to the assumption that dietary ppm is an equivalent exposure between species. However, U.S. EPA did not believe that this assumption is justified, since the calories/kg food consumed by humans is significantly different from that consumed by laboratory animals (primarily due to differences in moisture content). An empirically derived food factor, $f = F/W$

was used, which is the fraction of a species' body weight consumed per day as food. U.S. EPA (1986) gave the *f* values for humans, rats and mice as 0.028, 0.05 and 0.13, respectively.

Dietary exposures expressed as concentrations in ppm were converted to mg/surface area using the following relationship:

$$\frac{m}{r * W^{2/3}} = \frac{\text{ppm} * F}{W^{2/3}} = \frac{\text{ppm} * f * W}{W^{2/3}} = \text{ppm} * f * W^{2/3}$$

Exposures expressed as mg/kg/day ($m/Wr = s$) were converted to mg/surface area using the relationship:

$$\frac{m}{rW^{2/3}} = s * W^{2/3}$$

The calculation of dose when exposure is via inhalation was performed for cases where 1) the chemical is either a completely water-soluble gas or aerosol and is absorbed proportionally to the amount of inspired air, or 2) where the chemical is a partly water-soluble gas which reaches an equilibrium between the inspired air and body compartments. After equilibrium is attained, the rate of absorption is proportional to metabolic rate, which is proportional to the rate of oxygen consumption, which is related to surface area.

Exposure expressed as mg/day to completely water-soluble gas or aerosols can be calculated using the expression $m = I * v * r$, where I is the inspiration rate/day in m^3, v is the concentration of the chemical in air (mg/m^3), and r is the absorption fraction (assumed to be the same for all species in the absence of data to the contrary; usually 1). For humans, the default inspiration rate of 20 m^3 has been adopted. Inspiration rates for 113 g rats and 25 g mice have been reported to be 105 and 34.5 liters/day, respectively. Surface area proportionality can be used to determine inspiration rate for rats and mice of other weights; for mice, $I = 0.0345\ (W / 0.025)^{2/3}$ m^3/day; for rats, $I = 0.105\ (W / 0.113)^{2/3}$ m^3/day. The empirical factors for air intake/kg/day (i) for humans, rats and mice are 0.29, 0.64 and 1.3, respectively. Equivalent exposures in mg/surface area can be calculated using the relationship:

$$\frac{m}{W^{2/3}} = \frac{Ivr}{W^{2/3}} = \frac{iWvr}{W^{2/3}} = iW^{1/3}vr$$

Exposure expressed as mg/day to partly water-soluble gases is proportional to surface area and to the solubility of the gas in body fluids (expressed as an absorption coefficient r for that gas). Equivalent exposures in mg/surface area can be calculated using the relationships $m = kW^{2/3} * v * r$, and $d = m/W^{2/3} = kvr$. The further assumption is made that in the case of route-to-route extrapolations (*e.g.*, where animal exposure is via the oral route, and human exposure is via inhalation, or vice versa), unless pharmacokinetic data to the contrary exist, absorption is equal by either exposure route.

Adjustments were made for experimental exposure durations shorter than the lifetime of the test animal; the slope q_1^* was increased by the factor $(L/L_e)^3$, where L is the normal lifespan of the experimental animal and L_e is the duration of the experiment. This assumed that if the average dose d is continued, the age-specific rate of cancer will continue to increase as a constant function of the background rate. Since age-specific rates for humans increase by at least the 2nd power of the age, and often by a considerably higher power (Doll, 1971), there is an expectation that the cumulative tumor rate, and therefore q_1^*, will increase by at least the 3rd power of age. If the slope q_1^* is calculated at age L_e, it would be expected that if the experiment was continued for the full lifespan L at the same average dose, the slope q_1^* would have been increased by at least $(L/L_e)^3$.

U.S. EPA Calculation of Carcinogenic Potency Based on Human Data

U.S. EPA stated that existing human epidemiologic studies with sufficiently valid exposure characterization are always used in evaluating the cancer potency of a chemical. If they showed a carcinogenic effect, the data were analyzed to provide an estimate of the linear dependence of cancer rates on lifetime cancer dose (equivalent to the factor q_1^*). If no carcinogenic effect was demonstrated and carcinogenicity had been demonstrated in animals, then it was assumed that a risk does exist, but it is smaller than could have been observed in the epidemiologic study. An upper limit of cancer incidence was calculated assuming that the true incidence is just below the level of detection in the cohort studied, which is largely determined by the cohort size. Whenever possible, human data are used in preference to animal data. In human epidemiologic studies, the response is measured as the relative risk of the exposed cohort of individuals compared to the control group. The excess risk ($R(X)$ - 1, where $R(X)$ is relative risk) was assumed to be proportional to the lifetime average exposure X, and to be the same for all ages. The carcinogenic potency is then equal to $[R(X) - 1]/X$ multiplied by the lifetime risk at that site in the general population. According to this original procedure, the confidence limit for the excess risk was not usually calculated. This decision was ascribed to the difficulty in accounting for inherent uncertainty in the exposure and cancer response data. More recent assessments have taken the opposite view and attempted to calculate and characterize this uncertainty by determining confidence limits, *inter alia*.

Guidelines for Carcinogen Risk Assessment (U.S. EPA, 2005a)

U.S. EPA revised its "Guidelines for Carcinogen Risk Assessment" (referred to henceforth as the "U.S. EPA Guidelines") in 2005. Compared to the 1986 version of this document, more emphasis is placed on establishing a "mode of action" (MOA). The following excerpt provides a definition of this term:

> "The term "mode of action" is defined as a sequence of key events and processes, starting with interaction of an agent with a cell, proceeding through operational and anatomical changes, and resulting in cancer formation. A "key event" is an empirically observable precursor step that is itself a necessary element of the mode of action or is a biologically based marker for such an element. Mode of action is contrasted with "mechanism of action," which implies a more detailed understanding and description of events, often at the molecular level, than is meant by mode of action".

Cancer risk assessments performed under the prior U.S. EPA Guidelines sometimes included a MOA description. However, the 1986 U.S. EPA Guidelines did not explicitly mandate the development of a MOA description in cancer risk assessments.

The MOA information is then used to govern how a cancer risk assessment shall proceed. Tumor incidence data sets arising from a MOA judged to be not relevant to humans are not used to extrapolate a cancer potency factor. If an MOA cannot be determined or is determined to have a low-dose linear dose-response and a nonmutagenic MOA, then a linear extrapolation method is used to develop a cancer potency factor. The same linear extrapolation is used for all lifestages, unless chemical specific information on lifestage or population sensitivity is available. Carcinogens that act via an MOA judged to have a nonlinear low-dose dose response are modeled using MOA data, or the RfD/RfC risk assessment method is used as a default. Adjustments for susceptible lifestages or populations are to be performed as part of the risk assessment process.

If a carcinogen is deemed to act via a mutagenic MOA, then the data from the MOA analysis is evaluated to determine if chemical-specific differences between adults and juveniles exist and can be used to develop a chemical-specific risk estimate incorporating lifestage susceptibility. If this cannot be done, then early-life susceptibility is assumed, and age-dependent adjustment factors (ADAFs) are applied as appropriate to develop risk estimates. In cases where it is not possible to develop a toxicokinetic model to perform cross-species scaling of animal tumor data sets which arise from oral exposures, the U.S. EPA Guidelines state that administered doses should be scaled from animals to humans on the basis of equivalence of $mg/kg^{3/4}$-d (milligrams of the agent normalized by the 3/4 power of body weight per day). This is a departure from the 1986 U.S. EPA guidelines, which used a 2/3 power of body weight normalization factor. Other adjustments for dose timing, duration and route are generally assumed to be handled in similar fashion to that described for the 1986 guidelines, although of course updated parameter values would be used where available.

The 2005 U.S. EPA Guidelines also use benchmark dose methodology (described above, page 27) to develop a "point-of departure" (POD) from tumor incidence data. For linear extrapolation, the POD is used to calculate a cancer potency factor, and for nonlinear extrapolation the POD is used in the calculation of a reference dose (RfD) or reference concentration (RfC).

It should be noted that none of the cancer potency factors listed in this document were obtained from U.S. EPA risk assessments performed under the 2005 U.S. EPA Guidelines. All U.S. EPA IRIS cancer potency values contained in this document were obtained from risk assessments using the 1986 U.S. EPA Guidelines.

Office of Environmental Health Hazard Assessment (OEHHA), California Environmental Protection Agency

The cancer risk assessment procedures originally used by the Office of Environmental Health Hazard Assessment (OEHHA) are outlined in "Guidelines for Chemical Carcinogen Risk Assessments and their Scientific Rationale" (referred to below as the Guidelines) (CDHS, 1985). These procedures were generally used in generating Toxic Air Contaminant (TAC) cancer potency values, standard Proposition 65 cancer potency values and Public Health Goal (PHG) cancer

potency values. Expedited Proposition 65 cancer potency values depart somewhat from those procedures and are discussed separately below.

OEHHA cancer risk assessment methodology as described by CDHS (1985) generally resembled that used at that time by U.S. EPA (Anderson *et al*., 1983; U.S. EPA, 1986). OEHHA risk assessment practice similarly reflects the evolution of the technical methodology (*e.g.*, as described in U.S. EPA, 2005a) since the original guidelines were published. The basic principles and procedures described below are still considered applicable. More recent additions to OEHHA cancer risk assessment methods such as the use of benchmark dose methodologies and early-lifestage cancer potency adjustments are discussed above. The Guidelines state that both animal and human data, when available, should be part of the dose-response assessment.

OEHHA Calculation of Carcinogenic Potency Based on Animal Data

The procedures used to extrapolate low-dose human cancer risk from animal carcinogenicity data assumed that a carcinogenic change induced in a cell is transmitted to successive generations of cell descendants, and that the initial change in the cell is an alteration (*e.g.*, mutation, rearrangement, etc.) in the cellular DNA. Non-threshold models are used to extrapolate to low-dose human cancer risk from animal carcinogenicity data.

Several models were proposed for extrapolating low-dose human cancer risk from animal carcinogenicity data in the original Guidelines. These models include the Mantel-Bryan method (log-probit model), the one-hit model, the linearized multistage procedure, the gamma multihit model, and a number of time-to-tumor models. The Guidelines stated that time-to-tumor models (i.e., a Weibull-in-time model) should be used for low-dose extrapolation in all cases where supporting data are available, particularly when survival is poor due to competing toxicity. However, the Guidelines also noted the difficulty of determining the actual response times in an experiment. Internal tumors are generally difficult to detect in live animals and their presence is usually detected only at necropsy. Additionally, use of these models often requires making the determination of whether a tumor was the cause of death, or was found only coincidentally at necropsy when death was due to other causes. Further, competing causes of death, such as chemical toxicity, may decrease the observed time-to-tumor for nonlethal cancers by allowing earlier necropsy of animals in higher dose groups. The linearized multistage (LMS) procedure was noted as being an appropriate method for dose extrapolation in most cases, with the primary exception being a situation in which sufficient empirical data are available to indicate a dose-response curve of a "quasi-threshold" type (*e.g.*, flat for two or three dose levels, then curving sharply upwards). In this case, the LMS procedure may underestimate the number of stages and overestimate the low-dose risks. In this case, the gamma multihit model was suggested as being a potential alternative. The Mantel-Bryan model was described as having little biological basis as applied to carcinogenesis, and being likely to underestimate risks at low doses. The Guidelines stated that this model should not be used for low dose extrapolation. More recent practice has departed from these original guidelines in some respects, for instance by experimenting with cell-proliferation based models in a few cases. However, the LMS model remained the preferred extrapolation model for most purposes. Some of the difficulties in achieving a satisfactory fit to tumor incidence data were found to be alleviated by application of toxicokinetic models and use of an internal rather than applied dose metric with the LMS model. This has resulted in the alternative models originally advocated (Gamma multihit, Mantel-Bryan) being mostly

abandoned. As noted above (Dose-Response Assessment, page 23), the use of allegedly biologically based statistical models such as LMS has fallen from favor in recent years, and benchmark dose methodology has become the preferred method for extrapolating cancer potency values from animal cancer incidence data. However, it should also be noted that results generated by the LMS model and benchmark dose methodology from the same data set are often quite similar.

The 1985 Guidelines stated that both animal and human data, when available, should be part of the dose-response assessment. Although preference was given to human data when these were of adequate quality, animal studies may provide important supporting evidence. Low-dose extrapolation of human cancer risk from animal carcinogenicity data was generally based on the most sensitive site, species and study demonstrating carcinogenicity of a particular chemical, unless other evidence indicates that the data set in question is not appropriate for use. Where both benign and malignant tumors are induced at the same site and the benign tumors are considered to have the potential to progress to malignant tumors, the incidence data for both types of tumors could be combined to form the basis for risk assessment. Pharmacokinetic data on chemical metabolism, effective dose at target site, or species differences between laboratory test animals and humans were considered in dose-response assessments when available. In performing exposure scaling from animals to humans, the "surface area" correction (correcting by the 2/3 power of body weight) was used unless specific data indicate that this should not be done. The Guidelines assumed that in the absence of evidence to the contrary, chemicals that cause cancer after exposure by ingestion will also cause cancer after exposure by inhalation, and vice versa. These original proposals have continued in use with little change except that currently, TAC and PHG cancer potency factor calculations use a 3/4 power of body weight correction for interspecies scaling, in line with current U.S. EPA practice. The standard Proposition 65 cancer potency factor calculations still use a 2/3 power correction because the cancer potency calculation method is specified in regulation (California Health and Safety Code 25249.5 *et seq*.).

Cancer unit risk factors [in units of $(\mu g/m^3)^{-1}$] have been calculated from cancer potency factors [in units of $(mg/kg\text{-}day)^{-1}$] using the following relationship:

$$UR = \frac{CPF * 20\ m^3}{70\ kg\ *\ CV}$$

where UR is the cancer unit risk, CPF is the cancer potency factor, 70 kg is the reference human body weight, 20 m^3 is the reference human inspiration rate/day, and CV is the conversion factor from mg to µg (= 1000). The cancer unit risk describes the excess cancer risk associated with an inhalation exposure to a concentration of 1 $\mu g/m^3$ of a given chemical; the cancer potency factor describes the excess cancer risk associated with exposure to 1 mg of a given chemical per kilogram of body weight.

It should be noted that although this default method is still used in deriving published cancer unit risk values, for site-specific risk assessments age-appropriate distributions and percentile values are used in the current version of the Hot Spots exposure assessment document. Where exposure to children occurs (as it does in most exposures to the general population surrounding a source

site) it is also necessary to apply the age-specific adjustment factors for the appropriate durations in accordance with the guidance offered above (Page 30 *et seq.*).

OEHHA Calculation of Carcinogenic Potency Based on Human Data

Human epidemiologic studies with adequate exposure characterization are used to evaluate the cancer potency of a chemical. If they show a carcinogenic effect, the data are analyzed to provide an estimate of the linear dependence of cancer rates on lifetime cancer dose. The 1985 Guidelines stated that with continuous exposure, age-specific incidence continues to increase as a power function (*e.g.*, t^3 or t^4) of the elapsed time since initial exposure. Lifetime risks can be estimated by applying such a power function to the observed data and extrapolating beyond the actual followup period. OEHHA has generally undertaken the calculation of study power and confidence bounds on the potency estimate as important tools to establish the credibility of the estimate obtained and in comparing this with other estimates (from other human studies or from animal data). Due to the diversity in quality and type of epidemiological data, the specific approaches used in OEHHA risk assessments based on human epidemiologic studies vary on a case by case basis rather than following explicit general guidelines. Examples of the methods used can be observed in the Toxic Air Contaminant documents (these documents are listed in Appendix D: the methods used are described in the compound summaries provided in Appendix B).

Expedited Proposition 65 Cancer Risk Assessment Methodology

Expedited cancer potency values developed for several agents listed as carcinogens under Proposition 65 (California Health and Safety Code 25249.5 *et seq*.) were derived from selected animal carcinogenicity data sets of the Carcinogenic Potency Database (CPDB) of Gold *et al.* (1984, 1986, 1987, 1989, 1990, 1997) using default procedures specified in the administrative regulations for Proposition 65 (Title 22 California Code of Regulations [CCR] 12703). OEHHA hazard assessments usually describe all relevant data on the carcinogenicity (including dose-response characteristics) of the chemical under examination, followed by an evaluation of any pharmacokinetic and mechanistic (*e.g.*, genotoxicity) data. An evaluation of the data set for the chemical may indicate that adjustments in target dose estimates or use of a dose response model different from the default are appropriate. The procedure used to derive expedited Proposition 65 cancer potency values differs from the usual methodology in two ways. First, it relies on cancer dose response data evaluated and extracted from the original literature by Gold *et al.* Second, the choice of a linearized multistage procedure for generating cancer potency values is automatic, and pharmacokinetic adjustments are not performed. The methods used to develop expedited cancer potency values incorporate the following assumptions:

1. The dose response relationship for carcinogenic effects in the most sensitive species tested is representative of that in humans.
2. Observed experimental results can be extrapolated across species by use of the interspecies factor based on "surface area scaling."
3. The dose to the tissue giving rise to a tumor is assumed to be proportional to the administered dose.
4. The linearized multistage polynomial procedure can be used to extrapolate potency outside the range of experimental observations to yield estimates of "low" dose potency.

5. Cancer risk increases with the third power of age.

The Carcinogenic Potency Database of Gold *et al.* (1984, 1986, 1987, 1989, 1990) contains the results of more than 4000 chronic laboratory animal experiments on 1050 chemicals by combining published literature with the results of Federal chemical testing programs (Technical Reports from the Carcinogenesis Bioassay Program of the National Cancer Institute (NCI)/National Toxicology Program (NTP) published prior to June 1987). The published literature was searched (Gold *et al*., 1984) through the period December 1986 for carcinogenicity bioassays; the search included the Public Health Service publication "Survey of Compounds Which Have Been Tested for Carcinogenic Activity" (1948-1973 and 1978), monographs on chemical carcinogens prepared by the International Agency for Research on Cancer (IARC) and Current Contents. Also searched were Carcinogenesis Abstracts and the following journals: British Journal of Cancer, Cancer Letters, Cancer Research, Carcinogenesis, Chemosphere, Environmental Health Perspectives, European Journal of Cancer, Food and Chemical Toxicology, Gann, International Journal of Cancer, Journal of Cancer Research and Clinical Oncology (formerly Zeitschrift fur Krebsforschung und Klinische Onkologie), Journal of Environmental Pathology and Toxicology, Journal of Toxicology and Environmental Health, Journal of the National Cancer Institute, and Toxicology and Applied Pharmacology. Studies were included in the database if they met the following conditions:

1. The test animals were mammals.
2. Chemical exposure was started early in life (100 days of age or less for hamsters, mice and rats).
3. Route of administration was via the diet, drinking water, gavage, inhalation, intravenous injection or intraperitoneal injection.
4. The test chemical was administered alone (not in combination with other chemicals).
5. Chemical exposure was chronic (*i.e.* duration of exposure was at least one-fourth the standard lifespan for that species), with not more than 7 days between exposures.
6. The experiment duration was at least half the standard lifespan for the species used.
7. The study design included a control group and at least 5 animals/exposure group.
8. No surgical interventions were performed.
9. Pathology data were reported for the number of animals with tumors (not total number of tumors).
10. All results reported were original data (not analysis of data reported by other authors).

Included in their data set tabulations are estimates of average doses used in the bioassay, resulting tumor incidences for each of the dose levels employed for sites where significant responses were observed, dosing period, length of study and histopathology. Average daily dose levels were calculated assuming 100% absorption. Dose calculations follow procedures similar to those of Cal/EPA and U.S. EPA; details on methods used and standard values for animal lifespans, body weights, and diet, water and air intake are listed in Gold *et al.* (1984). OEHHA (1992) reviewed the quality assurance, literature review, and control procedures used in compiling the data and found them to be sufficient for use in an expedited procedure. Cancer potency estimates were

derived by applying the mathematical approach described in the section below to dose response data in the Gold *et al.* database.

The following criteria were used for data selection:

1. Data sets with statistically significant increases in cancer incidence with dose ($p \leq 0.05$) were used. (If the authors of the bioassay report considered a statistically significant result to be unrelated to the exposure to the carcinogen, the associated data set was not used.)
2. Data sets were not selected if the endpoint was specified as "all tumor-bearing animals" or results were from a combination of unrelated tissues and tumors.
3. When several studies were available, and one study stood out as being of higher quality due to numbers of dose groups, magnitude of the dose applied, duration of study, or other factors, the higher quality study was chosen as the basis for potency calculation if study results were consistent with those of the other bioassays listed.
4. When there were multiple studies of similar quality in the sensitive species, the geometric mean of potencies derived from these studies was taken. If the same experimentalists tested two sexes of the same species/strain under the same laboratory conditions, and no other adequate studies were available for that species, the data set for the more sensitive sex was selected.
5. Potency was derived from data sets that tabulate malignant tumors, combined malignant and benign tumors, or tumors that would have likely progressed to malignancy.

Cancer potency was defined as the slope of the dose response curve at low doses. Following the default approach, this slope was estimated from the dose response data collected at high doses and assumed to hold at very low doses. The Crump linearized multistage polynomial (Crump *et al.*, 1977) was fit to animal bioassay data:

$$\text{Probability of cancer} = 1 - \exp[-(q_0 + q_1 d + q_2 d^2 + ...)]$$

Cancer potency was estimated from the upper 95% confidence bound on the linear coefficient q_1, which is termed q_1^*.

For a given chemical, the model was fit to a number of data sets. As discussed in the section above, the default was to select the data for the most sensitive target organ in the most sensitive species and sex, unless data indicated that this was inappropriate. Deviations from this default occur, for example, when there are several bioassays or large differences exist between potency values calculated from available data sets.

Carcinogenicity bioassays using mice and/or rats will often use an exposure duration of approximately two years. For standard risk assessments, this is the assumed lifespan for these species. Animals in experiments of shorter duration are at a lower risk of developing tumors than those in the standard bioassay; thus potency is underestimated unless an adjustment for experimental duration is made. In estimating potency, short duration of an experiment was taken into account by multiplying q_1^* by a correction factor equal to the cube of the ratio of the assumed standard lifespan of the animal to the duration of the experiment (T_e). This assumes that the cancer hazard would have increased with the third power of the age of the animals had they lived longer:

$$q_{animal} = q_1^* * (104 \text{ weeks}/T_e)^3$$

In some cases excess mortality may occur during a bioassay, and the number of initial animals subject to late occurring tumors may be significantly reduced. In such situations, the above described procedure can, at times, significantly underestimate potency. A time-dependent model fit to individual animal data (i.e., the data set with the tumor status and time of death for each animal under study) may provide better potency estimates. When Gold *et al.* indicated that survival was poor for a selected data set, a time-dependent analysis was attempted if the required data were available in the Tox Risk (Crump *et al.*, 1991) data base. The Weibull multistage model (Weibull-in-time; multistage-in-dose) was fit to the individual animal data.

To estimate human cancer potency, q_{animal} values derived from bioassay data were multiplied by an interspecies scaling factor (K; the ratio of human body weight (bw_h) to test animal body weight (bw_a), taken to the 1/3 power (Anderson *et al.*, 1983)):

$$K = (bw_h/bw_a)^{1/3}$$

Thus, cancer potency = $q_{human} = K * q_{animal}$

Chemical-specific Descriptions of Cancer Potency Value Derivations

Unit Risk and potency values for chemicals whose cancer potency values were obtained from Toxic Air Contaminant documents, standard or expedited Proposition 65 documents, U.S. EPA's Integrated Risk Information System (IRIS) documents and Health Effects Assessment Summary Table (HEAST) entries, or from other documents prepared by OEHHA's Air Toxicology and Epidemiology Branch or Pesticide and Environmental Toxicology Branch are presented in Appendix A. Information summaries for these chemicals are presented in Appendix B.

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Exhibit H

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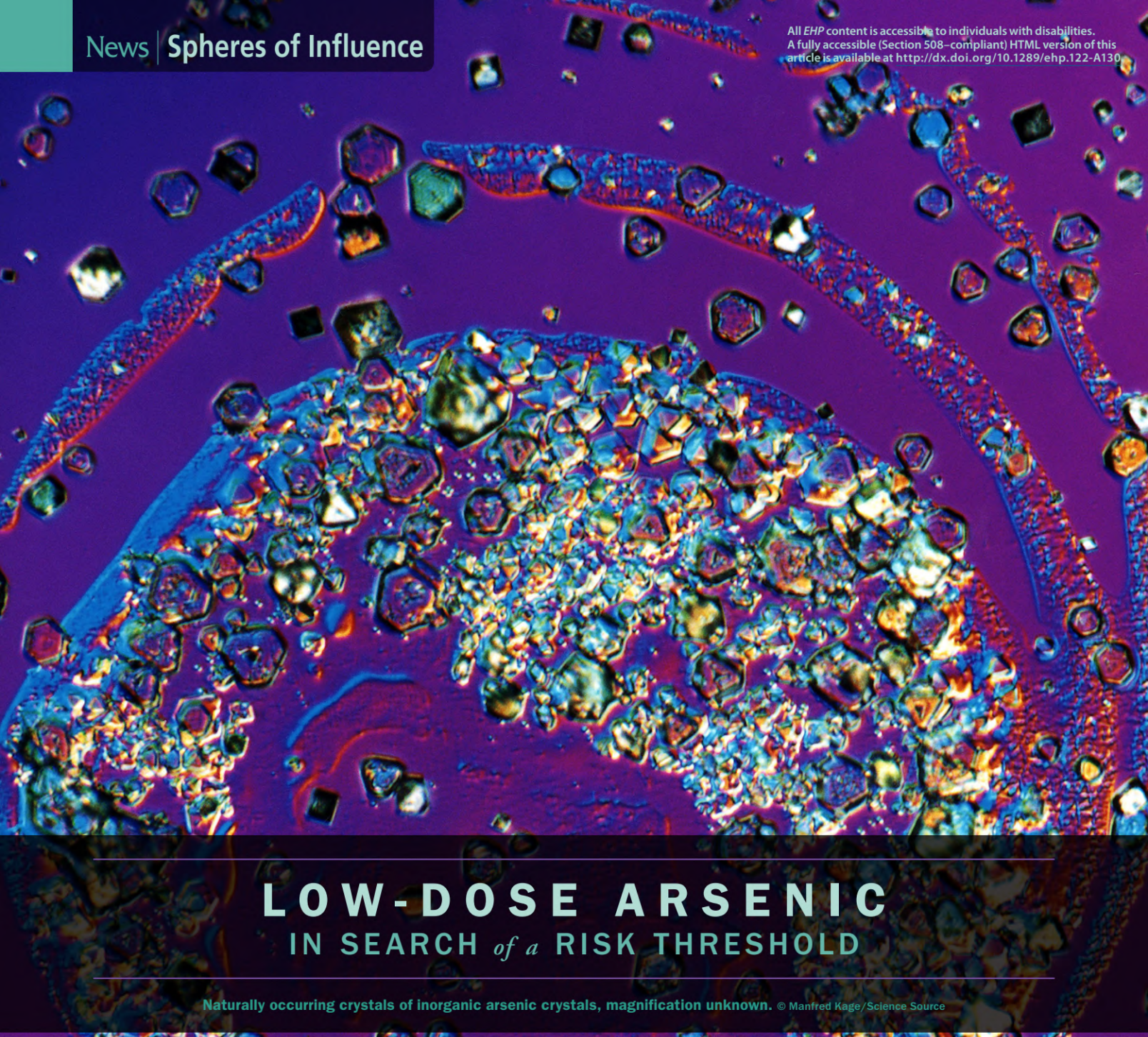

LOW-DOSE ARSENIC
IN SEARCH *of a* RISK THRESHOLD

Naturally occurring crystals of inorganic arsenic crystals, magnification unknown. © Manfred Kage/Science Source

Scientists long ago linked high levels of arsenic in groundwater to cancer and other environmental illnesses, particularly in Taiwan, Bangladesh, and South America, where the contamination can often reach extraordinarily high levels of 1,000 ppb or more. Now concerns are shifting to the health effects of much lower doses such as those that many Americans live with every day.

Margaret Karagas, who directs the Children's Environmental Health and Disease Prevention Research Center at Dartmouth College, says researchers increasingly believe that arsenic risks are more widespread than previously recognized, particularly during vulnerable periods such as pregnancy and childhood. Protecting against low-level exposure is challenging, however, given that arsenic is a natural element in the Earth's crust and ubiquitous throughout the environment.

Moreover, the evidence for low-dose effects is controversial. One view holds that arsenic has a dose threshold below which exposures aren't harmful. But controversial studies in the peer-reviewed literature increasingly suggest this threshold may not exist, so that any exposure—no matter how small—could boost risks for diabetes, heart disease, immunological problems, and cancer.[1,2,3,4,5,6]

The disagreement is a problem for regulators who face mounting pressure to set or reduce standards for arsenic. The U.S. Environmental Protection Agency (EPA) is grappling with a revised estimate of arsenic carcinogenicity that, if enacted, would result in unattainable clean-up standards, according to Susan Griffin, a senior toxicologist with the EPA's Region 8 office in Denver, Colorado. The U.S. Food and Drug Administration (FDA) is also under pressure to regulate arsenic in foods, especially rice, which readily absorbs the metal as it grows, making it a top source of dietary exposure.

The focus on rice comes on the heels of a new "action level" of 10 ppb for arsenic in apple juice that was proposed by the FDA in July 2013.[7] This new value, which tightens the agency's previous "level of concern" of 23 ppb (and which has yet to be formally adopted), was motivated in part by mounting publicity over low doses of arsenic in the diet, including media-directed efforts by the public-interest group Consumers Union (CU) to raise awareness on the issue. Growing public scrutiny has put a spotlight on the complex question of how very low arsenic exposures may affect human health.

A Historical View

That arsenic can be lethal has been known since antiquity. But lethal doses of arsenic are difficult to quantify, and they depend on solubility, valence states, and other factors. The Agency for Toxic Substances and Disease Registry suggests that the minimal lethal exposure in humans ranges from 1 to 3 ppm, with death resulting from cardiovascular collapse and hypovolemic shock.[8]

Researchers didn't perceive arsenic as an environmental health threat until studies in Taiwan, and later in Chile, linked levels in groundwater with skin cancers such as squamous cell carcinoma (which is rarely fatal) and a condition called black foot disease (which affects blood vessels, leading to gangrene). Villagers were exposed to the arsenic beginning in the early twentieth century after artesian wells were drilled throughout southwestern Taiwan to avoid saltwater intrusion from shallower wells.[9] The U.S. Public Health Service aimed to protect against the arsenic-related skin problems seen in Taiwan when it set a 50-ppb standard for arsenic in drinking water in 1942, which was then adopted by the EPA in 1975.[10]

The levels deemed "low" in early environmental health research on arsenic were much higher than what's considered low today. Studies from Taiwan up to the 1980s described groundwater levels of up to 300 ppb as low, of up to 600 ppb as moderate, and values beyond that as high.[10,11] These delineations were based on a view that consuming arsenic in groundwater, while harmful, wasn't fatal in the long run.

Two pivotal studies led researchers to reconsider that point. Chien-Jen Chen, who was then a teaching assistant at the National Taiwan University College of Medicine, and colleagues showed that arsenic could, in fact, boost risks for fatal malignancies at groundwater concentrations far less than 600 ppb. Published in 1985, the first study reported statistically significant associations between chronic exposure to artesian well water in Southwestern Taiwan and elevated mortality from cancers of the lung, bladder, and other internal organs.[12,13] And in their follow-up study, Chen and colleagues reported that this relationship was dose-dependent—i.e., that cancer rates grew with higher arsenic exposure—and that mortality rates were especially high in areas where blackfoot disease also was endemic.[11]

Joseph Graziano, a professor of environmental health sciences and pharmacology at Columbia University, says Chen's data had far-reaching consequences that scientists are still grappling with today. Without evidence to the contrary, the EPA defaulted to what is still a standard regulatory assumption: namely that any exposure to a carcinogen, no matter how small, increases cancer risk to some degree. Therefore, the National Research Council (NRC) now describes arsenic levels beyond 150 ppb as high, between 150 ppb and 50 ppb as moderate, and below 50 ppb as low.[14]

But linear assumptions drive considerable risk even at low exposures. Extrapolating from high-dose human data, the NRC predicted in 1999 that the 50-ppb water standard could induce cancer in as many as 1 in 100 people.[15]

By that time, the EPA had already been engaged in technical review on arsenic for years. The agency ultimately evaluated more than 300 studies and drew on expert opinions from the NRC, the National Drinking Water Council, and its own Science Advisory Board (SAB) before it finally dropped the standard from 50 to 10 ppb in 2001[16]—a level the NRC estimated might lead to a cancer risk of approximately 1 in 300 for people exposed over a lifetime.[17] According to Craig Steinmaus, an associate adjunct professor in epidemiology at the University of California, Berkeley, School of Public Health, the EPA by necessity had to factor cost and technical feasibility as well as health into the 10-ppb drinking water standard.

Debating the Standard

The EPA's risk assumptions on arsenic were criticized by researchers who felt it was inappropriate to extrapolate low-dose effects from the high-dose Taiwanese studies. Samuel Cohen, a professor of pathology and microbiology at the University of Nebraska Medical Center, has long maintained that arsenic has a dose threshold below which exposures are not harmful. According to Cohen's own research with rodents (in addition to *in vitro* and *in vivo* studies by other researchers), arsenic is carcinogenic only at doses high enough to induce cytotoxicity followed by regenerative cell proliferation. If prolonged, he says, that mechanism can spawn tumors in the bladder, lungs, and skin.

But Cohen insists this whole process depends on the generation of reactive arsenic metabolites that, in turn, interact with sulfhydryl groups in critical cell proteins. And at minimal doses (below 10 ppb in drinking water given to experimental animals or 100 ppb in well water consumed by humans, he says), arsenic exposure doesn't generate enough reactive metabolites to induce tumor growth, suggesting that arsenic has a dose threshold. Moreover, Cohen claims that only direct reactions with DNA produce linear, nonthreshold dose responses for cancer, but according to the evidence, he says, inorganic arsenic is not DNA-reactive.[18]

"A linear dose–response line goes against what we know about arsenic's basic biology," Cohen says. "What we show in the lab shows there must be a threshold phenomenon."

Other scientists disagree. Steinmaus, for instance, counters that rodents may not be good models for human arsenic metabolism given that "they don't get cancer at doses that clearly cause cancer in humans." He says, "You need to interpret those data cautiously."

Moreover, high-dose human data from Taiwan are valuable because they remove some of the uncertainty associated with

Arsenic in U.S. Private Wells

Despite the 10-ppb upper limit on inorganic arsenic in municipal water, neither the EPA nor state governments regulate arsenic in private wells. However, a 2001 EPA study found that 13 million U.S. residents get their drinking water from private wells that exceed the federal arsenic standard.[35,36,37] Similarly, in 2009 the U.S. Geological Survey (USGS) tested 1,774 private wells nationwide and found that 6.8% of them exceeded the EPA standard (these are the most recent national data available on arsenic in private wells).[38]

According to Leslie DeSimone, a water quality specialist with the USGS, 90% of the exceedances were below 50 ppb, but measured concentrations ranged as high as 242 ppb, with the highest levels detected in the West, Midwest, parts of Texas, and New England. During a survey of Maine wells conducted in the mid to late 2000s, USGS scientists measured a concentration of 3,100 ppb in the coastal town of Danforth.[39] Maine resides within a belt of arsenic-laden bedrock that extends north from New York.

Bill Wilber, chief of the USGS National Water Quality Assessment Program, says in some cases simply drilling a well introduces oxygen and other elements that alter the chemistry of the underlying geology, liberating arsenic from bedrock and allowing it to seep into the water column. "So you can find a big exceedance in one well and not in another that's just fifty feet away," Wilber says.

According to Andy Smith, state toxicologist with the Maine Division of Environmental Health, the cost of a home-based system to remove arsenic from well water ranges from $300 for a point-of-use system (i.e., at the faucet) to as much as $9,000 for point-of-entry systems that treat water for the whole household. Federal or state assistance to purchase these systems generally isn't available, Smith says.

exposure, Steinmaus claims. Villagers in Taiwan often spend much of their lives in one general location, so the arsenic measured in local well water likely reflects their actual long-term intake. By contrast, populations in the United States and other developed countries with lower arsenic levels in groundwater are more mobile, leading to a strong likelihood of exposure misclassification. This statistical bias occurs when individual subjects in epidemiology studies are classified as having consumed more—or less—of a substance over a given duration than they actually ingested, making it difficult to accurately estimate disease associations.

Thus, the EPA SAB concluded in 2010 that—given the size and stability of the population, as well as the inclusion of long-term exposure patterns—the Taiwanese data were "still the most appropriate source for estimating bladder and lung cancer risk to humans."[10] But the SAB also stated that published studies from countries with low levels of arsenic in drinking water (which the SAB defined as up to 160 ppb) should be critically evaluated.[10]

Evidence for Low-Dose Impacts

Low-dose studies are now ongoing in a number of countries, including various locations throughout the United States. For instance, in 2013 Ana Navas-Acien, an associate professor of environmental sciences and epidemiology at the Johns Hopkins Bloomberg School of Public Health, published results from a prospective study showing that urinary arsenic concentrations reflecting low and moderate drinking water exposures were associated with lung, prostate, and pancreatic cancer,[5] as well as with cardiovascular disease,[2] among Native Americans living in Arizona, Oklahoma, and the Dakotas.

Navas-Acien's team measured arsenic in urine samples that had been collected and frozen between 1989 and 1991. The cohort of nearly 4,000 individuals had originally been assembled for the Strong Heart Study (SHS), an evaluation of cardiovascular health in Native Americans launched by the National Heart, Lung and Blood Institute in 1988. According to Navas-Acien, Native Americans included in the SHS tend to be more geographically stable than the general U.S. population, limiting the potential for exposure misclassification.[5] "They get the same exposure to arsenic year after year that they got at birth," she explains.

By matching local well water data collected by the EPA and urinary arsenic measures from the SHS samples with information from death certificates up through 2008, Navas-Acien could study the relationship between arsenic exposure and cancer mortality. Her team's results suggested that arsenic had a linear dose response with lung cancer in particular, although Navas-Acien points out that confidence intervals were wide at doses below 5 ppb in well water, indicating uncertainty at the lowest exposure levels.

A similar linear response was also estimated for prostate and pancreatic cancer, but with even wider confidence intervals at the lowest doses. However, the excess relative risks estimated for prostate and pancreatic cancer in Navas-Acien's study are much greater than they are for lung cancer; this is inconsistent with findings from other areas such as Taiwan, and therefore raises questions among some researchers about the validity of the findings. Navas-Acien's team didn't evaluate bladder cancer or skin cancer because of the small number of cases.

In a separate study of the same SHS cohort, Navas-Acien reported an association between low-dose arsenic exposures and higher rates of cardiovascular disease.[2] That study is one of the first prospective cohort studies to evaluate arsenic-related cardiovascular risk, including both incidence and mortality, in a population from the United States.

These findings add to a wealth of data emerging from what could be the largest evaluation of arsenic toxicity yet undertaken: the Health Effects of Arsenic Longitudinal Study (HEALS), which launched in Bangladesh in 2000.[19] Coordinated by Graziano and Habibul Ahsan, a professor of epidemiology, medicine, and human genetics at the University of Chicago, HEALS has over time assembled a cohort of tens of thousands of individuals living in the district of Araihazar, where arsenic levels measured in well water have ranged from nondetectible to more than 900 ppb.

The HEALS team first reported an association between arsenic and high blood pressure in 2007 at well water concentrations of 10–40 ppb. Since then, HEALS has yielded dozens of papers associating arsenic at levels below 50 ppb with health conditions including heart disease, hematuria (blood in the urine), and impaired lung function.[20,21,22] Studies also showed that increased total urinary arsenic was associated with skin lesions such as melanosis and keratosis, which are known precursors to skin cancer.[23,24] "HEALS is an ongoing effort, and we are expanding the design and questions that we can answer with longer follow-up," Ahsan says.

The Regulatory Landscape

Confronted with mounting evidence of arsenic's low-dose effects, its commercial uses are being phased out. Of particular concern are uses in agriculture, which can result in potentially significant human exposures. According to a November 2013 NRC report, foods dominate human arsenic exposures when the levels in drinking water drop below 50 ppb (drinking water drives the exposures when its arsenic content exceeds that amount).[14]

In some cases, agricultural soils are naturally high in arsenic, but arsenical herbicides also can leave residues that accumulate in crops. Most of these herbicides have now been phased out (with some exceptions made for turfgrass and cotton),[25,26] but what remains in soil from past applications has been especially problematic in apple orchards, where these herbicides were routinely used, and in rice grown on old cotton fields that were treated with the chemicals.

Arsenical feed additives used to promote growth and prevent disease in poultry and swine may also be problematic for human consumers. However, these additives are also being phased out. Production of the feed additive roxarsone ceased voluntarily in 2011 after the FDA detected inorganic arsenic in the livers of chickens that ate it.[27] The manufacturers of roxarsone and two other arsenical feed additives have requested that the FDA withdraw approval of these products.[28] The agency is currently considering a request to ban a fourth additive, nitarsone.[28]

Now the FDA is weighing how to impose standards for arsenic in foods. The proposed standard of 10 ppb in apple juice was a first step in this direction, but advocates with CU say the agency should go further by imposing a 120-ppb standard for inorganic arsenic in rice.[29] In November 2012 CU published the results of a study showing that 223 samples of rice and rice-based products sold in the United States contained inorganic arsenic at concentrations ranging from 29.4 to 210 ppb.[30] In addition, Dartmouth investigators reported that brown rice syrup, a sweetener, might expose consumers to "significant concentrations" of inorganic arsenic.[31] (Arsenic tends to accumulate in the aleurone layer of the rice grain, which gives brown rice its color. This layer is removed to produce white rice.[31])

The FDA followed up with its own report on 1,300 samples of rice and rice products, which found that concentrations of inorganic arsenic ranged from an average 0.1 µg per serving in infant formula to an average 7.2 µg per serving in brown rice.[32] For perspective, Aaron Barchowsky, a professor of environmental and occupational health at the University of Pittsburgh School of Public Health, says that daily consumption of 3 liters of water at the 10-ppb standard amounts to a 30-µg dose of inorganic arsenic.

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In a 6 September 2013 statement, the FDA said the amount of detectable arsenic in the sampled rice and rice products was too low to cause "any immediate or short-term adverse health effects."[33] FDA spokesperson Shelly Burgess says the statement referred to short-term effects only, and not skin, bladder, or lung cancer.

But Michael Crupain, director of *Consumer Reports*' Food Safety and Sustainability Center, insists that chronic low-level exposures over time are still a concern, especially for infants fed formula made with brown rice syrup, which had the highest levels detected in CU's survey. The FDA is now performing a draft risk assessment for arsenic in rice, which agency officials say could guide further actions.

Also on the regulatory front, the EPA is grappling with its numerical estimate of arsenic's cancer potency. This value, known as a cancer slope factor (CSF), guides important regulatory policies, including clean-up standards at contaminated waste sites. Set in 1998, the original CSF for arsenic was based on nonmelanoma skin cancers observed in the early Taiwanese studies.

In 2010 the EPA proposed a revised CSF as part of an arsenic reassessment under the agency's Integrated Risk Information System (IRIS).[10] The proposed CSF, which was based on newer reports of associations with more dangerous lung and bladder cancers, was 17 times greater than the older value. But that new value was protested by industry and other affected stakeholders, even some of the agency's own scientists. Griffin, of EPA Region 8, says that with the revised CSF, arsenic clean-up levels would drop 100-fold, which is below natural background levels of arsenic in western states.

The proposal was subsequently dropped by the EPA, and under a congressional mandate the agency is now revising its arsenic reassessment with a focus on both cancer and noncancer end points. On 7 November 2013 the NRC presented a report that the EPA will use for guidance in drafting a new IRIS document.[14] Graziano, who chairs the NRC committee, says the EPA will submit the revised document by 2015. And at that point, he says, NRC scientists will review it to ensure that dose–response relationships between inorganic arsenic and its effects are "appropriately estimated and characterized."

Continued Debate

Meanwhile the debate over low-dose health risks from arsenic will likely continue on two fronts: how to apply mechanistic findings from animal and *in vitro* research to human responses, and how to address fundamental uncertainties in the human data.

A key question is whether the recent epidemiological literature supports estimates of cancer risk predicted from linear dose–response models. Dozens of studies over the last 15 years have investigated human cancer risk from arsenic exposure at sites around the world. According to a 2011 review published by Herman Gibb, president of environmental consulting firm Tetra Tech Sciences, these studies provide conflicting evidence, in part because the sample sizes needed to quantify risks at drinking water doses less than 100 ppb are larger than what's ordinarily achievable.[34]

Steinmaus argues that the high-dose epidemiology data may ultimately be most suitable for risk assessment, "but when you extrapolate down from those doses, the risks are huge." He adds, "This raises the question of whether linear extrapolations are suitable, and herein lies the big controversy."

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Exhibit I

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Arsenic and cancer: evidence and mechanisms

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Abstract

Arsenic is a potent carcinogen and poses a significant health concern worldwide. Exposure occurs through ingestion of drinking water and contaminated foods and through inhalation due to pollution. Epidemiological evidence shows arsenic induces cancers of the skin, lung, liver, and bladder among other tissues. While studies in animal and cell culture models support arsenic as a carcinogen, the mechanisms of arsenic carcinogenesis are not fully understood. Arsenic carcinogenesis is a complex process due its ability to be metabolized and because of the many cellular pathways it targets in the cell. Arsenic metabolism and the multiple forms of arsenic play distinct roles in its toxicity and contribute differently to carcinogenic endpoints, and thus must be considered. Arsenic generates reactive oxygen species increasing oxidative stress and damaging DNA and other macromolecules. Concurrently, arsenic inhibits DNA repair, modifies epigenetic regulation of gene expression, and targets protein function due its ability to replace zinc in select proteins. While these mechanisms contribute to arsenic carcinogenesis, there remain significant gaps in understanding the complex nature of arsenic cancers. In the future improving models available for arsenic cancer research and the use of arsenic induced human tumors will bridge some of these gaps in understanding arsenic driven cancers.

Keywords

arsenic; cancer; carcinogenesis; DNA damage; mechanism

INTRODUCTION

Over millennia, humans have harnessed the unique properties of arsenic for medicinal, agricultural, commercial, and decorative purposes. At the same time, humans have been subject to the stealthy toxicity of arsenic as an odorless and tasteless, intentional or unintentional, poison. Our complicated relationship with arsenic continues to this day.

Therapeutic uses of arsenic have been documented for thousands of years in traditional Chinese medicine and early western medicine. Two forms of arsenic were included in the

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Shennong Materia Medica in 200 BCE and Hippocrates is believed to use arsenic pastes to treat skin disorders (Au, 2011; Hughes et al., 2011; Paul et al., 2022; Chen & Costa, 2021). In 1786 Thomas Fowler reported on the medicinal effects of his arsenic solution for a broad range of infectious diseases and skin and blood disorders, in addition to other health conditions. The noted antimicrobial properties of arsenic led to the development of Salvarsan in the early 1900s as an effective treatment of syphilis garnering a Nobel prize for Paul Ehrlich in 1908. In the past, various forms of arsenic, including those used in traditional Chinese medicine and Fowler's solution, were employed as cancer therapeutics especially for cancers of the blood and skin (Au, 2011; Hughes et al., 2011; Paul et al., 2022; Chen & Costa, 2021). The FDA approved arsenic trioxide as a chemotherapeutic for leukemia in 2000 bringing an ancient drug into the modern era.

Other arsenic compounds have been beneficial as rodenticides, pesticides for agricultural crops and wood preservatives (Hughes et al., 2011; Bencko and Foong, 2017). Arsenic-based pigments were used in paints, fabrics and wallpapers based on a coveted emerald green color (Hughes et al., 2011). However, the medicinal and non-medicinal uses of arsenic revealed human toxicities based on unintended exposures. Widespread use of lead arsenate as a pesticide in apple and cherry orchards ultimately led to an official ban in the United States in 1988 (Hughes et al., 2011). The lasting legacy of this use is evident in millions of acres of land contaminated with lead arsenate. Chromated copper arsenate continues to be used as a wood preservative for non-residential purposes and organic arsenicals remain in restricted use as broad-spectrum herbicides. The potential for further contamination of soils and water by inorganic and organic arsenic compounds is under periodic review by the US Environmental Protection Agency (EPA).

Arsenic toxicity has been exploited for political gains through strategic poisonings leading to the often quoted statement labeling arsenic as the "king of poisons and poison of kings". Modern toxicological focus largely centers on the human health consequences of medicinal, occupational and environmental exposures to arsenic. Studies on health effects of human exposures through natural or anthropogenic arsenic contamination in soils and water led to adoption of drinking water standards worldwide currently at 10 ppb. Despite efforts to limit arsenic exposures, it is estimated that 200 million people or more are exposed to toxic levels of arsenic worldwide (Costa 2021). This chapter will focus on arsenic carcinogenicity and cover human population evidence for arsenic as a carcinogen, mechanisms of arsenic carcinogenicity, the carcinogenic potential of different forms of arsenic and conclude with a brief discussion of areas for future research.

SECTION 1: HUMAN STUDIES

Arsenic is a worldwide health concern due to prevalence in the environment and established human toxicity (Podgorski, 2020; Agency for Toxic Substances and Disease Registry (ATSDR), 2007; ATSDR, 2016; Naujokas et al., 2013). Arsenic is present in rocks, soil and water, and background environmental levels may be increased by mining, burning of fossil fuels, and application of agricultural pesticides and herbicides (Gundert-Remy et al., 2015). In recognition of its toxic potential, arsenic is at the top of the ASTDR Priority List (https://www.atsdr.cdc.gov/spl/index.html). Occupational exposures are limited by the US

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Occupational Safety and Health Administration to 10 μg/m^3, and recommended drinking water exposure limits of 10 μg/L (10 ppb) have been established by the EPA and the World Health Organization (WHO) (WHO, 2011; EPA, 2014).

The majority of human population studies focus on chronic arsenic ingestion through drinking water as the predominant exposure route (Andrew et al., 2003; Banerjee et al., 2007; Podgorski, 2020, ATSDR, 2007, ATSDR, 2016; WHO, 2011). Many parts of the world have high levels of arsenic in groundwater and aquifers with populations that use these water sources for household needs. One arsenic prediction model based on household groundwater-usage statistics estimates that between 94 and 220 million people may be exposed to high arsenic concentrations (Podgorski, 2020). Indeed, many seminal health studies have focused on populations in areas of the world with high levels of arsenic in water sources including, but not limited to, Bangladesh, India, Taiwan and Chile (ATSDR, 2007; ATSDR, 2016; Banerjee et al., 2017; Farzan et al., 2021; Moore et al., 2002). Some studies have established the relationship between arsenic levels in water and arsenic in biological specimens such as urine, hair and nails (Mahata et al., 2003; Maki-Paakkanen et al., 1998; Ruíz-Vera et al., 2019).

More recently, greater attention has been paid to food as a source of arsenic exposure (Oberoi 2014; Gundert-Remy 2015; Arslan et al., 2017; Wong et al., 2022). Food crops may contain elevated arsenic levels through irrigation with arsenic-containing water, cultivation in arsenic contaminated fields, or use of agricultural products containing arsenic (Gundert-Remy et al., 2015; Wong et al., 2022). Rice has become a notable concern due to arsenic's uptake and accumulation in this plant compared to other common grains such as wheat (Karagas et al., 2019). There is evidence of greater urinary arsenic in individuals reporting higher rice consumption compared to those with low rice consumption even in areas of low arsenic drinking water exposure (Gossai et al., 2017).

The relationships between arsenic exposure and cancer are clear. Cancer is one of the health effects of concern; arsenic is classified as a Class I human carcinogen by the International Agency for Research on Cancer (IARC) with strong experimental and human population evidence to support arsenic carcinogenicity (IARC, 2004; Moore et al., 2002; Srinivas et al., 2019; Tam et al., 2020). The strongest evidence for organ-specific arsenic carcinogenicity is in skin, lung, bladder and kidney with evidence for arsenic contributions to other cancers (WHO, ATSDR, 2007, ATSDR, 2016; Palma-Lara et al., 2020) (Figure 1).

Skin Cancer

Various non-cancerous skin lesions are associated with long term exposure to inorganic arsenic including changes in pigmentation, plantar-palmar hyperkeratinization and hyperkeratotic warts and corns (ASTDR, 2007; Hunt et al., 2014). These skin changes are most common in areas with high arsenic levels in drinking water and are viewed as sensitive indicators of chronic arsenic exposure (ASTDR, 2007; Hunt et al., 2014; Cheng et al., 2016). Skin lesions and cancer appear to be more prevalent at exposures to drinking water levels in excess of 50 μg/L and evidence linking arsenic to skin cancer is less conclusive at lower arsenic levels (Boffetta et al., 2020, Lamm et al., 2021; Karagas et al., 2015). Recent

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findings suggest that ingestion of arsenic containing foods in the diet such as rice may also contribute to skin cancer risk (Karagas et al., 2019; Gossai et al., 2017).

The most common tumors associated with arsenic exposure are keratinocytic tumors including squamous cell carcinomas, which may develop from hyperkeratotic warts or corns, and basal cell carcinomas (ASTDR, 2007; Karagas et al., 2015; Palma-Lara et al., 2020). There is less consistent evidence for arsenic-associated melanoma although it has been reported in Bangladesh (Choudhury et al., 2018), but not in the United States (Langston et al., 2022; Bedaiwi et al., 2021; Yager et al., 2016) or there are too few studies to draw firm conclusions (Matthews et al., 2019).

Lung Cancer

Epidemiological evidence indicates increased incidence of lung cancer in workers exposed to arsenic in the copper mining and smelting industry and ingestion through contaminated water (ASTDR 2007; Smith et al., 2012; Steinmaus et al., 2014; Palma-Lara et al., 2020). Studies conducted in Chilean cohorts born during periods of low versus high arsenic exposure from water reveal increased incidence of several cancers, including lung cancer, associated with the high exposure period (ASTDR, 2010; Smith et al., 2006). Similarly, mitigation efforts to decrease arsenic ingestion from contaminated water in Taiwan led to reduction in lung cancer rates (Su et al., 2011). No associations were identified for lung cancer and arsenic in soil in Taiwan despite reported associations between lung cancer and other metals in the same soils (Huang et al., 2013). These findings and others support the conclusion that lung cancer is increased upon chronic exposure to arsenic in drinking water (ASTDR, 2007; Kuo et al., 2017a; Su et al., 2011; Chen et al., 2010; Heck et al., 2009). There is evidence for dose dependence (Chen et al., 2010); however, the associations are less strong at low arsenic exposures (Shao et al., 2021; Tsuij et al., 2019)

The most common type of lung cancer associated with arsenic exposure is squamous cell carcinoma (Kuo et al., 2017; Heck et al., 2009; Taeger et al., 2009). The correlation between arsenic and squamous cell carcinoma was more pronounced at higher exposure levels; adenocarcinoma and small cell carcinoma of the lung were not associated with arsenic level in the drinking water in a Taiwan population (Kuo et al., 2017) although other investigators reported increased adenocarcinoma and small cell carcinomas of the lung with arsenic exposure (Chen et al., 2010; Guo et al., 2004). A study of former German uranium miners exposed to arsenic found that the arsenic-related type of lung cancer differed in miners based on evidence of silicosis. Arsenic was associated with increased squamous cell carcinoma in miners without silicosis. In contrast non-small cell lung cancer was related to arsenic exposure in miners with silicosis (Taeger et al., 2009) suggesting that other underlying factors may influence the specific lung cancer arising because of arsenic exposure.

Bladder Cancer

Population studies identify a clear relationship between elevated arsenic levels in drinking water and bladder cancer (IARC, 2004; ASTDR, 2007; Smith et al., 2012; Krajewski et al., 2021). A recent study found evidence for oxidative DNA damage in residents exposed to arsenic from artesian well-water in Taiwan and concluded that arsenic exposure and

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DNA damage predicted the risk of bladder cancer (Tsai et al., 2021). In the US, arsenic concentrations in drinking water were positively associated with bladder cancer in both men and women (Mendez et al., 2017; Baris et al., 2016) and a spatial cluster analysis of bladder cancer mortality identified significant hot spots. Further study concluded that there was a significant association between bladder cancer mortality and arsenic intake from well water (Amin et al., 2019; Baris et al., 2016). Notably, well water is not subject to federal regulation and may exceed the EPA recommended maximum contaminant level. As with other arsenic-associated cancers, there is not uniform agreement on risks linked to lower exposures (Kayajanian, 2003) although a meta-analysis suggested that exposure to 10 μg/L of arsenic in drinking water may double the risk of bladder cancer (Saint-Jacques et al., 2014). Arsenic ingestion through food is also considered a potentially important source of exposure that may contribute to bladder and other cancers (Gundert-Remy et al., 2015; Oberoi et al., 2014; Karagas et al., 2019).

There are several studies that indicate arsenic exposure may influence bladder cancer progression and clinical outcomes. Comparisons of clinicopathological characteristics in bladder cancer patients from an arsenic contaminated region versus two reference areas found significantly greater proportions of locally advanced and high-grade tumors in the arsenic-exposed patients (Fernandez et al., 2020). Patients from areas of high arsenic exposure in Taiwan versus low arsenic exposure found worse prognosis in the patients from areas of high arsenic and this was most pronounced in the disease-free survival of early-stage disease (Chang et al., 2021). Similar findings were reported for patients in West Bengal, India where measured arsenic accumulation in bladder tumor tissue was associated with advanced tumors, poor prognosis and disease recurrence after treatment (Ghosh et al., 2021). These observations may be related to distinct mechanisms of arsenic carcinogenesis (Zhou et al., 2021; Palma-Lara et al., 2020) as described in Section 2.

Additional Cancers and Cancer Risk Due to Prenatal and Early Life Exposure

Although the evidence for arsenic-associated cancers is strongest for skin, lung and bladder tumors, there are other cancers that are linked to arsenic exposure. There is significant evidence for arsenic induced kidney cancer (Smith et al., 2012; Krajewski et al., 2021; Saint-Jacques et al., 2014; Ferreccio et al., 2013a; Naujokas et al., 2013; Palma-Lara et al., 2020; Chen and Costa, 2021) and liver cancer (Naujokas et al., 2013; Palma-Lara et al., 2020; Chen & Costa, 2021; ASTDR, 2010). There is more limited evidence for increased gastrointestinal tract (Krajewski et al., 2021; ASTDR, 2010), laryngeal (Smith et al., 2012), prostate (Lamm et al., 2021) and breast cancer (Moslehi et al., 2020) risk with elevated arsenic exposure (Abuawad et al., 2021). In the case of breast cancer, it appears that genetic factors may play an important modifying role in arsenic-associated risk (Moslehi et al., 2020).

Gestational and early life exposure to arsenic is associated with a variety of long-term health effects including increased risk of cancer in humans (Smeester and Fry, 2018; Martinez and Lam, 2021). Studies conducted in Northern Chile provide strong evidence for the cancer consequences of prenatal and early life arsenic exposures. In 1958, the levels of arsenic in drinking water increased nearly 10-fold to 870 ppb and remediation efforts in the 1970s

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reduced arsenic in drinking water to near pre-1958 levels. This led to human cohorts with different levels and timing of arsenic exposure (Smith et al., 2012). Increased mortality rates were observed for bladder, laryngeal, lung, kidney, liver and other cancers (Smith et al., 2012; Ferreccio et al., 2013b; Steinmaus et al., 2014). Long latency patterns of 25 years or more after early life exposure have been reported for liver, kidney and bladder cancers, often accompanied by evidence for higher incidence and cancer mortality in children and young adults (Yuan et al., 2010; Marshall et al., 2007; Liaw et al., 2008). These findings point to arsenic cancer risks that can persist decades after exposure in early life stages. Given evidence from experimental animal models that prenatal arsenic exposure elevates cancer development (Martinez and Lam, 2021; Waalkes et al., 2007), arsenic exposures across the entire lifespan are a concern.

Modifying Factors of Arsenic Carcinogenesis

Arsenic is one of a limited number of metals or metalloids that is metabolized to methylated forms (Roy et al., 2020). Biotransformation of inorganic arsenic to mono and dimethyl forms (MMA and DMA, respectively) occurs through the enzyme arsenic methyltransferase (AS3MT) and arsenic is excreted as a mixture of inorganic and methylated forms (Roy et al., 2020, see also Section 3). Population studies suggest that the different forms of arsenic are not equivalent in carcinogenic potential. Studies of the proportion of inorganic and methylated arsenic species found that individuals with high urinary inorganic percent or low DMA present were more likely to develop bladder cancer (Chung et al., 2013) and a meta-analysis found that bladder and lung cancer were increased significantly with increasing MMA percent in the urine (Melak et al., 2014). Positive associations between percent urinary MMA and cancers of the breast and skin in addition to lung and bladder also have been reported (Abuawad 2021; Gamboa-Loira et al., 2017; Huang et al., 2018). There is increasing evidence that polymorphisms and expression levels of AS3MT may lead to differences in arsenic metabolism (Delgado et al., 2021) and are important factors in arsenic-related cancer risk and outcomes (Song et al., 2020; Huang et al., 2018; Lin et al., 2018; De la Rosa et al., 2017).

Co-exposures of arsenic and DNA damaging agents can amplify carcinogenesis with the greatest evidence in human populations for skin, lung and bladder cancers. The risk of arsenic-associated skin lesions that can be precursors to cancer was greater with sun exposure (Chen et al., 2006). Furthermore, arsenic exposure and smoking increase risk of lung and bladder cancers with evidence for significant arsenic dose effect (Tsuda et al., 1995; Karagas et al., 2004; Chen et al., 2010; Chen et al., 2004; Koutros et al., 2018; Ferreccio et al., 2013b). These population-based findings are consistent with experimental findings of arsenic co-carcinogenesis (Zhou et al., 2021). Cumulatively, the evidence derived from studies of human populations exposed to arsenic indicate that arsenic is a human carcinogen both as a single agent and the carcinogenic effects can be modified by multiple factors including genetic polymorphisms and toxic co-exposures.

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SECTION 2: MECHANISMS OF ARSENIC CARCINOGENESIS

The diverse range of cellular effects of arsenic exposure create a complex landscape for studying arsenic carcinogenesis. Many processes affected by arsenic exposure are interconnected further complicating our understanding of arsenic's effects. This section will discuss key mechanisms of arsenic carcinogenesis focusing on oxidative stress, the role of DNA damage and repair in genotoxicity, epigenetic changes, and how arsenic interacts with proteins to affect major pathways of carcinogenesis.

Oxidative Stress

Oxidative stress is a cornerstone of arsenic toxicity and carcinogenesis. It plays a role in DNA damage, repair inhibition and cellular mechanisms related to cell stress and cell death. Arsenic induces elevated levels of reactive oxygen species (ROS) and reactive nitrogen species (RNS) that are damaging to macromolecules in the cell including DNA and protein (Ding et al., 2005; Wang et al., 2013) (Figure 2). Oxidative stress due to arsenic exposure is initiated by intracellular metabolism of arsenic, which involves glutathione (GSH) as a necessary mediator. GSH depletion during arsenic metabolism may result in reduced ability to ameliorate damaging ROS, both endogenous and those produced by the direct effects of arsenic in the cell. Arsenic metabolism also produces additional reactive intermediates. For example, the dimethylarsenic peroxyl radical, which is formed in the metabolism of dimethylarsenic acid, a methylated form of inorganic arsenic, further requires antioxidant remediation, and this intermediate has been shown to induce DNA damage (Flora et al., 2007; Yamanaka, 1994; Yamanaka et al., 1995). Specific forms of arsenic and their effects on oxidative stress are discussed in Section 3.

In general, reactive species arise due to the reduction of molecular oxygen to form superoxide radical anions ($O_2^{\cdot -}$), hydrogen peroxide (H_2O_2), hydroxyl radicals (•OH), hydroperoxyl radicals (HOO•), singlet oxygen (O_2), and peroxyl radicals (ROO•) (Wiseman and Halliwell, 1996). Arsenic facilitates the formation of these species by targeting several different processes. The role of arsenic in production of ROS is observed in the mitochondria where it causes dysregulation of the electron transport chain (Hosseini et al., 2013). Arsenic inhibits succinate dehydrogenase activity responsible and altering the balance of oxidative phosphorylation and O_2 production which perpetuates formation of additional ROS while also altering mitochondrial membrane potential (Hosseini et al., 2013; Yen et al., 2012). Mitochondria also contain elevated levels of sulfhydryl containing enzymes due to their redox-prominent role making many enzymes in the mitochondria molecular targets of arsenic exposure (Netto et al., 2002). Arsenic induced ROS also leads to formation of oxidative DNA damage, which can be measured as 8-hydroxy-2'-deoxyguanosine (8-OHdG) (Chayapong et al., 2017; Ding et al., 2005; Kessel et al., 2002). NADPH oxidase (NOX), which is activated by arsenic and stimulates increased generation of ROS, is one mechanism of increase DNA damage through oxidative stress (Cooper et al., 2022).

Arsenic causes various forms of cellular damage, which enhances the formation of radicals in the cell, adding to oxidative stress. For example, arsenic exposure leads to the formation of oxidized lipids, which can be used as a biomarker for arsenic-induced oxidative

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stress. Lipid peroxidation contributes to protein damage and compromised mitochondrial permeability forming a cycle of increased damage to macromolecules and ROS (Li et al., 2020; Mahajan et al., 2018; Nutt et al., 2005).

Arsenic generates RNS including nitric oxide (NO•), which further interacts with another product of arsenic exposure, $O_2^{\cdot -}$, to produce peroxynitrite ($ONOO^-$), which can affect DNA and proteins (Pace et al., 2017). $ONOO^-$ induces the nitration of tyrosine in proteins potentially altering their function. $ONOO^-$ also can cause S-nitrosation of cysteine residues in proteins, which was demonstrated in a study on the DNA repair protein, PARP-1 and was inhibited by the production of ROS and RNS after exposure to arsenic (Zhou et al., 2019). Additionally, $ONOO^-$ interacts with guanine forming 8-nitroguanine, which is used as a biomarker for RNS production (Kawanishi and Hiraku, 2006). Levels of arsenic exposure have been correlated with increased levels of 8-nitroguanine in epidemiology studies (Navasumrit et al., 2019; Phookphen et al., 2017). Arsenic-induced ROS and RNS increase oxidative stress leading to direct and indirect damage to DNA, proteins, and signaling pathways involved in maintaining genomic integrity. These effects are further discussed in the following sections.

Genotoxicity

Arsenic carcinogenesis is a complex process. However, the current body of research suggests genotoxicity arising as damage to genetic information is a key driver of arsenic-induced cancers and is a result of combined induction of DNA damage, inhibited DNA repair, and aberrant cell division. Genotoxicity begins with damage to genetic material. There is sufficient data showing arsenic exposure results in various forms of DNA damage including DNA double- and single-strand breaks and other lesions such as 8-nitroguanine and 8-OHdG as discussed above (Ding et al., 2005; Dong and Luo, 1993; Dutta et al., 2015; Okayasu et al., 2003). However, arsenic does not directly interact with DNA to cause damage, and there is a lack of strong evidence of arsenic forming adducts with DNA. Instead, studies show arsenic induced oxidative stress is responsible for the majority of DNA damage after arsenic exposure (Kumar et al., 2016). Studies show RNS and ROS inhibitors and pre-treatment with antioxidants attenuate DNA damage after arsenic exposure suggesting oxidative stress is a major contributor in arsenic-induced DNA damage (Ding et al., 2005; Lynn et al., 1998; Nesnow et al., 2002). This effect was also observed in arsenic-exposed human populations (Biswas et al., 2010) and animal studies (Balakumar et al., 2012; Kadirvel et al., 2007)

DNA double strand breaks are a particularly lethal form of DNA damage and if left unrepaired result in cell death. Arsenic-induced DNA double strand breaks have been identified in a number of studies (Guillamet et al., 2004; Mouron et al., 2006; Okayasu et al., 2003; Xie et al., 2014). If mis-repaired, these DNA double strand breaks in sites of key tumor suppressor genes may lead to changes to the genetic material and carcinogenesis. This result is also true of single-strand breaks and the formation of intra-DNA adducts and crosslinks with proteins and other cellular molecules (Bau et al., 2002; Dong et al., 1993; Mouron et al., 2001; Wang et al., 2001). DNA adducts and DNA-protein adducts may also contribute to the formation of DNA double strand breaks if mis-repaired (Bau et al., 2002, Wang et al., 2001). Several studies show arsenic exposure results in crosslinking of

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proteins, including DNA repair proteins, with DNA potentially inhibiting repair processes and contributing to genomic instability (Garman et al., 1997; Gebel et al., 1998; Mustra et al., 2007). In another study arsenic-induced DNA-protein crosslinks were observed with gross chromosomal changes including sister chromatid exchanges, a hallmark of genomic instability (Mouron et al., 2005).

Genomic instability is a common driver of cancers and is associated with exposure to many metals including arsenic (Mitkovska et al., 2020; Wu et al., 2019; Wise and Wise, 2012). DNA damage and dysregulation of cell division induced by arsenic ultimately leads to gross changes to genetic material including formation of micronuclei (Basu et al., 2004; Navasumrit et al., 2019), both numerical and structural chromosome instability (States, 2015), and microsatellite instability (Wu et al., 2017). Numerical chromosome instability associated with arsenic exposure has been observed in both human populations (Dulout et al., 1996), cell culture models (Eguchi et al., 1997; Salazar et al., 2010; Sciandrello et al., 2002), and animal studies (Kashiwada et al., 1998). Numerical chromosome instability can arise due to uncoupling mechanisms involved in cell division, such as changes in mitotic checkpoints and centrosome dysregulation, and is considered a driving force of carcinogenesis (Sansregret and Swanton, 2017). Arsenic induces prolonged mitotic arrest resulting in aneuploidy (Eguchi et al., 1997; Yih et al., 1997). Other studies have shown arsenic disrupts centrosome function (States et al., 2002; Suzuki et al., 2009), which can be carried down through cell populations even after removal of arsenic suggesting these changes may be permanent and heritable (Sciandrello et al., 2002). Another endpoint of altered cell division is the formation of micronuclei, which form as a result of lagging chromosomes and chromosome fragments, and these events have been observed in arsenic-exposed cells (Moore et al., 1996), workers (Lewińska et al., 2007; Vuyyuri et al., 2006), and in populations exposed to arsenic in drinking water (Tian et al., 2001; Warner et al., 1994).

Structural chromosomal changes including chromatid exchanges, ring structures, and dicentric chromosomes have been identified in arsenic-exposed human populations (Banerjee et al., 2007; Ghosh et al., 2006; Mahata et al., 2003). Other studies have identified chromatid gaps associated with arsenic exposure and urine levels (Maki-Paakkanen et al., 1998). Importantly for carcinogenesis, increases in chromosomal aberrations have been associated with arsenic-induced cancers and pre-cancerous lesions. For example, chromosome aberrations were found in patients with arsenic-induced Bowen's disease (Ghosh et al., 2007), arsenic-induced stomach cancer (Boffetta et al., 2007), and were higher in bladder cancer patients with arsenic exposure than those without (Moore et al., 2002).

Telomere maintenance and stability is closely tied to maintaining genomic stability. Several recent studies in an arsenic exposed human population found exposure was associated with altered telomere length, which is also attributed to enhanced chromosomal instability and cancer (Chatterjee et al., 2018; Villarreal et al., 2019). Guanine bases are a target of arsenic-induced oxidative damage. Thus, telomeres, rich in guanine, are a target of arsenic exposure. For example, Coluzzie et al., 2014 showed telomeric changes, included enriched DNA damage and shortening, occurred because of arsenic-induced oxidative stress. These telomeric changes may contribute to compromised protection provided by telomeres in

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maintaining chromosomal integrity. Other studies have identified arsenic-induced oxidative stress as a source of telomere attrition and structural chromosome instability arising as end-to-end fusions, and these effects were reduced by the addition of antioxidants (Liu et al., 2003). Epidemiology studies have confirmed arsenic exposure is associated with decreased telomere length and increased risk of skin carcinomas (Farzan et al., 2021; Grau-Perez et al., 2019; Srinivas et al., 2019) while other studies have shown the opposite (Gao et al., 2015).

The literature supports genomic instability represented as structural and numerical chromosome instability and alterations to chromosome maintenance (telomeres) as a prominent mechanism of arsenic-induced carcinogenesis. While these changes are evident the mechanisms of how they arise are important in understanding arsenic carcinogenesis. Changes in cell division were discussed above in association with numerical chromosome instability. However, structural chromosome instability is most associated with DNA damage (discussed above) and failure of robust DNA repair pathways as discussed below.

DNA repair

Arsenic induces a variety of DNA lesions, each with distinct repair pathways (Figure 3). Inhibited DNA repair after arsenic exposure is considered a driving mechanism of genomic instability and arsenic-induced cancers and research in this area has uncovered detailed cellular mechanisms of arsenic carcinogenesis. Mechanistic studies show arsenic affects critical repair factors in pathways of DNA repair including excision repair pathways, nucleotide excision repair (NER), base excision repair (BER) and strand break repair pathways, homologous recombination (HR), and non-homologous end joining (NHEJ).

Excision repair mechanisms are used to remove oxidative damage to nucleotides. Non-bulky damage to DNA bases, such as arsenic-induced 8-oxoguanine and apurinic and apyrimidinic sites, are repaired by BER. BER has been shown to be essential in repairing oxidative damage after arsenic exposure (Lai et al., 2011). Meanwhile BER genes were found to have decreased expression in HaCaT cells exposed to arsenic exposure (Ding et al., 2021). Specifically, human 8-oxoguanine DNA glycosylase I (Ebert et al., 2011), DNA polymerase β, and APE1 (Sykora and Snow, 2008) were found to have suppressed or altered expression and activity in human lung cells after arsenic exposure contributing to repressed BER function.

NER is responsible for repairing bulky type DNA lesions and is particularly important when considering arsenic as a co-carcinogen. NER repairs bulky lesions such as cyclobutane DNA photoproducts induced by ultraviolet radiation (UVR) and DNA adducts as a result of polyaromatic hydrocarbon (PAH) exposure. Arsenic alters NER through several mechanism. Individuals exposed to arsenic in drinking water were found to have decreased expression of DNA repair genes across in cell culture and human populations (Andrew et al., 2003; Andrew et al., 2006). Studies focused on NER after arsenic exposure have identified specific protein targets of arsenic including XPC, XPA, and ERCC1 (Holcomb et al., 2017; Huestis et al., 2016; Muenyi et al., 2011; Nollen et al., 2009; Zhou et al., 2014). Other mechanisms of arsenic-inhibited NER include inhibited protein function. Arsenic inhibits the activity of DNA ligase III and DNA ligase I (Hu et al., 1998). Extensive studies have also found zinc finger proteins in the NER pathway, including XPA are targeted by arsenic exposure altering

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their function and are further discussed in Section 3 below (Huestis et al., 2016; Zhou et al., 2014). In addition to direct protein effects, polymorphisms in NER genes were found to be associated with non-melanoma skin cancer and arsenic exposure (Applebaum et al., 2007).

If NER or BER fail to repair DNA damage, double strand breaks can arise. These breaks are repaired by NHEJ or HR as a final attempt to repair the damage and maintain genomic integrity. However, studies show that both NHEJ and HR are impaired by arsenic exposure. Notably Morales et al., 2016 found arsenic shifted repair to the more error-prone alt-NHEJ pathway from the high-fidelity HR repair pathway potentially resulting in mis-repaired DNA double strand breaks and increased genomic instability. Arsenic has been shown to affect HR repair by altering recruitment of HR repair factors including BRCA1 and RAD51 (Zhang et al., 2014). Arsenic increased sumoylation of Mus18, an endonuclease involved in cyclobutane pyrimidine dimers (CPDs) and 6,4'PP HR repair, resulting in compromised DNA damage response (Hu et al., 2017). PARP-1 may play a role in double strand break repair due to changes to PARylation and therefore recruitment of DNA double strand break repair factors. PARP-1 also plays a role in BER, NHEJ, single strand break repair, and as a zinc finger protein has been shown to be a primary target of arsenic exposure, which will be discussed in Section 3.

Epigenetic changes

While studies have identified DNA repair deficiency as a mechanism of arsenic carcinogenesis, epigenetic regulation contributes to changes in DNA repair after arsenic exposure. Decreased gene expression is an established effect of arsenic exposure and studies show arsenic alters DNA methylation patterns across the genome with some sex differences (Bailey et al., 2013; Broberg et al., 2014; Nohara et al., 2011). Increased methylation of promotors involved in DNA repair has been associated with modified expression after arsenic exposure and was observed across different repair pathways. For example, BRCA1, ERCC2, MLH1, and OGG1 all had increased promoter methylation after arsenic exposure often associated with decreased expression (Hossain et al., 2012; Paul et al., 2014; Selmin et al., 2019; Wang et al., 2021). These studies support the finding that DNA methylation is associated with persistent genomic instability (Mauro et al., 2015). Confirming the importance of these finding are studies showing altered methylation patterns in populations exposed to arsenic (Bhattacharjee et al., 2018; Intarasunanont et al., 2012).

DNA methylation may be affected by the metabolism of arsenic, which involved methylation steps. Long term arsenic exposure has been associated with DNA hypomethylation as a result of depleted S-adenosylmethionine (SAM) (Reichard et al., 2007). While the mechanisms are not fully understood, SAM depletion results in decreased DNA methyltransferase activity, which may contribute to this effect (Du et al., 2018). Depletion of SAM and methylation activity may also affect histone methylation.

Posttranslational histone modifications, including methylation and acetylation, play an important role in gene expression. Arsenic has been shown to affect each of these posttranslational modifications creating a complicated landscape for understanding how they alter gene expression and accessibility and recruitment of DNA repair factors to sites of DNA damage. One study found the altered balance of H3K9me2, H3K36me3

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and H4K20me2 after arsenic exposure may lead to decreased repair ability at sites of DNA damage (Li et al., 2016). Directly related to expression of DNA repair genes, arsenic increased H3K9me2 was found to reduced expression of genes involved in BER (Ding et al., 2021). Other studies show global histone methylation patterns after arsenic exposure are a contributing factor in malignant transformation (Ge et al., 2018) and cell transformation (Qiu et al., 2021). Zhang et al., 2020 found histone demethylase JDHM2A is responsible for regulating H3K9 dimethylation after arsenic exposure as a potential mechanism.

Arsenic altered levels of histone acetylases may also contribute to changes in gene expression, especially of DNA repair genes. H3K18ac was downregulated after arsenic exposure and this effect was notable in the promoter regions of NER protein genes (Zhang et al., 2020). Arsenic may also inhibit accessibility to repair sites of DNA damage through decreased histone acetylation. For example, arsenic decreased global H4K16Ac, notable for its role in relaxing chromatin, with concentration and time (Jo et al., 2009). Mechanisms of altered histone acetylation, including the effect of arsenic on histone acetyltransferases following arsenic exposure has been linked to zinc finger protein interactions (Tam et al., 2017).

Epigenetic alteration of gene expression is also affected by arsenic-induced changes in microRNAs, which have been linked to inhibited DNA repair, increased sensitivity to oxidative stress, and cellular transformation, and have been proposed to be used as biomarkers of arsenic exposure (Sturchio et al., 2014). Various cohorts of arsenic exposed people around the world have been evaluated for changes in microRNA expression to understand which microRNAs may be playing a role in disease progression (Al-Eryani et al., 2018a; Banerjee et al., 2019; Beck et al., 2018; Ruiz-Vera et al., 2019). Specific microRNAs have been linked with arsenic-induced skin lesions and cancers. For example, Banerjee et al., 2017 found miR-21 contributes to skin lesion and cancer in chronically exposed individuals.

Cell culture studies have looked closely at the role of specific microRNAs altered by arsenic exposure in targeted pathways of cancers. A study of prolonged exposure to arsenic used HaCaT cells as a model for skin cancer and identified dynamic changes in microRNA expression at different stages of exposure and transformation (Banerjee et al., 2022). Looking at specific microRNAs, Gonzalez et al., 2015 found arsenic upregulated miR-21, miR-200a, and miR-141 expression, and determined a likely association with pathways of melanoma progression. Another cell culture study found miR-200b was associated with malignant transformation of bronchial epithelial cells (Wang et al., 2011). These studies have investigated associations between microRNAs and cellular transformation and carcinogenesis. Others have focused on earlier processes in arsenic carcinogenesis. For example, arsenic altered microRNAs were implicated in targeting specific pathways such as the TP53 pathway, implicated to have early effects contributing to carcinogenesis (Al-Eryani et al., 2018b). An *in vivo* study in rats found arsenic-responsive microRNAs are likely involved in pathways of oxidative stress, specifically related to genes that regulate GSH levels (Ren et al., 2015).

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MicroRNA studies in human populations and in experimental models have been used to understand how they may affect DNA repair. For example, Wei et al., 2018 found miR-145 was upregulated in individuals exposed to toxic levels of arsenic, and this effect was replicated in a cell culture model where it was found to target expression of ERCC2, potentially having a negative impact on DNA repair. From these studies it is likely microRNAs play a role in pathways of arsenic-induced carcinogenesis and modulating expression DNA repair genes.

Protein Effects

Arsenic-dependent changes to protein expression were discussed above. However, arsenic also affects protein directly. Recent studies have focused on how arsenic affects protein folding signaling pathways and protein function. For example, arsenic induced endoplasmic reticulum protein folding stress, which contributed to autophagy defects but not oxidative stress suggesting this effect is independent of ROS (Dodson et al., 2018). Endoplasmic reticulum protein folding effects have been observed in other arsenic studies as well and is associated with autophagy (Wadgaonkar and Chen, 2021).

While arsenic-altered protein expression and processing contribute to carcinogenic mechanisms, studies show arsenic can interact with zinc finger proteins causing inhibited function, and as briefly mentioned in Section 1, has a significant effect on zinc finger protein interactions. Zinc finger proteins are highly sensitive to oxidation due to thiol groups that play a central role in their function (Krishna et al., 2003). This structure is protected and maintained by a zinc ion, which coordinates a combination of 4 cysteine and histidine residues within the zinc finger domain. Zinc fingers can be found in several arrangements of cysteine and histidine including C2H2, C3H1, C4 and more complex structures like C4C4 ring domains (Klug et al., 2010; Razin et al., 2012). These structures are largely responsible for protein binding nucleic acids and with other proteins (Eom et al., 2016; Fu and Blackshear, 2017).

The mechanisms of arsenic disruption of zinc finger proteins involves the direct displacement of zinc by arsenic within the zinc finger domain. However, different forms of arsenic bind the specific zinc finger orientations depending on the ratio of cysteine and histidine. In general, arsenic has a lower binding affinity for protein with one or two cysteines compared to those with three or four (Asmuss et al., 2000; Kitchin and Wallace, 2006a; Kitchen and Wallace, 2006b). However, while arsenite and arsenic trioxide show a preference to bind to C3H1 and C4 zing finger domains methylated arsenic can bind to all three C2H2, C3H1, and C4 types (Zhou et al., 2014). Details of specific forms of arsenic in carcinogenic mechanisms is discussed in Section 3. Arsenic is similar enough to zinc to competitively displace it from the zinc finger, but in doing so induces a conformational shift within the domain altering how the protein functions (Quintal et al., 2011). The selectivity of different forms of arsenic to bind zinc finger domains with specific combinations of cysteine and histidine also suggests binding selectivity and may impact specific carcinogenic mechanisms differently.

Arsenic displacement of zinc has significant implications for protein in many cell regulatory pathways affecting DNA repair and gene expression (Huestis et al., 2016; Zhou et al.,

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2020a). Many studies have focused on the impact of arsenic on zinc finger proteins involved in DNA repair (Cooper et al., 2014; Ding et al., 2017; Tam et al., 2020; Zhou et al., 2011; Zhou et al., 2015). After DNA damage, repair proteins must form complexes around the damage site, which requires binding to the damaged DNA. DNA-binding proteins use zinc fingers for this purpose, and therefore if disrupted, can destabilize DNA repair complexes at sites of damage and inhibit repair. The DNA repair protein PARP-1 is a C3H1 zinc finger DNA binding protein shown to be a sensitive target of arsenic exposure inhibiting its function (Ding et al., 2009; Walter et al., 2007). This disruption interferes with DNA binding and recruitment of other DNA repair factors involved in different pathways of repair including NER and BER (Chaudhuri et al., 2017). Arsenic was also found to bind and displace zinc in XPA, a critical DNA repair factor in NER (Huestis et al., 2016).

Arsenic may impact DNA repair by modulating access to sites of DNA damage. Zhang et al., 2014 found arsenic was able to bind to RNF20 and RNF40 RING finger domains causing a conformational shift in these proteins. The RNF20 and RNF40 RING fingers are responsible for the monoubiquitinating histone H2B and promoting access of DNA double strand break repair factors to sights of DNA damage (Zhang et al., 2014). Indeed, Recruitment of DNA repair factors including the HR repair protein, RAD51, to sites of double strand breaks was impaired after arsenic exposure. Similarly, arsenic was found to bind the FANCL E3 ubiquitin ligase and RING finger protein, altering recruitment of DNA repair factors to sites of DNA interstrand crosslinks (Jiang et al., 2017). These studies demonstrate arsenic can impact the function of different types of zinc finger proteins. Additionally, this interference affects different mechanisms of DNA damage repair and recruitment highlighting the dynamic and vast effect arsenic can have on cellular processes.

Signaling Pathways

Altered signaling after arsenic exposure contributes to checkpoint control, DNA repair response, and cell survival changes linking them together. Many pathways altered by arsenic exposure are interconnected and likely affect multiple mechanisms of arsenic carcinogenesis. One study using arsenic as a case study predicted top pathways associated with arsenic exposure include stress response, apoptosis, cell cycle, and protein signaling pathways such as MAPK, Jak-STAT, and p53 (Davis et al., 2008). MAPK signaling disruption has been observed in cell culture studies to increase cell invasiveness (Tingting et al., 2010). Predictions on arsenic's effect in signaling pathways including JNK, EGFR, AKT, PI3L, mTOR, and Nrf2-Keap1 have been extensively validated in other studies as well (Chen et al., 2013; Kang and Lee, 2008; Fu et al., 2021; Wang et al., 2017). These pathways are interconnected but are largely related to cell survival and escape from cell death and transformation.

The EGFR pathway has been closely linked with alterations of DNA repair and cell proliferation after arsenic exposure. Tong et al., 2015 found DNA mismatch repair was inhibited after arsenic exposure by promoting EGFR expression. Another study found EGFR and HB-EGF were activated in arsenic-transformed cells to promote cell proliferation (Wang et al., 2020). Recently a study in lung epithelial cells found EGFR expression was enhanced

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after acute and chronic arsenic exposure, but the mechanism responsible for these changes was different depending on the exposure time (Kim et al., 2020).

The balance of cell survival and cell death pathways are shifted after arsenic exposure (Dreval et al., 2018; Watcharasit et al., 2012). The Nrf2-Keap1 signaling pathway is a cellular mechanism implicated in promoting cell survival and when dysregulated is considered to have cancer-promoting functions. Specifically, constitutively active Nrf2 leads to a variety of downstream implications including altered expression of growth factors, antioxidant proteins, transcription factors, and protein processing due to its activity in binding antioxidant response elements (AREs) in the promoter of genes (Hayes et al., 2010). Studies show arsenic constitutively activates Nrf2 is closely tied to the alteration of the autophagy pathway (Lau et al., 2013; Zhou et al., 2020b). Indeed, studies show arsenic increases autophagy activity (Bolt et al., 2010; Pucer et al., 2010).

Many studies have investigated the PI3K AKT, and mTOR pathways in arsenic cellular transformation and malignancy (Chen and Costa, 2018). When these pathways are unregulated normal cell growth becomes aberrant. Chronic arsenic exposure alters the PI3K/AKT pathway and is associated with anchorage-independent growth and cell migration (Carpenter and Jiang, 2013). Other studies have found autophagy dysfunction is tied to PI3K and mTOR signaling (Liang et al., 2020). Evidence shows in arsenic-transformed cells the AKT pathway is implicated in enhancing invasiveness (Wang et al., 2012) while being regulated upstream by JNK to promote alterations in phosphorylation of proteins involved in altering expression of tumor suppressors and oncogenes (Chen et al., 2013).

SECTION 3: CHEMICAL FORMS OF ARSENIC AND CARCINOGENESIS

Inorganic and Organic Arsenic Forms, Exposure, and Metabolism

Arsenic exists in several different oxidation states and various chemical forms (Carlin at al., 2016; Bolt and Henglestler, 2018). There are two major oxidation states of arsenicals, trivalent and pentavalent. Both oxidation states exist naturally (Carlin at al., 2016; Zhu et al., 2014). Arsenic occurs naturally in many minerals, usually in combination with sulfur and metals. Humans can be exposed to arsenic through different forms and oxidation states, and metabolism of arsenic also converts one form or oxidation state to another (Watanabe and Hirano, 2013). Each form/oxidation state may have different exposure routes, organ/tissue distribution, toxicity, and carcinogenic effects (Watanabe and Hirano, 2013; Sattar et al., 2016). There are two major forms of arsenicals, inorganic and organic. Inorganic arsenicals are the major form of arsenic exposure, occupationally and environmentally. Organic arsenicals are mainly acknowledged as metabolites of arsenic, specifically, in methylated forms (Negro Silva et al., 2017; Cohen et al. 2006).

Trivalent arsenicals are found in the form of sodium/potassium arsenite and arsenic trioxide (Dopp et al., 2005). Pentavalent arsenicals are mainly found as sodium arsenate. The environmental existence of inorganic arsenicals is in two major phases, solid and a liquid. Inorganic arsenicals in ground water can be found in both trivalent and pentavalent forms (Zheng et al., 2017). The trivalent and pentavalent forms mainly exist in oxic and anoxic

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waters, respectively, due to their chemical properties. Drinking water is a major source of environmental exposure of inorganic arsenicals (Carlin at al., 2016; Zhu et al., 2014; Mantha et al., 2017). As mentioned in Section 1 arsenicals may also be accumulated in plants through irrigation (Zhu et al., 2014; Mantha et al., 2017; Dominguez-Gonzales et al., 2020), such as rice and vegetables, which also serve as a significant source of inorganic arsenic exposures. Trivalent and pentavalent arsenicals also exist in soil which leads to inhalation exposure from dust (Liu et al., 2016, Alamdar et al., 2016). Occupational exposure of arsenic can occur in facilities that manufacture pesticides, herbicides, and other agricultural products (Baker et al., 2018). Mine smelters and woodworking facilities are also major sources of occupational inorganic arsenic exposures.

Organic arsenicals are not commonly found naturally in the environment. Organic arsenicals include arsanilic acid, arsenosugars, and methylated arsenicals. Methylated arsenicals are produced as a consequence of inorganic arsenic biotransformation in various organisms. Humans may be exposed to methylated arsenicals from ingestion of seafood and meat (Yoshinaga and Narukawa, 2021; Naess et al., 2020).

Trivalent arsenic uptake into eukaryotes is mediated mainly by proteins in the aquaporin superfamily (AQPs) (Agre et al., 2002). Mammalian AQPs were first identified to transport trivalent arsenic in rat and mice as AQP9 and AQP7, respectively (Liu et al., 2002). Meanwhile, trivalent arsenic has also been shown to be taken up by glucose transporters such as GLUT1 (Liu et al., 2006) and hexose permeases (Liu et al., 2004). Both aquaglyceroporins and glucose permeases are bidirectional routes of trivalent arsenic into and out of cells.

Organic arsenic forms contribute to arsenic toxicity mainly through metabolic pathways. The metabolism of arsenic after absorption consists of two major types of reactions; oxidative methylation and reduction (Li et al., 2017; Hughes et al., 2011) (Figure 4). First, arsenite is oxidatively methylated into monomethylarsonic acid (MMA^{V}). MMA^{V} is thus reduced into monomethylarsonous acid (MMA^{III}). Second, MMA^{III} is oxidatively methylated into dimethylarsonic acid (DMA^{V}), then reduced into dimethylarsonous acid (DMA^{III}). The metabolism of arsenic plays a critical role in toxicity and carcinogenesis. The exact mechanisms of action of different arsenic forms is still unclear, but various hypotheses have been proposed.

Under drinking water exposure, an animal study of organ distribution of arsenicals suggested that kidney, lung and liver contain highest levels of arsenic (Li et al., 2013). In lung, the major form is DMA^{III} at almost all time points (Kenyon et al., 2005). At early stages of exposure, liver and kidney contain all forms of arsenicals, such as MMA^{III}, MMA^{V}, DMA^{III}, DMA^{V}, and inorganic arsenic. At later stages, both liver and kidney show an increase in the percentage of DMA^{III} in arsenicals (Kenyon et al., 2005). In contrast, blood and brain contains the lowest level of all arsenic forms compared to other organs across all time points. Inorganic and organic arsenicals were also reported to be strongly accumulated in reproductive organs (Pant et al., 2004).

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The subcellular distribution of arsenicals largely depends on the cell type. According to the characteristics of arsenic metabolism, there are two different types of cells, methylating (such as hepatocytes) and non-methylating (such as urothelial cells) (Dopp et al., 2010). The membrane permeability and the efficacy of arsenic uptake depend upon both the arsenic species and the cell type (Dopp et al., 2005). Uptake rates of MMA^{III} and DMA^{III} were highest and exceeded those of their pentavalent counterparts by several orders of magnitude. Non-methylating cells accumulate higher amounts of arsenic within the cell than the methylating cells, and cellular uptake and efflux seem to be faster in methylating cells. Elevated concentrations of arsenic are present in the ribosomal fraction of non-methylating cells and in nucleic and mitochondrial fractions of methylating cells. However, cytotoxic and genotoxic effects are more pronounced in methylating cells (Dopp et al. 2008), which also suggests that methylated forms of arsenic may have greater cytotoxic effects than inorganic arsenic forms.

Carcinogenesis of Arsenic Forms

Arsenic exposure is mainly in the form of trivalent inorganic arsenic through gastrointestinal absorption. Different forms and oxidation state of arsenicals play various roles in carcinogenesis (Wadgaonkar and Chen, 2021). Some research indicates that organic arsenic forms such as MMA and DMA are most relevant to skin and bladder cancers (Gamboa-Loira et al., 2017). MMA and DMA are both positively related to almost all types of cancers (Gamboa-Loira et al., 2017; Di Giovanni et al., 2020; Kuo et al., 2017; Jomova et al., 2011). However, DMA level was found to be negatively correlated to lung cancer only (Gamboa-Loira et al., 2017).

MMA^{III} induces malignant transformation in a human bladder urothelial cell line (Bredfeldt et al., 2006), and this kind of transformation is irreversible (Wnek et al., 2010). Acute and chronic MMA^{III} exposure induces MAPK and COX-2, which may be a mechanism of bladder carcinogenesis (Eblin et al., 2007). Also, MMA^{III} alters histone modification patterns in human bladder cells (Ge et al., 2018). There are still gaps in research progress on organic arsenic forms and liver and lung cancers.

The molecular mechanisms of arsenic induction of various cancers can be summarized into two major categories: a) the trivalent arsenicals activate or inhibit signaling proteins or alter protein structure by reacting with proteinaceous thiol groups and b) inorganic or organic arsenicals activate ROS signaling or ROS-related signaling pathways. Carcinogenesis of inorganic arsenicals is related to both mechanisms. However, organic arsenicals are predominantly reported to correspond to ROS-dependent mechanisms at present (Huang et al., 2017). Current literature suggests that both inorganic and organic arsenicals contribute to arsenic carcinogenesis. It remains to be determined which specific form of arsenic is the most carcinogenic, although the answer may likely depend on the chemical properties of arsenical and the target organ.

Forms of Arsenic and Reactive Oxygen Species

Almost all forms and oxidation states of arsenicals can induce ROS and relevant signaling pathways (Lee et al., 2016). For example, for arsenic trioxide, superoxide induction occurs

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through HO-1, hydrogen peroxide and also RNS such as nitric oxide and peroxynitrite (Zhou et al., 2019; Chen et al., 2008; Gurr et al., 2003). In murine embryonic maxillary mesenchymal cells, pentavalent arsenic leads to oxidative injury initiating cell death cascade, triggering cytotoxicity, mitochondrial dysfunction, and activation of caspase-9 (Singh et al., 2010). Specifically, the antioxidant N-acetylcysteine attenuates the effect of pentavalent arsenic, suggesting that ROS production may contribute to the mechanism of pentavalent arsenic cytotoxicity.

In human bladder urothelial cells, MMA^{III} is known to produce ROS (Wnek et al., 2011). In smooth muscle cells, MMA^{III} has been reported as a mitochondria toxicant that elevates ROS through mitochondrial and non-mitochondrial pathways (Pace et al., 2016). In rat liver cells, MMA^{III} has the highest potential of ROS generation, followed by DMA^{III}, then arsenic trioxide (Naranmandura et al., 2011). In human bladder urothelial cells, MMA^{III} was also observed to generate higher ROS than the same concentration of arsenic trioxide (Eblin et al., 2006). In human myeloid leukemic HL-60 cells, MMA^{III} and DMA^{III} cause apoptosis through inhibition to mitochondrial membrane potential and oxidative stress (Rehman et al., 2014). Caspase-9 and caspase-3 were significantly activated by MMA^{III} and DMA^{III} exposure. Similarly, antioxidant N-acetylcysteine is also able to reverse these effects (Rehman et al., 2014).

In HepG2 cells, MMA^{V}, DMA^{V}, or trimethylarsine (TMA^{V}) significantly induced CYP1A1 and NQO1 through an Hsp90 pathway (Anwar-Mohamed et al., 2014). ROS production by MMA^{V} exposure is also significantly higher than arsenic trioxide. Overall, MMA^{V} and DMA^{V} have moderate effect when compared to MMA^{III} and DMA^{III}, but the effects become stronger in a reductive environment, for example when there is a low ROS/GSH ratio (Sakurai et al., 2005).

In total, inorganic and organic arsenicals both contribute to ROS generation and ROS-dependent signaling pathways. However, there are still debates on which arsenic form generates higher ROS *in vivo*. It is still largely unclear whether metabolism of arsenic could enhance or reduce the strength of ROS effect. In addition, there is still limited knowledge on the differences of ROS type generated from different arsenicals, which should be of importance to ROS-related mechanisms.

Forms of Arsenic and DNA Damage/Repair

As mentioned in Section 2, trivalent arsenic inhibits DNA repair through direct interaction with zinc finger DNA repair proteins such as PARP-1 and XPA. For pentavalent arsenicals, there is no evidence currently demonstrating direct interaction with zinc fingers. However, pentavalent arsenicals are able to generate ROS which are not only able to induce DNA damage but also impair DNA repair pathways (Flora, 2011; Schwerdtle et al., 2003). Therefore, in contrast to trivalent arsenicals, which inhibit DNA repair through both direct and ROS pathways, pentavalent arsenicals inhibit DNA repair only through ROS-dependent signaling pathways.

In natural killer cells, at low concentration, MMA^{III} induces oxidative stress, DNA damage, and inhibits cell growth. DNA damage positively correlates with oxidative stress, indicating

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that at environmentally relevant concentrations, MMA^{III} has a genotoxic effect (Xu and Wang, 2018). In human bladder urothelial cells, low-level chronic exposure to MMA^{III} elevates DNA damage, which remains at a high level after removal of MMA^{III}, and elevated levels of ROS also play a role in MMA^{III} induced-DNA damage (Wnek et al., 2009). While pentavalent arsenicals only act through ROS-dependent pathways, MMA^{III} has two potential interdependent mechanisms for human bladder urothelial cell transformation; elevated levels of MMA^{III}-induced DNA damage through the production of ROS and the direct MMA^{III}-induced inhibition of PARP-1 (Wnek et al., 2011), which has been confirmed *in vitro* (Zhou et al., 2014).

In T cells, MMA^{III} induces strong genotoxicity in the early developing T cells in the thymus. In terms of MMA^{III} induced genotoxicity and apoptosis, double negative ($CD4^{-}$ $CD8^{-}$) T cells were much more sensitive than double positive cells (Xu et al., 2017). ROS-dependent mechanisms are particularly important. For example, superoxide is involved either directly or indirectly in producing DNA damage in cells exposed to trivalent methylated arsenicals. DMA^{III} and MMA^{III} produced significantly more DNA damage in the homozygous knockout mouse splenocytes than in the splenocytes from the wild-type or heterozygous mice (Tennant and Kligerman, 2011).

Overall, the DNA damage effect and DNA repair inhibition capabilities of various arsenic forms and oxidative states largely depend on the tissue or cell type. Intriguingly, in bladder or human urothelial cells, DMA^{III} and MMA^{III} are the most hazardous arsenicals when considering cytotoxicity and genotoxicity (Bailey et al., 2012; Wang et al., 2007). However, in lung and skin cells, trivalent arsenicals show higher potency for DNA damage (Bolt and Hengstler, 2018; Sattar et al., 2016). This may be because of a difference in metabolism or cellular arsenic uptake.

Conclusion

There is extensive and strong epidemiological evidence that links arsenic exposure with increased risk of developing various types of cancer. Arsenic is ranked number one by the Agency for Toxic Substances and Disease Registry (ATSDR) on their priority list of substances that are determined to pose the most significant potential threat to human health. The most effective and efficient strategy to decrease arsenic-induced cancer risk is to reduce arsenic exposure. Based on convincing research findings, in 2001, U.S. EPA adopted a new standard for arsenic in drinking water of 0.01 mg/l or 10 parts per billion (ppb), replacing the old standard of 50 ppb. The same standard has since been used by most countries around the world. However, it is estimated that over 200 million people world-wide remain exposed to arsenic above this level (Li and Costa 2022).

Over the last several decades, extensive research has been carried out to investigate and identify various molecular and cellular changes caused by arsenic that are associated with known carcinogenic processes. Despite tremendous progress to date, we still do not fully understand exactly how arsenic causes cancer development, and what are the key cancer-driving events that play critical roles in arsenic-induced cancer. One of the significant barriers in research is the lack of relevant and appropriate animal models that mimic the

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development of arsenic-induced cancer in humans, probably due to differences in genetics and arsenic metabolism between rodents and humans. Recent development in humanized mice could potentially provide an important tool to help resolve these critical questions (Koller et al., 2020).

Another major issue is that while current research has identified many individual molecular targets of arsenic involved in carcinogenic processes, it is difficult to assess which of these altered processes are predominantly responsible for arsenic-induced cancer in humans. The recent advances in whole genome sequencing and the associated informatics technology could help identify, using unbiased approaches, target molecules and processes that drive the mutation and tumorigenesis at the whole genome level.

Abbreviations

8-OHdG	8-hydroxy-2'-deoxyguanosine
AQP	aquaporin
AS3MT	arsenic methyltransferase
ATSDR	Agency for Toxic Substances and Disease Registry
BER	base excision repair
CPD	cyclobutene pyrimidine dimer
DMA	Dimethylated arsenic
DMA^{III}	dimethylarsonous acid
DMA^{V}	dimethylarsonic acid
EPA	US Environmental Protection Agency
GSH	glutathione
HR	homologous recombination
IARC	International Agency for Research on Cancer
MMA	Monomethylated arsenic
MMA^{III}	monomethylarsonous acid
MMA^{V}	monomethylarsonic acid
NER	nucleotide excision repair
NHEJ	non-homologous end joining
NOX	NADPH oxidase
PAH	polyaromatic hydrocarbons

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RNS	Reactive nitrogen species
ROS	Reactive oxygen species
TMA(V)	trimethylarsine
UVR	ultraviolet radiation
WHO	World Health Organization

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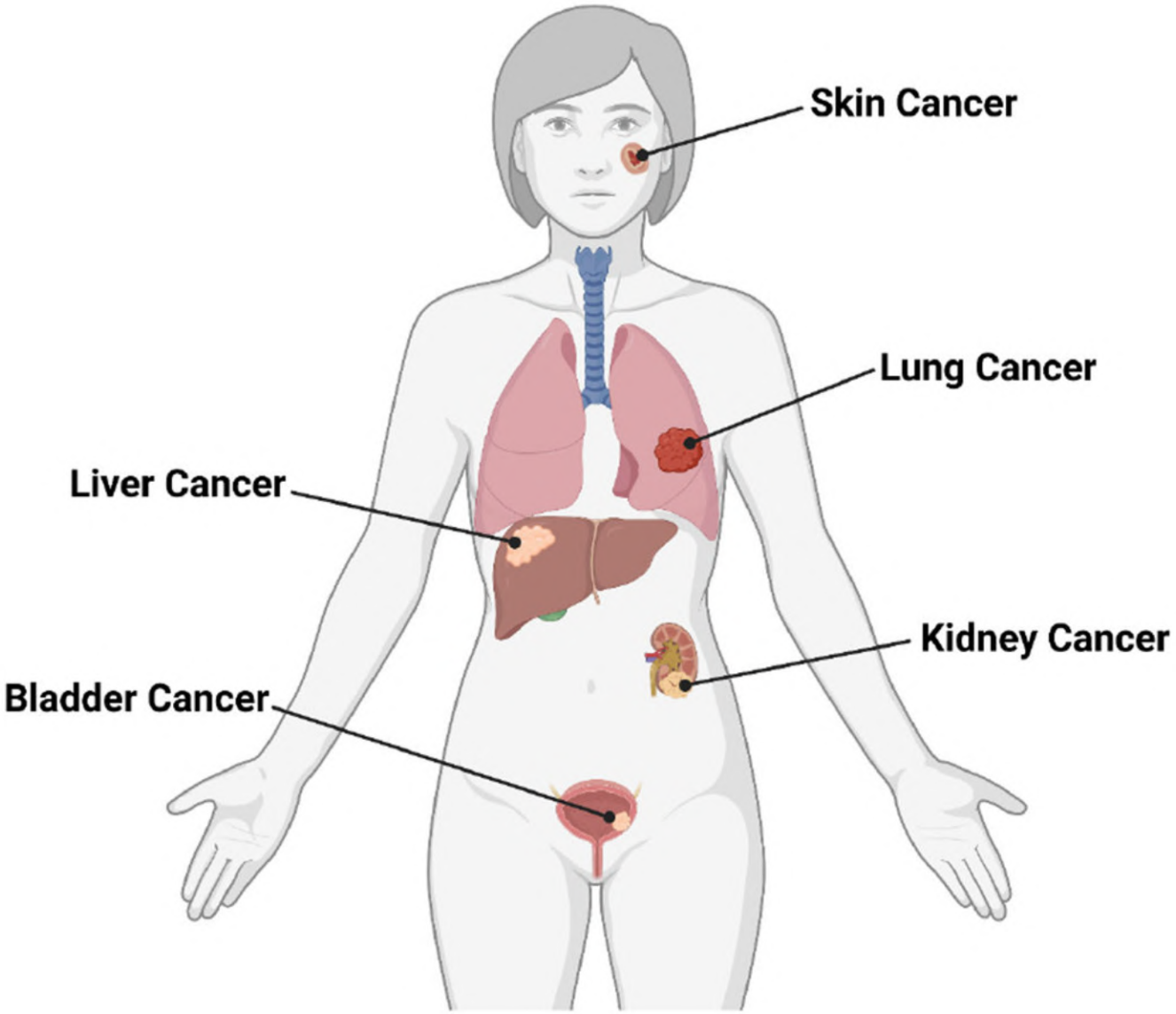

Figure 1.

Cancers associated with arsenic exposure. Epidemiology studies support the association of arsenic exposure through drinking water with increased risk of developing skin, lung, bladder, kidney, and liver cancers.

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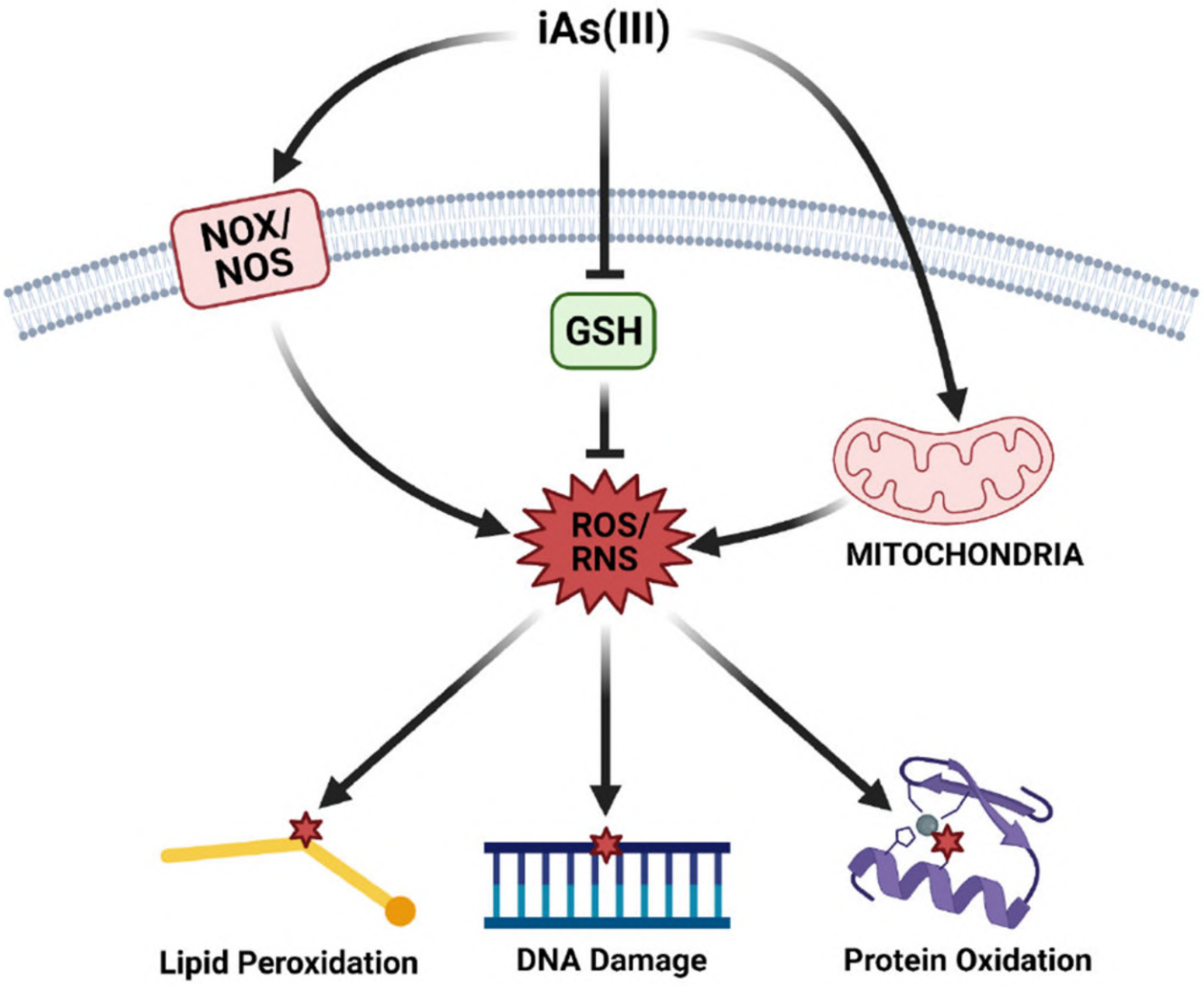

Figure 2. Mechanism of arsenic-induced ROS and oxidative damage to macromolecules.

Arsenic exposure stimulates the production of ROS and RNS through mechanisms such as the dysregulation of the electron transport chain and stimulation of enzymes such as NADPH oxidase and nitric oxide synthase. The depletion of GSH through the metabolism of arsenic further promotes redox imbalance. Consequently, macromolecules such as DNA, protein, and lipids are damaged by arsenic-induced ROS and RNS.

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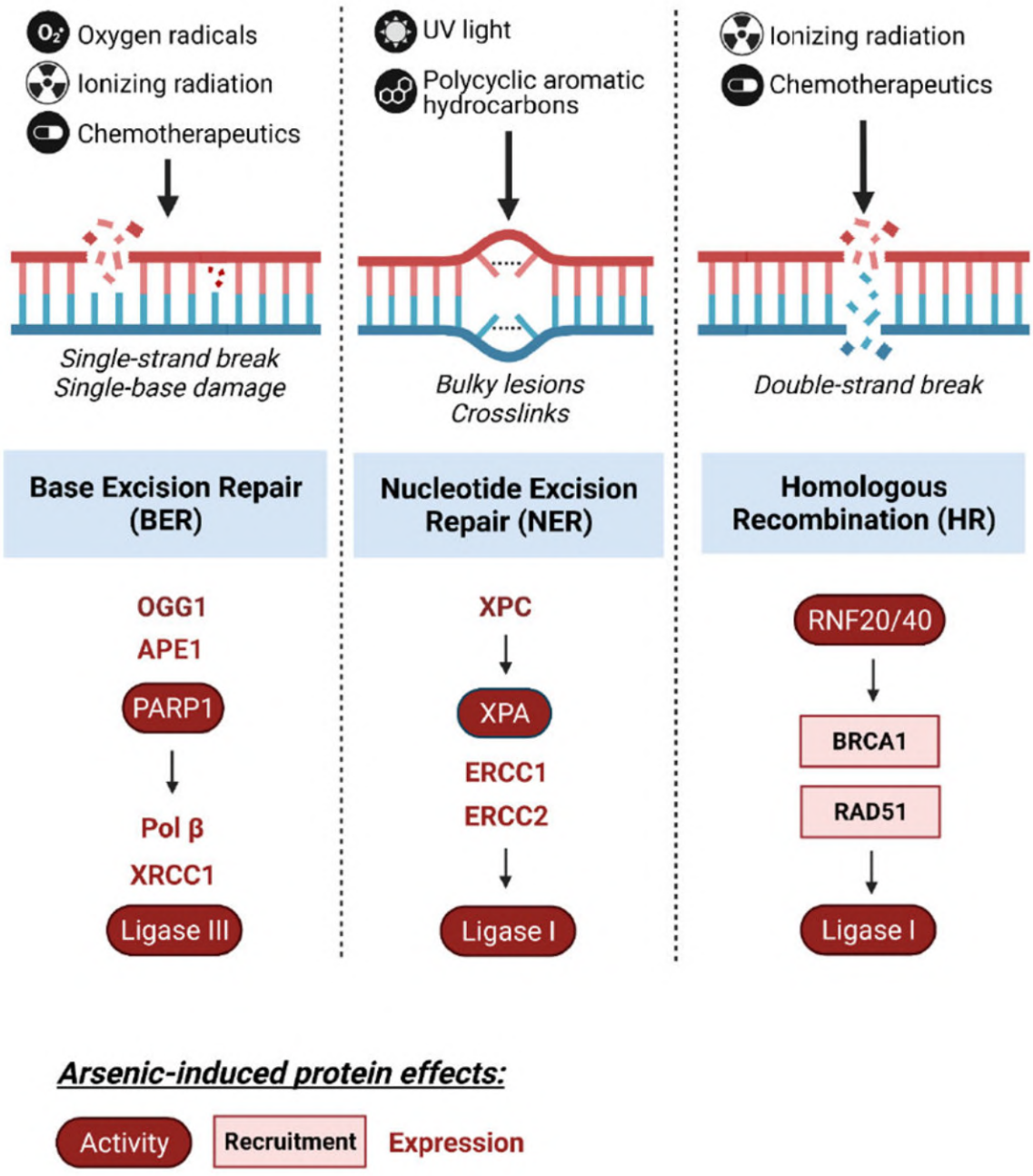

Figure 3. Arsenic inhibits DNA repair.

Exposure to DNA damaging agents such as ROS, UV light, and ionizing radiation can generate single-base damage, bulky lesions, and double-strand breaks, respectively. These types of damage are remediated by repair pathways which contain critical DNA repair proteins that facilitate the recruitment of repair proteins, removal of damage, and the synthesis and sealing of undamaged DNA. Arsenic alters the function of key DNA repair proteins through several means: zinc finger domain inhibition leading to loss of activity,

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disruption in recruitment to DNA damage, and the suppression of expression by altering transcription and protein turnover.

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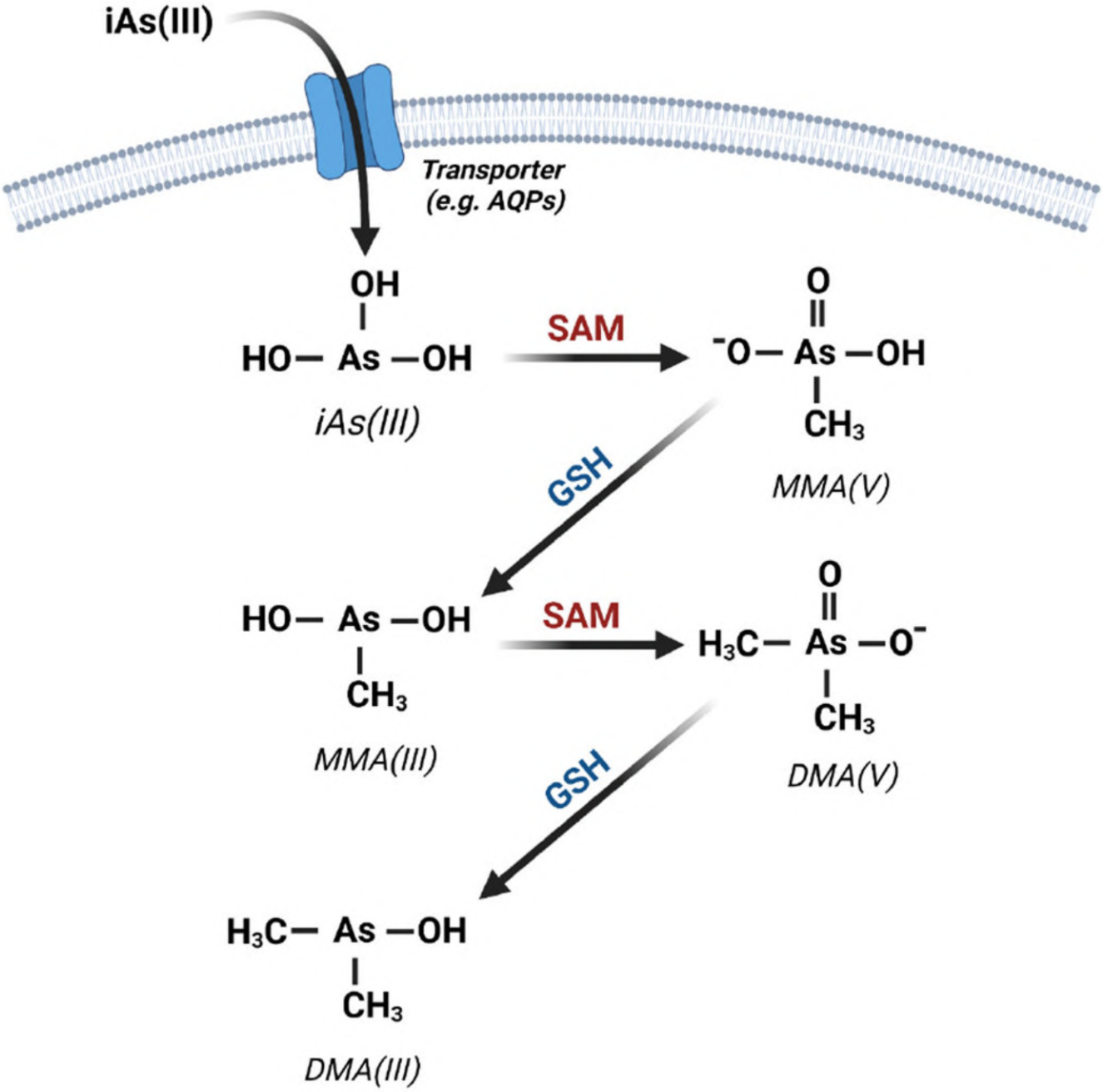

Figure 4.

The metabolism of arsenic. The uptake of trivalent arsenic into eukaryotes is mediated through several transporters such as AQPs. Trivalent arsenic is metabolized by successive oxidative methylation and reduction reactions. First, iAs(III) is oxidatively methylated into MMA(V) by S-adenosyl methionine (SAM), then reduced into MMA(III) by GSH. Second, MMA(III) is oxidatively methylated into DMA(V), then reduced into DMA(III)

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Exhibit J

A Section 508–conformant HTML version of this article is available at http://dx.doi.org/10.1289/ehp.1510144.

Estimating Children's Soil/Dust Ingestion Rates through Retrospective Analyses of Blood Lead Biomonitoring from the Bunker Hill Superfund Site in Idaho

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Background: Soil/dust ingestion rates are important variables in assessing children's health risks in contaminated environments. Current estimates are based largely on soil tracer methodology, which is limited by analytical uncertainty, small sample size, and short study duration.

Objectives: The objective was to estimate site-specific soil/dust ingestion rates through reevaluation of the lead absorption dose–response relationship using new bioavailability data from the Bunker Hill Mining and Metallurgical Complex Superfund Site (BHSS) in Idaho, USA.

Methods: The U.S. Environmental Protection Agency (EPA) *in vitro* bioavailability methodology was applied to archived BHSS soil and dust samples. Using age-specific biokinetic slope factors, we related bioavailable lead from these sources to children's blood lead levels (BLLs) monitored during cleanup from 1988 through 2002. Quantitative regression analyses and exposure assessment guidance were used to develop candidate soil/dust source partition scenarios estimating lead intake, allowing estimation of age-specific soil/dust ingestion rates. These ingestion rate and bioavailability estimates were simultaneously applied to the U.S. EPA Integrated Exposure Uptake Biokinetic Model for Lead in Children to determine those combinations best approximating observed BLLs.

Results: Absolute soil and house dust bioavailability averaged 33% (SD ± 4%) and 28% (SD ± 6%), respectively. Estimated BHSS age-specific soil/dust ingestion rates are 86–94 mg/day for 6-month- to 2-year-old children and 51–67 mg/day for 2- to 9-year-old children.

Conclusions: Soil/dust ingestion rate estimates for 1- to 9-year-old children at the BHSS are lower than those commonly used in human health risk assessment. A substantial component of children's exposure comes from sources beyond the immediate home environment.

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Introduction

Ingestion Rate Background

Consumption of fine soil and dust particulates, especially by young children, is the dominant route of exposure for lead and other contaminants (Laidlaw et al. 2014; Landrigan et al. 1975; Lanphear et al. 1998, 2003). Childhood soil and dust ingestion occurs via multiple pathways, including hand-to-mouth transfer, mouthing of objects, and contaminated food. These pathways are dependent on individual behaviors, exposure time, and environmental conditions (Zahran et al. 2013a). Accurate estimates of the soil and household dust ingestion rate (IR) pathway are needed to assess children's exposures and health risks associated with trace metals and persistent organic chemical residues in the home or play environment, and to make informed cleanup decisions.

Early estimates of soil/dust IRs in children were based on studies of trace elements in soil and feces, yielding uncertain estimates due to analytical uncertainty, limited sample size, and short study duration (Batelle 2005; Doyle et al. 2010; Sedman and Mahmood 1994; Stanek et al. 2012; U.S. EPA 2011, 2012). Currently, national U.S. Environmental Protection Agency (EPA) central tendency soil/dust IRs of 60 mg/day (children 6 weeks to < 12 months of age) and 100 mg/day (children 1 to < 6 years of age) are based on these tracer studies (U.S. EPA 2011). More recent studies have used dermal transfer to estimate soil and dust IRs. Ozkaynak et al. (2011) modeled the frequency of hand and object mouthing in children 3 years to < 6 years of age, resulting in a mean total soil/dust IR of 68 mg/day (95th percentile: 224 mg/day). Similarly, Wilson et al. (2013) used a mechanistic model including parameters for particle loading on skin, transfer to hands, hand surface area, mouthing surface area, hand-to-mouth frequency, saliva dissolution, and exposure time, to estimate an average combined soil/dust IR of 61 mg/day for children 7 months to 4 years of age. Meta-analysis of four major studies using stochastic modeling of the most reliable tracers resulted in an average soil ingestion estimate of 26 mg/day (95th percentile: 79 mg/day) for children 1–8 years of age (Stanek et al. 2012). Findings from large-scale reviews and integration of data from tracer, mechanistic, validation modeling/measurement, and empirical relation (biomonitoring/environmental concentration) studies suggest that mean IRs in children are < 100 mg/day and may be as low as 40–80 mg/day (Bierkens et al. 2011; Moya and Phillips 2014).

Soil/dust IR and bioavailability are sensitive parameters in the U.S. EPA Integrated Exposure Uptake Biokinetic (IEUBK) Model for Lead in Children. The IEUBK model currently uses default IRs ranging from 85 to 135 mg/day for 6-month- to 6-year-old children and 30% absolute bioavailability for ingested soil and indoor dust (U.S. EPA 2013). The first use of the IEUBK model to develop site-specific cleanup levels was at the Bunker Hill Mining and Metallurgical Complex Superfund Site (BHSS) in northern Idaho (CH2M Hill 1991; TerraGraphics 1990; U.S. EPA and IDHW 1991, 1992). The dose–response relationship observed between soil, dust, and blood lead levels (BLLs) was consistently lower at the BHSS than IEUBK model predictions using the default parameters (TerraGraphics 1990; von Lindern et al. 2003b). This was nominally attributed to lower soil/dust bioavailability (18%), although it was acknowledged that the reduced

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dose response was likely a combination of lower bioavailability and IRs (von Lindern et al. 2003b).

BHSS Background

In 1974, soon after the lead smelter operators bypassed emission controls destroyed by a baghouse fire, > 95% of children 1–9 years of age living within 3 mi of the smelter had BLLs exceeding 40 µg/dL (Yankel et al. 1977). Lead health interventions have been ongoing since that time. The smelter closed in 1981 and remediation began in 1986, representing one of the world's largest, most comprehensive, and well-documented lead health response cleanups (U.S. EPA 2005, 2010; von Lindern et al. 2003a, 2003b). From 1988 through 2002, soil from > 3,500 properties within the 21-mi^2 area surrounding the smelter was removed and replaced with up to 1 ft of clean fill averaging ≤ 50 mg/kg. Hundreds of families with children received lead health education and in-home follow-up investigations through a local Lead Health Intervention Program (LHIP). The LHIP tested children's BLLs, achieving participation rates > 50% among 0- to 9-year-old children for 15 consecutive years through door-to-door recruitment and incentive payments. Annual blood lead survey results were used to prioritize soil cleanup until the Remedial Action Objective (RAO) of < 5% of children with BLLs ≥ 10 µg/dL was achieved. From 1988 through 2002, homes of young children (0–6 years), pregnant women, and older children with BLLs ≥ 10 µg/dL were remediated first, regardless of location within the site. Beginning in 1994, all soils in contiguous neighborhoods with lead levels ≥ 1,000 mg/kg were removed and replaced, regardless of BLLs. This cleanup prioritization coupled with families moving within the affected communities resulted in a dynamic, complex combination of soil/dust exposures affecting individual children.

Blood lead data, collected during the seasonal peak in late summer, were matched to dust lead concentrations (from samples collected from household vacuum cleaners) and soil lead data to monitor the relationship between children's BLLs and environmental exposures to ensure cleanup was effective. Four variables were used to quantify soil and dust exposures throughout the cleanup: house dust, yard soil, neighborhood soil, and community soil lead concentrations. The neighborhood soil variable is the mean of all yard soils within a specific radius of the home, excluding the home's yard soil lead concentration. This was calculated for 200-ft, 500-ft, and 1,000-ft radii. The community soil variable is the mean of all yard soils within the community, excluding the home and neighborhood radius soil lead concentrations. The prioritized cleanup rapidly reduced the number of children residing in homes with soil lead concentrations ≥ 1,000 mg/kg and markedly decreased yard soil exposures for those families. Neighborhood soil lead concentrations progressively declined until the block-by-block cleanup strategy was implemented in 1994, and then decreased faster as contiguous neighborhoods were remediated. Community soil lead mean concentrations declined steadily until 2002 when yard soil replacement was mostly complete. House dust lead exposures (dust lead concentrations from homes of children with BLL measurements) decreased following the yard, neighborhood, community, and industrial complex cleanups but lagged the community soil means by a decade or more (von Lindern et al. 2003a).

By 2002, children's mean BLLs decreased to 2.2 µg/dL. In 2013, the health district conducted the first comprehensive blood lead survey since 2002, recruiting an estimated 50% of children 6 months to 9 years of age living within the 21-mi^2 area using incentive payments and door-to-door solicitation. The geometric mean BLL among 1- to 5-year-old children tested was 2.2 µg/dL (SD ± 1.8) compared with the most recent U.S. mean of 1.3 µg/dL (CDC 2013), with 2 of 276 children having levels ≥ 10 µg/dL, indicating that the cleanup continues to meet the RAO of 95% of children < 10 µg/dL (TerraGraphics 2015). Over the 15 years of active cleanup (1988–2002), education, and intervention, the LHIP amassed approximately 5,400 blood lead observations (referred to as the parent database) from nearly 2,340 individuals, yielding 2,176 records of blood/soil/dust lead concentrations (TerraGraphics 2004; von Lindern et al. 2003b, 2003a).

Subsequent to the cleanup at the BHSS, the U.S. EPA adopted an *in vitro* methodology to estimate site-specific bioavailability of lead in soil and dust (U.S. EPA 2012). This methodology was applied to a subset of archived soil and dust samples from the BHSS, and results were applied to the parent database. The objective of this study was to estimate age-specific soil/dust IRs through reanalysis of the dose–response relationship using new soil and house dust lead bioavailability data. In light of uncertainties and limitations of fecal tracer soil ingestion studies, these site-specific estimates likely have broader application to the IEUBK model and to human health risk assessment.

Methods

Blood lead samples collected from children participating in the LHIP were obtained through written informed consent from parents as well as child assent. The annual LHIP surveys are public health actions undertaken by state and local health authorities. TerraGraphics secured approval from the University of Idaho's Institutional Review Board for this project. No additional survey data or samples were collected from human subjects for this analysis.

Sample Analyses

In total, 271 samples (193 house dust samples, 73 yard soil samples, and 5 quality control samples) sieved to 80 mesh (or < 0.177 mm) were analyzed for total lead (Method 6010B) and *in vitro* bioaccessibility (TerraGraphics 2012; U.S. EPA 2007, 2012). U.S. EPA's *in vitro* assay measures the solubility, or bioaccessibility, of lead in soil and dust samples to estimate (*in vivo*) bioavailability. The 80 mesh sieve for both soil and dust was initiated at the BHSS in 1974 and focuses analyses on particle sizes more likely to adhere to hands and other surfaces and be ingested by children (Panhandle District Health Department et al. 1986; Ruby and Lowney 2012). Archived soil and dust samples collected between 1986 and 2002 were retrieved from storage. Those with intact seals, legible identification numbers, and sufficient mass for analysis were then checked to ensure that blood lead data and information on child age and sex, home location, and property remediation status were available. A temporal and geographic subset of samples meeting these criteria was randomly selected and analyzed at the laboratory. Reanalyzed soil and dust lead concentrations were compared to historical values using linear regression. *In vitro* bioaccessibility results were converted to *in vivo* relative bioavailability and absolute bioavailability (ABS) following U.S. EPA methods using comparison to a lead acetate reference (0.5) following Equation 1 (U.S. EPA 2007, 2009, 2012):

$$\mathrm{ABS} = (0.878 \times \mathrm{IVBA} - 0.028) \times 0.5, \quad [1]$$

where IVBA = *in vitro* bioaccessibility.

Community mean ABS values for unremediated yard soils and house dust, and site-wide ABS means for postremediation soils were integrated into the parent database. Annual site-wide ABS means were calculated using a weighted average of bioavailable lead (product of concentration and bioavailability) from remediated and unremediated yards.

Quantitative Analyses

Soil and dust partitions, age-specific IRs, and lead uptake from sources other than soil and dust were determined through structural equations modeling (SEM). SEM is a statistical multivariate methodology appropriate for pathways analysis, defined as a network of linear relations between variables. SEM was applied by von Lindern et al. (2003b) to reflect the exposure pathways of yard, community, and neighborhood soils (Ullman and Bentlar 2003). The 2003 SEM was

repeated using absorbed and bioavailable lead (instead of blood and total soil and dust lead levels), using SAS® software version 8 (SAS Institute Inc.). Several combinations of variables, including neighborhood soil means using radii of 200 ft, 500 ft, and 1,000 ft and age- and year-specific soil and dust categorical variables (i.e., grouped by both age and calendar year), were alternatively added, and model fit was evaluated by five criteria: *a*) convergence, *b*) chi-square probability test ($p > 0.05$), *c*) goodness of fit index (GFI) (> 0.90), *d*) parameters with significant t-statistics ($p < 0.05$), and *e*) parameter performance in subsequent IEUBK model analyses, described below (Carey 1998; SAS Institute Inc. 2008; Suhr 2006; Wothke 2010). Both the chi-square and GFI measure the difference between the expected and observed covariance matrices. Higher chi-square probability indicates better fit. The GFI ranges from 0 to 1.0, with higher values indicating better fit (Jöreskog and Sörbom 1988; SAS Institute Inc. 2008). SEM equations were solved using mean values for the independent variables and model parameters to estimate: *a*) soil and dust lead pathway parameters, *b*) neighborhood and community soil effects on lead uptake, *c*) age-specific and temporal effects in lead intake and uptake, and *d*) source partition scenarios for use in subsequent IEUBK modeling.

Ingestion Rate Estimates

Total lead uptake (µg/day) was calculated by dividing the measured BLLs (µg/dL) by the age-specific biokinetic slope factors, referred to as CR^{-1} (day/dL), used in the original IEUBK model (Harley and Kneip 1985; Jacobs Engineering et al. 1989; Kneip et al. 1983; TerraGraphics 1990, 2012; U.S. EPA 1994). Total lead uptake was partitioned into components used in the IEUBK model: air, diet, water, and soil/dust. Lead uptake from soil and dust was estimated by partitioned dust, yard soil, neighborhood soil (used only in the SEM), and community soil subcomponents by subtracting air, dietary, and drinking-water uptakes estimated from the IEUBK model default values (U.S. EPA 2001), as shown in Equation 2:

$$\begin{aligned} UP_{sd} = [&(C_d \times IR_d \times ABS_d) \\ &+ (C_{ys} \times IR_{ys} \times ABS_{ys}) \\ &+ (C_{cs} \times IR_{cs} \times ABS_{cs}) \\ &+ (C_{ns} \times IR_{ns} \times ABS_{ns})] \\ &= UP_{tot} - [UP_{air} + UP_{diet} + UP_{water}], \end{aligned} \quad [2]$$

where UP = lead uptake (µg/day); C = concentration (mg/kg); IR = ingestion rate (mg/day); ABS = absolute bioavailability (unitless); and (subscripts): sd = combined soil/dust sources; d = house dust; ys = yard soil; cs = community soil; ns = neighborhood soil (SEM); tot = total sources; air = airborne source; $diet$ = dietary source; $water$ = water source.

Equation 2 can be rearranged to calculate total soil/dust IRs [IR_{sd} (mg/day) is the sum of IR_d, IR_{ys}, IR_{cs}, and IR_{ns}] by assigning partition coefficients, i.e., fractional contributions to total soil/dust ingestion by each source, as follows in Equation 3:

$$\begin{aligned} IR_{sd} = 1{,}000 \times \{UP_{sd}/[&(C_d \times PT_d \times ABS_d) \\ &+ (C_{ys} \times PT_{ys} \times ABS_{ys}) \\ &+ (C_{cs} \times PT_{cs} \times ABS_{cs}) \\ &+ (C_{ns} \times PT_{ns} \times ABS_{ns})]\}, \end{aligned} \quad [3]$$

where PT = partition coefficient.

Partition coefficients used in these analyses included the IEUBK model default, those originally developed to support BHSS cleanup criteria, and values derived from SEM. Partition coefficients, resulting age-specific soil/dust IRs (using Equation 3), and bioavailability were input to the IEUBK model batch-mode analyses (IEUBKwin v1.1 build 11) to compare predicted and observed BLLs. The combined IR and partition scenarios showing best-predicted BLLs were evaluated by linear regression and sums of squared error (SSE). The slope nearest to 1.0 coupled with the highest r^2, highest F-statistic, and lowest sum of squared residuals from linear regression, as well as the SSE (squared difference between observed and predicted geometric mean BLLs), were used to determine the scenario(s) that best represent observed BLLs. The age-specific soil and dust IR estimates were then determined based on these scenario(s).

Results

Sample Analysis

The selected subset of historical data was considered generally representative of the parent database (e.g., lead concentration and child's age) (Table 1). The reanalyzed soil and dust lead concentrations were not significantly different

Table 1. Comparison of the parent BHSS database with the subset of records selected for reanalysis (historical data).

	Parent data set						Selected subset					
City	Minimum	Maximum	Average	SD	Geometric mean	Geometric SD	Minimum	Maximum	Average	SD	Geometric mean	Geometric SD
Kellogg	Parent data set $n = 3{,}054$						Selected subset $n = 118$					
Age (years)	0	9	5.1	2.7	—	—	1	9	5.5	2.6	—	—
Blood lead (µg/dL)	1	54	6.4	4.7	5.1	2.0	2	41	7.6	5.7	6.3	1.8
Soil lead (mg/kg)	100	13,400	954	1,625	274	4.4	100	6,930	1,407	1,849	435	5.2
Dust lead (mg/kg)	32	52,700	1,213	2,839	733	2.4	88	5,530	1,373	1,093	985	2.3
Page	Parent data set $n = 161$						Selected subset $n = 15$					
Age (years)	0	9	5.1	2.6	—	—	1	9	4.3	2.8	—	—
Blood lead (µg/dL)	1	26	7.0	4.7	5.7	1.9	3	12	5.6	2.4	5.2	1.5
Soil lead (mg/kg)	53	3,480	557	668	287	3.2	100	1,670	541	420	387	2.5
Dust lead (mg/kg)	69	2,070	678	496	478	2.6	86	1,680	706	567	467	2.9
Pinehurst	Parent data set $n = 1{,}369$						Selected subset $n = 117$					
Age (years)	0	9	5.1	2.6	—	—	1	9	5.2	2.4	—	—
Blood lead (µg/dL)	1	26	4.6	3.1	3.8	1.9	1	17	4.3	2.6	3.7	1.7
Soil lead (mg/kg)	31	3,060	438	424	312	2.3	37	1,700	469	356	369	2.0
Dust lead (mg/kg)	22	15,000	639	1,053	417	2.4	45	15,000	625	1,427	383	2.3
Smelterville	Parent data set $n = 642$						Selected subset $n = 57$					
Age (years)	0	9	4.9	2.7	—	—	1	9	4.5	2.6	—	—
Blood lead (µg/dL)	1	55	7.0	5.4	5.6	2.0	2	30	7.5	4.9	6.4	1.7
Soil lead (mg/kg)	100	10,700	953	1,921	245	4.3	100	8,170	1,037	1,821	242	4.8
Dust lead (mg/kg)	54	11,300	1,127	1,257	757	2.5	393	4,210	1,387	807	1,190	1.8
Wardner	Parent data set $n = 173$						Selected subset $n = 5$					
Age (years)	0	9	5.2	2.7	—	—	1	8	4.8	3.1	—	—
Blood lead (µg/dL)	1	20	6.6	3.8	5.5	1.9	2	8	4.6	2.2	4.2	1.6
Soil lead (mg/kg)	100	34,800	759	2,925	224	3.5	100	13,200	3,104	5,705	484	9.6
Dust lead (mg/kg)	130	6,000	1,005	1,112	700	2.3	307	2,220	1,147	697	959	2.1

from historical results (r^2 = 0.99, p < 0.01, n = 73; and r^2 = 0.91, p < 0.01, n = 193, respectively), indicating that samples were not compromised during storage. The reanalyzed sample results are summarized in Table 2. Mean soil bioavailability ranged from 30% to 39% by community, averaging 33% (SD ± 4%); dust bioavailability ranged from 27% to 30%, averaging 28% (SD ± 6%). Three "clean" soil samples were obtained in 2011 from borrow piles used to replace contaminated property soils. No clean yard soil samples were previously collected and archived. Consequently, these three samples represent postremediation replacement clean soils, and bioavailability results averaged 15% (SD ± 0.6%; data not shown). Linear regression relating soil and dust bioavailability to lead concentration showed a weak relationship (r^2 = 0.15, p = 0.0006 and r^2 = 0.045, p = 0.0028, respectively).

SEM Analyses

Several plausible SEM combinations met the model acceptance criteria. In each accepted model, bioavailable lead in dust and soils from the home yard, neighborhood, and community were all significant independent predictors of total blood lead uptake. Based on experience with the BHSS cleanup and development of the parent database, numerous combinations of spatial, temporal, and age-specific variable constructs and database time periods were explored (data not shown). Of the three neighborhood radii, 500 ft showed the best fit by combined chi-square test and parameter t-values. Age-specific coefficients for dust concentration among the youngest children (6 to < 24 months old) were significant (p < 0.01), implying different IRs, with a significant intercept representing uptake from other sources. Coefficients for age-specific and year-specific soil concentration variables were not significant (p > 0.05). The SEM with temporal variables showed marginally significant (p = 0.05) positive dust coefficients for 6- to 23-month-old children in 1994–1998, suggesting higher dust IRs during those years.

Source partitions using three SEM combinations were evaluated in subsequent IEUBK model analyses: Model 1 (1989–2002 database) included a term allowing calculation of year-specific IRs, and model 2 (1989–1998 database) and model 3 (1989–2002 database) assumed constant source contributions and IRs throughout each respective time period (Tables 3 and 4). Soil/dust IRs and source partitions were estimated by substitution of mean soil and dust lead concentrations in the model equations.

Model 2, shown in Equations 4 and 5 (chi-square test: p = 0.7416, n = 1,571; Table 3), was selected based on performance in subsequent IEUBK modeling:

$$\ln(UP_{tot}) = [0.1466 \times \ln(C_d \times ABS_d)] + [0.0516 \times \ln(C_{ys} \times ABS_{ys})] + [0.0440 \times \ln(C_d \times ABS_d \times \text{age0–1})] + [0.0613 \times \ln(C_d \times ABS_d \times \text{age1–2})] + [0.0661 \times \ln(C_{ns} \times ABS_{cs})] + [0.0954 \times \ln(C_{cs} \times ABS_{cs})] + 0.7666 \quad [4]$$

Table 2. Community averages of reanalyzed archived soil and house dust samples.

	Soil			Dust		
City	n	Soil lead (mg/kg) (mean ± SD)	Soil ABS (%) (mean ± SD)	n	Dust lead (mean ± SD) (mg/kg)	Dust ABS (%) (mean ± SD)
Kellogg	24	2,656 ± 1,624	34 ± 3	66	1,179 ± 934	28 ± 6
Page	7	778 ± 417	33 ± 4	12	753 ± 529	27 ± 5
Pinehurst	33	569 ± 463	32 ± 4	75	762 ± 2,131	28 ± 6
Smelterville	8	4,136 ± 2,192	39 ± 2	36	1,239 ± 550	30 ± 4
Wardner	1	2,030	30	4	892 ± 415	27 ± 5
Overall	73	1,686 ± 1,748	33 ± 4	193	996 ± 1,472	28 ± 6

ABS, absolute bioavailability.

Table 3. Structural equations modeling (SEM) results.

	Model 1 (1989–2002)			Model 2 (1989–1998)			Model 3 (1989–2002)		
Variables	Slope coefficient	t-Value[a]	Standardized coefficient	Slope coefficient	t-Value[a]	Standardized coefficient	Slope coefficient	t-Value[a]	Standardized coefficient
UP_{tot} (Equation 4)									
ln(UP_d)	0.1347	8.43	0.2575	0.1466	7.95	0.2762	0.1360	8.50	0.2598
ln(DUSTage0–1)	0.0450	2.80	0.0132	0.0440	2.24	0.0116	0.0450	2.79	0.0132
ln(DUSTage1–2)	0.0501	4.06	0.0273	0.0613	6.23	0.0333	0.0667	7.45	0.0363
ln(DUST1994–1998)	0.0336	1.95	0.0128	—	—	—	—	—	—
ln(UP_{ys})	0.0611	6.09	0.1027	0.0516	4.82	0.0866	0.0601	5.99	0.1010
ln(UP_{ns})	0.0647	3.30	0.1364	0.0661	2.41	0.1396	0.0636	3.24	0.1341
ln(UP_{cs})	0.1594	6.03	0.3439	0.0954	2.75	0.2050	0.1571	5.94	0.3389
Intercept	0.3639	3.34	0.1316	0.7666	5.55	0.2670	0.3820	3.52	0.1382
Error	—	—	0.2098	—	—	0.2021	—	—	0.2100
Bioavailable dust lead (Equation 5)									
ln(UP_{ys})	0.1039	7.57	0.0914	0.1054	7.31	0.0938	0.1039	7.57	0.0914
ln(UP_{ns})	0.0751	2.77	0.0828	0.1126	3.01	0.1262	0.0751	2.77	0.0828
ln(UP_{cs})	0.3350	9.35	0.3782	0.2582	5.50	0.2944	0.3350	9.35	0.3782
Intercept	2.3390	16.52	0.4418	2.5994	14.67	0.4804	2.3339	16.52	0.4418
Error	—	—	0.1523	—	—	0.1468	—	—	0.1523
Baseline bioavailable lead (µg/dL)	1.4			2.2			1.5		
Baseline bioavailable dust lead (mg/kg)	37.0			48.1			36.9		
n		2,034			1,571			2,034	
Goodness of fit index		0.9995			0.9999			0.9998	
χ^2		4.7284			0.598			1.5347	
Degrees of freedom		3			2			2	
Pr > χ^2		0.1928			0.7416			0.4642	
r^2 Total uptake		0.9560			0.9591			0.9559	
r^2 Bioavailable dust lead		0.9768			0.9785			0.9768	

Abbreviations: χ^2, chi-square; cs, community soil; d, dust; DUSTage0–1, bioavailable dust lead if the child was 6–11 months; DUSTage1–2, bioavailable dust lead if the child was 12–23 months; DUST1994–1998, bioavailable dust lead if the year was 1994, 1995, 1996, 1997, or 1998. ln, natural log; ns, neighborhood soil; Pr, probability; r^2, r-squared; tot, total; UP, uptake; ys, yard soil.
[a]t-Values ≥ 1.96 are equivalent to p-values < 0.05.

$$\ln(C_d \times ABS_d) = [0.1054 \times \ln(C_{ys} \times ABS_{ys})] + [0.1126 \times \ln(C_{ns} \times ABC_{cs})] + [0.2582 \times \ln(C_{cs} \times ABS_{cs})] + 2.5994, \quad [5]$$

where ln = natural log; C_{ns} = neighborhood soil arithmetic mean using 500-ft radius (mg/kg); age0–1 = 1 for 6–11 months, otherwise 0; age1–2 = 1 for 12–23 months, otherwise 0; ABS_{cs} applies to both C_{ns} and C_{cs} values.

The SEM standardized regression coefficients (Table 3) yielded partition coefficients of 50% house dust/25% yard soil/10% arithmetic mean neighborhood soil/15% arithmetic mean community soil (50/25/10/15) (Table 4) used in subsequent calculation of age-specific IRs.

Ingestion Rate Estimates

Figure 1 summarizes arithmetic and geometric mean soil/dust IRs calculated for four source partition scenarios: *a*) the IEUBK model default 55% dust/45% yard soil (55/45), *b*) the original BHSS model applying 40% dust/30% yard soil/30% geometric mean community soil (40/30/30G) (Panhandle District Health Department 1986), *c*) the same partition using arithmetic average community soil (40/30/30A), and *d*) the SEM (50/25/10/15). Calculated IRs were observed in three general ranges. The highest IR estimates were arithmetic means for the 55/45 partition and are near the IEUBK model recommended values (also shown in Figure 1). Mid- and low-range IR estimates are approximately one-third and one-half lower, respectively [corresponding numeric data with 95% confidence interval (CI) and percentiles are provided in Table S1].

IEUBK Model Results

The four IR and partition scenarios with the best agreement are from the mid-range IRs shown in Figure 1 (i.e., 40/30/30G-geometric mean IR (geoIR), 55/45-geoIR, 50/25/10/15-arithmetic mean IR (aveIR), 40/30/30A-aveIR; the high- and low-range IRs, respectively, over- and underpredicted observed BLLs (data not shown). Figure 2 shows the results of the SSE and linear regression analyses for annual observed and predicted geometric mean BLLs for the four scenarios with the best agreement. Observed geometric mean BLLs ranged from > 8 µg/dL in the late 1980s to near 2 µg/dL in 2002, and observed geometric standard deviations (GSDs) ranged from 1.52 to 2.12 (n = 2,176). GSDs calculated from the IEUBK batch runs for these four scenarios ranged from 1.42 to 2.10, with medians around 1.7 (see Table S2), consistent with the IEUBK model default GSD of 1.6.

Each of the four scenarios represents a plausible source partition and estimated lead intake scenario, produces similar IR estimates (Table 5), and shows temporal variability in the SSE, with the largest SSEs in 1988 (see Table S3). The scenarios with the smallest total SSE for 1989–2002 were 40/30/30G-geoIR, 55/45-geoIR, and 50/25/10/15-aveIR. The 40/30/30A-geoIR was similar to the 50/25/10/15-aveIR and had the next smallest SSE for those same years. Although all four scenarios showed temporal variation in predicting observed BLLs, the 50/25/10/15-aveIR had the lowest SSEs in the early and later years of the cleanup (1989–1990 and 1996–2002, respectively), whereas the 40/30/30G-geoIR had the lowest SSE in the middle years of the cleanup (1991–1995). Additionally, linear regression indicated that the 50/25/10/15-aveIR and the 40/30/30A-aveIR scenarios were best-fit models due to a slope coefficient nearest 1.0, in combination with highest r^2, largest F-statistic, and smallest sum of squared residuals (see

Table 4. Structural equations modeling (SEM) results for soil/dust contributions (%).

Variables	Model 1 (1989–2002) 0–2 years	Model 1 (1989–2002) 2–9 years	Model 1 (1989–2002) Value[a]	Model 2 (1989–1998) 0–2 years	Model 2 (1989–1998) 2–9 years	Model 2 (1989–1998) Value[a]	Model 3 (1989–2002) 0–2 years	Model 3 (1989–2002) 2–9 years	Model 3 (1989–2002) Value[a]
Contribution of dust/soil ingestion									
House dust	40	37	40	48	45	50	41	38	40
Yard	30	30	30	28	30	25	30	31	30
Neighborhood	11	11	10	9	10	10	11	11	10
Community	19	23	20	15	15	15	18	20	20
Contribution to lead in blood									
House dust			17			22			16
Yard			35			34			33
Neighborhood			14			15			14
Community			34			29			37

[a]Values are rounded to total 100%.

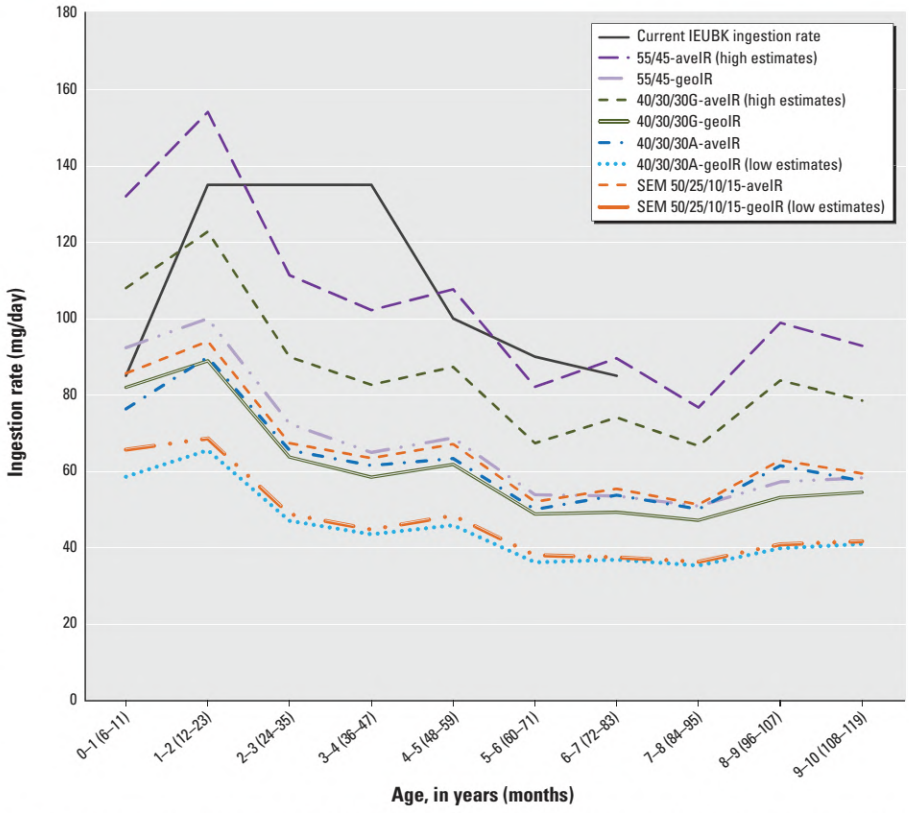

Figure 1. Arithmetic and geometric mean age-specific soil/dust ingestion rates (IRs) for four soil/dust partition scenarios. Included are current Integrated Exposure Uptake Biokinetic (IEUBK) model IRs and calculated age-specific mean soil/dust IRs for the four partition scenarios. For each age (6 months–9 years), arithmetic mean IRs (aveIR) and geometric mean IRs (geoIR) are shown. 55/45 is the partition of dust/yard soil, 40/30/30 is the partition of dust/yard/community soil, and SEM 50/25/10/15 is the partition of dust/yard/neighborhood/community soil. Corresponding numeric data, with 95% CI and percentile distributions for each model and age, are provided in Table S1.

Table S4). The age-specific IRs and 95% CIs for the 50/25/10/15-aveIR scenario are shown in Figure 3 because this scenario had the lowest SSEs in multiple years and was one of the best-fit linear regressions. Figure 3 also shows age-specific IRs recommended by U.S. EPA risk assessment guidance (U.S. EPA 1994, 2011).

Discussion

At the BHSS, children's soil/dust exposures have been investigated since the 1970s, and the IEUBK model has been used to evaluate the dose–response relationship since 1986. Use of the IEUBK model default IRs, bioavailability and soil/dust partition failed to account for soil sources beyond the immediate home yard and consistently overpredicted observed BLLs. In 1990, the BHSS cleanup criteria were developed using the 40/30/30G partition accounting for community soils and reduced soil/dust lead uptake (compared with the IEUBK model default). The overprediction of BLLs using default IEUBK model values was resolved by lowering soil and dust lead bioavailability, although it could have been explained by several combinations of reduced IRs or bioavailability. However at the time, it was not possible to determine which was predominant. In this study, we used a newly available laboratory method to estimate soil and house dust ABS. The soil and house dust bioavailability results of 33% and 28%, respectively, are similar to the recommended 30% IEUBK model default values and those found in other BHSS studies (Maddaloni et al. 1998). These findings suggest that IRs, not ABS, should be reduced by about 40% from the IEUBK default values to best represent the dose–response relationship observed at the BHSS.

In this study, the more rigorous SEM pathways analyses resulted in several plausible models, all suggesting that community and neighborhood soil sources, in addition to the yard soil source, are independent contributors to total lead uptake and bioavailable lead in house dust. Others have recently confirmed the importance of soil beyond the immediate home yard (Laidlaw et al. 2014; Zahran et al. 2013a, 2013b). The 50/25/10/15-aveIRs were derived from the only partition including neighborhood soils and exhibited the lowest SSEs in multiple years. These IRs were calculated using arithmetic-mean neighborhood and community soil exposures. The central tendency statistic that better approximates geographic area exposures has been the subject of debate and remains unresolved; the arithmetic mean represents an aggregate biased by high or low concentrations, and the geometric mean is the most likely concentration in the prescribed area. Two of the four select models employed arithmetic means, one used the geometric mean, and the IEUBK model default scenario uses individual observations and assumes the effect of soils beyond the home yard is included in house dust. However, all four models produced similar IRs with the average nearly identical to the 50/25/10/15-aveIRs, indicating the source partition is critical in describing lead intake.

Age-specific and temporal effects, also examined with SEM, suggested children 6–23 months of age exhibited greater lead intake rates from house dust than older children, consistent with the study by Wilson et al. (2013). Additionally, SEM analyses including year-specific variables suggested dust intake rates for younger children may have been lower early in the cleanup (1989–1993) and higher during the middle years of the cleanup (1994–1998). However, only age- and year-specific intake rates of interior dust were statistically significant predictors (Table 3); consequently, age- and year-specific IRs for soil intake (yard, neighborhood, or community) were not included in our final model (data not shown). Several factors may have caused temporal variations in IRs, or partition coefficients. Aggressive LHIP education and intervention programs may have resulted in a temporary reduction in soil/dust intake by children. Alternatively, elevated dust loadings caused by flooding and

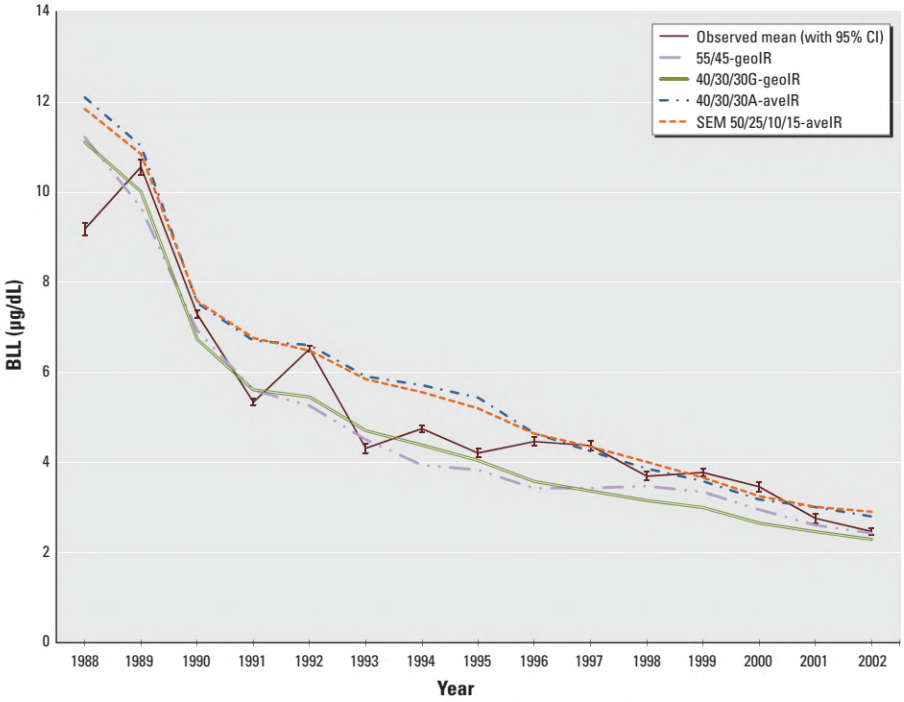

Figure 2. Observed and predicted geometric mean blood lead levels (BLLs) by year for four scenarios that best predict observed BLLs. Predicted geometric mean BLLs for the four scenarios are compared with observed BLLs from 1988 through 2002. Observed BLLs include error bars for the 95% confidence interval (CI). Abbreviations: aveIR, arithmetic mean ingestion rate; geoIR, geometric mean ingestion rate. 55/45 is the partition of dust/yard soil, 40/30/30 is the partition of dust/yard/community soil, and SEM 50/25/10/15 is the partition of dust/yard/neighborhood/community soil. Corresponding numeric data, with 95% CI and percentile distributions for each model and age, are provided in Table S1.

Table 5. Mean age-specific soil/dust ingestion rates (mg/day) for four scenarios that best predict observed blood lead levels.

Age[a] (years)	55/45[b]-geoIR	40/30/30G[c]-geoIR	40/30/30A[c]-aveIR	50/25/10/15[d]-aveIR	Average all models
0–1	92	82	76	86	84
1–2	100	89	90	94	93
2–3	72	64	66	67	67
3–4	65	58	62	63	62
4–5	69	62	63	67	65
5–6	54	49	50	52	51
6–7	54	49	54	55	53
7–8	51	47	50	51	50
8–9	57	53	61	63	59
9–10	58	54	57	59	57

Abbreviations: aveIR, arithmetic mean ingestion rate; geoIR, geometric mean ingestion rate.
[a]0–1 = 6–11 months, 1–2 = 12–23 months, 2–3 = 24–35 months, etc. [b]Dust/yard soil. [c]Dust/yard/community soil; G = geometric mean; A = arithmetic mean. [d]Dust/yard/neighborhood/community soil.

construction activities may have exacerbated ingestion in the middle years of the cleanup. However, SEM and IEUBK model sensitivity analyses investigating alternate time period (years) variable constructs suggested that variation in calculated IRs may be an artifact of the source partitions, nature of the data, or progression of the cleanup. At the beginning of the cleanup, there was little difference between community soil and neighborhood soil concentrations. As area-wide cleanups predominated, these variable concentrations diverged between 1994 and 1998 and returned to similar concentrations by 2000 (TerraGraphics 2004). The 50/25/10/15 SEM is the only partition scenario that captures spatial differentiation in soil outside the home yard through the neighborhood soil variable. It is also possible that various periods of the cleanup exhibited different partition ratios from landscape changes or LHIP activities.

The truncated 1989–1998 database was used to derive the select SEM partition because from 1999 forward, the yard, neighborhood, and community soil variables were dominated by remediated homes. Lead concentrations were not measured in remediated yards. Instead, a nominal value of 100 mg/kg was assigned to represent the maximum allowable recontamination level. Replacement soils, and presumably yard soil concentrations immediately following remediation, averaged ≤ 50 mg/kg (LFR Inc. 2008; McCulley, Frick & Gilman Inc. 1997). Consequently, remediated soil lead concentrations were likely biased high and reflected less variation in the final years of the cleanup. Including 1999–2002 in the SEM analyses could bias the standardized coefficients for soil lead parameters used to estimate source effects.

Additionally, SEM coefficients were based on 1,571 of 4,019 observations in the 1989–1998 database. Most missing variable measurements for the SEM subset were house dust lead levels, implying the home lacked a vacuum cleaner, and were associated with likely dustier homes and higher BLLs (TerraGraphics 2004; U.S. EPA 2000; von Lindern et al. 2003a, 2003b). As a result of the missing house dust levels, mean values for key variables in the SEM subset differ from those in the parent database; particularly, mean absorbed lead was about 11% greater for children with no dust lead observation. Because total absorbed lead was allocated to source variables, higher absorbed blood lead implies potentially higher soil/dust IRs, absorption rates, or dust lead concentrations, or a combination thereof among these underrepresented children. The LHIP provides free loaner high-efficiency particulate arresting vacuum cleaners to residents to address this need.

This study is part of larger cleanup and public health response. It was not a designed experiment. The LHIP paid participants a modest fee for blood and house dust samples specifically to identify and provide follow-up services to children at risk. Factors such as self-selection, repeat blood leads, uncontrolled vacuum dust samples, lack of a home vacuum cleaner, intervention responses, other lead sources, community awareness, and assumed clean soil values could bias the IRs higher or lower. Many of these factors were discussed in detail by von Lindern et al. (2003b).

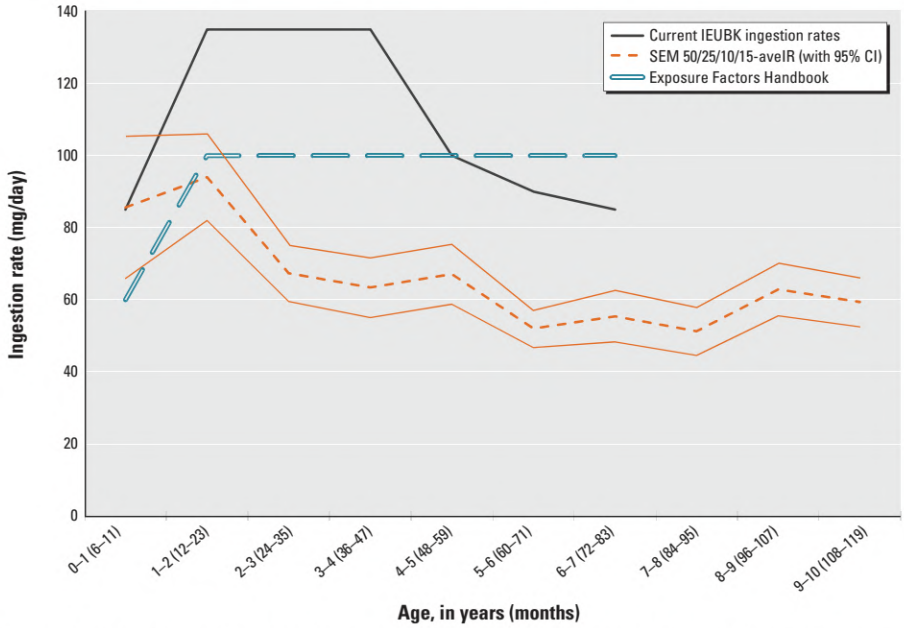

Figure 3. Mean age-specific ingestion rates (IRs) with 95% confidence intervals (CI) for the structural equations modeling (SEM) partition scenario. SEM 50/25/10/15 partition scenario (of dust/yard/neighborhood/community soil) with arithmetic mean IRs (aveIR) for ages 6 months–9 years, including 95% CI, are compared with current Integrated Exposure Uptake Biokinetic (IEUBK) model IRs and *Exposure Factors Handbook* IRs (ages 6 months–6 years only) (U.S. EPA 1994, 2011).

Conclusions

The addition of *in vitro* soil and house dust bioavailability estimates to the BHSS lead health database facilitated analysis of absorbed and bioavailable soil/dust lead, which improves understanding of the dose–response relationship and supports improved estimates of total soil/dust IRs. Bioavailability was substantially underestimated in the original BHSS risk assessment. The IEUBK model, using default bioavailability and default soil/dust IRs, consistently overpredicted BLLs collected from > 50% of resident children, and this was likely attributable to overestimating IRs. Although remediation activities were based on an inaccurate combination of IRs and bioavailability estimates, remediation was nonetheless effective in achieving the objective of < 5% of children with BLLs ≥ 10 µg/dL.

Soil and dust IRs at the BHSS from 1988 through 2002 averaged 66 mg/day (95% CI: 57, 75 mg/day) for children 6 months–9 years of age, and peaked at 94 mg/day (95% CI: 82, 106 mg/day) at age 12–23 months. The estimated IRs were lower than both IEUBK default and the U.S. EPA *Exposure Factors Handbook* recommended values for all ages except the youngest age group (< 12 months) (U.S. EPA 2001, 2011). The average IRs are 40% less than IEUBK default recommendations and 30% lower than estimates in the *Exposure Factors Handbook* (shown in Figure 3), and are consistent with recent studies and reviews suggesting values < 100 mg/day (Bierkens et al. 2011; Moya and Phillips 2014; Ozkaynak et al. 2011; Wilson et al. 2013).

Soil/dust IRs are among the most sensitive variables in the IEUBK and other risk assessment models used at hazardous waste sites (Griffin et al. 1999; TRW Lead Committee 2014). Accurately estimating lead intake requires simultaneously quantifying both soil/dust IRs and the soil/dust source partition. Inclusion of neighborhood and community soil exposures is essential to estimating soil/dust lead intake. These findings suggest that approximately half of the lead intake is from house dust and half is from soil, equally attributed to the immediate home yard and surrounding neighborhood/community. Additionally, the importance of soil outside the home environment varies with distance, not property boundaries, and intake estimates should account for soil sources in the immediate neighborhood and greater community.

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Exhibit K

ESTIMATION OF AGE-SPECIFIC SOIL AND DUST INGESTION RATES FOR U.S. CHILDREN: UPDATE TO THE DEFAULT VALUES FOR THE INTEGRATED EXPOSURE UPTAKE BIOKINETIC MODEL FOR LEAD IN U.S. CHILDREN

OVERVIEW

Since 1994, the Office of Land and Emergency Management (OLEM), formerly known as the Office of Solid Waste and Emergency Response (OSWER), has recommended the Integrated Exposure Uptake Biokinetic Model for Lead in Children (IEUBK model) as a risk assessment tool to support environmental cleanup decisions at current or future anticipated residential sites (U.S. EPA, 1994a, b). The IEUBK model predicts blood lead levels (PbB) in young children (birth to 7 years of age) exposed to lead from several sources and routes. The IEUBK model uses more than 100 input parameters that are initially set to default values. Of these, there are 46 parameters that may be input, or modified, by the user; the remainder are internal variables that are unavailable for modification (U.S. EPA, 1994a).

The IEUBK model uses empirical data from numerous studies of lead uptake and biokinetics, contact and intake rates of children with contaminated media, and data on the presence and behavior of environmental lead to predict a plausible distribution centered on the geometric mean (GM) of PbB for a hypothetical child or population of children (U.S. EPA, 2020).[1] The relative variability of PbB concentrations around the GM is defined as the geometric standard deviation (GSD). The GSD encompasses biological and behavioral differences, measurement variability from repeat sampling, variability as a result of sample locations and analytical variability.[2] From the distribution, the IEUBK model estimates the risk (*i.e.*, probability) that a child's or a population of children's PbB concentration will not exceed a certain PbB concentration (U.S. EPA, 1998, 1994a; White et al., 1998).

Ingestion of fine soil and dust particulates, especially by young children, is the dominant route of exposure for lead. (Laidlaw et al., 2014; Landrigan et al., 1975; Lanphear et al., 1998, 2003). Childhood soil and dust ingestion occurs via multiple pathways, including hand-to-mouth transfer, mouthing of objects, and contaminated food. The rate at which soil and dust is ingested are dependent on a child's age, individual behaviors, exposure time, total dust and soil accessible and environmental conditions (Zahran et al., 2013a,b). Age-specific estimates of the soil and dust ingestion rate pathway are needed to assess children's exposures in the home or play environment, and to make informed cleanup decisions.

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[1] The GM represents the central tendency estimate (*e.g.*, mean, 50th percentile) of PbB concentration of children from a hypothetical population (Hogan et al., 1998). If an arithmetic mean (or average) is used, the model provides a central point estimate for risk of an elevated PbB level. By definition a central tendency estimate is equally likely to over- or under-estimate the lead-intake at a contaminated site. Upper confidence limits (UCLs) can be used in the IEUBK model; however, the IEUBK model results could be interpreted as a more conservative estimate of the risk of an elevated PbB level. See U.S. EPA (1994a) for further information.

[2] The IEUBK model uses a log-normal probability distribution to characterize this variability (U.S. EPA, 1994a). The biokinetic component of the IEUBK model output provides a central estimate of blood lead concentration along with the distribution of possible blood lead concentrations in a population of similarly exposed children. In the IEUBK model, the GSD encompasses biological and behavioral differences, measurement variability from repeat sampling, variability as a result of sample locations, and analytical variability. The GSD is **not** intended to reflect variability in blood lead concentrations where different individuals are exposed to substantially **different** media concentrations of lead. The recommended default value for GSD (1.6) was derived from empirical studies with young children where both blood and environmental lead concentrations were measured (White et al., 1998).

The soil and dust ingestion rate is one of the most influential variables in the IEUBK model for lead in children (U.S. EPA, 1994a).

Early estimates of soil and dust ingestion rate in children were based on studies of trace elements in soil and feces (Battelle, 2005; Doyle et al., 2010; Sedman and Mahmood, 1994; U.S. EPA, 2011, 2012). The default values for the *Age-Dependent Soil and Dust Ingestion Rate* variable in the IEUBK model (v. 1.1, build 11) represent age-specific central tendency estimates for lead intake from soil and dust for children (6 to 84 months of age). The default values (v.1.1, build 11) are based on these tracer studies from a literature review and analysis performed during a review of the National Ambient Air Quality Standards (NAAQS) for lead (U.S. EPA, 1989, pp. A-16). The default soil and dust ingestion rate values are based on a study of soil ingestion in children (Sedman et al., 1989). This study utilized trace elements to quantify soil ingestion rates. The initial calibration of the IEUBK model employed these default values, and the results of a validation study performed in the early 1990s showed reasonably close agreement between model estimates using these intake values and empirical blood lead measurements (Hogan et al., 1998). The study that formed the basis for the existing default values did not, however, account for several factors that should be considered when designing a soil dust ingestion study (e.g., sieve to the currently recommended size fraction[3], sample household dust, soil outside of individual yards or the bioavailability of the lead in ingested soil or dust).

The purpose of this document is to provide the technical basis for an analysis of the currently available published literature to support an updated *Age-Dependent Soil and Dust Ingestion Rate (IRsd)* variable in the IEUBK model (Table 1). The updated age-specific soil and dust ingestion rate estimates for the *Age-Dependent Soil and Dust Ingestion Rate* variable in the IEUBK are based on soil and dust ingestion rates from scenario 3 of von Lindern et al. (2016). As described below in the Technical Analysis Section, this study was selected because it was determined that the approach employed by the authors provides the best central tendency estimate of age-specific soil and dust ingestion rates for use in the IEUBK to support risk assessments conducted under CERCLA or RCRA corrective action authority. The soil-dust ingestion rates from Scenario 3 results in soil-dust ingestion rates that are supported by other independent analyses that use dermal transfer to estimate soil and dust ingestion rate, specifically the modeled estimates from Ozkaynak et al. (2011) and Wilson et al. (2013) (see Table 2).

Soil/dust ingestion studies reviewed for this effort are not intended to specifically represent soil-dust ingestion for children who engage in pica behavior. The intake estimates for soil pica behavior would be greater than intake estimates for incidental ingestion of soil-dust, but reliable data for pica ingestion rates or frequency are not available[4].
The intended audience for this document is human health risk assessors familiar with using the IEUBK model in support of CERCLA and RCRA corrective action risk assessments. For further background information on both this variable and the use of the IEUBK model in Superfund lead risk assessment, refer to U.S. EPA (1994a) or the Technical Review Workgroup for Lead (TRW) website (https://www.epa.gov/superfund/lead-superfund-sites-guidance).

[3] Particle size should be similar to the fraction that adheres to skin to reflect the particles that are incidentally ingested during hand-to-mouth activity.
[4] See Chapter 5 of US EPA Exposure Factors Handbook for more information on pica.

Table 1. Recommended revision to default age-specific soil/ dust ingestion rates (mg/day) in the IEUBK model

Source	Age Category (months)							Basis for Age-Specific Value
	0<12	12<24	24<36	36<48	48<60	60<72	72<84	
IEUBK Model Default[a]	85	135	135	135	100	90	85	Methodology U.S. EPA, 1989 Data Source Sedman et al., 1989
Revised Soil/Dust Ingestion Rate	86	94	67	63	67	52	55	Methodology von Lindern et al., 2016 Ozkaynak et al., 2011 Wilson et al., 2013 Data Source von Lindern et al., 2016

[a]IEUBK model v. 1.1, build 11.

INTRODUCTION

The IEUBK model predicts PbB in young children (birth to 7 years of age) exposed to lead from several sources of exposure and routes. The IEUBK model uses more than 100 input parameters that are initially set to default values. Of these, there are 46 parameters that may be input, or modified, by the user; the remainder are locked (U.S. EPA, 1994a). Default values represent national averages or other central tendency values derived from empirical data in the open literature. Default values include a) lead concentrations in exposure media (*e.g.*, diet representative of national food sources); b) contact and intake rates (*e.g.*, soil/dust ingestion); and c) exposure durations (White et al., 1998). The representativeness of IEUBK model output is wholly dependent on the representativeness of the data (often assessed in terms of completeness, comparability, precision, and accuracy [U.S. EPA, 1994a]).

Representative site-specific data are essential for developing a risk assessment (as well as cleanup goals) that reflect the current or potential future conditions. The most common type of site-specific data is media-specific lead concentration information (air, water, soil, dust). Until recently, an inexpensive, validated method to estimate bioavailability of lead in soil or dust was not available. Receptor data (*e.g.*, age, body weight, breathing rate, or soil ingestion rate) does not typically vary from site to site.

To promote defensible and reproducible risk assessments and cleanup plans, while maintaining flexibility needed to respond to different site conditions, U.S. EPA recommends the Data Quality Objectives process (U.S. EPA, 2006). Data Quality Objectives provide a structured approach to collecting environmental data that will be sufficient to support decision-making (http://www.epa.gov/QUALITY/dqos.html).

TECHNICAL ANALYSIS

The initial default IEUBK total soil and dust ingestion rates were used in the development of the NAAQS (U.S. EPA, 1989). Rather than adding new data, many of the published studies since the initial default values were adopted in 1994 were reanalyzed data from previous studies. Moreover, the TRW identified a number of limitations of the re-analyses of the data that were published after 1994. For example, Stanek and Calabrese (2000) included estimates of daily soil ingestion that were significantly negative, biased by large negative values in the data. The decision to include the negative values and their consequent impact on the results was never addressed by the authors (Stifelman 2006). We have identified several newer and relevant studies on soil/dust ingestion from seven sources: Arnot et al., 2010; Bierkens and Cornelis, 2006; Jang et al., 2014; Ozkaynak et al., 2011; Stanek et al., 2012a,b; von Lindern et al., 2016; Wilson et al., 2013.

To evaluate these studies, the TRW Lead Committee used a data quality objective (DQO) approach (see Attachment 1). This approach (working through the first four steps of the DQO process) allowed the Committee to focus on identifying studies that provided information that would support a revision of the default age-specific soil-dust ingestion rates for use in the IEUBK model for assessing lead exposure at CERCLA and RCRA corrective action sites. Table 2 provides a summary of these literature sources.

The following studies were evaluated to support a revision to the soil and dust ingestion rate default parameter in the IEUBK. Arnot et al. (2010) described the Farfel Exposure Model (FHX) employed by Health Canada, which uses a soil/dust ingestion rate of 65 mg/day for children age 5-11 years, and 100 mg/day for toddlers (age 6-60 months). Bierkens and Cornelis (2006) derived a range of soil/dust ingestion values (23.2 to 116 mg/day assuming an 8-hour waking and outdoor period [alternate values for 12-hour waking and outdoor period shown in Table 2]) based on probabilistic modeling of other mouthing frequency and hand loading publications. A 4-day fecal study of Korean children age 0 to 84 months, using the limiting tracer method, calculated an arithmetic mean soil/dust ingestion rate of 118 mg/day and a geometric mean of 29.3 mg/day (Jang et al., 2014; tracer-specific data not provided in study). Ozkaynak et al. (2011) estimated a mean soil/dust ingestion rate for children 3 to 6 years of age (as compared to the age range of the IEUBK model which is children <72 months old) using stochastic human exposure and dose simulation (SHEDS) modeling, using activity diaries to estimate hand-to-mouth, and object-to-mouth contact rates. Stanek et al. (2012a,b) conducted a meta-analysis of their earlier four mass balance studies using stochastic modeling of the most reliable tracers of children from Amherst, Massachusetts; Anaconda, Montana; and Washington State. Soil pica data were excluded from their analysis. Soil/dust ingestion rates for children in specific age classes are shown in Table 2; an overall mean soil/dust ingestion rate of 25.5 mg/day (95th percentile 79.4 mg/day) was estimated. Similar to Ozkaynak et al. (2011), Wilson et al. (2013) calculated soil and dust ingestion rates using a mechanistic model including parameters for particle loading on skin, transfer to hands, hand surface area, mouthing surface area, hand-to-mouth frequency, saliva dissolution, and exposure time using deterministic and probabilistic methods. Results, which are dependent on exposure time, were calculated separately for soil and dust, then summed for a daily soil/dust ingestion rate.

In addition, the information available on soil and dust ingestion rate values in EPA's Exposure Factors Handbook (U.S. EPA, 2017) was also considered as part of this effort but was not included in the peer review of this document (which preceded the release of the Exposure Factors Handbook update). The difference between the soil and dust ingestion rate values in the

Exposure Factors Handbook (U.S. EPA, 2017) and those proposed herein was addressed by the Office of Research and Development evaluation of the IEUBK model. (U.S. EPA, 2020).

The study by von Lindern et al. (2016) satisfies many of the evaluation criteria described in the TRW Lead Committee's DQOs (see Attachment 1). The authors of that study used environmental information collected at the Bunker Hill Mining and Metallurgical Complex Superfund Site (BHSS) site in Idaho to compare archived soil and dust samples from the BHSS to children's blood lead levels monitored from 1989 through 2002 to calculate soil/dust ingestion rates using the IEUBK model. Over 15 years of active cleanup, the Lead Health Intervention Program amassed approximately 5,400 blood lead observations (referred to as the parent database) from nearly 2,340 children (ages 0–9 and with a >50% participation rate) and yielding 2,176 records of blood/soil/dust lead concentrations. The study by von Lindern et al. (2016) used measured peak blood leads, community soil, neighborhood soil, yard soil concentration, house dust concentration and bioavailability information with IEUBK model defaults for Air, Water, and Diet to estimate soil-dust ingestion rates (IRs_D) under different Structural Equations Modeling (SEM) scenarios.

In the Bunker Hill study, four variables were used to quantify soil and dust exposures: house dust, yard soil, neighborhood soil (the mean of all yard soils within 200, 500, and 1000 feet of the home, excluding the home's yard), and community soil (the mean of all yard soils within the community, excluding the home's yard and neighborhood). The 271 samples (193 house dust samples, 73 yard soil samples and 5 quality control samples) were sieved to 80 mesh (to account for the particle size that would likely adhere to a child's hands) and analyzed for total lead and bioavailability.

The default assumption for the IEUBK model is that the source of soil ingested is 55% dust and 45% yard soil (U.S. EPA, 1994b). Structural Equations Modeling (SEM) was used to evaluate three different scenarios of yard soil to dust, neighborhood soil, and community soil:

1. 55% house dust/45% yard soil (as currently in the IEUBK model),
2. 40% house dust/30% yard soil/30% community soil, (alternatively using arithmetic or geometric means for community soil) and
3. 50% house dust/25% yard soil/10% neighborhood soil/15% community soil (alternatively using arithmetic or geometric means for neighborhood and community soil).

Table 2. Data summary of average soil/dust ingestion rates in children from selected studies.

Source	Soil/Dust Ingestion Rate (mg/day)	Age Range	n	Summary of Evaluation
IEUBK Model Default Values[a]	85-135	Children 0-84 months (yearly values)	77	Existing IEUBK model soil-dust ingestion rates Based on technical analysis to support the NAAQS for Lead (U.S. EPA, 1989).
Arnot et al., 2010	100	Children 6 60 months (age range)	n/a[b]	Is not considered a support document for revising the soil/dust ingestion rate because these are assumed input parameters for an exposure model using exposure factors for the general population of Canada. They are based on Health Canada 1998, which is based on Binder et al., (1986), Clausing et al. (1987), Calabrese et al. (1989), and Van Wijnen et al. (1990). Farfel Exposure Model (FHX) and Health Canada. 1998.[b]
	65	Children age 5 to 144 months (age range)		
Bierkens and Cornelis, 2006[c]	23.2-116	Children 12-84 months (age range) 8-hr awake and outdoors	5,000 (model runs)	Supportive study based on the limited number of observations.. Ranges of ingestion rates derived from probabilistic modeling of data from other publications reporting mouthing frequency and hand loading (Holmes et al., 1999; AuYeung et al., 2003; and U.S. EPA exposure factors, 2017).
	34.8-174	Children 12-84 months (age range) 12-hr awake and outdoors		
Ozkaynak et al., 2011	68	Children 36-72 months (age range) Mean value	1,000 (model runs)	Supportive study based on lack of new observation data. The estimates are based on modeling using SHEDS and hand-to-mouth and object-to-mouth contacts.
Jang et al., 2014	118	Children 0-96 months Arithmetic mean	58 samples	New tracer data based on Korean children. Estimates based on aluminum. The publication lacked details of the study. Only feces and soil-dust collected. 5 children were used as control group to compensate for exposure from other sources.
	29.3	Children 0-96 months Geometric mean	58 samples	

Source	Soil/Dust Ingestion Rate (mg/day)	Age Range	n	Summary of Evaluation
Stanek et al., 2012a,b	3.8	Children 12 to 36 months old	39 samples	Meta-analysis of four existing mass balance studies. The reanalysis of existing data is not a direct measurement and is not considered a candidate for supporting a revised default age-specific soil-dust ingestion rate
	20.6	Children 24 to 36 months old	55 samples	
	32.2	Children 36 to 60 months old	47 samples	
	40.9	Children 48 to 108 months old	75 samples	
U.S EPA Exposure Factors Handbook (2017)	40 - 90	Children < 6 months, 6 months to < 1, 1 to <2 years, 2 to <6 years, 1 to <6 years , 6 to < 12 years	241 in key tracer studies, 2,599 biokinetic modeling studies, modeled estimates of 1,000 simulated individuals and 200,000 trials.	The overall rating was low based on criteria of Soundness, Applicability and Utility, Clarity and Completeness, Variability and Uncertainty, and Evaluation and Review.
von Lindern et al., 2016	52-94[d]	Children 12 to 72 months old (yearly values)	985[f] (measured PbB and environmental values used for model runs)	Reanalysis of archived soil and dust data from Bunker Hill Superfund Site, available information includes bioavailability data, particle size and children's blood lead levels monitored (in some cases longitudinal data) from 1988-2002. Evaluated various combinations of dust, yard soil, neighborhood soil, and community soil. Accurately predicted peak annual blood lead from children representing greater than 50% of all resident children for 15 consecutive years.
Wilson et al., 2013	61	Toddlers 7 to 60 months	200,000 (model runs)	The study is considered a supportive study due to new modeled data. This study models soil/dust ingestion rates in Canada using hand-to-mouth transfer.
	55	Children 60 to 144 months		

[a]IEUBK model v. 1.1, build 11.
[b]Health Canada values based on data from Binder et al., 1986; Clausing et al., 1987; Calabrese et al., 1989; and Van Wijnen et al., 1990.
[c]Study reports values in units of mg/hr. The range (2.9-14.5 mg/hour) was converted to mg/d assuming both an 8-hour and a 12-hour waking and outdoor period.
[d]Results of Structural Equations Modeling (SEM) assuming 50% dust, 25% yard soil, 10% neighborhood soil, and 15% community soil.
[e] von Lindern et al. (2016) employed a hybrid approach that measured peak blood leads, particle size, community soil concentration, neighborhood soil concentration, yard soil concentration, as well as house dust concentration, and used IEUBK Modeled defaults for Air, Water, and Diet to estimate IRs under different SEM scenarios to select the model which best fit the empirical distribution of blood leads, representative of over 50% of the community for 15 consecutive years.
[f] 985 is the sum of 12-72 month old children in the 50/25/10/15 partition from Table S-1 of Supplemental Material to von Lindern et al. (2016).

The authors selected the model that provided the best fit to the empirical distribution of blood leads, which represented over 50% of the community for 15 consecutive years. Though ingestion rates for all three scenarios were similar, scenario 3 above had the lowest sum of squared error (SSE) in the statistical evaluation[5]. For this scenario, the authors derived age-specific, arithmetic mean soil/dust ingestion rates ranging from 52 to 94 mg/day for children age 1 to 6 years, with 95% confidence intervals ranging from 47 to 106 mg/day (Table 3). The other two scenarios were less acceptable because they did not fit the data as well.

Table 3. Soil/dust ingestion rates for the 50% house dust/25% yard soil/10% neighborhood soil/15% community soil scenario for the 12-71 month age range that is used in the IEUBK model (von Lindern et al., 2016).

Age[a]	n	AvgIR (95% CI)[b]	Percentiles						
			5	10	25	50	75	90	95
0-12	54	86 (66, 105)	17	27	38	72	94	165	221
13-24	174	94 (82, 106)	16	22	42	69	123	188	250
25-36	202	67 (59, 75)	10	19	28	53	82	140	178
37-48	209	63 (55, 72)	10	14	26	47	76	130	156
49-60	192	67 (59, 75)	11	15	32	53	86	122	182
61-72	208	52 (47, 57)	10	12	23	41	74	102	126
73-84	218	55 (48,62)	7	11	21	41	68	116	171

[a] Months
[b] AvgIR (95% CI) = arithmetic mean ingestion rate (95% confidence intervals)

After evaluating the available literature using the DQOs (see Attachment 1), the TRW Lead Committee recommends the age-specific soil-dust ingestion rates from scenario 3 of von Lindern et al. (2016) as the basis for revising the default age-specific soil-dust ingestion rates in the IEUBK model for CERCLA and RCRA corrective action risk assessments. As described above, this study was selected because it was determined that the approach employed by the authors most closely fits the DQOs established by the TRW Lead Committee for this effort; the study by von Lindern et al. (2016) provides the best estimate of age-specific soil and dust ingestion rates for use in the IEUBK model at CERCLA and RCRA 5,400 blood lead observations from nearly 2,340 individuals, yielding 2,176 records of blood/soil/dust lead concentrations over a 15 year timeframe with a >50% participation rate. In total, 271 samples (193 house dust samples, 73 yard soil samples and 5 quality control samples) sieved to 80 mesh (the particle size that adheres to a child's hand and most likely to be ingested by children) were analyzed for total lead and *in vitro* bioaccessibility. Community mean absolute bioavailability values (ABS) for unremediated yards soils and house dust, and site-wide ABS means for post-remediation soils were integrated into the database. Annual site-wide ABS means were calculated using a weighted average of bioavailable lead from remediated and unremediated yards. Aggressive LHIP education and intervention programs may have resulted in a temporary reduction in soil-dust intake rates by children, although this conclusion is not supported by multiple systematic reviews (Nussbaumer-Streit, Yeoh *et al.* 2016). Alternatively, elevated dust loadings caused by flooding and construction activities may have exacerbated soil-dust ingestion rates in the middle years of the BHSS cleanup. However, SEM and IEUBK model sensitivity analysis suggested that variation in calculated ingestion rates may be an artifact of the source partitions, nature of the data, or progression of the cleanup. The data collected at the BHSS best represents conditions at most CERCLA and RCRA corrective action sites during the Remedial

[5] Sum of Squared Error (SSE) is a statistical measure of the discrepancy between empirical values and the estimation model results. Lower SSE means better model prediction

Investigation and Feasibility Study phase of the remedial process. The soil-dust ingestion rates from Scenario 3 of von Lindern et al. (2016) results in soil-dust ingestion rates for the IEUBK model that are supported by other independent analyses, specifically the modeled estimates from Ozkaynak et al. (2011) and Wilson et al. (2013) (see Table 2).

UNCERTAINTY

Several studies published since 1994 were not applicable to this variable; for example, they contained only adult data, evaluated sediment ingestion rates rather than soil ingestion rates, or were review papers summarizing or reanalyzing other studies. Among recent publications that provide new data for young children (see Table 2), the TRW Lead Committee considered the study by von Lindern et al. (2016) to provide the relevant age-specific estimates of soil-dust ingestion rates for young children because it satisfied the most evaluation criteria (see Attachment 1) compared with the other studies. The TRW Lead Committee acknowledges that the data used by von Lindern et al. (2016) are site-specific and consideration was given to whether the Bunker Hill site was representative of other hazardous waste sites in the US. The data collected for that study were from an area of known lead contamination and could represent higher levels of lead than found in some areas. Also, as these data were collected from a site where EPA and other authorities were actively engaged in public outreach to reduce exposure, the soil-dust ingestion rates could be lower than in communities lacking public education efforts to limit exposure to soil and dust and thus may not necessarily be appropriate as an estimate for the general population, although the effectiveness of education has not been demonstrated in any of the Cochrane systematic reviews (Nussbaumer-Streit et al., 2016). Alternatively, elevated dust loadings caused by flooding and construction activities may have exacerbated soil-dust ingestion rates in the middle years of the BHSS cleanup. However, SEM and IEUBK model sensitivity analysis suggested that variation in calculated ingestion rates may be an artifact of the source partitions, nature of the data, or progression of the cleanup. The TRW Lead Committee notes that these conditions would likely occur at any CERCLA or RCRA corrective action site where USEPA was engaged in a risk assessment and therefore this limitation may be considered a strength (in that the data are possibly a better fit for the intended purpose than soil-dust ingestion rates collected from a naïve population would be). Furthermore, the information from this study is supported by two independent studies (Ozkaynak et al., 2011; Wilson et al., 2013). Thus, in the absence of other high-quality information the estimates from von Lindern et al. (2016) shown in table 3 are likely to be most representative of soil dust ingestion rates for young children at CERCLA and RCRA corrective action sites. The TRW Lead Committee did not, as part of this review process, define study acceptance criteria (aside from using the DQOs to guide the evaluation), conduct a systematic review, or conduct quality assurance activities on the published data to identify anomalies such as incorrect units, duplicate samples, etc. Consideration of additional studies published in the future could inform further refinement of age-specific soil and dust ingestion rates.

RECOMMENDATIONS FOR THE IEUBK MODEL

Results from several new studies provide information on average soil dust ingestion rates from children 0-84 months old. In general, these studies support an average combined soil/dust ingestion rate from 50 to 100 mg/day for children younger than 84 months old that could be applied to children residing near a CERCLA or RCRA corrective action site. For example, the two supporting studies Ozkaynak et al. (2011) and Wilson et al. (2013) result in values of 68 mg/day and 55-61 mg/day, respectively. These values are consistent with the recommended age-specific soil-dust ingestion rates for some of the similar age groupings from von Lindern et al.

(2016). The age-specific soil/dust ingestion recommended as the default soil/dust ingestion rates in the IEUBK model are shown in Table 4.

Table 4. Recommended change to soil/dust ingestion rates for use in the IEUBK model.

Age (years)	Age-specific, Average Soil/Dust Ingestion Rate (mg/day)	Basis for Age-Specific Value
0-1	86	Age-specific arithmetic mean ingestion rates based on the best fit model from von Lindern et al., 2016 and supported by modeled estimates from Ozkaynak et al., 2011; Wilson et al., 2013
1-2	94	
2-3	67	
3-4	63	
4-5	67	
5-6	52	
6-7	55	

Based on the evaluation described in this document and many factors specific to CERCLA and RCRA corrective action sites, these soil-dust ingestion rates are appropriate for assessing exposure at contaminated areas where the IEUBK model is frequently used. The TRW Lead Committee recommends updating the default *Age-Dependent Soil and Dust Ingestion Rate* variable in the IEUBK model to the age-specific average soil/dust ingestion rates based on von Lindern et al. (2016) (Table 3). These default values are considered appropriate for all applications of the IEUBK model where current and future residential scenarios are being assessed for CERCLA and RCRA corrective action risk assessment. The updated age-specific soil-dust ingestion rates are incorporated into the IEUBK model as shown in Figure 1.

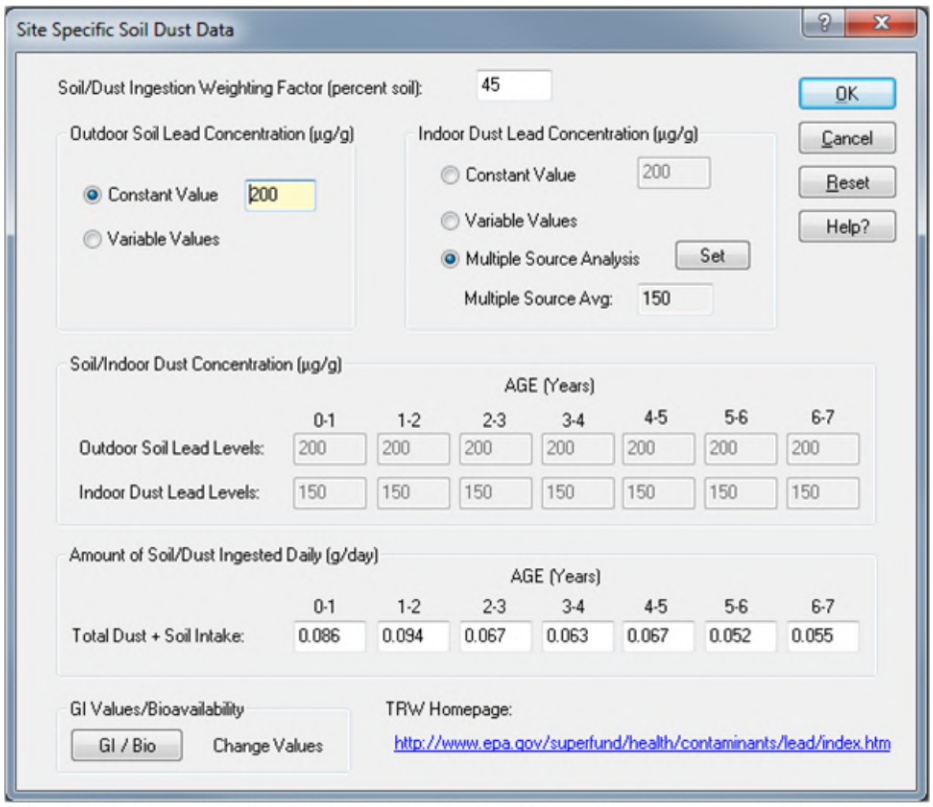

Figure 1. IEUBK Model Site Specific Soil Dust Data Entry Window with the Updated Soil/Dust Ingestion Rates.

IMPACT ON THE IEUBK MODEL PREDICTIONS

Using current IEUBK model (v.2) defaults for all parameters while implementing the proposed soil-dust rates will increase the preliminary remediation goal (PRG). Table 5 presents the updated estimates as well as the estimates from the previous analyses.

The PRGs in Table 5 are used to illustrate the impact when developing a screening level for lead in soil. As examples, the PRGs corresponding to PbBs of 10 µg/dL and 5 µg/dL are presented for illustrative purposes.

Table 5. Effects of changing the Soil-Dust Ingestion Rate (mg/day) in the IEUBK model

Study	Age Range	IRsd	P10 PRG[†]	P5 PRG[‡]
IEUBK Model (v1.1 build 11) default values	0-1 yr 1-2 yrs 2-3 yrs 3-4 yrs 4-5 yrs 5-6 yrs 6-7 yrs	85 mg/d 135 mg/d 135 mg/d 135 mg/d 100 mg/d 90 mg/d 85 mg/d	418 ppm	153 ppm
Proposed Update (based on von Lindern et al.	0-1 yr 1-2 yrs 2-3 yrs	86 mg/d 94 mg/d 67 mg/d	605 ppm	200 ppm

Study	Age Range	IRsd	P10 PRG[†]	P5 PRG[‡]
[2016]) using IEUBK v.2 default values	3-4 yrs 4-5 yrs 5-6 yrs 6-7 yrs	63 mg/d 67 mg/d 52 mg/d 55 mg/d		

[†] P10 PRG is the preliminary remediation goal for soil lead based on no more than 5% probability of exceeding a blood lead concentration of 10 µg/dL using IEUBK (v1.1. build 11) with default values for the 0-84 month age range.

[‡] P5 PRG is the preliminary remediation goal for soil lead based on no more than 5% probability of exceeding a blood lead concentration of 5 µg/dL using IEUBK (v1.1. build 11) with default values for the 0-84 month age range.

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ATTACHMENT 1. DATA QUALITY OBJECTIVES FOR THE SOIL-DUST INGESTION RATE LITERATURE EVALUATION

1. State the Problem
    a. Current IEUBK Model soil-dust ingestion rates do not reflect recent studies, which have addressed many of the problems of previous studies
        i. Age-specific rates
        ii. Dust rates
        iii. Confidence limits
        iv. Analytical uncertainty
            1. CV
            2. Negative values
        v. Study duration
            1. 5-20 days
        vi. Untested tracer bioavailability assumptions
        vii. Biomarkers
        viii. Sampling uncertainty
            1. Particle size
            2. Dust
            3. Exposure area
        ix. Number of subjects
        x. Transparency
            1. Stanek & Calabrese Data was not shared, despite requests & assurances
        xi. Consistency with other studies
            1. Multiple analyses of single datasets produce multiple estimates
        xii. Potential Conflict (or appearance) of interest
            1. PRP funding

2. Identify the Decisions
    a. IEUBK default
        i. Age-specific values
        ii. CTE values

3. Identify Inputs to the Decision
    a. Literature search
    b. Evaluation criteria
    c. Peer review

4. Define the Study Boundaries
    a. Timing
    b. Schedule
    c. Review process
    d. Impacts to programs & agencies

FMI see https://www.epa.gov/fedfac/guidance-systematic-planning-using-data-quality-objectives-process

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Exhibit L

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October 6, 2021

Kelli Wetzel
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Subject: **Facility ID No. 085-00011, Perpetua Resources Idaho, Inc., Stibnite Gold Project –TAP Addendum Report**

Dear **Ms. Wetzel**:

Perpetual Resources, Inc. is providing the enclosed TAP Addendum report (Addendum) for the Stibnite Gold Project. The Addendum contains the hazardous air pollutant (HAP) and toxic air pollutant (TAP) emissions calculations provided in the PTC application and as requested by IDEQ, supplements that information to support IDEQ's responses to comments.

If you have any questions regarding this submittal, please contact me at 208-901-3053 or alan.haslam@perpetua.us.

Thank you for reviewing this information.

Sincerely,
Perpetua Resources

Alan Haslam
Vice President – Permitting

Enclosure: TAP Addendum Report

AIR SCIENCES INC.

DENVER • PORTLAND • LOS ANGELES

Stibnite Gold Project Permit to Construct Application

TAP Addendum

Prepared For:
PERPETUA RESOURCES IDAHO, INC.

PROJECT NO. 335-21-404
OCTOBER 5, 2021

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Appendix A – HAP/TAP Emission Calculations
Appendix B – Modeled Emissions per Modeling Scenario and Source
Appendix C – TAP Modeling Results
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1.0 INTRODUCTION

On September 10, 2020 and February 18, 2021, the Idaho Department of Environmental Quality (IDEQ) provided notices for public comment on the Perpetua Resources Idaho, Inc. (hereafter referred to as Perpetua Resources) Stibnite Gold Project (SGP) complete application materials (Application), draft permit to construct (Draft PTC), and statement of basis (SOB). The public comments received included requests for additional information regarding hazardous air pollutant (HAP) and toxic air pollutant (TAP) emission estimates and modeling.

The purpose of this TAP Addendum (Addendum) is to provide that additional information to support IDEQ's responses to comments. The information provided in this Addendum confirms the following determinations made by Perpetua Resources and IDEQ at the time of the public notices:

1. The SGP is an area source for HAP emissions.

2. The SGP complies with the Idaho TAP provisions (IDAPA 58.01.01.210).

3. The SGP complies with the Idaho mercury rule (IDAPA 58.01.01.215).

This Addendum supplements information in the complete Application and supports those determinations highlighted during the public comment. Section 2.0 provides a description of the HAP/TAP emission calculations and source status. Section 3.0 provides a TAP emissions evaluation and modeling analysis, including TAP emission sources covered by IDAPA 58.01.01.210.20. Section 4.0 compares arsenic modeling analyses for actual and potential arsenic emissions. Section 5.0 provides a discussion of the emission reductions that demonstrate compliance with carcinogenic TAPs. Section 6.0 provides a Toxic Air Pollutant Reasonably Available Control Technology (T-RACT) analysis. Section 7.0 provides proposed permit conditions for demonstrating compliance with carcinogenic TAPs, and Section 8.0 provides a discussion of mercury emissions, including mercury emission sources covered by IDAPA 58.01.01.215.01.

IDAPA 58.01.01.210 and 215 reduce the information required from a PTC applicant and streamline the PTC review required by IDEQ in those circumstances where the HAP/TAP emissions are covered or addressed by federal regulations (IDAPA 58.01.01.210) or the mercury emissions are below a specific exemption threshold (IDAPA 58.01.01.215). Perpetua Resources referenced these rules in the Application and relied on these provisions to present a complete HAP/TAP emissions inventory that aligned with these rules. To support IDEQ's responses to public comments, IDEQ requested that Perpetua Resources expand its HAP/TAP analyses beyond the requirements of these rules and reconfirm compliance with TAP thresholds. This additional work reconfirms IDEQ's earlier findings that the SGP is an area source, and the proposed HAP/TAP emissions comply with IDAPA 58.01.01.210 and 215.

2.0 HAP/TAP EMISSIONS

During the two IDEQ public comment periods, IDEQ received comments regarding the following:

1. SGP source status for HAPs
2. Metal HAP/TAP emissions from fugitive dust
3. Metal HAP/TAP emissions from the autoclave and lime kiln processes
4. Fugitive emissions of hydrogen cyanide (HCN)

To support IDEQ's responses to comments and confirm the SGP area source status, the potential-to-emit (PTE)[1] HAP/TAP emission inventory in Appendix A of this Addendum contains emission calculations for all HAPs and TAPs emitted from all the SGP processes, including:

- Metals from mining fugitive dust emissions
- Metals from ore processing, ore concentration and refining, and lime, aggregate, and concrete production
- Antimony (Sb) emissions from the Sb drying and bagging circuit
- Sulfuric acid (H_2SO_4) and hydrogen sulfide (H_2S) from the autoclave, and hydrochloric acid (HCl) emissions and lime kiln
- Evaporative HCN from cyanide leaching and the tailings storage facility
- Various HAPs/TAPs from fuel storage and combustion
- Carbon disulfide emissions from the use of xanthate
- Evaporative mercury from mining surfaces

This HAP/TAP emission inventory was conducted for all 14 modeling scenarios evaluated in the Application. The emissions provided in Appendix A reflect the highest emissions scenario (HAP/TAP Emission Calculations – Scenario W3, 180,000 T/day).[2]

---

[1] PTE in this Addendum refers to the potential emissions after applying all proposed *air pollution control equipment and restrictions on hours of operation or on the type or amount of material combusted, stored or processed* per IDAPA 58.01.01.006.88 (i.e., PTE is the proposed permitted emissions).

[2] HAP/TAP Emission Calculations – Scenario W3, 180,000 T/day: HAP/TAP emissions based on the potential mining production rate of 180,000 tons per day (T/day) and the highest emissions scenario (Modeling Scenario W3).

2.1 Description of HAP Source Status

2.1.1 Controlled HAP Emissions

The controlled HAP emissions (PTE) from the SGP are below the major source thresholds; therefore, the SOB classified the SGP as an area source for HAP emissions. This is consistent with EPA's determination that all U.S. gold mine ore processing and production facilities are area sources.[3] The emissions inventory provided in Appendix A shows the total HAP emissions are 3.67 tons per year (ton/yr) for a single HAP and 12.56 ton/yr for all the HAPs combined for the highest emissions scenario (Modeling Scenario W3). The major source levels are 10 ton/yr for a single HAP and/or 25 ton/yr for all the HAPs combined.

2.1.2 Uncontrolled HAP Emissions

Uncontrolled HAP emissions are estimated to exceed 25 ton/yr, combined; therefore, to support the area source designation, Perpetua Resources committed to operational limitations and emission controls in the Application that achieve area source status.

2.2 Description of HAP/TAP Emission Calculations

This section provides a brief description of the methods used to calculate the HAP/TAP emissions provided in Appendix A. The references used for the HAP/TAP calculations were presented in the Application. Any new references are provided in this section.

2.2.1 Metal Emissions from Mining Fugitive Dust

The metal HAP/TAP emissions from fugitive dust generated by mining activities (drilling, blasting, excavating, hauling, etc.) were calculated by multiplying the HAP/TAP-specific median metal concentration in the ore[4] by the activity-specific total particulate matter (PM) emissions. The median metal concentrations were derived from over 55,000 core samples taken primarily from the more mineralized zones of the SGP pits (i.e., in and around gold ore deposits).

This emissions inventory does not reflect any of the emission reductions described in Section 5.0 for carcinogenic TAP compliance.

[3] *EPA recently gathered data and evaluated emissions of other HAP, including cyanide and non-mercury metals. The data indicate that the gold mining processing and production category consists of only area sources (i.e., facilities that emit less than ten tons per year of any one HAP and less than 25 tons per year of any combination of HAP)* (EPA 2010).

[4] Iron (Fe) and selenium (Se) were not included in the Application because the concentrations of these metals were similar to typical crustal abundance levels. In response to comments on HAPs/TAPs emissions, the concentrations of these metals (18,200 ppm of Fe and 0.4 ppm of Se) are provided (Midas Gold 2020).

2.2.2 Metal Emissions from Ore Processing and Lime/Aggregate Production

2.2.2.1 Crushing, Screening, and Material Handling

The metal HAP/TAP emissions generated by process and production sources (the crushing, screening, and handling of ore, limestone, lime, and aggregate) were calculated by multiplying the PM emissions from these sources by the median concentration of metals in the ore, limestone, lime, or aggregate. The ore median metal concentrations are discussed in Section 2.2.1. The limestone, lime, and aggregate metal concentrations are provided in Table 1.

The limestone metal concentrations were measured from core hole samples through the middle marble formation in the proposed limestone quarry's footprint. These rock samples were specifically analyzed to assess the formation as a viable limestone source. As a conservative estimate, the limestone metal profile was also used for aggregate production.

Table 1. Metal TAP Concentrations for Limestone and Lime

CAS	TAP Name	Concentration (ppm) [1]
7440-38-2	Arsenic	23
7440-41-7	Beryllium	0.8
7440-43-9	Cadmium	0.25
7440-48-4	Cobalt	4
7440-47-3	Chromium	15
7439-97-6	Mercury	0.02
7439-96-5	Manganese	236.5
7440-02-0	Nickel	5
7439-92-1	Lead	3
7440-36-0	Antimony	2.5
7723-14-0	Phosphorus	130
7440-22-4	Silver	0
7429-90-5	Aluminum	22,600
7440-39-3	Barium	145
1317-65-3	Calcium Carbonate [2]	274,500
1305-78-8	Calcium Oxide [3]	740,000
7440-50-8	Copper	5
7439-89-6	Iron	10,350
7439-98-7	Molybdenum	0.5
7440-28-0	Thallium	5
7440-61-1	Uranium	5

CAS	TAP Name	Concentration (ppm) [1]
7440-62-2	Vanadium	15.5
7440-33-7	Tungsten	5
7440-66-6	Zinc	18

[1] Median of 98 samples of the SGP limestone material (M3 2018).
[2] Calcium carbonate ($CaCO_3$) is used for limestone processing.
[3] Calcium oxide (CaO) is used for lime processing. 40% to 74% CaO (NLA 2007).

2.2.2.2 Lime Kiln

The non-mercury metal HAP/TAP emissions from the lime kiln were calculated by multiplying the PM emissions by the median concentration of metals in the limestone shown in Table 1. The mercury emissions from the lime kiln were conservatively estimated by assuming all mercury in the limestone feed is volatilized and emitted.

2.2.2.3 Autoclave

Mercury emissions from the SGP autoclave were based on the SysCAD modeling of the SGP autoclave performed by Perpetua Resources' engineering contractor: M3 Engineering. This modeling predicted 0.0105 grams per second of mercury emissions exiting the autoclave mercury control system, which is comprised of a venturi scrubber, a vent gas cleaning tower, a vent gas steam condensation tower, and one or more sulfur-impregnated activated carbon filters.

The non-mercury metal HAP/TAP emissions from the autoclave mercury control system are expected to be less than the mercury emissions because non-mercury HAP/TAP emissions are only particulates and more easily controlled by the emissions control system. Mercury emissions move through the control system as both particulate and gas. For this review, the non-mercury HAP/TAP emissions were conservatively assumed to be equal to the mercury emissions.

2.2.2.4 EW Cells, Pregnant Solution Tank, Retort, Furnace, and Carbon Kiln

Mercury emissions from the SGP electrowinning (EW) cells, pregnant solution tank, mercury retort, induction melting furnace, and carbon regeneration kiln were calculated based on stack test data from similar sources utilizing similar mercury control systems at Nevada gold mines.

The non-mercury metal HAP/TAP emissions exiting these mercury control systems are expected to be less than the mercury emissions because non-mercury HAP/TAP emissions are only particulates and more easily controlled by the emissions control system. Mercury emissions move through the control system as both particulate and gas. For this review, the non-mercury HAP/TAP emissions were conservatively assumed to be equal to the respective mercury emissions.

2.2.2.5 Antimony Dryer and Dry Bagging

The Sb circuit proposed in the Application was replaced with a new dewatering/packaging circuit. The new circuit eliminates the potential for metal emissions from dust and mercury evaporation emissions from concentrate heating. Instead, the Sb concentrate will be dewatered using a filter press and then bagged as a wet (damp) product. There are no HAP/TAP emissions associated with this new circuit.

2.2.3 Metal Emissions from Concrete Production

The metal HAP/TAP emissions from concrete production were calculated using EPA emission factors from AP-42 Section 11.12, Concrete Batching. This section provides controlled emission factors for cement silo filling and central mix batching. There are no emission factors for cement silo unloading. Therefore, the cement silo filling factors were used for cement silo unloading as a conservative estimate.

Chromium (VI) percentages of the total chromium were provided by IDEQ for cement silo filling and central mix batching. These percentages were used to calculate chromium (VI) emissions from cement silo filling and unloading and central mix batching.

There are no HAP/TAP emission factors for the dust generated from aggregate handling in the concrete production process. As a conservative estimate, the limestone metals profile provided in Table 1 of Section 2.2.2.1 was used to estimate the HAP/TAP emissions from aggregate handling.

2.2.4 H_2SO_4 and H_2S Emissions from the Autoclave

H_2SO_4 and H_2S emissions from the SGP autoclave were calculated based on source test data from similar autoclaves at gold mines in Nevada.

2.2.5 HCl Emissions from the Lime Kiln

The HCl emissions from the lime kiln were calculated using the HCl emission factor obtained from EPA's EPCRA Section 313 Guidance for Reporting Hydrochloric Acid (EPA 1999b).

2.2.6 HCN Emissions from Cyanide Leaching and Tailings Storage Facility

The evaporative HCN emissions from cyanide leaching and the tailings storage facility were calculated using the flux methodology developed by EPA and the Nevada Mining Association as part of the 40 CFR 63 rule-making process. The methodology is based on empirical measurements at several gold mines in Nevada taken under the direction of EPA. Numerous gold mines in several states have used this method since its development in 2010.

2.2.7 HAP/TAP Emissions from Fuel Storage and Fuel Combustion

HAP/TAP emissions from fuel combustion (propane and diesel) were calculated using fuel combustion rates and the applicable EPA AP-42 emission factors.

HAP/TAP emissions from fuel storage (gasoline) were calculated from the tank volatile organic compound (VOC) emissions multiplied by the weight percentages of HAP/TAP in the fuel. The percentages were obtained from EPA's EPCRA Section 313 Industry Guidance Metal Mining Facilities, Table 3-8 for gasoline (EPA 1999a).

2.2.8 Carbon Disulfide Emissions from Xanthate

Carbon disulfide (CS_2) emissions from potassium amyl xanthate (PAX) use were calculated based on the decomposition of xanthate to CS_2 gas. The decomposition rate was determined from published experimental data.

2.2.9 Evaporative Mercury Emissions from Mining Surfaces

Mercury can evaporate from rock surfaces in pits, tailings facilities, development rock storage facilities, and stockpiles. The rate of mercury evaporation (or flux) is a function of the mercury concentration in the material. Mercury flux rates and concentration measurements taken at a gold mine in Nevada were adjusted for the SGP mercury concentrations to estimate mercury flux emissions from the SGP pits, tailings facility, development rock storage facilities, and ore stockpiles.

3.0 TAP ANALYSIS

A complete inventory of the PTE TAP emissions is provided in Appendix A, as discussed in Section 2.0. Appendix A also identifies the applicability of IDAPA 58.01.01.210.20. According to IDAPA 58.01.01.210.20, no further demonstration of compliance with the TAP provisions is required to obtain a PTC for new source emissions, such as the SGP, from:

a. The equipment or activities covered by a New Source Performance Standards (NSPS) or National Emissions Standards for Hazardous Air Pollutants (NESHAP); or

b. The source category of equipment or activities addressed by a NSPS or NESHAP even if the specific equipment or activity is not subject to compliance requirements under the federal rule.

After applying IDAPA 58.01.01.210.20 as described in Section 3.1, the remaining TAP emissions are subject to further compliance demonstration and are compared to the screening emission levels (EL) described in Section 3.3. TAP emissions that below the screening EL, require no further demonstration of compliance with the TAP provisions. TAP emissions above the screening EL require modeling, as described in Section 3.4. To identify the TAPs subject to review, Section 3.2 provides a comparison of the metals analyzed in the SGP ore, development rock, and limestone to the TAPs listed in IDAPA 58.01.01.585 and IDAPA 58.01.01.586.

3.1 Equipment or Activities Covered or Addressed by NESHAP or NSPS

In accordance with IDAPA 58.01.01.210.20, the equipment and activities at the SGP that are either covered or addressed by NESHAP or NSPS are discussed in the following subsections. TAPs emitted from these sources that are also HAPs require no further evaluation to demonstrate compliance with the TAP provisions. TAP emissions from these sources that are not HAPs require additional review to demonstrate compliance with the TAP provisions.

3.1.1 NESHAP Subpart ZZZZ

40 CFR 63, Subpart ZZZZ, NESHAP for Stationary Reciprocating Internal Combustion Engines covers HAP emissions from the SGP emergency generators and fire pump (Source ID No. EDG1, EDG2, EDG3, and EDFP). IDAPA 58.01.01.210.20(a) applies to Source ID No. EDG1, EDG2, EDG3, and EDFP.

3.1.2 NESHAP Subpart AAAAA

40 CFR 63, Subpart AAAAA, NESHAP for Lime Manufacturing Plants addresses HAP emissions from the SGP lime manufacturing sources (Source ID No. LS12, LK, LS-L/U, LCR, and LKC).[5] IDAPA 58.01.01.210.20(b) applies to Source ID No. LS12, LK, LS-L/U, LCR, and LKC.

3.1.3 NESHAP Subpart CCCCCC

40 CFR 63, Subpart CCCCCC, NESHAP for Source Category: Gasoline Dispensing Facilities covers the SGP gasoline storage tanks (Source ID No. TG1 and TG2). IDAPA 58.01.01.210.20(a) applies to Source ID No. TG1 and TG2.

3.1.4 NESHAP Subpart EEEEEEE

40 CFR 63, Subpart EEEEEEE, NESHAP: Gold Mine Ore Processing and Production Area Source Category covers HAP emissions from the SGP autoclave (Source ID No. AC) and the EW cells, pregnant solution tank, mercury retort, induction melting furnace, and carbon regeneration kiln (Source ID No. EW, MR, MF, and CKD). IDAPA 58.01.01.210.20(a) applies to Source ID No. AC, EW, MR, MF, and CKD.

The NESHAP source category addresses HAP emissions from mining activities, specifically fugitive dust-generating activities (drilling, blasting, excavating, hauling, etc.), explosives use and storage (Source ID No. PS), cyanide leaching (Source ID No. CIP Leach 1-4, CIL 1-6, CIP 1-6, and CN Detox 1-2), tailings storage, ore processing (Source ID No. OC1-13), ore processing heating (Source ID No. ACB, CKB, PV, and HS), and the ore processing reagent use of PAX and sodium cyanide (NaCN). The NESHAP source category is defined as "*Gold Ore Mining ..., NAICS code 212221, Establishments primarily engaged in developing the mine site, mining, and/or beneficiating (i.e., preparing) ores valued chiefly for their gold content. Establishments primarily engaged in transformation of the gold into bullion or doré bar in combination with mining activities are included in this industry*" (EPA 2011b). EPA's rule-making docket (Docket ID EPA-HQ-OAR-2010-0239) provides documents evaluating HAP metal emissions from mining fugitive dust, HCN emissions from cyanide leaching, and downwind HCN ambient concentrations.[6]

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[5] NESHAP Subpart AAAAA defines the affected source as follows: *each lime kiln and its associated cooler, each individual PSH [processed stone handling] system. The individual types of emission units in a PSH system are conveying system transfer points, bulk loading or unloading systems, screening operations, bucket elevators, and belt conveyors-if they follow the processed stone storage bin or storage pile in the sequence of PSH operations. The materials processing operations (MPO) associated with lime products (such as quicklime and hydrated lime), lime kiln dust handling, quarry or mining operations, limestone sizing operations, and fuels are not subject to today's final NESHAP. Processed stone handling operations are further distinguished in the final NESHAP as follows: (1) whether their emissions are vented through a stack, (2) whether their emissions are fugitive emissions, (3) whether their emissions are vented through a stack with some fugitive emissions from the partial enclosure, and/or (4) whether the source is enclosed in a building* (69 Fed. Reg. 394, 397 (January 5, 2004)).

[6] EPA-HQ-OAR-2010-0239-0132, *Profile of the Metal Mining Industry;* EPA-HQ-OAR-2010-0239-0157, *Recommended Methodology for Quantification of Fugitive Dust Metals Emissions from Mining Activities for Title V Applicability;* EPA-HQ-OAR-2010-0239-0102, *QAPP Comprehensive Air Emissions Testing for Hydrogen Cyanide;* EPA-HQ-OAR-2010-0239-0134, -0135 -0136 -0137 -0161 -0162 -0378, *Meteorological and Hydrogen Cyanide (HCN) Fence Line Monitoring* reports.

In response to public comments, this Addendum applies IDAPA 58.01.01.210.20(a) to those sources of HAP emissions at the SGP that are covered by Subpart EEEEEEE. This Addendum provides further evaluation of the sources of HAP emissions that are addressed by the NESHAP per IDAPA 58.01.01.210.20(b) – the mining emissions.[7]

3.1.5 NSPS Subpart LL

40 CFR 60, Subpart LL, Standards of Performance for Metallic Mineral Processing Plant covers the SGP ore processing (Source ID No. OC1-13). IDAPA 58.01.01.210.20(a) applies to Source ID No. OC1-13.

3.1.6 NSPS Subpart OOO

40 CFR 60, Subpart OOO, Standards of Performance for Nonmetallic Mineral Processing Plants covers the SGP limestone processing sources (Source ID LS1-11 and LSBM), aggregate production (Source ID No. PCSP1 and PCSP2), and aggregate handling in the concrete production process (Source ID No. CA-L/U). IDAPA 58.01.01.210.20(a) applies to Source ID No. LS1-11, LSBM, PCSP1, PCSP2, CA-L/U.

3.2 Metals Review for TAP Provisions Applicability

Table 2 provides a comparison of the metals analyzed in the SGP ore, development rock, and limestone to the TAPs listed in IDAPA 58.01.01.585 and IDAPA 58.01.01.586.

Table 2. Metals Comparison to IDAPA 58.01.01.585-586 TAPs

Metal			TAP		
CAS	**Name**	**HAP?**	**CAS**	**Name**	**Is the Metal a TAP?**
7440-57-5	Gold	No	7440-57-5	Not listed	No
7440-22-4	Silver	No	7440-22-4	Silver - Including metal soluble compounds, as Ag	Yes, same CAS Yes, similar form No
7429-90-5	Aluminum	No	7429-90-5	Aluminum, including: Metal & Oxide Pyro powders Soluble salts	Yes, same CAS Yes, similar form No No
7440-36-0	Antimony	Yes	7440-36-0	Antimony & compounds, as Sb (handling & use)	Yes, same CAS
7440-38-2	Arsenic	Yes	7440-38-2	Arsenic compounds	Yes, same CAS
7440-39-3	Barium	No	7440-39-3	Barium, soluble compounds, as Ba	Yes, same CAS
7440-41-7	Beryllium	Yes	7440-41-7	Beryllium & compounds	Yes, same CAS

[7] A demonstration of compliance that applied IDAPA 58.01.01.210.20(a) and (b) to the sources of HAP emissions covered and addressed by the NESHAP is presented in the SOB (February 18, 2021).

Metal			TAP		
CAS	**Name**	**HAP?**	**CAS**	**Name**	**Is the Metal a TAP?**
7440-69-9	Bismuth	No	1304-82-1	Bismuth telluride undoped Bismuth telluride if selenium doped	No, Bi compounds are expected to be bismuthinite ($Bi2S_3$) and bismite (Bi_2O_3) [1]
7440-43-9	Cadmium	Yes	7440-43-9	Cadmium and compounds	Yes, same CAS
7440-70-2	Calcium	No	1317-65-3 156-62-7 1305-62-0 1305-78-8 1344-95-2 13397-24-5	Calcium carbonate Calcium cyanamide Calcium hydroxide Calcium oxide Calcium silicate (synthetic) Calcium sulfate	Yes [2] No, different CAS No, different CAS Yes [2] No, different CAS No, different CAS
7440-47-3	Chromium	Yes	7440-47-3 7440-47-3 16065-83-1 18540-29-9	Chromium metal, including: Chromium (II) compounds, as Cr Chromium (III) compounds, as Cr Chromium (VI) & compounds, as Cr+6	Yes, same CAS Yes, same CAS No, different CAS No, different CAS
7440-48-4	Cobalt	Yes	10210-68-1 16842-03-8 7440-48-4	Cobalt carbonyl, as Co Cobalt hydro carbonyl, as Co Cobalt metal, dust, and fume	No, different CAS No, different CAS Yes, same CAS
7440-50-8	Copper	No	7440-50-8	Copper: Fume Dusts & mists, as Cu	Yes, same CAS No Yes, similar form
7440-55-3	Gallium	No		Not listed	No
7439-89-6	Iron	No	1309-37-1 13463-40-6 7439-89-6	Iron oxide fume (Fe2O3), as Fe Iron pentacarbonyl, as Fe Iron salts, soluble, as Fe	No, different CAS No, different CAS Yes, same CAS
7439-91-0	Lanthanum	No		Not listed	No
7440-09-7	Potassium	No	1310-58-3	Potassium hydroxide	No, different CAS
7439-92-1	Lead	Yes		Not listed	No, criteria pollutant
7439-95-4	Magnesium	No	1309-48-4	Magnesium oxide fume	No, different CAS
7439-96-5	Manganese	Yes	7439-96-5	Manganese, as Mn, including: Dust & compounds Fume	Yes, same CAS Yes, similar form No
7439-97-6	Mercury	Yes		Not listed	No, regulated by mercury rules
7439-98-7	Molybdenum	No	7439-98-7	Molybdenum, as Mo, including: Soluble compounds Insoluble compounds	Yes, same CAS No Yes, similar form
7440-02-0	Nickel	Yes	7440-02-0 12035-72-2 7440-02-0	Nickel Nickel Subsulfide Nickel Refinery Dust	No, see Ni refinery dust No, different CAS Yes, same CAS and form

Metal			TAP		
CAS	Name	HAP?	CAS	Name	Is the Metal a TAP?
7723-14-0	Phosphorus	Yes	7723-14-0	Phosphorus	Yes, same CAS
			10025-87-3	Phosphorus oxychloride	No, different CAS
			10026-13-8	Phosphorus penta-chloride	No, different CAS
			1313-80-3	Phosphorus penta-sulfide	No, different CAS
			1314-56-3	Phosphorus pentoxide (ID)	No, different CAS
			7719-12-2	Phosphorus trichloride	No, different CAS
7782-49-2	Selenium	Yes	7782-49-2	Selenium and compounds, as Se	Yes, same CAS
7440-23-5	Sodium	No	26628-22-8	Sodium azide (CL)	No, different CAS
			7631-90-5	Sodium bisulfite	No, different CAS
			136-78-7	Sodium 2,4-dichloro-phenoxyethyl sulfate; see Sesone	No, different CAS
			62-74-8	Sodium fluoroacetate	No, different CAS
			1310-73-2	Sodium hydroxide	No, different CAS
			7681-57-4	Sodium metabisulfite	No, different CAS
7440-20-2	Scandium	No		Not listed	No
7440-24-6	Strontium	No		Not listed	No
7440-28-0	Thallium	No	7440-28-0	Thallium, soluble compounds, as Tl	Yes, same CAS
7440-29-1	Thorium	No		Not listed	No
7440-32-6	Titanium	No		Not listed	No
7440-33-7	Tungsten	No	7440-33-7	Tungsten, including: Insoluble compounds Soluble compounds	Yes, same CAS Yes, similar form No
7440-61-1	Uranium	No	7440-61-1	Uranium (natural) soluble & insoluble compounds, as U	Yes, same CAS
7440-62-2	Vanadium	No	1314-62-1	Vanadium, as V_2O_5 Respirable dust & fume	No, different CAS [3]
			12604-58-9	Ferrovanadium dust	No, different CAS
7440-66-6	Zinc	No	7440-66-6	Zinc metal (ID)	Yes, same CAS
			7646-85-7	Zinc chloride fume	No, different CAS
			1314-13-2	Zinc oxide fume	No, different CAS
			1314-13-2	Zinc oxide dust	No, different CAS

[1] Over 95% of the samples were at or below the detection limit for Bismuth of 2 ppm. Limited sampling for tellurium indicates 90% of the samples are below 0.5 ppm. Mineralogical studies have not identified telluride minerals as a significant phase in the deposits. Based on these low levels and deposit mineralogy, no significant bismuth telluride is expected to be found in the ore body or development rock.

[2] Although the CAS numbers do not match, the calcium in the ore, limestone, and aggregate is expected to be in the form of calcium carbonate ($CaCO_3$). For lime, the calcium will be in the form of calcium oxide (CaO).

[3] The principal vanadium mineral in Idaho shale-hosted vanadium deposits is metahewettite ($CaV_6O_{162} \bullet H2O$) (USGS n.d.). Although not a TAP, vanadium in the ore, limestone, and aggregate is conservatively assumed to be V_2O_5 for the purpose of the TAP evaluation included in this HAP/TAP Addendum.

3.3 Screening Level Analysis of TAP Emissions

As discussed in Section 2.0, the highest TAP emissions scenario is Model Scenario W3, that estimates emissions from a potential throughput of 180,000 T/day. Table A in Appendix A

provides a summary of the TAP emissions for Model Scenario W3, identifies whether the sources are covered or addressed by IDAPA 58.01.01.210.20(a) or (b) (Section 3.1), and notes the TAP screening EL. TAPs that exceed the screening EL are highlighted in Table A. These TAPs require further demonstrations of compliance with the applicable ambient air concentration (AAC) and are listed in Table 3 below.

Table 3. TAPs Exceeding the Screening Emission Level

CAS	TAP Name	Carcinogenic	SGP PTE (lb/hr) [1]	Screening EL (lb/hr)
7429-90-5	Aluminum	No	58.50	0.667
7440-38-2	Arsenic	Yes	0.544	0.0000015
7440-39-3	Barium	No	0.659	0.033
7440-41-7	Beryllium	Yes	0.00261	0.000028
7440-43-9	Cadmium	Yes	0.000435	0.0000037
1317-65-3	Calcium Carbonate	No	13.65	0.667
1305-78-8	Calcium Oxide	No	0.696	0.133
592-01-8	Cyanide	No	0.453	0.333
50-00-0	Formaldehyde	Yes	0.00189	0.00051
7439-89-6	Iron	No	15.04	0.067
7439-96-5	Manganese	No	0.244	0.067
7440-02-0	Nickel	Yes	0.00169	0.000027
7723-14-0	Phosphorus	No	0.530	0.007
7664-93-9	Sulfuric Acid	No	2.03	0.067
7440-28-0	Thallium	No	0.00867	0.007
7440-62-2	Vanadium	No	0.0237	0.003

[1] Model Scenario W3, 180,000 T/day Emissions

3.4 Modeling of TAP Emissions

To maintain consistency with the National Ambient Air Quality Standards (NAAQS) compliance analyses reviewed by IDEQ, the TAP modeling was performed using the same IDEQ-approved datasets and model versions described in the SOB from February 18, 2021. TAP modeling was conducted for the 14 modeling scenarios consistent with the NAAQS analyses. Scenario W5 was eliminated from the arsenic modeling, as discussed in Section 3.4.5.

3.4.1 Meteorological Data and Deposition

The meteorological dataset used for the TAP modeling was processed using EPA's Qian and Venkatram (Q&V) meteorological processing method. This method, which does not use the BULKRN keyword, is approved by EPA as a default method.

As discussed in the PTC application, EPA evaluated the performance of the model with the Q&V processed meteorological dataset as part of its model approval determination. This evaluation quantified the bias between the modeled concentrations and the actual observed concentrations. The results of EPA's evaluation showed a conservative bias of the model to overpredict concentrations by a factor of 1.41 to 3.21 (Air Sciences 2020, A-8 of Attachment A). Therefore, the meteorological dataset used in the TAP modeling is expected to predict conservatively high concentrations.

The particulate deposition parameters used in the NAAQS compliance analysis were derived for PM_{10} and $PM_{2.5}$. See Tables 24 and 25 in the SOB from February 18, 2021. Dust-related metal TAP emissions include total particulates (all size fractions of PM up to PM_{30}). Therefore, the deposition parameters for PM were calculated using the same methodology and EPA references used for PM_{10} and $PM_{2.5}$ in the NAAQS compliance analysis. The PM deposition parameters are provided in Table 4.

Table 4. PM Deposition Parameters by Source Category

Source Category	Parameter	PM				
		Bin 1	Bin 2	Bin 3	Bin 4	Bin5
Haul Roads	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.02	0.23	0.75	--	--
	Mass Mean Diameter (µm)	2.50	10.00	30.00	--	--
	Density (g/cm³) (DR average of YP, HF, WE)	2.46	2.46	2.46	--	--
Material Handling (Ore, DR, Limestone)	Bin Upper Diameter (µm)	2.50	5.00	10.00	30.00	--
	Mass Fraction	0.07	0.20	0.20	0.53	--
	Mass Mean Diameter (µm)	2.50	5.00	10.00	30.00	--
	Density (g/cm³) (Ore)	Pit-specific, see Table 5				
	Density (g/cm³) (DR)	Pit-specific, see Table 5				
	Density (g/cm³) (Limestone)	1.09	1.09	1.09	1.09	--
Baghouses	Bin Upper Diameter (µm)	2.50	6.00	10.00	30.00	--
	Mass Fraction	0.25	0.45	0.20	0.10	--
	Mass Mean Diameter (µm)	2.50	6.00	10.00	30.00	--
	Density (g/cm³) (Ore)	Pit-specific, see Table 5				
Diesel Engines	Bin Upper Diameter (µm)	1.00	2.50	6.00	10.00	30.00
	Mass Fraction	0.82	0.08	0.03	0.03	0.04
	Mass Mean Diameter (µm)	1.00	2.50	6.00	10.00	30.00
	Density (g/cm³) (Diesel Combustion)	1.00	1.00	1.00	1.00	1.00
Heaters and Boilers	Bin Upper Diameter (µm)	1.00	2.50	6.00	10.00	30.00
	Mass Fraction	0.23	0.22	0.25	0.09	0.21
	Mass Mean Diameter (µm)	1.00	2.50	6.00	10.00	30.00
	Density (g/cm³) (Propane Combustion)	1.24	1.24	1.24	1.24	1.24
	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--

Source Category	Parameter	PM				
		Bin 1	Bin 2	Bin 3	Bin 4	Bin5
Lime Loading and Unloading (Quick, Pebble)	Mass Fraction	0.05	0.29	0.66	--	--
	Mass Mean Diameter	2.50	10.00	30.00	--	--
	Density (g/cm^3) (Quick)	0.44	0.44	0.44	--	--
	Density (g/cm^3) (Pebble)	0.96	0.96	0.96	--	--
Lime Unloading (Quick, Pebble)	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.09	0.49	0.42	--	--
	Mass Mean Diameter (µm)	2.50	10.00	30.00	--	--
	Density (g/cm^3) (Quick)	0.44	0.44	0.44	--	--
	Density (g/cm^3) (Pebble)	0.96	0.96	0.96	--	--
Cement and Aggregate Loading and Unloading	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.05	0.29	0.66	--	--
	Mass Mean Diameter (µm)	2.50	10.00	30.00	--	--
	Density (g/cm^3) (Cement)	1.44	1.44	1.44	--	--
	Density (g/cm^3) (Aggregate)	1.28	1.28	1.28	--	--
Prill Loading and Unloading	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.05	0.30	0.65	--	--
	Mass Mean Diameter (µm)	2.50	10.00	30.00	--	--
	Density (g/cm^3) (Prill)	0.84	0.84	0.84	--	--
Refining Processes	Bin Upper Diameter (µm)	1.00	2.50	6.00	10.00	30.00
	Mass Fraction	0.72	0.10	0.07	0.03	0.08
	Mass Mean Diameter (µm)	1.00	2.50	6.00	10.00	30.00
	Density (g/cm^3) (Diesel Combustion)	1.00	1.00	1.00	1.00	1.00
Portable Crushing and Screening Plant	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.05	0.32	0.63	--	--
	Mass Mean Diameter (µm)	2.50	10.00	30.00	--	--
	Density (g/cm^3) (DR average of YP, HF, WE)	2.46	2.46	2.46	--	--
Lime Kiln and Ball Mill	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--
	Mass Fraction (Kiln)	0.27	0.28	0.45	--	--
	Mass Fraction (Ball Mill)	0.30	0.54	0.16	--	--
	Mass Mean Diameter (µm)	2.50	10.00	30.00	--	--
	Density (g/cm^3)	1.09	1.09	1.09	--	--
Blasting and Drilling	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.03	0.49	0.48	--	--
	Mass Mean Diameter (µm)	2.50	10.00	30.00	--	--
	Density (g/cm^3) (Ore or DR)	Pit-specific, see Table 5				
Dozing	Bin Upper Diameter (µm)	2.50	10.00	15.00	30.00	--
	Mass Fraction	0.11	0.08	0.06	0.75	--
	Mass Mean Diameter (µm)	2.50	10.00	15.00	30.00	--
	Density (g/cm^3) (Waste)	Pit-specific, see Table 5				

Table 5. Pit-Specific Ore and DR Densities for Deposition

Pit	Material	Density (g/cm^3)
YP	Ore	2.59
BT	Ore	2.00
HF	Ore	2.59
WE	Ore	2.68
YP	DR	2.48
BT	DR	2.00
HF	DR	2.34
WE	DR	2.57
Average (YP, HF, WE)	DR	2.46

3.4.2 Modeling for Non-Carcinogenic TAPs

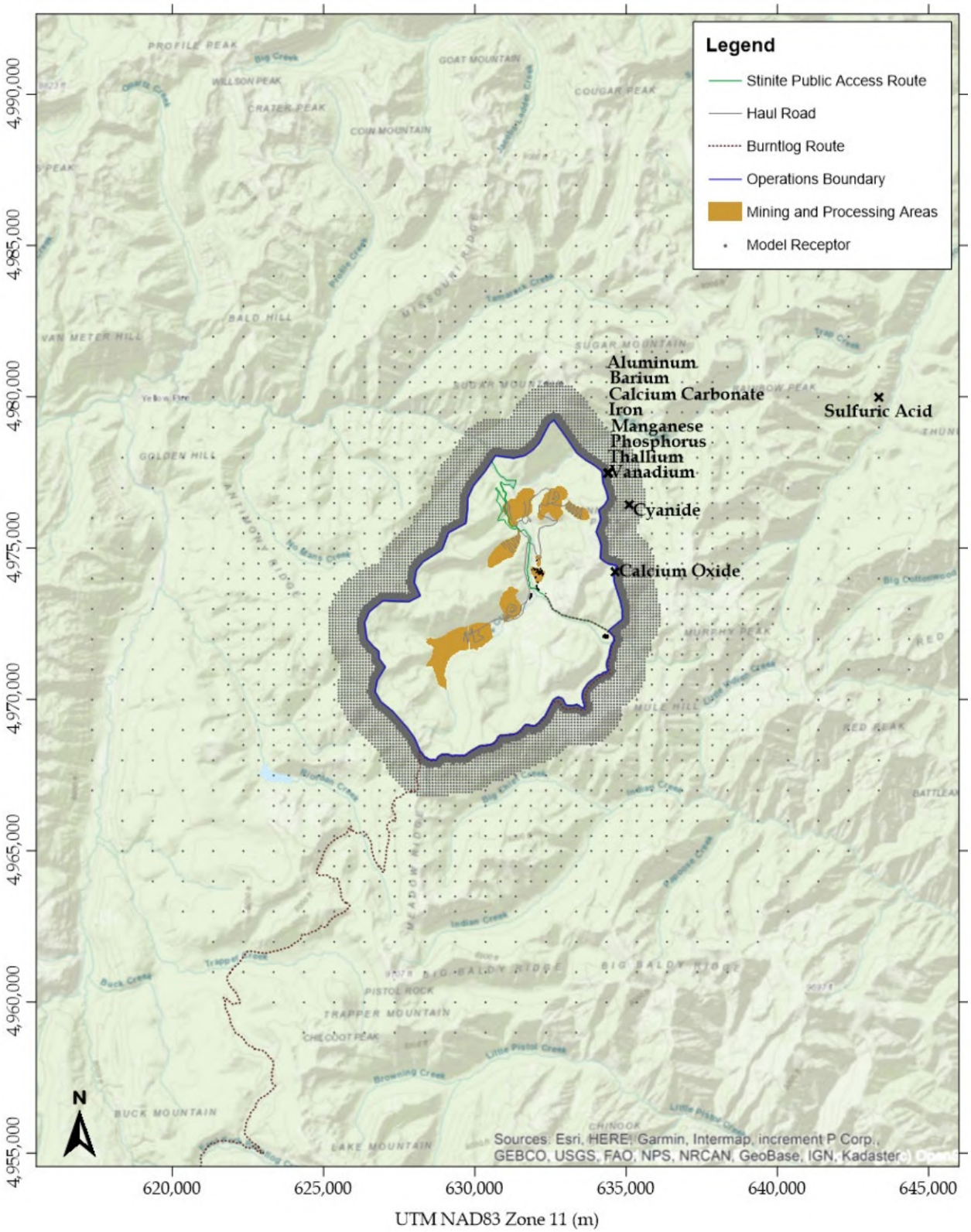
The non-carcinogenic TAPs subject to the AACs per IDAPA 58.01.01.585 were modeled at the emission levels shown in Table 3 above. The maximum 24-hour modeled concentration for each of the 14 modeling scenarios demonstrates compliance with the applicable AAC, as summarized in Table 6.

Table 6. Compliance Demonstration for Non-Carcinogenic TAPs

CAS	TAP Name	Highest Model Scenario	SGP Maximum 24-hr Concentration (µg/m³)	AAC (µg/m³)	TAP Compliance
7429-90-5	Aluminum	W5	6.17	500	Yes
7440-39-3	Barium	W5	0.07	25	Yes
1317-65-3	Calcium Carbonate	W5	1.22	500	Yes
1305-78-8	Calcium Oxide	ALL	0.15	100	Yes
592-01-8	Cyanide	ALL	0.20	250	Yes
7439-89-6	Iron	W5	1.58	50	Yes
7439-96-5	Manganese	W5	0.03	250	Yes
7723-14-0	Phosphorus	W5	0.06	5	Yes
7664-93-9	Sulfuric Acid	ALL	0.41	50	Yes
7440-28-0	Thallium	W5	0.001	5	Yes
7440-62-2	Vanadium	W5	0.002	2.5	Yes

The modeled emissions for each modeling scenario and source are provided in Appendix B. The modeled concentration per modeling scenario is provided in Appendix C. The predicted locations of the maximum concentrations for each non-carcinogenic TAP are presented in Figure 1.

Figure 1. Non-Carcinogenic Maximum TAP Concentration (µg/m³) Locations



3.4.3 Modeling Carcinogenic TAPs

The carcinogenic TAPs subject to the acceptable ambient concentrations for carcinogens (AACC) per IDAPA 58.01.01.586 were modeled using an emission inventory that includes the following T-RACT controls, long-term mining production limits, and other emission inventory refinements, as described below:

- Installing and operating dust collection systems on drilling rigs (T-RACT)
- Capping the haul roads that are outside of the pits and development rock storage facilities (DRSFs) with clean development rock (T-RACT)
- Limiting long-term mining production to 135,000 T/day (5-year rolling total)
- Constructing the Burntlog access road with offsite materials containing background level arsenic concentrations
- Updating the bulldozing emission factor using the SGP site-specific silt content.

The above emission inventory reductions are discussed in more detail in Section 5.0. The T-RACT analysis is provided in Section 6.0. A comparison of the 180,000 T/day TAP emissions shown in Table 3 and the T-RACT TAP emissions is shown in Table 7.

Table 7. Comparison of 180,000 T/day and T-RACT Emissions

CAS	TAP Name	Carcinogenic	180,000 T/day Emissions (lb/hr) [1]	T-RACT Emissions (lb/hr) [2]
7440-38-2	Arsenic	Yes	0.544	0.232
7440-41-7	Beryllium	Yes	0.00261	0.00185
7440-43-9	Cadmium	Yes	0.000435	0.000317
50-00-0	Formaldehyde	Yes	0.00189	0.00189
7440-02-0	Nickel	Yes	0.00169	0.00121

[1] Model Scenario W3 emissions from Table 3
[2] T-RACT emission levels for the demonstration of carcinogenic TAP compliance. See Table A-W3, T-RACT Emissions in Appendix A, pp. A-45 to A-49.

The maximum modeled concentration for each of the 14 modeling scenarios demonstrated compliance with the applicable AACC, as summarized in Table 8. The AACCs listed in Table 8 were increased by a factor of ten (10) per IDAPA 58.01.01.210.12(b); T-RACT adjustment. The SGP maximum concentrations were adjusted to account for the life-of-mine (LOM) production limits, which affect the lifetime exposure, and to account for the elimination of Modeling Scenario W5. See Sections 3.4.4 and 3.4.5 for more detail.

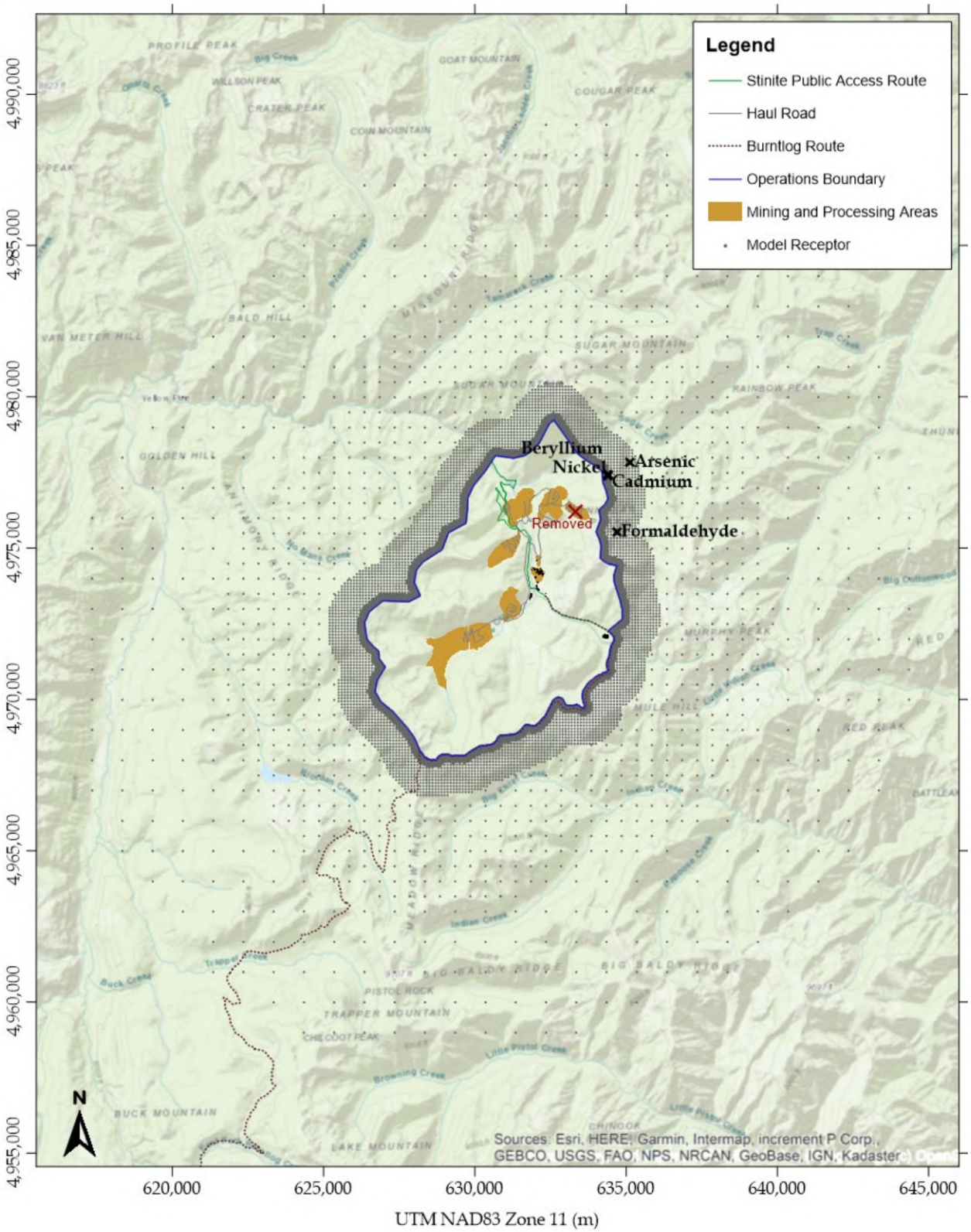
Table 8. Compliance Demonstration for Carcinogenic TAPs

CAS	TAP Name	Model Scenario	SGP Maximum Lifetime Exposure Concentration (µg/m³) [1]	AACC (µg/m³) [2]	TAP Compliance
7440-38-2	Arsenic	W2	0.00095	0.0023	Yes
7440-41-7	Beryllium	W1	0.00001	0.042	Yes
7440-43-9	Cadmium	W1	0.000002	0.0056	Yes
50-00-0	Formaldehyde	ALL	0.00007	0.77	Yes
7440-02-0	Nickel	W1	0.00001	0.42	Yes

[1] The lifetime exposure concentrations are based on the proposed restrictions discussed in Sections 3.4.4 and 3.4.5.
[2] The AACCs are increased by a factor of ten per IDAPA 58.01.01.210.12(b); T-RACT adjustment.

The modeled emissions for each modeling scenario and source are provided in Appendix B. The modeled concentration per modeling scenario is provided in Appendix C. The locations of the maximum concentrations for each carcinogenic TAP are presented in Figure 2.

Figure 2. Carcinogenic Maximum TAP Concentration (µg/m³) Locations



3.4.4 Carcinogenic TAP Modeling Lifetime Exposure Adjustment

The AACCs provided in IDAPA 58.01.01.586 were developed *based on the probability of developing excess cancers over a seventy (70) year lifetime exposure to one (1) microgram per cubic meter (1 ug/m3) of a given carcinogen and expressed in terms of a screening emission level or an acceptable ambient concentration for a carcinogenic toxic air pollutant* (IDAPA 58.01.01.006.125). Therefore, the highest modeled annual carcinogenic TAP concentration from each of the 14 modeling scenarios was evaluated for lifetime exposure as follows:

$$Lifetime\ expsoure\ \left(\frac{\mu g}{m^3}\right) = \frac{Highest\ annual\ concentration\ \left(\frac{\mu g}{m^3}\right) \times 16\ (mine\ operation\ years)}{70\ (years, lifetime\ exposure)}$$

This equation conservatively assumes that the highest annual concentration from the 14 modeling scenarios is repeated for 16 years of mining operation. This is then averaged over 70 years to calculate the 70-year lifetime exposure.

Calculating lifetime exposure based on 16 years of mining operation is also conservative. The annual emissions for carcinogenic TAP modeling are based on 135,000 T/day (see Section 3.4.3) and 365 days per year. Over 16 years, this equates to a potential mining production of 788.4 million tons:

$$\frac{135{,}000\left(\frac{ton}{day}\right) \times 365\left(\frac{day}{year}\right) \times 16\ years}{1{,}000{,}000\left(\frac{ton}{million\ ton}\right)} = 788.4\ million\ tons$$

The actual LOM total production as described in the SGP Refined Proposed Action (ModPRO2) mine plan is only 402.86 million tons (Perpetua 2021a), which is 51.1% of the potential LOM production represented in the above equation and related emissions evaluations.

3.4.5 Arsenic Compliance Demonstration for Modeling Scenarios W1–W5

To demonstrate compliance with the AACC for arsenic, two addition operating limitations were applied:

- The removal of Modeling Scenario W5 as a potential operating scenario
- Limiting the West End pit's LOM potential mining production to 50% of the total LOM potential mining production of 788.4 million tons: 50% * 788.4 = 394.2 million tons

Perpetua Resources has determined that the West End DRSF will not be constructed. This change eliminated Modeling Scenario W5 from the arsenic modeling evaluation. The remaining four West End pit modeling scenarios (W1–W4) are evaluated using the 70-year lifetime exposure equation from Section 3.4.4 and adjusting for the proposed West End pit LOM production limit of 50% of the total production as follows:

$$lifetime\ expsoure\ \left(\frac{\mu g}{m^3}\right) = \left(\frac{\left[Wi\left(\frac{\mu g}{m^3}\right)(50\%) + nonW\left(\frac{\mu g}{m^3}\right)(50\%)\right] \times 16\ (mine\ operation\ years)}{70\ (years, lifetime\ exposure)}\right)$$

Where:

$Wi = the\ modeled\ annual\ arsenic\ concentration\ from\ Scenario\ Wi;\ i = 1\ to\ 4$

$nonW = the\ modeled\ annual\ arsenic\ concentration\ of\ the\ highest\ nonW\ scenario;$

B1, B2, H1, H2, H3, H4, Y1, Y2, or Y3

The above equation was used to calculate the lifetime arsenic exposure from the West End pit scenarios (W1–W4) on a receptor-by-receptor basis. Combining the concentrations from Modeling Scenarios W1–W4 with the highest concentration from the remaining non-West End pit scenarios (B1, B2, H1, H2, H3, H4, Y1, Y2, or Y3) ensures that the maximum concentration is evaluated.

Calculating lifetime arsenic exposure based on the proposed West End pit LOM production limit of 50% of the total production is conservative. The actual LOM total production from the West End pit as described in the ModPRO2 mine plan is only 198.26 million tons (Perpetua 2021a), which is 50.3% of the proposed West End pit LOM production limit of 394.2 million tons.

4.0 COMPARISON OF ACTUAL ARSENIC MODELING TO POTENTIAL ARSENIC MODELING

Additional analyses of arsenic emissions were prompted by public comments on the draft PTC. IDEQ requested that Perpetua Resources conduct an arsenic modeling analysis based on the actual mining operation and production described in the ModPRO2 mine plan. Those modeling results were submitted to IDEQ in a report on July 8, 2021, titled "Stibnite Gold Project Permit to Construct Application Arsenic Modeling Addendum" (Air Sciences 2021).

While that report provided an assessment of the actual arsenic concentrations expected from the actual mining operation and production over the life of the SGP ("actual analysis"), the analysis described in Section 3.0 above is based on potential operating scenarios ("potential analysis"). These analyses ensure that public health is protected under all operating conditions.

A comparison between the actual analysis and the potential analysis for the lifetime exposure of arsenic is summarized in Table 9.

Table 9. Actual Analysis vs. Potential Analysis for Arsenic Lifetime Exposure

Model Parameter	Actual Data	Potential Data	Actual Data Basis	Potential Data Basis
Process emissions (lb/hr)	0.004514	0.004514	Equipment design rate	Equipment design rate
Mining emissions (lb/hr); varies	Max: 0.0854 Min: 0.0058 Avg: 0.0451	Max: 0.232 Min: 0.061	ModPRO2 – 16 years of operation	14 potential worst-case scenarios
Emissions included in modeling (lb/yr)	100%	98%	Actual analysis of all emissions	Includes IDAPA 58.01.01.210.20
LOM production (million tons)	402.86	788.4	ModPRO2	135,000 ton/day * 365 day/yr * 16 years
Lifetime exposure modeling	Average concentration over 16 years of operation	Highest scenario concentration assumed for 16 years	Actual analysis	Potential worst-case analysis
Maximum modeled concentration ($\mu g/m^3$)	0.00015	0.00095	Actual analysis	Potential worst-case analysis
Applicable AACC ($\mu g/m^3$)	0.0023	0.0023	IDAPA 58.01.01. 210.12(b) and .586	IDAPA 58.01.01. 210.12(b) and .586

A brief discussion of Table 9 is provided below:

- AACC Results: In both the actual and potential analyses, the maximum modeled arsenic concentrations are below the AACC, demonstrating compliance with IDAPA 58.01.01.210.

- Process emissions: The process arsenic emissions in both analyses are identical. This is because both emission inventories were based on the maximum design rates of the process equipment.

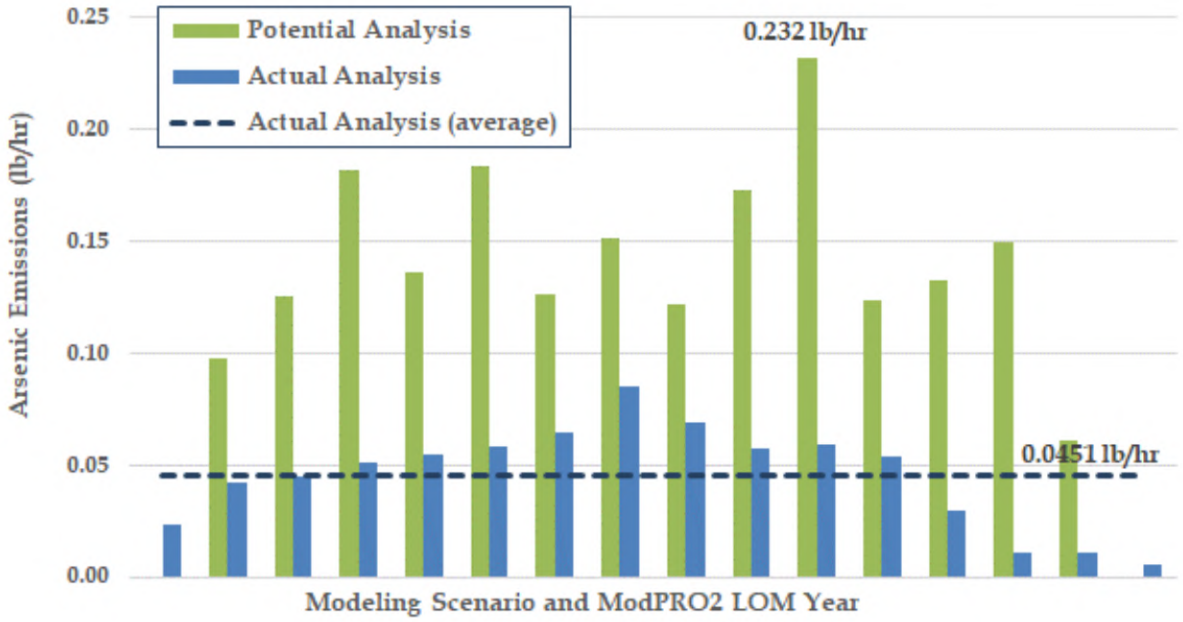
- Mining emissions: The arsenic emissions in the actual analysis (0.0451 lb/hr average) are only 19% of the arsenic emissions in the potential analysis (0.232 lb/hr highest scenario). This is because the actual mining operation and production activities (e.g., drilling, blasting, material product, hauling miles, etc.) in ModPRO2 are far less than the potential mining (PTC) operating scenarios. Figure 3 compares the ModPRO2 arsenic emissions from mining for each year of operation (actual analysis) to the PTC arsenic emissions from mining for each worst-case operating scenario (potential analysis).

- In both analyses, all the arsenic emissions are included in the modeling, except emissions from covered or addressed sources, IDAPA 58.01.01210.20(a) and (b). See Section 3.1.

- The actual analysis LOM production of 402.86 million tons is 51.1% of the potential analysis production of 788.4 million tons.

- When modeling the lifetime arsenic exposure, the actual analysis is based on modeling each year of the ModPRO2 mine plan and then averaging the yearly results on a receptor-by-receptor basis. In addition to the lower actual arsenic emissions, the mining activity locations vary, which reduced the average arsenic concentration at any given location outside the operations boundary. In contrast, the potential analysis is based on higher (potential) emissions and the highest modeling scenario, which are assumed to occur for 16 consecutive years. This potential approach resulted in significantly higher and more conservative arsenic hot-spot concentrations.

Figure 3. Actual Arsenic Mining Emissions vs. Potential Arsenic Mining Emissions



The concentrations and maximum locations of the arsenic lifetime exposure (70 years) are presented in Figure 4 for the actual analysis and Figure 5 for the potential analysis. As shown in these figures, the maximum arsenic concentrations are below the applicable AACC per IDAPA 58.01.01.210.12(b) and 586.

Figure 4. Actual Arsenic Concentrations (µg/m³) and Maximum Location

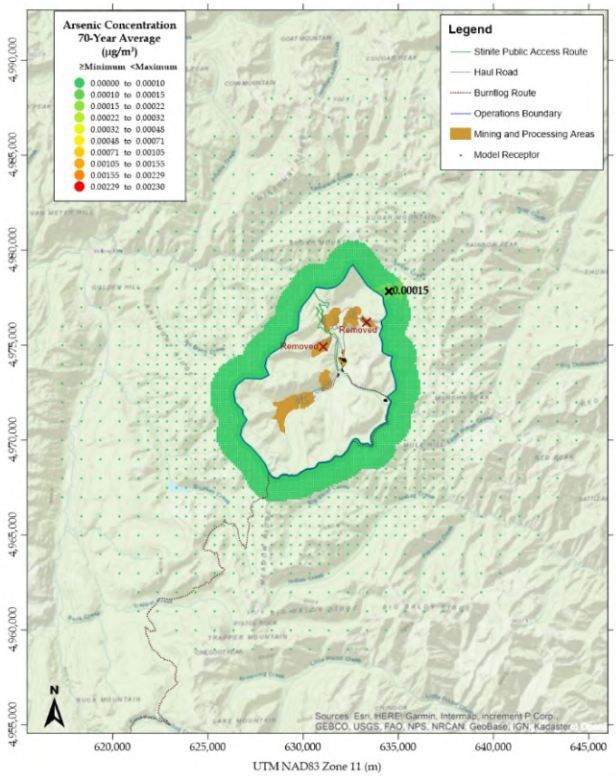
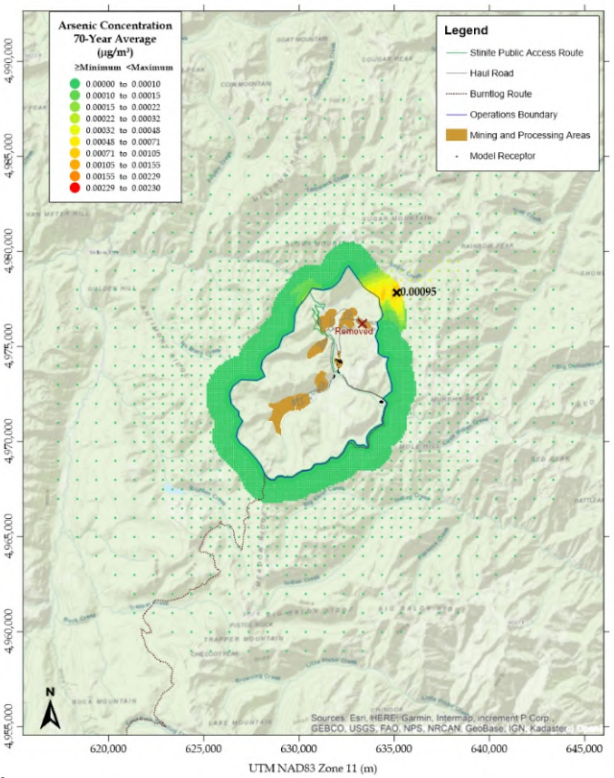


Figure 5. Potential Arsenic Concentrations (µg/m³) and Maximum Location



5.0 EMISSION INVENTORY FOR CARCINOGENIC TAPS

As discussed in Section 3.4.3, carcinogenic TAPs were modeled using an emission inventory adjusted for T-RACT controls, long-term mining production limits, and other refinements. These emission inventory changes are described in the following sections. The detailed emission calculations for the T-RACT emission inventory are provided in Appendix A (HAP/TAP Emission Calculations – Scenario W3, T-RACT Emissions).[8] The changes to these emission inventory inputs are highlighted on page A-41 of Appendix A.

5.1 Drilling Dust Control System

To reduce dust-related metal TAP emissions from drilling, Perpetua Resources will install and operate drilling rigs mounted with dust collection systems. *These systems have the ability to operate in various climates, i.e., they are not subject to freezing at lower temperatures as with the use of water, and they can be up to 99 percent efficient if properly maintained* (CDC 2012). The arsenic emissions inventory in Appendix A conservatively assumes a dust control efficiency of 90% for these systems.

5.2 Haul Road Capping

To reduce dust-related arsenic emissions from haul roads, Perpetua Resources will cap the haul roads that are outside of the pits and DRSFs with clean (low arsenic) development rock. Haul roads within the pits and DRSFs cannot be capped with this material because of steep grades and periodic road rerouting as mining areas develop. The median arsenic concentration of the clean development rock is 90 parts per million (ppm) (Perpetua 2021g).

5.3 Long-Term Mining Production Limits

To limit long-term dust-related metal TAP emissions, Perpetua Resources proposes limiting mining production to 135,000 T/day based on a 5-year rolling averaging period. This long-term mining production limit will be in addition to the current short-term daily limit of 180,000 T/day.

Limiting the long-term mining production limit to 135,000 T/day (5-year rolling average) is conservative. The highest 5-year rolling average mining production rate as described in ModPRO2 is only 95,700 T/day (Perpetua 2021a), which is 70.9% of the proposed limit.

[8] HAP/TAP Emission Calculations – Scenario W3, T-RACT: The HAP and TAP emissions based on T-RACT controls, a long-term mining production limit of 135,000 T/day (5-year rolling average), other refinements, and the highest emissions scenario (Modeling Scenario W3).

5.4 Burntlog Access Road Refinement

To reduce dust-related arsenic emissions from vehicle travel on the Burntlog access road, Perpetua Resources will construct this road with borrow material located outside of the mine site ambient air boundary. Analyses of the borrow sites show low arsenic levels of 2.5 ppm (ALS 2018), which are consistent with the background soil levels (DHHS 2007).

5.5 Bulldozing Refinement

Perpetua Resources and Air Sciences conducted a thorough review of the SGP emissions inventory to identify any potential dust-related metal TAP emission control measures (as discussed in the previous sections) and emission factor refinements. The only emission factor refinement identified was changing the bulldozing emission factor silt content from the EPA default of 6.9% to the SGP site-specific silt content of 4.0% (Midas Gold 2015). EPA recommends the use of site-specific data when available.[9]

[9] *In using the equations to estimate emissions from sources found in a specific western surface mine, it is necessary that reliable values for correction parameters be determined for the specific sources of interest if the assigned quality ratings of the equations are to be applicable. For example, actual silt content of coal or overburden measured at a facility should be used instead of estimated values. In the event that site-specific values for correction parameters cannot be obtained, the appropriate geometric mean values from Table 11.9-3 may be used, but the assigned quality rating of each emission factor equation should be reduced by 1 level (e.g., A to B)* (EPA 1998).

6.0 T-RACT ANALYSIS

Per IDAPA 58.01.01.210.14(a), this section documents the T-RACT control technologies.

6.1 Drilling Dust Control System

As discussed in Section 5.1, Perpetua Resources will install and operate drilling rigs mounted with dust collection systems. The following paragraphs evaluate this control as T-RACT:

Identification of all possible control technologies

Drilling operations create dust-related metal TAP emissions. The possible control technologies for these emissions are as follows:

- Applying best management practices
- Wet drilling with water injection
- Dry drilling with dust collectors

Best management practices include: (1) avoiding drilling operations during high dust conditions, and (2) shrouding drill areas to limit dust emissions.

Wet drilling includes injected water flows through the center of the drill and out though the drill bit to reduce dust emissions by 96% to 98%.[10]

Dry drilling includes rigs equipped with dust collection systems that shroud dust generated from the drilling area, capture, and remove dust through a dust collection system composed of an exhaust fan and filters that can achieve up to 99% control efficiency (CDC 2012).

Elimination of technologically infeasible or unreasonable technologies

Wet drilling at the SGP has the following disadvantages:

- It is subject to freezing at the low temperatures expected for the SGP location.
- It can result in drill bit plugging, drill rotation binding, and drill bit degradation.
- A wet drill hole can interfere with the blasting agent.

Based on the above disadvantages of wet drilling, it is considered an infeasible or unreasonable technology for the SGP.

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[10] *Testing has demonstrated that dust control efficiencies of up to 98 percent can be obtained using the water separator sub while dust control efficiencies of wet drilling without the water separator sub were 96 percent* (CDC 2012).

Ranking the remaining technologies by control effectiveness

The ranking of the possible control technologies for drilling by control effectiveness is as follows (highest to lowest):

1. Dry drilling with dust collectors – up to 99% control efficiency
2. Best management practices

Evaluation of the most effective control technology and selection of T-RACT

Perpetua Resources selects the top (most effective) control technology of dry drilling with dust collectors as T-RACT. Selecting the top control negates the need for considering economic, energy, and environmental impacts regarding the other control technologies.

6.2 Haul Road Dust and Arsenic Control

Dust emissions from unpaved roads are caused by vehicle traffic on these roads. Particles are lifted and dropped from the rolling wheels, and the turbulent wake behind the vehicles causes these particulates to become air borne. Dust control options include surface improvement (paving) or surface treatment (chemical suppressant application or watering).

As discussed in the SOB from February 18, 2021, Perpetua Resources will control dust emissions from haul roads by treating the surface with frequent watering and the periodic application of a chemical suppressant. Reducing dust emissions reduces dust-related metal TAP emissions. In addition, Perpetua Resources will reduce arsenic emissions by capping the haul roads outside of the pits and DRSFs with clean (low arsenic) development rock, as discussed in Section 5.2. The following sections evaluate these control measures as T-RACT.

6.2.1 Dust Control Technologies

Identification of all possible control technologies

Vehicle traffic on unpaved haul roads creates dust-related metal TAP emissions. The possible control technologies for these emissions are as follows:

- Paving
- Application of a chemical dust suppressant
- Watering

Paving: *The control efficiencies achievable by paving can be estimated by comparing emission factors for unpaved and paved road conditions* (EPA 2006). The particulate emission factor for a paved road with a silt loading of 0.2 g/m^2 (based on the EPA default value for the SGP average daily traffic of 500–5,000 trips per day) (EPA 2011a) and the SGP average vehicle weight of 182.6 tons is

0.515 lb/VMT. The SGP unpaved road particulate emission factor is 14.43 lb/VMT (uncontrolled). Based on these emission factors, the estimated control efficiency of paving the haul roads is 96%.

Dust suppressant and watering: The SGP dust emissions from unpaved haul roads are calculated based on a surface treatment control efficiency of 90% (annual basis) for the application of a chemical dust suppressant supplemented with frequent watering. As discussed in the SGP Application, this control efficiency is supported by EPA's AP-42 13.2.2 referenced test reports, which show that a chemical dust suppressant alone can achieve 90% to 99% control efficiency and 98% for magnesium chloride in particular (Air Sciences 2020, Appendix A to Attachment A). A control efficiency of 90% is also supported by the control efficiency limits established under Reasonable Achievable Control Technology (RACT), Best Available Control Technology (BACT), and Lowest Achievable Emission Rate (LAER) determinations under EPA's New Source Review permitting program.

The EPA RACT/BACT/LAER Clearinghouse (RBLC) database contains case-specific information on the air pollution technologies required by major stationary sources seeking a permit under EPA's New Source Review (NSR) program. This database was queried for all listings of air pollution technologies for unpaved roads using chemical dust suppressants or a combination of chemical dust suppressants and watering. The results of the query identified 10 projects containing a control efficiency of 90% or greater for unpaved roads. These determinations are listed in Table 10.

Table 10. EPA RBLC Determinations for 90% or Greater Control Efficiency of Unpaved Roads

State	Facility Name	RBLC-ID	Dust Control	Dust Control Efficiency
AK	Donlin Gold Project	AK-0084	water/chem	90%
AR	Turk Power Plant	AR-0094	water/chem	90%
CO	Rio Grande Portland Cement Corp.	CO-0043	water/chem	90%
IN	Nucor Steel	IN-0034	chem	90%
LA	Nucor Steel Louisiana	LA-0239	water/chem	90%
MO	Lafarge Corp.	MO-0048	chem	90%
NV	Sloan Quarry	NV-0045	chem	98%
NV	Nellis Air Force Base	NV-0047	water/chem	90%
OH	Unlimited Concrete	OH-0126	water/chem	90%
OH	Unlimited Concrete	OH-0131	water/chem	90%

(EPA 2021)

Elimination of technologically infeasible or unreasonable technologies

Paving haul roads at the SGP has the following disadvantages:

- The paving of haul roads is not conventional practice at mining operations.
- Paved highway weight limits are only approximately 20,000 pounds (10 tons).
- Paving is costly.

The conventional practice for mining operations is to utilize unpaved haul roads with treated surfaces to control fugitive dust. Haul trucks are single axle vehicles with a gross loaded weight of 60 tons to 685 tons. The loaded weight range for the SGP haul trucks is 60 to 260 tons. These weights significantly exceed regulatory weight limits for paved highways of 10 tons. Furthermore, the SGP mining activity locations move as mining progresses. This requires haul roads to be rerouted as necessary. Due to the temporary nature of hauling routes and the heavy weight of haul trucks, paving is considered an infeasible or unreasonable technology for the SGP.

Ranking the remaining technologies by control effectiveness

The ranking of the possible control technologies for drilling by control effectiveness is as follows (highest to lowest):

1. Application of a chemical dust suppressant – 90% to 99% control efficiency

2. Watering – 75% to 95% control efficiency (EPA 2006, Figure 13.2.2-2)

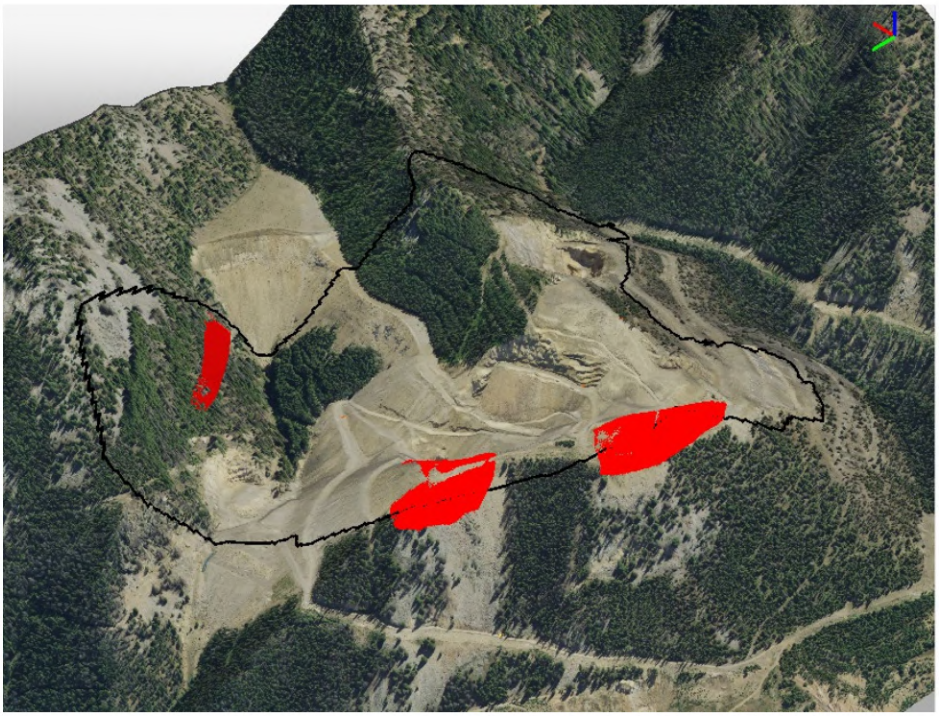
Evaluation of the most effective control technology and selection of T-RACT

After eliminating paving as a viable control option, Perpetua Resources selects the next most effective control technologies of the application of a chemical dust suppressant supplemented with frequent watering as T-RACT.

6.2.2 Arsenic Control Technologies

After applying T-RACT for dust control, as discussed in Section 6.2.1, dust-related arsenic emissions can only be further reduced by capping the haul roads with clean (low-arsenic) development rock. The median arsenic concentration of the SPG onsite material is 667 ppm (Midas Gold 2017c). However, there are quartzite rock deposits at the West End pit that have significantly lower mineralization and, thus, lower arsenic levels. The median arsenic concentration of this quartzite rock is 90 ppm (Perpetua 2021g), and there is approximately 3 million tons of this material available. Figure 6 shows the locations of the quartzite rock deposits.

Figure 6. Quartzite Rock Areas



Perpetua Resources proposes capping the haul roads that are outside of the pits and DRSFs with clean (low-arsenic) development rock as a T-RACT work practice, in addition to the T-RACT dust control measures discussed in Section 6.2.1. Haul roads within the pits and DRSFs cannot be capped with this material because of steep grades and periodic road rerouting as mining areas develop.

7.0 PROPOSED PERMIT CONDITIONS FOR CARCINOGENIC TAP COMPLIANCE

IDEQ is required to establish limits and standards as part of the permit to construct to ensure compliance with the TAP provisions in accordance with IDAPA 58.01.01.210.12(d) and 14(e). Per these two rules, Perpetua Resources proposes the following permit conditions:

7.1 Conditions per IDAPA 58.01.01.210.12(d)

Per IDAPA 58.01.01.210.12(d), *[t]he Department shall include emission limits and other permit terms for the toxic air pollutant in the permit to construct that assure that the facility will be operated in the manner described in the preconstruction compliance demonstration*. As discussed in Section 5.2, Perpetua Resources is proposing long-term mining production limits to demonstrate compliance with carcinogenic TAPs. The following are proposed permit conditions to address this TAP provision:

- The permittee shall haul no more than 135,000 tons per day (T/day) of ore and rock, based on a 5-year rolling average.
    - Each year, the permittee shall monitor and record the amount of ore and rock transported on haul trucks in tons per year (T/yr), and calculate the 5-year rolling average (T/day) based on 365 days per year.
- The permittee shall haul no more than 788.4 million tons (MT) of ore and rock from all deposits over the life of the mine.
- The permittee shall haul no more than 394.2 MT of ore and rock from the West End deposit over the life of the mine.
    - Each year, the permittee shall monitor and record the amount of ore and rock transported on haul trucks (T/yr) from all deposits and the amount of ore and rock transported on haul trucks (T/yr) from the West End deposit, and calculate the life-of-mine rolling total (MT) for each.

7.2 Conditions per IDAPA 58.01.01.210.14(e)

Per IDAPA 58.01.01.210.14(e), *[i]f the Department determines that the applicant has proposed T-RACT, the Department shall determine which of the options, or combination of options, will result in the lowest emission of toxic air pollutants, develop the emission standards constituting T-RACT and incorporate the emission standards into the permit to construct.* As discussed in Section 6.2, Perpetua Resources is proposing T-RACT controls to demonstrate compliance with carcinogenic TAPs. The following are proposed permit conditions to address this TAP provision:

- The permittee shall use drilling rigs equipped with dust collection systems. Control efficiency: 90%.
    - Within 60 days after startup, the permittee shall develop and maintain an Operation and Maintenance (O&M) manual. The O&M manual shall be a permittee-developed document based upon, but independent from, manufacturer-supplied operating manuals. The permittee shall operate the dust collection systems in accordance with the O&M manual at all times. The requirements in the O&M manual shall be incorporated by reference to this permit and shall be enforceable permit conditions. The O&M manual shall be submitted to DEQ within 60 days after initial startup.
- The permittee shall cap haul roads that are outside of the pits and DRSFs with low-arsenic material.
    - The permittee shall develop and maintain a plan that:
        - identifies the low-arsenic quartzite rock deposits in the West End pit based on core sample analyses,
        - requires periodic inspections (at least quarterly) of the capped haul roads and recapping as needed, and
        - includes record keeping of the inspections and any recapping of roads, noting the date and road section.
    - The permittee shall use the low-arsenic quartzite rock deposits from the West End pit, or other material with equal or lower arsenic concentration, as capping material.
        - If other material is used, it must be analyzed for arsenic concentration and a record of the median arsenic concentration shall be maintained.

The Draft PTC currently includes conditions for treating haul road surfaces with a chemical suppressant and water to control 90% of the dust (on an annual basis). See Conditions 1.2, 2.1–2.6, 2.8, 3.2, and 3.9. Therefore, no new conditions are needed or proposed for this dust control practice.

8.0 MERCURY EMISSIONS ANALYSIS

A complete inventory of mercury emissions is provided in Appendix A, as discussed in Section 2.0. This section categorizes these emissions into mercury emissions covered or not covered by IDAPA 58.01.01.215. According to IDAPA 58.01.01.215:

No owner or operator may commence construction or modification of a stationary source or facility that results in an increase in annual potential emissions of mercury of twenty-five (25) pounds or more unless the owner or operator has obtained a permit to construct under Sections 200 through 228 of these rules. The permit to construct application shall include an MBACT analysis for the new source or sources for review and approval by the Department. A determination of applicability under Section 215 shall be based upon the best available information. Fugitive emissions shall not be included in a determination of applicability under Section 215.

01. Exemptions. New or modified stationary sources within a source category subject to 40 CFR Part 63 are exempt from the requirements of Section 215.

Table 11 summarizes the SGP mercury sources and potential emissions for the highest emissions year (Model Scenario W3, 180,000 T/day Emissions). This table also provides the mercury emissions without considering the above exemptions, the exemption criteria, and the non-exempt mercury emissions for each source. As shown in this table, under IDAPA 58.01.01.215.01, the total potential non-exempt mercury emissions are 5.40E-5 ton/yr (0.108 lb/yr), which is well below the 25 lb/yr emission threshold.

Table 11. Mercury Source and Emissions Summary

Source	All Emissions ton/yr	Fugitive/ NESHAP Exemption	Non-Exempt Emissions ton/yr
Mining			
Fugitive Dust (drilling, blasting, excavating, hauling, etc.)	0.0021	Fugitive	0
Fugitive Evaporative (pits, tailings, DRSFs, stockpiles)	0.0036	Fugitive	0
Ore Processing			
Crushing, Screening, and Transfers	2.47E-05		2.47E-05
Prill Silos	0		0
Ore Concentration and Refining			
Autoclave	0.00010	7E	0
EW, Pregnant Tank, Retort, Furnace, Carbon Kiln	0.0017	7E	0
Process Heating			
POX, Carbon Kiln, Propane Vaporizers, Solution Heater	8.28E-06		8.28E-06
Lime Production			
Lime Kiln Combustion	2.09E-05	5A	0
Limestone Crushers, Screens, Mill, and Transfers	3.86E-07		3.86E-07
Lime Kiln, Kiln Feed, Lime Mill, and Pebble Lime Silo	0.0010	5A	0
Lime Silos and Lime Mill Crushing	4.05E-09		4.05E-09
Aggregate Production			
Portable Crushers, Screens, and Transfers	1.10E-07		1.10E-07
Concrete Production			
Central Mixer	0		0
Cement Silo Loading and Unloading	0		0
Aggregate Bin	6.90E-08		6.90E-08
HVAC			
Heaters	2.04E-05		2.04E-05
Emergency Power			
Emergency Generators and Fire Pump	0	4Z	0
Fuel Storage			
Gasoline Fuel Tanks	0	6C	0
Total	**0.00863**		**5.40E-05**

9.0 REFERENCES

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Appendix A – HAP/TAP Emission Calculations

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Table A-W3. HAP/TAP Emissions and Exemptions – Scenario W3, T-RACT Emissions A-45

Air Sciences Inc.	PROJECT TITLE: Stibnite Gold Project	BY: K. Lewis
	PROJECT NO: 335-20-3	PAGE: 1 OF: 19 SHEET: Calcs
AIR EMISSION CALCULATIONS	SUBJECT: HAP/TAP Emission Calculations	DATE: October 4, 2021

Model Scenario W3 180,000 T/day Emissions

Hazardous Air Pollutants (HAP)/Toxic Air Pollutants (TAP) Emissions Summary

		Emissions[1]									
		Fuel Combustion		Process/Prod/Leach		Mining		Total			
CAS	HAP/TAP	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	HAP	TAP
106-99-0	1,3-Butadiene	8.4E-07	3.7E-06	0	0	0	0	8.4E-07	3.7E-06	Y	Y
91-57-6	2-Methylnaphthalene	1.1E-06	4.6E-06	0	0	0	0	1.1E-06	4.6E-06	Y	N
56-49-5	3-Methylchloranthrene	7.8E-08	3.4E-07	0	0	0	0	7.8E-08	3.4E-07	Y	Y
57-97-6	7,12-Dimethylbenz(a)anthracene	7.6E-07	3.0E-06	0	0	0	0	7.6E-07	3.0E-06	Y	N
83-32-9	Acenaphthene	5.7E-06	7.1E-06	0	0	0	0	5.7E-06	7.1E-06	Y	N
208-96-8	Acenaphthylene	1.1E-05	1.4E-05	0	0	0	0	1.1E-05	1.4E-05	Y	N
75-07-0	Acetaldehyde	2.5E-05	1.1E-04	0	0	0	0	2.5E-05	1.1E-04	Y	Y
107-02-8	Acrolein	1.6E-05	2.0E-05	0	0	0	0	1.6E-05	2.0E-05	Y	Y
120-12-7	Anthracene	1.7E-06	2.4E-06	0	0	0	0	1.7E-06	2.4E-06	Y	N
7440-36-0	Antimony	0	0	5.7E-04	2.5E-03	1.9E-02	8.2E-02	1.9E-02	8.5E-02	Y	Y
7440-38-2	Arsenic	8.7E-06	3.8E-05	4.5E-03	2.0E-02	0.54	2.38	0.55	2.40	Y	Y
56-55-3	Benz(a)anthracene	3.1E-07	1.4E-06	0	0	0	0	3.1E-07	1.4E-06	Y	Y
71-43-2	Benzene	3.6E-04	1.6E-03	7.0E-03	3.1E-02	0	0	7.4E-03	3.2E-02	Y	Y
50-32-8	Benzo(a)pyrene	1.4E-07	6.1E-07	0	0	0	0	1.4E-07	6.1E-07	Y	Y
205-99-2	Benzo(b)fluoranthene	4.4E-07	1.9E-06	0	0	0	0	4.4E-07	1.9E-06	Y	Y
191-24-2	Benzo(g,h,i)perylene	7.5E-07	1.1E-06	0	0	0	0	7.5E-07	1.1E-06	Y	N
207-08-9	Benzo(k)fluoranthene	1.5E-07	6.6E-07	0	0	0	0	1.5E-07	6.6E-07	Y	Y
7440-41-7	Beryllium	5.2E-07	2.3E-06	4.3E-04	1.9E-03	2.6E-03	1.1E-02	3.0E-03	1.3E-02	Y	Y
92-52-4	Biphenyl	0	0	4.4E-05	1.9E-04	0	0	4.4E-05	1.9E-04	Y	Y
7440-43-9	Cadmium	4.8E-05	2.1E-04	4.1E-04	1.8E-03	4.1E-04	1.8E-03	8.7E-04	3.8E-03	Y	Y
75-15-0	Carbon Disulfide	0	0	1.4E-02	6.3E-02	0	0	1.4E-02	6.3E-02	Y	Y
7440-47-3	Chromium	6.6E-05	2.7E-04	6.1E-04	2.5E-03	7.3E-03	3.2E-02	8.0E-03	3.5E-02	Y	Y
18540-29-9	Cr (VI)	0	0	3.4E-07	1.5E-06	0	0	3.4E-07	1.5E-06	Y	Y
218-01-9	Chrysene	5.8E-07	2.5E-06	0	0	0	0	5.8E-07	2.5E-06	Y	Y
7440-48-4	Cobalt	4.0E-06	1.6E-05	4.7E-04	2.0E-03	3.3E-03	1.4E-02	3.7E-03	1.6E-02	Y	Y
592-01-8	Cyanide	0	0	0.45	1.99	0	0	0.45	1.99	Y	Y
53-70-3	Dibenzo(a,h)anthracene	1.8E-07	7.7E-07	0	0	0	0	1.8E-07	7.7E-07	Y	Y
106-46-7	Dichlorobenzene	5.7E-05	2.3E-04	0	0	0	0	5.7E-05	2.3E-04	Y	Y
206-44-0	Fluoranthene	5.5E-06	7.0E-06	0	0	0	0	5.5E-06	7.0E-06	Y	N
86-73-7	Fluorene	1.7E-05	2.1E-05	0	0	0	0	1.7E-05	2.1E-05	Y	N
50-00-0	Formaldehyde	3.3E-03	1.5E-02	0	0	0	0	3.3E-03	1.5E-02	Y	Y
110-54-3	Hexane	8.5E-02	0.34	3.1E-02	0.14	0	0	0.12	0.48	Y	Y
7647-01-0	Hydrogen Chloride	0	0	0.99	3.67	0	0	0.99	**3.67**	Y	Y
193-39-5	Indeno(1,2,3-cd)pyrene	2.2E-07	9.6E-07	0	0	0	0	2.2E-07	9.6E-07	Y	Y
7439-92-1	Lead	0	0	4.8E-04	2.1E-03	6.5E-03	2.9E-02	7.0E-03	3.1E-02	Y	N
7439-96-5	Manganese	1.8E-05	7.2E-05	4.6E-03	1.7E-02	0.24	1.07	0.25	1.08	Y	Y
7439-97-6	Mercury	1.2E-05	5.0E-05	6.9E-04	2.9E-03	1.3E-03	5.7E-03	2.0E-03	8.6E-03	Y	N
91-20-3	Naphthalene	1.9E-04	3.1E-04	1.9E-03	8.5E-03	0	0	2.1E-03	8.8E-03	Y	Y
7440-02-0	Nickel	9.1E-05	4.0E-04	4.6E-04	2.0E-03	1.6E-03	7.1E-03	2.2E-03	9.5E-03	Y	Y
85-01-8	Phenanthrene	5.1E-05	6.3E-05	0	0	0	0	5.1E-05	6.3E-05	Y	N
108-95-2	Phenol	0	0	2.4E-04	1.1E-03	0	0	2.4E-04	1.1E-03	Y	Y
7723-14-0	Phosphorus	0	0	5.6E-03	2.3E-02	0.53	2.32	0.54	2.34	Y	Y
129-00-0	Pyrene	5.0E-06	6.6E-06	0	0	0	0	5.0E-06	6.6E-06	Y	N
7782-49-2	Selenium	1.1E-06	4.6E-06	4.1E-04	1.8E-03	3.3E-04	1.4E-03	7.4E-04	3.2E-03	Y	Y
108-88-3	Toluene	5.2E-04	1.1E-03	3.2E-02	0.14	0	0	3.2E-02	0.14	Y	Y
1330-20-7	Xylene	2.5E-04	3.0E-04	3.1E-02	0.14	0	0	3.2E-02	0.14	Y	Y
Total HAP		9.0E-02	0.36	1.58	6.25	1.36	5.95	3.03	12.56		

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

	0.2155	0.8650	8.3307	31.6474	86.1858	377.4936	94.7319	410.0060
TRUE	0.2155	0.8650	8.3307	31.6474	86.1858	377.4936	94.7319	410.0060
	chk	chk	chk-15	chk	chk	chk	chk	chk

Hazardous Air Pollutants (HAP)/Toxic Air Pollutants (TAP) Emissions Summary - continued

		Emissions[1]									
		Fuel Combustion		Process/Prod/Leach		Mining		Total			
CAS	**Non-HAP TAP**	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	HAP	TAP
7429-90-5	Aluminum	0	0	0.65	2.58	57.86	253.41	58.50	255.98	N	Y
7440-39-3	Barium	2.1E-04	8.4E-04	6.6E-03	2.7E-02	0.65	2.86	0.66	2.88	N	Y
1317-65-3	Calcium Carbonate	0	0	2.24	8.12	11.41	49.97	13.65	58.09	N	Y
1305-78-8	Calcium Oxide	0	0	0.70	0.95	0	0	0.70	0.95	N	Y
7440-50-8	Copper	4.0E-05	1.6E-04	4.9E-04	2.1E-03	4.1E-03	1.8E-02	4.6E-03	2.0E-02	N	Y
110-82-7	Cyclohexane	0	0	1.0E-03	4.6E-03	0	0	1.0E-03	4.6E-03	N	Y
7783-06-4	Hydrogen Sulfide	0	0	0.90	3.94	0	0	0.90	3.94	N	Y
7439-89-6	Iron	0	0	0.21	0.81	14.83	64.96	15.04	65.77	N	Y
7439-98-7	Molybdenum	5.2E-05	2.1E-04	4.2E-04	1.8E-03	8.1E-04	3.6E-03	1.3E-03	5.6E-03	N	Y
109-66-0	Pentane	0.12	0.50	0	0	0	0	0.12	0.50	N	Y
7440-22-4	Silver	0	0	4.1E-04	1.8E-03	4.1E-04	1.8E-03	8.2E-04	3.6E-03	N	Y
7664-93-9	Sulfuric Acid	0	0	2.03	8.89	0	0	2.03	8.89	N	Y
7440-28-0	Thallium	0	0	5.2E-04	2.2E-03	8.1E-03	3.6E-02	8.7E-03	3.8E-02	N	Y
7440-61-1	Uranium	0	0	5.2E-04	2.2E-03	8.1E-03	3.6E-02	8.7E-03	3.8E-02	N	Y
7440-62-2	Vanadium	1.1E-04	4.4E-04	7.3E-04	3.0E-03	2.3E-02	1.0E-01	2.4E-02	0.10	N	Y
25551-13-7	Trimethyl benzene	0	0	1.1E-02	4.8E-02	0	0	1.1E-02	4.8E-02	N	Y
7440-33-7	Tungsten	0	0	5.2E-04	2.2E-03	8.1E-03	3.6E-02	8.7E-03	3.8E-02	N	Y
7440-66-6	Zinc	1.4E-03	5.5E-03	8.0E-04	3.3E-03	2.9E-02	0.12	3.1E-02	0.13	N	Y
Total Non-HAP TAP		0.13	0.50	6.75	25.40	84.83	371.54	91.71	397.44		

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

Conversions
2,000 lb/ton
8,760 hr/yr
24 hr/day

PROPANE COMBUSTION

Source Data

Source ID	Description	MMBtu/day	MMBtu/yr
Lime Process Heating			
LKC	PFR Shaft Lime Kiln Combustion	529.0	163,935
Ore Process Heating			
ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	17.0	510
CKB	Carbon Regeneration Kiln (Burners)	54.1	19,754
PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	2.4	876
HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	120.0	43,800
Subtotal		193.5	64,940
HVAC			
H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	96.0	35,040
H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	96.0	35,040
HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	96.0	35,040
HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	6.0	2,190
HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	6.0	2,190
HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	6.0	2,190
HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	12.0	4,380
HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	48.0	17,520
HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	72.0	26,280
Subtotal		438.0	159,870

PROPANE COMBUSTION - CONTINUED

HAP/TAP Emission Factors and Emissions

O.Heat_pph O.Heat_tpy L.Heat_pph L.Heat_tpy HVAC_pph HVAC_tpy lb/hr ton/yr

		Emission Factor[2]		Emissions[1] Ore Proc Heat		Lime Proc Heat		HVAC		Total			
CAS	Pollutant	lb/MMscf	lb/MMBtu[3]	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	TAP	A/C
91-57-6	2-Methylnaphthalene	2.4E-05	2.35E-8	1.9E-07	7.6E-07	5.2E-07	1.9E-06	4.3E-07	1.9E-06	1.1E-06	4.6E-06	N	
56-49-5	3-Methylchloranthrene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
57-97-6	7,12-Dimethylbenz(a)ant	< 1.6E-05	1.57E-8	1.3E-07	5.1E-07	3.5E-07	1.3E-06	2.9E-07	1.3E-06	7.6E-07	3.0E-06	N	
83-32-9	Acenaphthene	< 1.8E-06	1.76E-9	1.4E-08	5.7E-08	3.9E-08	1.4E-07	3.2E-08	1.4E-07	8.5E-08	3.4E-07	N	
208-96-8	Acenaphthylene	< 1.8E-06	1.76E-9	1.4E-08	5.7E-08	3.9E-08	1.4E-07	3.2E-08	1.4E-07	8.5E-08	3.4E-07	N	
120-12-7	Anthracene	< 2.4E-06	2.35E-9	1.9E-08	7.6E-08	5.2E-08	1.9E-07	4.3E-08	1.9E-07	1.1E-07	4.6E-07	N	
7440-38-2	Arsenic	2.0E-04	1.96E-7	1.5E-06	6.4E-06	3.7E-06	1.6E-05	3.6E-06	1.6E-05	8.7E-06	3.8E-05	Y	C
56-55-3	Benz(a)anthracene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
71-43-2	Benzene	2.1E-03	2.06E-6	1.5E-05	6.7E-05	3.9E-05	1.7E-04	3.8E-05	1.6E-04	9.1E-05	4.0E-04	Y	C
50-32-8	Benzo(a)pyrene	< 1.2E-06	1.18E-9	8.7E-09	3.8E-08	2.2E-08	9.6E-08	2.1E-08	9.4E-08	5.2E-08	2.3E-07	Y	C
205-99-2	Benzo(b)fluoranthene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
191-24-2	Benzo(g,h,i)perylene	< 1.2E-06	1.18E-9	9.5E-09	3.8E-08	2.6E-08	9.6E-08	2.1E-08	9.4E-08	5.7E-08	2.3E-07	N	
207-08-9	Benzo(k)fluoranthene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
7440-41-7	Beryllium	< 1.2E-05	1.18E-8	8.7E-08	3.8E-07	2.2E-07	9.6E-07	2.1E-07	9.4E-07	5.2E-07	2.3E-06	Y	C
7440-43-9	Cadmium	1.1E-03	1.08E-6	8.0E-06	3.5E-05	2.0E-05	8.8E-05	2.0E-05	8.6E-05	4.8E-05	2.1E-04	Y	C
7440-47-3	Chromium	1.4E-03	1.37E-6	1.1E-05	4.5E-05	3.0E-05	1.1E-04	2.5E-05	1.1E-04	6.6E-05	2.7E-04	Y	A
218-01-9	Chrysene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
7440-48-4	Cobalt	8.4E-05	8.24E-8	6.6E-07	2.7E-06	1.8E-06	6.8E-06	1.5E-06	6.6E-06	4.0E-06	1.6E-05	Y	A
53-70-3	Dibenzo(a,h)anthracene	< 1.2E-06	1.18E-9	8.7E-09	3.8E-08	2.2E-08	9.6E-08	2.1E-08	9.4E-08	5.2E-08	2.3E-07	Y	C
106-46-7	Dichlorobenzene	1.2E-03	1.18E-6	9.5E-06	3.8E-05	2.6E-05	9.6E-05	2.1E-05	9.4E-05	5.7E-05	2.3E-04	Y	A
206-44-0	Fluoranthene	3.0E-06	2.94E-9	2.4E-08	9.5E-08	6.5E-08	2.4E-07	5.4E-08	2.4E-07	1.4E-07	5.7E-07	N	
86-73-7	Fluorene	2.8E-06	2.75E-9	2.2E-08	8.9E-08	6.1E-08	2.3E-07	5.0E-08	2.2E-07	1.3E-07	5.3E-07	N	
50-00-0	Formaldehyde	7.5E-02	7.35E-5	5.5E-04	2.4E-03	1.4E-03	6.0E-03	1.3E-03	5.9E-03	3.3E-03	1.4E-02	Y	C
110-54-3	Hexane	1.8E+00	1.76E-3	1.4E-02	5.7E-02	3.9E-02	1.4E-01	3.2E-02	1.4E-01	8.5E-02	3.4E-01	Y	A
193-39-5	Indeno(1,2,3-cd)pyrene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
7439-96-5	Manganese	3.8E-04	3.73E-7	3.0E-06	1.2E-05	8.2E-06	3.1E-05	6.8E-06	3.0E-05	1.8E-05	7.2E-05	Y	A
7439-97-6	Mercury	2.6E-04	2.55E-7	2.1E-06	8.3E-06	5.6E-06	2.1E-05	4.7E-06	2.0E-05	1.2E-05	5.0E-05	N	
91-20-3	Naphthalene	6.1E-04	5.98E-7	4.8E-06	1.9E-05	1.3E-05	4.9E-05	1.1E-05	4.8E-05	2.9E-05	1.2E-04	Y	A
7440-02-0	Nickel	2.1E-03	2.06E-6	1.5E-05	6.7E-05	3.9E-05	1.7E-04	3.8E-05	1.6E-04	9.1E-05	4.0E-04	Y	C
85-01-8	Phenanthrene	1.7E-05	1.67E-8	1.3E-07	5.4E-07	3.7E-07	1.4E-06	3.0E-07	1.3E-06	8.1E-07	3.2E-06	N	
129-00-0	Pyrene	5.0E-06	4.90E-9	4.0E-08	1.6E-07	1.1E-07	4.0E-07	8.9E-08	3.9E-07	2.4E-07	9.5E-07	N	
7782-49-2	Selenium	< 2.4E-05	2.35E-8	1.9E-07	7.6E-07	5.2E-07	1.9E-06	4.3E-07	1.9E-06	1.1E-06	4.6E-06	Y	A
108-88-3	Toluene	3.4E-03	3.33E-6	2.7E-05	1.1E-04	7.3E-05	2.7E-04	6.1E-05	2.7E-04	1.6E-04	6.5E-04	Y	A
109-66-0	Pentane	2.6E+00	2.55E-3	2.1E-02	8.3E-02	5.6E-02	2.1E-01	4.7E-02	2.0E-01	1.2E-01	5.0E-01	Y	A
7440-39-3	Barium	4.4E-03	4.31E-6	3.5E-05	1.4E-04	9.5E-05	3.5E-04	7.9E-05	3.4E-04	2.1E-04	8.4E-04	Y	A
7440-50-8	Copper	8.5E-04	8.33E-7	6.7E-06	2.7E-05	1.8E-05	6.8E-05	1.5E-05	6.7E-05	4.0E-05	1.6E-04	Y	A
7439-98-7	Molybdenum	1.1E-03	1.08E-6	8.7E-06	3.5E-05	2.4E-05	8.8E-05	2.0E-05	8.6E-05	5.2E-05	2.1E-04	Y	A
7440-62-2	Vanadium	2.3E-03	2.25E-6	1.8E-05	7.3E-05	5.0E-05	1.8E-04	4.1E-05	1.8E-04	1.1E-04	4.4E-04	Y	A
7440-66-6	Zinc	2.9E-02	2.84E-5	2.3E-04	9.2E-04	6.3E-04	2.3E-03	5.2E-04	2.3E-03	1.4E-03	5.5E-03	Y	A
Total				3.6E-02	1.4E-01	9.8E-02	3.6E-01	8.1E-02	3.5E-01	2.1E-01	8.6E-01		

(1) *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

(2) *AP-42, Table 1.4-3 & 1.4-4 (7/98) Natural Gas Combustion* 1.07e6 1.07e6

(3) *Natural Gas Higher Heating Value* 1,020 *MMBtu/MMscf* chk

Air Sciences Inc.	PROJECT TITLE: Stibnite Gold Project	BY: K. Lewis
	PROJECT NO: 335-20-3	PAGE: 5 OF: 19 SHEET: Calcs
AIR EMISSION CALCULATIONS	SUBJECT: HAP/TAP Emission Calculations	DATE: October 4, 2021

DIESEL COMBUSTION

Source Data

Source ID	Description	Power Rating kW	Power Rating hp	Operation hr/day	Operation hr/yr	Fuel Consumption[1] & [2] MMBtu/day	Fuel Consumption[1] & [2] MMBtu/yr
EDG1	Camp Emergency Generator	1,000	1,341	1	100	9.39	938.70
EDG2	Plant Emergency Generator #1	1,000	1,341	1	100	9.39	938.7
EDG3	Plant Emergency Generator #2	1,000	1,341	1	100	9.39	938.7
EDFP	Mill Fire Pump	200	268	1	100	1.88	187.7
Total						30.0	3,003.8

[1] *Based on brake specific fuel consumption for diesel generators* 7,000 *Btu/hp-hr* *AP-42 Tbl 3.3-1*

[2] *Heat Content of* 0.137 *MMBtu/gal* 1E+6 *Btu/MMBtu* 1.341 *hp/kW*

HAP/TAP Emission Factors and Emissions

		Factor (lb/MMBtu)		Emissions (≤600 hp)		Emissions (>600 hp)		Total Emissions[1]			
	Pollutant	≤600 hp[2]	>600hp[3]	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	TAP	A/C
106-99-0	1,3-Butadiene	< 3.9E-05		8.4E-07	3.7E-06	0.0E+00	0.0E+00	8.4E-07	3.7E-06	Y	C
83-32-9	Acenaphthene	< 1.4E-06	4.7E-06	1.1E-07	1.3E-07	5.5E-06	6.6E-06	5.6E-06	6.7E-06	N	
208-96-8	Acenaphthylene	< 5.1E-06	9.2E-06	4.0E-07	4.7E-07	1.1E-05	1.3E-05	1.1E-05	1.3E-05	N	
75-07-0	Acetaldehyde	7.7E-04	2.5E-05	1.6E-05	7.2E-05	8.1E-06	3.5E-05	2.5E-05	1.1E-04	Y	C
107-02-8	Acrolein	< 9.3E-05	7.9E-06	7.2E-06	8.7E-06	9.2E-06	1.1E-05	1.6E-05	2.0E-05	Y	A
120-12-7	Anthracene	1.9E-06	1.2E-06	1.5E-07	1.8E-07	1.4E-06	1.7E-06	1.6E-06	1.9E-06	N	
56-55-3	Benz(a)anthracene	1.7E-06	6.2E-07	3.6E-08	1.6E-07	2.0E-07	8.8E-07	2.4E-07	1.0E-06	Y	C
71-43-2	Benzene	9.3E-04	7.8E-04	2.0E-05	8.8E-05	2.5E-04	1.1E-03	2.7E-04	1.2E-03	Y	C
50-32-8	Benzo(a)pyrene	< 1.9E-07	< 2.6E-07	4.0E-09	1.8E-08	8.3E-08	3.6E-07	8.7E-08	3.8E-07	Y	C
205-99-2	Benzo(b)fluoranthene	< 9.9E-08	< 1.1E-06	2.1E-09	9.3E-09	3.6E-07	1.6E-06	3.6E-07	1.6E-06	Y	C
191-24-2	Benzo(g,h,i)perylene	< 4.9E-07	< 5.6E-07	3.8E-08	4.6E-08	6.5E-07	7.8E-07	6.9E-07	8.3E-07	N	
207-08-9	Benzo(k)fluoranthene	< 1.6E-07	< 2.2E-07	3.3E-09	1.5E-08	7.0E-08	3.1E-07	7.3E-08	3.2E-07	Y	C
218-01-9	Chrysene	3.5E-07	1.5E-06	7.6E-09	3.3E-08	4.9E-07	2.2E-06	5.0E-07	2.2E-06	Y	C
53-70-3	Dibenzo(a,h)anthracene	< 5.8E-07	< 3.5E-07	1.2E-08	5.5E-08	1.1E-07	4.9E-07	1.2E-07	5.4E-07	Y	C
206-44-0	Fluoranthene	7.6E-06	4.0E-06	6.0E-07	7.1E-07	4.7E-06	5.7E-06	5.3E-06	6.4E-06	N	
86-73-7	Fluorene	2.9E-05	1.3E-05	2.3E-06	2.7E-06	1.5E-05	1.8E-05	1.7E-05	2.1E-05	N	
50-00-0	Formaldehyde	1.2E-03	7.9E-05	2.5E-05	1.1E-04	2.5E-05	1.1E-04	5.1E-05	2.2E-04	Y	C
193-39-5	Indeno(1,2,3-cd)pyrene	< 3.8E-07	< 4.1E-07	8.0E-09	3.5E-08	1.3E-07	5.8E-07	1.4E-07	6.2E-07	Y	C
91-20-3	Naphthalene	8.5E-05	1.3E-04	6.6E-06	8.0E-06	1.5E-04	1.8E-04	1.6E-04	1.9E-04	Y	A
85-01-8	Phenanthrene	2.9E-05	4.1E-05	2.3E-06	2.8E-06	4.8E-05	5.7E-05	5.0E-05	6.0E-05	N	
129-00-0	Pyrene	4.8E-06	3.7E-06	3.7E-07	4.5E-07	4.4E-06	5.2E-06	4.7E-06	5.7E-06	N	
108-88-3	Toluene	4.1E-04	2.8E-04	3.2E-05	3.8E-05	3.3E-04	4.0E-04	3.6E-04	4.3E-04	Y	A
1330-20-7	Xylene	2.9E-04	1.9E-04	2.2E-05	2.7E-05	2.3E-04	2.7E-04	2.5E-04	3.0E-04	Y	A
Total				1.4E-04	3.6E-04	1.1E-03	2.2E-03	1.2E-03	2.6E-03		

lb/hr ton/yr

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

[2] *AP-42, Tab. 3.3-2, 10/96, diesel engines (≤ 600 hp)* chk chk

[3] *AP-42, Tabs. 3.4-3 & 3.4-4, 10/96, large diesel engines (> 600 hp)*

ORE PROCESSING

Source Data

Source ID	Description	PM Emissions lb/day	PM Emissions ton/yr
OC1	Loader Transfer of Ore to Grizzly	3.500	0.639
OC2	Grizzly to Apron Feeder	3.500	0.639
OC3	Apron Feeder to Dribble Conveyor	3.500	0.639
OC4	Apron Feeder to Vibrating Grizzly	3.500	0.639
OC5	Dribble Conveyor to Vibrating Grizzly	3.500	0.639
OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	3.500	0.639
OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	30.000	5.475
OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	3.500	0.639
OC9	Stockpile Transfers to Reclaim Conveyors	16.560	3.022
OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	16.560	3.022
OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	16.560	3.022
OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge C	33.120	6.044
OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	3.864	0.705
Total		141.164	25.762

HAP/TAP Emission Factors and Emissions

CAS No.	Pollutant	Concentration ppm[2]	Emissions[1] lb/hr	Emissions[1] ton/yr	TAP	A/C
7440-38-2	Arsenic	667	3.9E-03	1.7E-02	Y	C
7440-41-7	Beryllium	3.2	1.9E-05	8.2E-05	Y	C
7440-43-9	Cadmium	0.50	2.9E-06	1.3E-05	Y	C
7440-48-4	Cobalt	4	2.4E-05	1.0E-04	Y	A
7440-47-3	Chromium	9	5.3E-05	2.3E-04	Y	A
7439-97-6	Mercury [3]	0.96	5.6E-06	2.5E-05	N	
7439-96-5	Manganese	299	1.8E-03	7.7E-03	Y	A
7440-02-0	Nickel	2	1.2E-05	5.2E-05	Y	C
7439-92-1	Lead	8	4.7E-05	2.1E-04	N	
7440-36-0	Antimony	23	1.4E-04	5.9E-04	Y	A
7723-14-0	Phosphorus	650	3.8E-03	1.7E-02	Y	A
7782-49-2	Selenium [4]	0.40	2.4E-06	1.0E-05	Y	A
7440-22-4	Silver	0.50	2.9E-06	1.3E-05	Y	A
7429-90-5	Aluminum	71,000	4.2E-01	1.8E+00	Y	A
7440-39-3	Barium	800	4.7E-03	2.1E-02	Y	A
1317-65-3	Calcium Carbonate	14,000	8.2E-02	3.6E-01	Y	A
7440-50-8	Copper	5	2.9E-05	1.3E-04	Y	A
7439-89-6	Iron [4]	18,200	1.1E-01	4.7E-01	Y	A
7439-98-7	Molybdenum	1	5.9E-06	2.6E-05	Y	A
7440-28-0	Thallium	10	5.9E-05	2.6E-04	Y	A
7440-61-1	Uranium	10	5.9E-05	2.6E-04	Y	A
7440-62-2	Vanadium	28	1.6E-04	7.2E-04	Y	A
7440-33-7	Tungsten	10	5.9E-05	2.6E-04	Y	A
7440-66-6	Zinc	35	2.1E-04	9.0E-04	Y	A
Total			6.2E-01	2.7E+00		

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

[2] *(Midas Gold 2017c) Median concentration of 55,000 SGP samples.*

[3] *(Midas Gold 2018e) Median ore concentration of 151,000 SGP samples; resource block model.*

[4] *(Midas Gold 2020) Median concentration of 56,000 SGP samples for Fe and 1,500 SGP samples for Se.*

1E+6 parts/ppm

Air Sciences Inc.	PROJECT TITLE: Stibnite Gold Project	BY: K. Lewis
	PROJECT NO: 335-20-3	PAGE: 7 OF: 19 SHEET: Calcs
AIR EMISSION CALCULATIONS	SUBJECT: HAP/TAP Emission Calculations	DATE: October 4, 2021

ORE CONCETRATION AND REFINING

Source Data

Source ID	Description	Subpart 7E Allowable Limit lb/yr[1]	Oper. hr/yr	% of Subpart 7E for Controlled Systems %	Controlled Hg Emissions lb/hr	ton/yr	lb/yr
AC	Autoclave	213.4	8,760	[2]	0.000023	0.00010	0.20
EW,MR,MF,CKD	Refinery Sources (C. Kiln, EW, Retort, Furr	16.8		20% [3]	0.000384	0.00168	3.36
7439-97-6 Mercury	Total	230.2			0.000407	0.00178	3.56

[1] *Subpart 7E Limit - Ore Pretreatment Processes (CFR 2018b)*

$$\frac{84\ lb}{MMton} \times \frac{2{,}540{,}400\ ton}{yr} \times \frac{MMton}{1.0E{+}6\ ton} = \frac{213.4\ lb}{yr}$$

[1] *Subpart 7E Limit - Carbon Processes with Mercury Retorts*

$$\frac{0.8\ lb}{ton} \times \frac{21\ ton}{yr} = \frac{16.8\ lb}{yr}$$

[2] *Controlled SysCAD modeled emissions from Autoclave:* 0.0105 g/hr 2.3E-05 lb/hr 0.20 lb/yr (M3 2019)

[3] *Based on similar source (but with much higher ore Hg content) Hg reporting levels provided below:*

Goldstrike Refinery (2015 & 2016 Hg Reports) (NDEP 2015a) (NDEP 2016)

$$\frac{28.79\ lb}{yr} \times \frac{yr}{251.00\ ton} = \frac{0.11\ lb}{MMton} \times \frac{ton}{0.8\ lb} = 14.3\%$$

Twin Creeks Refinery (2015 & 2016 Hg Reports) (NDEP 2015a) (NDEP 2016)

$$\frac{31.27\ lb}{yr} \times \frac{yr}{142.77\ ton} = \frac{0.22\ lb}{MMton} \times \frac{ton}{0.8\ lb} = 27.4\%$$

HAP/TAP Emission Factors and Emission

AC_pph AC_tpy Refin_pph Refin_tpy lb/hr ton/yr

CAS No.	Pollutant	Emission Factor[1]	Autoclave lb/hr	Autoclave ton/yr	Refinery lb/hr	Refinery ton/yr	Total Emissions lb/hr	Total Emissions ton/yr	TAP	A/C
7440-38-2	Arsenic	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	C
7440-41-7	Beryllium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	C
7440-43-9	Cadmium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	C
7440-48-4	Cobalt	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-47-3	Chromium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7439-97-6	Mercury	see above	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	N	
7439-96-5	Manganese	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-02-0	Nickel	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	C
7439-92-1	Lead	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	N	
7440-36-0	Antimony	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7723-14-0	Phosphorus	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7782-49-2	Selenium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-22-4	Silver	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7429-90-5	Aluminum	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-39-3	Barium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
1317-65-3	Calcium Carbonate	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-50-8	Copper	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7439-89-6	Iron	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7439-98-7	Molybdenum	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-28-0	Thallium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-61-1	Uranium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-62-2	Vanadium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-33-7	Tungsten	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-66-6	Zinc	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
Total			5.5E-04	2.4E-03	9.2E-03	4.0E-02	9.8E-03	4.3E-02		

[1] *Hg is the most difficult metal to control due to it existing in both particulate and gaseous form. Therefore, all other metals are conservatively estimated to be equal to or less than the Hg emissions.*

0.0525 0.0525 chk

7664-93-9	Sulfuric Acid	Autoclave	2.03	8.89			2.03	8.89
7783-06-4	Hydrogen Sulfic	Autoclave	0.90	3.94			0.90	3.94
592-01-8	Cyanide	Point Sources - 5 EW Cells			0.0012	0.0053	0.00	0.01
Total			2.93	12.84	0.01	0.05	2.94	12.88

ORE CONCETRATION AND REFINING - CONTINUED

Source Data

Source ID	Description	Throughput ton/day	Throughput ton/yr	Operation hr/day	Operation hr/yr
AC	Autoclave	6,960	2,540,400	24	8,760

Autoclave HAP/TAP Emission Factors and Emission lb/hr ton/yr

CAS No.	Pollutant	Emission Factor		Emissions[1] lb/hr	Emissions[1] ton/yr
7664-93-9	Sulfuric Acid	0.007	lb/ton[2]	2.03	8.89
7783-06-4	Hydrogen Sulfide	0.9	lb/hr[3]	0.90	3.94

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

[2] *H2SO4 is based on Acidic Autoclave test data (APT 2010)*

[3] *H2S is based on Acidic Autoclave test data (APT 2013)*

LEACHING OPERATION

Cyanide (HCN) Source Data, Emission Factors, and Emissions

Source ID	Description	Dia. ft[1]	pH[1]	Free CN- g/m3[1]	T C[1]	pKa	a0	H	kG[2] m/s	Fa*Fw	g/s	lb/hr	ton/yr
TSF	***Fugitive Sources***												
TSF	Tailings Maint. Pond	76	7.75	1	3.74	9.803	0.9912	0.0025	1.89E-05	0.641	1.27E-05	0.0001	0.0004
MILLTA	CN Detox Tank 1	40	8.5	25	25	9.250	0.8490	0.0055	0.000311	0.688	0.002891	0.0229	0.101
MILLTA	CN Detox Tank 2	40	8.5	25	25	9.250	0.8490	0.0055	0.000311	0.688	0.002891	0.0229	0.101
MILLTA	CIP Leach Tank 1	52	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.668	0.001435	0.0114	0.050
MILLTA	CIP Leach Tank 2	52	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.668	0.001435	0.0114	0.050
MILLTA	CIP Leach Tank 3	52	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.668	0.001435	0.0114	0.050
MILLTA	CIP Leach Tank 4	52	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.668	0.001435	0.0114	0.050
MILLTA	CIL Tank 1	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA	CIL Tank 2	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA	CIL Tank 3	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA	CIL Tank 4	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA	CIL Tank 5	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA	CIL Tank 6	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA	CIP Tank 1	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
MILLTA	CIP Tank 2	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
MILLTA	CIP Tank 3	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
MILLTA	CIP Tank 4	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
MILLTA	CIP Tank 5	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
MILLTA	CIP Tank 6	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
		Acres[1]											
TSF	Tails, Aqueous Surface	110.222	7.75	1	3.74	9.803	0.9912	0.0025	1.89E-05	0.421	0.008845	0.0702	0.307
TSF	Tails, Wet Sediment	110.222							5.31E-08	0.421	0.009961	0.0791	0.346
TSF	Tails, Dry Sediment	110.222							2.33E-08	1	0.010375	0.0823	0.361
		330.666											
592-01-8	Cyanide Fugitive Sources - Subtotal											0.4527	1.983
75-15-0	Carbon Disulfide											0.01446	0.06332
	Point Sources												
EW	EW Cells	[3]										0.0006	0.003
EW	Preg/Barren Tanks	[3]										0.0006	0.003
592-01-8	Cyanide Point Sources - Subtotal											0.0012	0.0053
	Total											0.454	1.988

[1] *(Midas Gold 2016)(M3 2017c)(M3 2017d)*

[2] *The emission factors and caculation methodology are from the EPA directed HCN study: (Card, T. 2009)(EPA 2009)(Schmidt 2010)*

[3] *(APT 2009)*

Carbon Disulfide Emissions from Xanthate Decomposition

CAS No.	Pollutant	Xanthate[1] ton/yr	Molar Decomp.[2]	CS_2 MW Ratio	Temperature Adj. Factor[3]	Emissions lb/hr	Emissions ton/yr
75-15-0	Carbon Disulfide	1,700	0.99%	0.376	1%	0.0145	0.063

	MW	
Xanthate (PAX)	202.37	$C6H11KOS_2$
Carbon disulfide	76.139	CS_2

[1] *(Midas Gold 2016) p. 12-11*

[2] *(Air Sciences 2020) molar decomposition of xanthate in solution to CS2 gas*

[3] *(Air Sciences 2020) based on the comparison of CS2 generation at 25C and 70C*

Conversions

8,760	hr/yr	453.5929	g/lb	Wind adjustment factor Fw	1
2,000	lb/ton	3.28084	ft/m		
4,046.86	m2/acre	3,600	s/hr		

Air Sciences Inc.	PROJECT TITLE: Stibnite Gold Project	BY: K. Lewis		
	PROJECT NO: 335-20-3	PAGE: 10	OF: 19	SHEET: Calcs
AIR EMISSION CALCULATIONS	SUBJECT: HAP/TAP Emission Calculations	DATE: October 4, 2021		

LIME PRODUCTION

Source Data

Source ID	Description	Throughput ton/day	Throughput ton/yr	PM Emissions lb/day	PM Emissions ton/yr
LS1	Limestone transfer to Primary Crusher Hopper			3.39	0.48
LS2	Primary Crushing and Associated Transfers In and Out			6.10	0.86
LS3	Primary Screening and Associated Transfers In and Out			28.25	3.97
LS4	Secondary Crushing and Associated Transfers In and Out			6.10	0.86
LS5	Secondary Screening and Associated Transfers In and Out			28.25	3.97
LS6	Limestone transfer to Ball Mill Feed Bin			3.39	0.48
LS7	Limestone transfer to Ball Mill Feed Conveyor			3.39	0.48
LS8	Ball Mill Feed transfer to Ball Mill			3.39	0.48
LSBM	Limestone Ball Mill			45.65	6.42
LS9	Limestone transfer to Kiln Feed Bin			0.80	0.12
LS10	Limestone transfer to Lime Kiln Feed Conveyor			0.80	0.12
LS11	Fines Screening and Associated Transfers In and Out			6.68	1.03
Subtotal LS1-11				136.18	19.28
LS12	Kiln Feed transfer to PFR Shaft Lime Kiln			0.80	0.12
LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	169	52,377	21.97	3.40
Subtotal LS12,LK				22.77	3.53
Total				158.95	22.80

HAP/TAP Emission Factors and Emissions

LS_pph LS_tpy LS12_pph LS12_tpy LK_pph LK_tpy lb/hr ton/yr

CAS No.	Pollutant	Concentration ppm[2]	LS1-11,LSBM lb/hr	LS1-11,LSBM ton/yr	LS12 lb/hr	LS12 ton/yr	Lime Kiln lb/hr	Lime Kiln ton/yr	Emissions[1] lb/hr	Emissions[1] ton/yr	TAP	A/C
7440-38-2	Arsenic	23	1.01E-04	4.43E-04	6.51E-07	2.85E-06	1.79E-05	7.83E-05	1.20E-04	5.24E-04	Y	C
7440-41-7	Beryllium	0.8	3.52E-06	1.54E-05	2.27E-08	9.92E-08	6.22E-07	2.72E-06	4.17E-06	1.82E-05	Y	C
7440-43-9	Cadmium	0.25	1.10E-06	4.82E-06	7.08E-09	3.10E-08	1.94E-07	8.51E-07	1.30E-06	5.70E-06	Y	C
7440-48-4	Cobalt	4	2.27E-05	7.71E-05	1.34E-07	4.96E-07	3.66E-06	1.36E-05	2.65E-05	9.12E-05	Y	A
7440-47-3	Chromium	15	8.51E-05	2.89E-04	5.01E-07	1.86E-06	1.37E-05	5.11E-05	9.93E-05	3.42E-04	Y	A
7439-97-6	Mercury [3]	0.02	1.13E-07	3.86E-07	6.68E-10	2.48E-09	2.82E-04	1.05E-03	2.82E-04	1.05E-03	N	
7439-96-5	Manganese	236.5	1.34E-03	4.56E-03	7.89E-06	2.93E-05	2.16E-04	8.05E-04	1.57E-03	5.39E-03	Y	A
7440-02-0	Nickel	5	2.20E-05	9.64E-05	1.42E-07	6.20E-07	3.89E-06	1.70E-05	2.60E-05	1.14E-04	Y	C
7439-92-1	Lead	3	1.70E-05	5.78E-05	1.00E-07	3.72E-07	2.75E-06	1.02E-05	1.99E-05	6.84E-05	N	
7440-36-0	Antimony	2.5	1.42E-05	4.82E-05	8.34E-08	3.10E-07	2.29E-06	8.51E-06	1.66E-05	5.70E-05	Y	A
7723-14-0	Phosphorus	130	7.38E-04	2.51E-03	4.34E-06	1.61E-05	1.19E-04	4.43E-04	8.61E-04	2.96E-03	Y	A
7440-22-4	Silver	0	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	Y	A
7429-90-5	Aluminum	22600	1.28E-01	4.36E-01	7.54E-04	2.80E-03	2.07E-02	7.69E-02	1.50E-01	5.15E-01	Y	A
7440-39-3	Barium	145	8.23E-04	2.79E-03	4.84E-06	1.80E-05	1.33E-04	4.94E-04	9.60E-04	3.31E-03	Y	A
1317-65-3	Calcium Carbonate	274500	1.56E+00	5.29E+00	9.16E-03	3.40E-02	2.51E-01	9.35E-01	1.82E+00	6.26E+00	Y	A
7440-50-8	Copper	5	2.84E-05	9.64E-05	1.67E-07	6.20E-07	4.58E-06	1.70E-05	3.31E-05	1.14E-04	Y	A
7439-89-6	Iron	10350	5.87E-02	1.99E-01	3.45E-04	1.28E-03	9.47E-03	3.52E-02	6.85E-02	2.36E-01	Y	A
7439-98-7	Molybdenum	0.5	2.84E-06	9.64E-06	1.67E-08	6.20E-08	4.58E-07	1.70E-06	3.31E-06	1.14E-05	Y	A
7440-28-0	Thallium	5	2.84E-05	9.64E-05	1.67E-07	6.20E-07	4.58E-06	1.70E-05	3.31E-05	1.14E-04	Y	A
7440-61-1	Uranium	5	2.84E-05	9.64E-05	1.67E-07	6.20E-07	4.58E-06	1.70E-05	3.31E-05	1.14E-04	Y	A
7440-62-2	Vanadium	15.5	8.79E-05	2.99E-04	5.17E-07	1.92E-06	1.42E-05	5.28E-05	1.03E-04	3.53E-04	Y	A
7440-33-7	Tungsten	5	2.84E-05	9.64E-05	1.67E-07	6.20E-07	4.58E-06	1.70E-05	3.31E-05	1.14E-04	Y	A
7440-66-6	Zinc	18	1.02E-04	3.47E-04	6.01E-07	2.23E-06	1.65E-05	6.13E-05	1.19E-04	4.10E-04	Y	A
Subtotal			1.75E+00	5.94E+00	1.03E-02	3.82E-02	2.82E-01	1.05E+00	2.04E+00	7.03E+00	9.0667	9.0667
7647-01-0	Hydrogen Chloride	0.14 lb/ton product[4]					0.99	3.67	0.99	3.67		chk

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

[2] *(M3 2018) Median concentrations of SGP limestone material. Metals with medians below the detection limit (DL) are set to 1/2DL.*

[3] *Hg emissions from the Lime Kiln are conservatively estimated assuming 100% volatilization of all Hg in the limestone*

[4] *(EPA 1999b)*

1E+6 parts/ppm

LIME PRODUCTION - CONTINUED

Source Data

Source ID	Description	PM Emissions lb/day (PM_ppd)	PM Emissions ton/yr (PM_tpy)
LS1L	Mill Lime Silo #1 Loading	0.248	0.002
LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	1.200	0.011
MillS2L	Mill Lime Silo #2 Loading	0.248	0.002
MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	1.200	0.011
ACS1L	AC Lime Silo #1 Loading	0.990	0.009
ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.304	0.042
ACS2L	AC Lime Silo #2 Loading	0.990	0.009
ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.304	0.042
ACS3L	AC Lime Silo #3 Loading	0.990	0.009
ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.304	0.042
ACS4L	AC Lime Silo #4 Loading	0.495	0.004
ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	2.304	0.021
Subtotal - Mill & AC Lime Silos		15.576	0.203
LCR	Lime Mill Crushing and associated transfers In and Out	6.828	1.058
LSL	Pebble Lime Silo Loading via Bucket Elevator	0.149	0.023
LSU	Pebble Lime Silo discharge to Lime Slaker	0.015	0.002
Subtotal - Lime Mfg		6.991	1.083
Total		22.567	1.286

HAP/TAP Emission Factors and Emissions

CAS No.	Pollutant	Concentration ppm[2]	Mill and AC lb/hr (MillAC_pph)	Mill and AC ton/yr (MillAC_tpy)	Lime Mfg lb/hr (LimeM_pph)	Lime Mfg ton/yr (LimeM_tpy)	Emissions[1] lb/hr	Emissions[1] ton/yr	TAP	A/C
7440-38-2	Arsenic	23	1.06E-06	4.66E-06	5.69E-06	2.49E-05	6.75E-06	2.96E-05	Y	C
7440-41-7	Beryllium	0.8	3.70E-08	1.62E-07	1.98E-07	8.67E-07	2.35E-07	1.03E-06	Y	C
7440-43-9	Cadmium	0.25	1.16E-08	5.07E-08	6.18E-08	2.71E-07	7.34E-08	3.22E-07	Y	C
7440-48-4	Cobalt	4	2.60E-06	8.11E-07	1.17E-06	4.33E-06	3.76E-06	5.14E-06	Y	A
7440-47-3	Chromium	15	9.74E-06	3.04E-06	4.37E-06	1.63E-05	1.41E-05	1.93E-05	Y	A
7439-97-6	Mercury	0.02	1.30E-08	4.05E-09	5.83E-09	2.17E-08	1.88E-08	2.57E-08	N	
7439-96-5	Manganese	236.5	1.53E-04	4.79E-05	6.89E-05	2.56E-04	2.22E-04	3.04E-04	Y	A
7440-02-0	Nickel	5	2.31E-07	1.01E-06	1.24E-06	5.42E-06	1.47E-06	6.43E-06	Y	C
7439-92-1	Lead	3	1.95E-06	6.08E-07	8.74E-07	3.25E-06	2.82E-06	3.86E-06	N	
7440-36-0	Antimony	2.5	1.62E-06	5.07E-07	7.28E-07	2.71E-06	2.35E-06	3.22E-06	Y	A
7723-14-0	Phosphorus	130	8.44E-05	2.63E-05	3.79E-05	1.41E-04	1.22E-04	1.67E-04	Y	A
7440-22-4	Silver	0	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	Y	A
7429-90-5	Aluminum	22,600	1.47E-02	4.58E-03	6.58E-03	2.45E-02	2.13E-02	2.91E-02	Y	A
7440-39-3	Barium	145	9.41E-05	2.94E-05	4.22E-05	1.57E-04	1.36E-04	1.86E-04	Y	A
1305-78-8	Calcium Oxide	740,000 [3]	4.80E-01	1.50E-01	2.16E-01	8.02E-01	6.96E-01	9.52E-01	Y	A
7440-50-8	Copper	5	3.25E-06	1.01E-06	1.46E-06	5.42E-06	4.70E-06	6.43E-06	Y	A
7439-89-6	Iron	10350	6.72E-03	2.10E-03	3.01E-03	1.12E-02	9.73E-03	1.33E-02	Y	A
7439-98-7	Molybdenum	0.5	3.25E-07	1.01E-07	1.46E-07	5.42E-07	4.70E-07	6.43E-07	Y	A
7440-28-0	Thallium	5	3.25E-06	1.01E-06	1.46E-06	5.42E-06	4.70E-06	6.43E-06	Y	A
7440-61-1	Uranium	5	3.25E-06	1.01E-06	1.46E-06	5.42E-06	4.70E-06	6.43E-06	Y	A
7440-62-2	Vanadium	15.5	1.01E-05	3.14E-06	4.52E-06	1.68E-05	1.46E-05	1.99E-05	Y	A
7440-33-7	Tungsten	5	3.25E-06	1.01E-06	1.46E-06	5.42E-06	4.70E-06	6.43E-06	Y	A
7440-66-6	Zinc	18	1.17E-05	3.65E-06	5.24E-06	1.95E-05	1.69E-05	2.31E-05	Y	A
Total			5.02E-01	1.57E-01	2.25E-01	8.38E-01	7.27E-01	9.95E-01		

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

[2] *See LIME PRODUCTION, page 10*

[3] *(NLA 2007) 40% to 74% CaO in lime*

1E+6 parts/ppm

AGGREGATE PRODUCTION

Source Data

PM_ppd PM_tpy

Source ID	description Description	PM Emissions lb/day	ton/yr
PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conve	15.00	2.74
PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conve	15.00	2.74
Total		30.00	5.48

HAP/TAP Emission Factors and Emissions

lb/hr ton/yr

CAS No.	Pollutant	Concentration ppm[2]	Emissions[1] lb/hr	ton/yr	TAP	A/C
7440-38-2	Arsenic	23	2.88E-05	1.26E-04	Y	C
7440-41-7	Beryllium	0.8	1.00E-06	4.38E-06	Y	C
7440-43-9	Cadmium	0.25	3.13E-07	1.37E-06	Y	C
7440-48-4	Cobalt	4	5.00E-06	2.19E-05	Y	A
7440-47-3	Chromium	15	1.88E-05	8.21E-05	Y	A
7439-97-6	Mercury	0.02	2.50E-08	1.10E-07	N	
7439-96-5	Manganese	236.5	2.96E-04	1.29E-03	Y	A
7440-02-0	Nickel	5	6.25E-06	2.74E-05	Y	C
7439-92-1	Lead	3	3.75E-06	1.64E-05	N	
7440-36-0	Antimony	2.5	3.13E-06	1.37E-05	Y	A
7723-14-0	Phosphorus	130	1.63E-04	7.12E-04	Y	A
7440-22-4	Silver	0	0.00E+00	0.00E+00	Y	A
7429-90-5	Aluminum	22600	2.83E-02	1.24E-01	Y	A
7440-39-3	Barium	145	1.81E-04	7.94E-04	Y	A
1317-65-3	Calcium Carbonate	274500	3.43E-01	1.50E+00	Y	A
7440-50-8	Copper	5	6.25E-06	2.74E-05	Y	A
7439-89-6	Iron	10350	1.29E-02	5.67E-02	Y	A
7439-98-7	Molybdenum	0.5	6.25E-07	2.74E-06	Y	A
7440-28-0	Thallium	5	6.25E-06	2.74E-05	Y	A
7440-61-1	Uranium	5	6.25E-06	2.74E-05	Y	A
7440-62-2	Vanadium	15.5	1.94E-05	8.49E-05	Y	A
7440-33-7	Tungsten	5	6.25E-06	2.74E-05	Y	A
7440-66-6	Zinc	18	2.25E-05	9.86E-05	Y	A
Total			3.85E-01	1.69E+00		

(1) *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

(2) *See LIME PRODUCTION, page 10*

1E+6 parts/ppm

CONCRETE PRODUCTION

Source Data

TP_unit/day TP_unit/yr

Source ID	description Description	Throughput ton/day	ton/yr
CS1L	Cement/Shotcrete Silo #1 Loading	164	60,000
CS1U	Cement/Shotcrete Silo #1 Unloading	164	60,000
CS2L	Cement/Shotcrete Silo #2 Loading	164	60,000
CS2U	Cement/Shotcrete Silo #2 Unloading	164	60,000
CM	Central Mixer Loading	164	60,000
	Subtotal Cement Silo Filling	658	240,000
	Subtotal Central Mix Batching	164	60,000

HAP/TAP Emission Factors and Emissions

CF_pph CF_tpy CM_pph CM_tpy lb/hr ton/yr

CAS No.	HAP/TAP	Silo Fill lb/ton[2]	Central Mixer lb/ton[3]	Cement Silo L/U lb/hr	Cement Silo L/U ton/yr	Central Mix Batching lb/hr	Central Mix Batching ton/yr	Total Emissions[3] lb/hr	Total Emissions[3] ton/yr	TAP	A/C
7440-38-2	Arsenic	4.24E-09	2.96E-07	1.16E-7	5.09E-7	2.03E-6	8.88E-6	2.14E-6	9.39E-6	Y	C
7440-41-7	Beryllium	4.86E-10		1.33E-8	5.83E-8	--	--	1.33E-8	5.83E-8	Y	C
7440-43-9	Cadmium		7.10E-10	--	--	4.86E-9	2.13E-8	4.86E-9	2.13E-8	Y	C
7440-47-3	Chromium	2.90E-08	1.27E-07	7.95E-7	3.48E-6	8.70E-7	3.81E-6	1.66E-6	7.29E-6	Y	A
18540-29-9	Cr (VI)	5.80E-09	2.70E-08	1.59E-7	6.96E-7	1.85E-7	8.11E-7	3.44E-7	1.51E-6	Y	C
7439-92-1	Lead	1.09E-08	3.66E-08	2.99E-7	1.31E-6	2.51E-7	1.10E-6	5.49E-7	2.41E-6	N	
7439-96-5	Manganese	1.17E-07	3.78E-06	3.21E-6	1.40E-5	2.59E-5	1.13E-4	2.91E-5	1.27E-4	Y	A
7440-02-0	Nickel	4.18E-08	2.48E-07	1.15E-6	5.02E-6	1.70E-6	7.44E-6	2.84E-6	1.25E-5	Y	C
7723-14-0	Phosphorus		1.20E-06	--	--	8.22E-6	3.60E-5	8.22E-6	3.60E-5	Y	A
Total				5.73E-6	2.51E-5	3.91E-5	1.71E-4	4.49E-5	1.97E-4		

(1) *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

(2) *AP-42, Table 11.12-8, (06/06) Cement Silo Filing, Controlled.* 20% *Cr (VI), IDEQ email on 11/23/2020* 0.0002 0.0002

(3) *AP-42, Table 11.12-8, (06/06) Central Mix Batching, Controlled.* 21.29% *Cr (VI), IDEQ email on 11/23/2020* chk

Conversions

24 hr/day

CONCRETE PRODUCTION - CONTINUED

Source Data PM_ppd PM_tpy

Source ID	description Description	PM Emissions lb/day	ton/yr
CAL	Aggregate Bin Loading	16.56	1.73
CAU	Aggregate Bin Unloading	16.56	1.73
Total		33.12	3.45

HAP/TAP Emission Factors and Emissions lb/hr ton/yr

CAS No.	Pollutant	Concentration ppm[2]	Emissions[1] lb/hr	ton/yr	TAP	A/C
7440-38-2	Arsenic	23	1.81E-05	7.94E-05	Y	C
7440-41-7	Beryllium	0.8	6.30E-07	2.76E-06	Y	C
7440-43-9	Cadmium	0.25	1.97E-07	8.63E-07	Y	C
7440-48-4	Cobalt	4	5.52E-06	1.38E-05	Y	A
7440-47-3	Chromium	15	2.07E-05	5.18E-05	Y	A
7439-97-6	Mercury	0.02	2.76E-08	6.90E-08	N	
7439-96-5	Manganese	236.5	3.26E-04	8.16E-04	Y	A
7440-02-0	Nickel	5	3.94E-06	1.73E-05	Y	C
7439-92-1	Lead	3	4.14E-06	1.04E-05	N	
7440-36-0	Antimony	2.5	3.45E-06	8.63E-06	Y	A
7723-14-0	Phosphorus	130	1.79E-04	4.49E-04	Y	A
7440-22-4	Silver	0	0.00E+00	0.00E+00	Y	A
7429-90-5	Aluminum	22600	3.12E-02	7.80E-02	Y	A
7440-39-3	Barium	145	2.00E-04	5.00E-04	Y	A
7440-50-8	Copper	5	6.90E-06	1.73E-05	Y	A
7439-89-6	Iron	10350	1.43E-02	3.57E-02	Y	A
7439-98-7	Molybdenum	0.5	6.90E-07	1.73E-06	Y	A
7440-28-0	Thallium	5	6.90E-06	1.73E-05	Y	A
7440-61-1	Uranium	5	6.90E-06	1.73E-05	Y	A
7440-62-2	Vanadium	15.5	2.14E-05	5.35E-05	Y	A
7440-33-7	Tungsten	5	6.90E-06	1.73E-05	Y	A
7440-66-6	Zinc	18	2.48E-05	6.21E-05	Y	A
Total			4.63E-02	1.16E-01		

(1) *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

(2) *See LIME PRODUCTION, page 10*

1E+6 parts/ppm

FUEL STORAGE - GASOLINE

Source Data

Source ID	Description	VOC Emissions lb/day	VOC Emissions ton/yr
TG1	Mine Site Gasoline Tank #1	5.25	0.96
TG2	Mine Site Gasoline Tank #2	5.25	0.96
Total		10.49	1.91

HAP/TAP Emission Factors and Emissions

CAS No.	Pollutant	Concentration wt. %[2]	Emissions[1] lb/hr	Emissions[1] ton/yr	TAP	A/C
71-43-2	Benzene	1.608%	7.03E-03	3.08E-02	Y	C
92-52-4	Biphenyl	0.010%	4.37E-05	1.91E-04	Y	A
110-82-7	Cyclohexane	0.240%	1.05E-03	4.60E-03	Y	A
110-54-3	Hexane	7.138%	3.12E-02	1.37E-01	Y	A
91-20-3	Naphthalene	0.444%	1.94E-03	8.50E-03	Y	A
108-95-2	Phenol	0.055%	2.40E-04	1.05E-03	Y	A
108-88-3	Toluene	7.212%	3.15E-02	1.38E-01	Y	A
25551-13-7	Trimethyl benzene	2.500%	1.09E-02	4.79E-02	Y	A
1330-20-7	Xylene	7.170%	3.13E-02	1.37E-01	Y	A
Total			1.15E-01	5.05E-01		

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

[2] *(EPA 1999a)*

MINING FUGITIVE EMISSIONS

Dust Emissions

Source Data **Model Scenario** **W3** **180,000 T/day Emissions**

Operating schedule 365 day/yr

Clean rock cap (CR) >0% [1]

[1] *(Perpetua 2021h) Percent of VMTs on haul roads capped with CR*
Roads outside of the pits and DRSFs are capped with CR

Source ID	Description	PM Emissions lb/day	PM Emissions ton/yr
YPP	Yellow Pine Pit	--	--
HFP	Hangar Flats Pit	--	--
WEP	West End Pit	1,887.91	344.54
BT	Bradley Tailings	--	--
YPPBL	Yellow Pine Pit Blasting	--	--
HFPBL	Hangar Flats Pit Blasting	--	--
WEPBL	West End Pit Blasting	643.03	117.35
BTBL	Bradley Tailings Blasting	--	--
STKP	PC Stockpile	--	--
FDRSF	Fiddle DRSF	--	--
HFDRSF	Hangar Flats DRSF	289.91	52.91
YPDRSF	Yellow Pine DRSF	--	--
WEDRSF	West End DRSF	--	--
HR000	Haul Roads	16,697.74	3,047.34
TSF	Tailing Storage Facility	--	--
ACCRD	Access Roads	38.10	6.95
UGEXP	Scout Portal	0.008	0.002
Total		19,556.71	3,569.10

TSF, ACCRD, UGEXP 38.11 6.95 chk 3569.10

HAP/TAP Emission Factors		ORE	DR	CR	HRD	Borrow	AR
		Concentration					
CAS No.	Pollutant	ppm[1]	ppm[1]	ppm[3]	ppm[4]	ppm[5]	ppm
7440-38-2	Arsenic	667	667	90	667	2.5	667
7440-41-7	Beryllium	3.2	3.2		3.2		3.2
7440-43-9	Cadmium	0.5	0.5		0.5		0.5
7440-48-4	Cobalt	4	4		4		4
7440-47-3	Chromium	9	9		9		9
7439-97-6	Mercury [2]	0.96	0.6		0.6		0.6
7439-96-5	Manganese	299	299		299		299
7440-02-0	Nickel	2	2		2		2
7439-92-1	Lead	8	8		8		8
7440-36-0	Antimony	23	23		23		23
7723-14-0	Phosphorus	650	650		650		650
7782-49-2	Selenium	0.4	0.4		0.4		0.4
7440-22-4	Silver	0.5	0.5		0.5		0.5
7429-90-5	Aluminum	71000	71000		71000		71000
7440-39-3	Barium	800	800		800		800
1317-65-3	Calcium Carbonate	14000	14000		14000		14000
7440-50-8	Copper	5	5		5		5
7439-89-6	Iron	18200	18200		18200		18200
7439-98-7	Molybdenum	1	1		1		1
7440-28-0	Thallium	10	10		10		10
7440-61-1	Uranium	10	10		10		10
7440-62-2	Vanadium	28	28		28		28
7440-33-7	Tungsten	10	10		10		10
7440-66-6	Zinc	35	35		35		35

[1] *(Midas Gold 2017c)* *Median concentration of 55,000 SGP samples.* *1E+6 parts/ppm*
[2] *(Midas Gold 2018e)* *Median ore and development rock (DR) concentrations of 151,000 samples; resource block model.*
[3] *(Perpetua 2021g)* *Median concentration of 265 SGP samples.*
[4] *HRD: haul road - emissions calculated based on 0% of the total VMT occuring on CR*
[5] *(ALS 2018)* *Median concentration of 8 SGP samples.*

DR DR DR DR DR DR DR DR ORE DR DR DR DR HRD DR/AR

MINING FUGITIVE EMISSIONS - CONTINUED **Model Scenario W3** DR **180,000 T/day Emissions**

HAP/TAP Emissions

Hourly [1] YPP_pph HFP_pph WEP_pph BT_pph YPPBL_pph HFPBL_pph WEPBL_ppl BTBL_pph STKP_pph FDRSF_pph HFDRSF_pph YPDRSF_pph WEDRSF_pph HR000_pph CCRD, UGE lb/hr

CAS No.	Pollutant	YPP lb/hr	HFP lb/hr	WEP lb/hr	BT lb/hr	YPPBL lb/hr	HFPBL lb/hr	WEPBL lb/hr	BTBL lb/hr	STKP lb/hr	FDRSF lb/hr	HFDRSF lb/hr	YPDRSF lb/hr	WEDRSF lb/hr	HR000 lb/hr	TSF, ACCRD, UGEXP lb/hr	Total lb/hr
7440-38-2	Arsenic	0	0	0.052	0	0	0	0.018	0	0	0	8.1E-3	0	0	0.464	1.1E-3	0.544
7440-41-7	Beryllium	0	0	2.5E-4	0	0	0	8.6E-5	0	0	0	3.9E-5	0	0	2.2E-3	5.1E-6	2.6E-3
7440-43-9	Cadmium	0	0	3.9E-5	0	0	0	1.3E-5	0	0	0	6.0E-6	0	0	3.5E-4	7.9E-7	4.1E-4
7440-48-4	Cobalt	0	0	3.1E-4	0	0	0	1.1E-4	0	0	0	4.8E-5	0	0	2.8E-3	6.4E-6	3.3E-3
7440-47-3	Chromium	0	0	7.1E-4	0	0	0	2.4E-4	0	0	0	1.1E-4	0	0	6.3E-3	1.4E-5	7.3E-3
7439-97-6	Mercury	0	0	4.7E-5	0	0	0	1.6E-5	0	0	0	7.2E-6	0	0	4.2E-4	9.5E-7	4.9E-4
7439-96-5	Manganese	0	0	0.024	0	0	0	8.0E-3	0	0	0	3.6E-3	0	0	0.208	4.7E-4	0.244
7440-02-0	Nickel	0	0	1.6E-4	0	0	0	5.4E-5	0	0	0	2.4E-5	0	0	1.4E-3	3.2E-6	1.6E-3
7439-92-1	Lead	0	0	6.3E-4	0	0	0	2.1E-4	0	0	0	9.7E-5	0	0	5.6E-3	1.3E-5	6.5E-3
7440-36-0	Antimony	0	0	1.8E-3	0	0	0	6.2E-4	0	0	0	2.8E-4	0	0	0.016	3.7E-5	0.019
7723-14-0	Phosphorus	0	0	0.051	0	0	0	0.017	0	0	0	7.9E-3	0	0	0.452	1.0E-3	0.530
7782-49-2	Selenium	0	0	3.1E-5	0	0	0	1.1E-5	0	0	0	4.8E-6	0	0	2.8E-4	6.4E-7	3.3E-4
7440-22-4	Silver	0	0	3.9E-5	0	0	0	1.3E-5	0	0	0	6.0E-6	0	0	3.5E-4	7.9E-7	4.1E-4
7429-90-5	Aluminum	0	0	5.585	0	0	0	1.902	0	0	0	0.858	0	0	49.397	0.113	57.855
7440-39-3	Barium	0	0	0.063	0	0	0	0.021	0	0	0	9.7E-3	0	0	0.557	1.3E-3	0.652
1317-65-3	Calcium Ca:	0	0	1.101	0	0	0	0.375	0	0	0	0.169	0	0	9.740	0.022	11.408
7440-50-8	Copper	0	0	3.9E-4	0	0	0	1.3E-4	0	0	0	6.0E-5	0	0	3.5E-3	7.9E-6	4.1E-3
7439-89-6	Iron	0	0	1.432	0	0	0	0.488	0	0	0	0.220	0	0	12.662	0.029	14.831
7439-98-7	Molybdenu	0	0	7.9E-5	0	0	0	2.7E-5	0	0	0	1.2E-5	0	0	7.0E-4	1.6E-6	8.1E-4
7440-28-0	Thallium	0	0	7.9E-4	0	0	0	2.7E-4	0	0	0	1.2E-4	0	0	7.0E-3	1.6E-5	8.1E-3
7440-61-1	Uranium	0	0	7.9E-4	0	0	0	2.7E-4	0	0	0	1.2E-4	0	0	7.0E-3	1.6E-5	8.1E-3
7440-62-2	Vanadium	0	0	2.2E-3	0	0	0	7.5E-4	0	0	0	3.4E-4	0	0	0.019	4.4E-5	0.023
7440-33-7	Tungsten	0	0	7.9E-4	0	0	0	2.7E-4	0	0	0	1.2E-4	0	0	7.0E-3	1.6E-5	8.1E-3
7440-66-6	Zinc	0	0	2.8E-3	0	0	0	9.4E-4	0	0	0	4.2E-4	0	0	0.024	5.6E-5	0.029
Total		0	0	8.320	0	0	0	2.834	0	0	0	1.278	0	0	73.586	0.168	86.185

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.* chk 86.1849 86.1849

DR DR DR DR DR DR DR DR ORE DR DR DR DR HRD DR/AR

MINING FUGITIVE EMISSIONS - CONTINUED **Model Scenario W3** DR **180,000 T/day Emissions**

HAP/TAP Emissions

Annual

		YPP_tpy	HFP_tpy	WEP_tpy	BT_tpy	YPPBL_tpy	HFPBL_tpy	WEPBL_tpy	BTBL_tpy	STKP_tpy	FDRSF_tpy	HFDRSF_tpy	YPDRSF_tpy	WEDRSF_tpy	HR000_tpy	CCRD, UGE	ton/yr
		YPP	HFP	WEP	BT	YPPBL	HFPBL	WEPBL	BTBL	STKP	FDRSF	HFDRSF	YPDRSF	WEDRSF	HR000	TSF, ACCRD, UGEXP	Total
CAS No.	Pollutant	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr
7440-38-2	Arsenic	0	0	0.230	0	0	0	0.078	0	0	0	0.035	0	0	2.033	4.6E-3	2.381
7440-41-7	Beryllium	0	0	1.1E-3	0	0	0	3.8E-4	0	0	0	1.7E-4	0	0	9.8E-3	2.2E-5	0.011
7440-43-9	Cadmium	0	0	1.7E-4	0	0	0	5.9E-5	0	0	0	2.6E-5	0	0	1.5E-3	3.5E-6	1.8E-3
7440-48-4	Cobalt	0	0	1.4E-3	0	0	0	4.7E-4	0	0	0	2.1E-4	0	0	0.012	2.8E-5	0.014
7440-47-3	Chromium	0	0	3.1E-3	0	0	0	1.1E-3	0	0	0	4.8E-4	0	0	0.027	6.3E-5	0.032
7439-97-6	Mercury	0	0	2.1E-4	0	0	0	7.0E-5	0	0	0	3.2E-5	0	0	1.8E-3	4.2E-6	2.1E-3
7439-96-5	Manganese	0	0	0.103	0	0	0	0.035	0	0	0	0.016	0	0	0.911	2.1E-3	1.067
7440-02-0	Nickel	0	0	6.9E-4	0	0	0	2.3E-4	0	0	0	1.1E-4	0	0	6.1E-3	1.4E-5	7.1E-3
7439-92-1	Lead	0	0	2.8E-3	0	0	0	9.4E-4	0	0	0	4.2E-4	0	0	0.024	5.6E-5	0.029
7440-36-0	Antimony	0	0	7.9E-3	0	0	0	2.7E-3	0	0	0	1.2E-3	0	0	0.070	1.6E-4	0.082
7723-14-0	Phosphorus	0	0	0.224	0	0	0	0.076	0	0	0	0.034	0	0	1.981	4.5E-3	2.320
7782-49-2	Selenium	0	0	1.4E-4	0	0	0	4.7E-5	0	0	0	2.1E-5	0	0	1.2E-3	2.8E-6	1.4E-3
7440-22-4	Silver	0	0	1.7E-4	0	0	0	5.9E-5	0	0	0	2.6E-5	0	0	1.5E-3	3.5E-6	1.8E-3
7429-90-5	Aluminum	0	0	24.463	0	0	0	8.332	0	0	0	3.756	0	0	216	0.494	253
7440-39-3	Barium	0	0	0.276	0	0	0	0.094	0	0	0	0.042	0	0	2.438	5.6E-3	2.855
1317-65-3	Calcium Ca:	0	0	4.824	0	0	0	1.643	0	0	0	0.741	0	0	42.663	0.097	49.967
7440-50-8	Copper	0	0	1.7E-3	0	0	0	5.9E-4	0	0	0	2.6E-4	0	0	0.015	3.5E-5	0.018
7439-89-6	Iron	0	0	6.271	0	0	0	2.136	0	0	0	0.963	0	0	55.462	0.127	64.958
7439-98-7	Molybdenu	0	0	3.4E-4	0	0	0	1.2E-4	0	0	0	5.3E-5	0	0	3.0E-3	7.0E-6	3.6E-3
7440-28-0	Thallium	0	0	3.4E-3	0	0	0	1.2E-3	0	0	0	5.3E-4	0	0	0.030	7.0E-5	0.036
7440-61-1	Uranium	0	0	3.4E-3	0	0	0	1.2E-3	0	0	0	5.3E-4	0	0	0.030	7.0E-5	0.036
7440-62-2	Vanadium	0	0	9.6E-3	0	0	0	3.3E-3	0	0	0	1.5E-3	0	0	0.085	1.9E-4	0.100
7440-33-7	Tungsten	0	0	3.4E-3	0	0	0	1.2E-3	0	0	0	5.3E-4	0	0	0.030	7.0E-5	0.036
7440-66-6	Zinc	0	0	0.012	0	0	0	4.1E-3	0	0	0	1.9E-3	0	0	0.107	2.4E-4	0.125
Total		0	0	36.441	0	0	0	12.412	0	0	0	5.596	0	0	322	0.736	377
															chk	377.4900	377.4900

MINING FUGITIVE EMISSIONS - CONTINUED

Mercury Evaporative Flux Emissions

Fugitive Mercury Flux and Emissions

			Area		Hg Flux	Emissions[1] lb/hr	Emissions[1] ton/yr	Emissions[1] lb/yr
CAS No.	Pollutant	Source	m^2	ha	$\mu g/m^2$-yr	lb/hr	ton/yr	lb/yr
		Stockpiles	52,623	5.3	556	7.37E-6	3.2E-5	6.5E-2
		Rock Dumps	2,063,990	206.4	76.2	3.96E-5	1.7E-4	0.35
		Tailings	1,338,158	133.8	2,144	7.22E-4	3.2E-3	6.32
		Pits	1,504,919	150.5	132.3	5.01E-5	2.2E-4	0.44
7439-97-6	Mercury					8.2E-4	3.6E-3	7.17

(1) *Hourly emissions based on:* 8,760 *hours per year of operation*

Fugitive Mercury Emission Factors

	Twin Creeks (TC)		Ore Hg Adjusted	Stibnite	
	Hg Flux (1)	Hg (2)	$\mu g/m^2$/yr	Hg Flux (3)	Hg (4)
Source	$\mu g/m^2$-yr	µg/g	TC	$\mu g/m^2$-yr	µg/g
Stockpiles	5,609	33	556	556	0.96
Rock Dumps	768	3.5	76.2	76.2	0.60
Tailings	21,621	33	2,144	2,144	0.96
Pits	1,334	9.5	132	132.3	0.60

(1) *(Eckley 2010)* *Table 1: Hg flux* $\mu g/m^2$*-yr*

(2) *(Eckley 2010)* *Table 1: Average Hg flux mg/g: " Stockpiles - high-grade stockpiles, Rock Dumps - waste rock dumps, Tailings - high-grade stockpiles as a surrogate; Pits - pit"*

(3) *(Eckley 2010)* *Figure 2: log(y) = m*log(x) + b*

y = Hg Flux (ng/m^2*-d)*
x = material Hg concentration (µg/g)]

Slope =	*Solar*	*TC*
	Low	*0.59*
	Medium	*0.6*
	High	*0.77*
	Average	*0.65*

(4) *(Midas Gold 2018e)*

Sample Calculation: m = log (y1/y2) / log(x1/x2)

m=	0.65	unitless
y1=	5,609	$\mu g/m^2$-yr
x1=	33	$\mu g/m^2$-yr
x2=	0.96	$\mu g/m^2$-yr
log(x1/x2)=	1.536243	unitless
log(y1/y2)=	1.003679	unitless
y1/y2=	10.08506	unitless
y2=	556.2	$\mu g/m^2$-yr

Conversions

2,000	lb/ton
10,000	m2/ha
453.593	g/lb

TABLE A-W3. HAP/TAP Emissions and Exemptions

180,000 T/day Emissions						MINING										LEACHING	
chk						*Mining*	*Model Scenario W3*									*CN Leach/PAX*	
						YPP,HFP,WEP,BT		YPPBL,HFPBL,WEPBL,BTBL		HR000		STKP, FDRSF, HFDRSF, YPDRSF, WEDRSF		TSF,ACCRD,UGEXP			
CAS	HAP/TAP	HAP	TAP			Pits		Blasting		Haul Roads		Stockpiles and DRFS		Tails, Access Road, Exploration		CN Leach and PAX	
	NSPS or NESHAP HAP/TAP -->			*Y*													
	Non-Carcinogenic Acute (A) or Carcinogenic (C) -->				*A/C*	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr
106-99-0	1,3-Butadiene	Y	Y	Y	C				0	0	0		0				
91-57-6	2-Methylnaphthalene	Y	N	n/a								0					
56-49-5	3-Methylchloranthrene	Y	Y	Y	C												
57-97-6	7,12-Dimethylbenz(a)anthracene	Y	N	n/a													
83-32-9	Acenaphthene	Y	N	n/a													
208-96-8	Acenaphthylene	Y	N	n/a													
75-07-0	Acetaldehyde	Y	Y	Y	C												
107-02-8	Acrolein	Y	Y	Y	A												
120-12-7	Anthracene	Y	N	n/a													
7440-36-0	Antimony	Y	Y	Y	A	1.8E-3	7.9E-3	6.2E-4	2.7E-3	0.016	0.070	2.8E-4	1.2E-3	3.7E-5	1.6E-4		
7440-38-2	Arsenic	Y	Y	Y	C	0.052	0.230	0.018	0.078	0.464	2.033	8.1E-3	0.035	1.1E-3	4.6E-3		
71-43-2	Benzene	Y	Y	Y	C												
50-32-8	Benzo(a)pyrene	Y	Y	Y	C												
56-55-3	Benz(a)anthracene	Y	Y	Y	C												
205-99-2	Benzo(b)fluoranthene	Y	Y	Y	C												
207-08-9	Benzo(k)fluoranthene	Y	Y	Y	C												
218-01-9	Chrysene	Y	Y	Y	C												
53-70-3	Dibenzo(a,h)anthracene	Y	Y	Y	C												
193-39-5	Indeno(1,2,3-cd)pyrene	Y	Y	Y	C												
191-24-2	Benzo(g,h,i)perylene	Y	N	n/a													
7440-41-7	Beryllium	Y	Y	Y	C	2.5E-4	1.1E-3	8.6E-5	3.8E-4	2.2E-3	9.8E-3	3.9E-5	1.7E-4	5.1E-6	2.2E-5		
92-52-4	Biphenyl	Y	Y	Y	A												
7440-43-9	Cadmium	Y	Y	Y	C	3.9E-5	1.7E-4	1.3E-5	5.9E-5	3.5E-4	1.5E-3	6.0E-6	2.6E-5	7.9E-7	3.5E-6		
75-15-0	Carbon Disulfide	Y	Y	Y	A											0.014	0.063
7440-47-3	Chromium	Y	Y	Y	A	7.1E-4	3.1E-3	2.4E-4	1.1E-3	6.3E-3	0.027	1.1E-4	4.8E-4	1.4E-5	6.3E-5		
18540-29-9	Cr (VI)	Y	Y	Y	C												
7440-48-4	Cobalt	Y	Y	Y	A	3.1E-4	1.4E-3	1.1E-4	4.7E-4	2.8E-3	0.012	4.8E-5	2.1E-4	6.4E-6	2.8E-5		
592-01-8	Cyanide	Y	Y	Y	A											0.453	1.983
106-46-7	Dichlorobenzene	Y	Y	Y	A												
206-44-0	Fluoranthene	Y	N	n/a													
86-73-7	Fluorene	Y	N	n/a													
50-00-0	Formaldehyde	Y	Y	Y	C												
110-54-3	Hexane	Y	Y	Y	A												
7647-01-0	Hydrogen Chloride	Y	Y	Y	A												
7439-92-1	Lead	Y	N	n/a		6.3E-4	2.8E-3	2.1E-4	9.4E-4	5.6E-3	0.024	9.7E-5	4.2E-4	1.3E-5	5.6E-5		
7439-96-5	Manganese	Y	Y	Y	A	0.024	0.103	8.0E-3	0.035	0.208	0.911	3.6E-3	0.016	4.7E-4	2.1E-3		
7439-97-6	Mercury	Y	N	n/a		9.7E-5	4.3E-4	1.6E-5	7.0E-5	4.2E-4	1.8E-3	5.4E-5	2.4E-4	7.2E-4	3.2E-3		
91-20-3	Naphthalene	Y	Y	Y	A												
7440-02-0	Nickel	Y	Y	Y	C	1.6E-4	6.9E-4	5.4E-5	2.3E-4	1.4E-3	6.1E-3	2.4E-5	1.1E-4	3.2E-6	1.4E-5		
85-01-8	Phenanthrene	Y	N	n/a													
108-95-2	Phenol	Y	Y	Y	A												
7723-14-0	Phosphorus	Y	Y	Y	A	0.051	0.224	0.017	0.076	0.452	1.981	7.9E-3	0.034	1.0E-3	4.5E-3		
129-00-0	Pyrene	Y	N	n/a													
7782-49-2	Selenium	Y	Y	Y	A	3.1E-5	1.4E-4	1.1E-5	4.7E-5	2.8E-4	1.2E-3	4.8E-6	2.1E-5	6.4E-7	2.8E-6		
108-88-3	Toluene	Y	Y	Y	A												
1330-20-7	Xylene	Y	Y	Y	A												
7429-90-5	Aluminum	N	Y	N	A	5.585	24.463	1.902	8.332	49.397	216	0.858	3.756	0.113	0.494		
7440-39-3	Barium	N	Y	N	A	0.063	0.276	0.021	0.094	0.557	2.438	9.7E-3	0.042	1.3E-3	5.6E-3		
1317-65-3	Calcium Carbonate	N	Y	N	A	1.101	4.824	0.375	1.643	9.740	42.663	0.169	0.741	0.022	0.097		
1305-78-8	Calcium Oxide	N	Y	N	A												
7440-50-8	Copper	N	Y	N	A	3.9E-4	1.7E-3	1.3E-4	5.9E-4	3.5E-3	0.015	6.0E-5	2.6E-4	7.9E-6	3.5E-5		
110-82-7	Cyclohexane	N	Y	N	A												
7783-06-4	Hydrogen Sulfide	N	Y	N	A												
7439-89-6	Iron	N	Y	N	A	1.432	6.271	0.488	2.136	12.662	55.462	0.220	0.963	0.029	0.127		
7439-98-7	Molybdenum	N	Y	N	A	7.9E-5	3.4E-4	2.7E-5	1.2E-4	7.0E-4	3.0E-3	1.2E-5	5.3E-5	1.6E-6	7.0E-6		
109-66-0	Pentane	N	Y	N	A												
7440-22-4	Silver	N	Y	N	A	3.9E-5	1.7E-4	1.3E-5	5.9E-5	3.5E-4	1.5E-3	6.0E-6	2.6E-5	7.9E-7	3.5E-6		
7664-93-9	Sulfuric Acid	N	Y	N	A												
7440-28-0	Thallium	N	Y	N	A	7.9E-4	3.4E-3	2.7E-4	1.2E-3	7.0E-3	0.030	1.2E-4	5.3E-4	1.6E-5	7.0E-5		
7440-61-1	Uranium	N	Y	N	A	7.9E-4	3.4E-3	2.7E-4	1.2E-3	7.0E-3	0.030	1.2E-4	5.3E-4	1.6E-5	7.0E-5		
7440-62-2	Vanadium	N	Y	N	A	2.2E-3	9.6E-3	7.5E-4	3.3E-3	0.019	0.085	3.4E-4	1.5E-3	4.4E-5	1.9E-4		
25551-13-7	Trimethyl benzene	N	Y	N	A												
7440-33-7	Tungsten	N	Y	N	A	7.9E-4	3.4E-3	2.7E-4	1.2E-3	7.0E-3	0.030	1.2E-4	5.3E-4	1.6E-5	7.0E-5		
7440-66-6	Zinc	N	Y	N	A	2.8E-3	0.012	9.4E-4	4.1E-3	0.024	0.107	4.2E-4	1.9E-3	5.6E-5	2.4E-4		
HAP TOTAL						***0.131***	***0.574***	***0.045***	***0.196***	***1.160***	***5.079***	***0.020***	***0.088***	***3.4E-3***	***0.015***	***0.467***	***2.046***
MERCURY TOTAL (exempt)						***9.7E-5***	***4.3E-4***	***1.6E-5***	***7.0E-5***	***4.2E-4***	***1.8E-3***	***5.4E-5***	***2.4E-4***	***7.2E-4***	***3.2E-3***		
MERCURY TOTAL (non-exempt)																	
TAP TOTAL (HAP-TAP addressed by NSPS/NESHAP)																	
TAP TOTAL (For EL Evaluation)						***8.319***	***36.438***	***2.834***	***12.411***	***73.580***	***322***	***1.278***	***5.595***	***0.168***	***0.735***	***0.467***	***2.046***

TABLE A-W3. HAP/TAP Emissions and Exemptions

180,000 T/day Emissions						PROCESSING AND PRODUCTION											
chk						*Ore Processing*				*Ore Concentration and Refining*				*Process Heating*			
						OC1-13		PS		AC		EW,MR,MF,CKD		ACB, CKB, PV, HS		LKC	
CAS	HAP/TAP	HAP	TAP			Crushers & Xfers		Prill Silos		Autoclave		EW, Preg Tank, Retort, Furnace, Carbon Kiln		POX Boiler, C. Kiln Comb., Prop. Vap., Sol'n Heater		Lime Kiln Combustion	
	NSPS or NESHAP HAP/TAP -->			*Y*		*LL*	*LL*			*7E*	*7E*	*7E*	*7E*			*5A*	*5A*
	Non-Carcinogenic Acute (A) or Carcinogenic (C) -->				*A/C*	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr
106-99-0	1,3-Butadiene	Y	Y	Y	C												
91-57-6	2-Methylnaphthalene	Y	N	n/a										1.9E-7	7.6E-7	5.2E-7	1.9E-6
56-49-5	3-Methylchloranthrene	Y	Y	Y	C									1.3E-8	5.7E-8	3.3E-8	1.4E-7
57-97-6	7,12-Dimethylbenz(a)anthracene	Y	N	n/a										1.3E-7	5.1E-7	3.5E-7	1.3E-6
83-32-9	Acenaphthene	Y	N	n/a										1.4E-8	5.7E-8	3.9E-8	1.4E-7
208-96-8	Acenaphthylene	Y	N	n/a										1.4E-8	5.7E-8	3.9E-8	1.4E-7
75-07-0	Acetaldehyde	Y	Y	Y	C												
107-02-8	Acrolein	Y	Y	Y	A												
120-12-7	Anthracene	Y	N	n/a										1.9E-8	7.6E-8	5.2E-8	1.9E-7
7440-36-0	Antimony	Y	Y	Y	A	1.4E-4	5.9E-4			2.3E-5	1.0E-4	3.8E-4	1.7E-3				
7440-38-2	Arsenic	Y	Y	Y	C	3.9E-3	0.017			2.3E-5	1.0E-4	3.8E-4	1.7E-3	1.5E-6	6.4E-6	3.7E-6	1.6E-5
71-43-2	Benzene	Y	Y	Y	C									1.5E-5	6.7E-5	3.9E-5	1.7E-4
50-32-8	Benzo(a)pyrene	Y	Y	Y	C									8.7E-9	3.8E-8	2.2E-8	9.6E-8
56-55-3	Benz(a)anthracene	Y	Y	Y	C									1.3E-8	5.7E-8	3.3E-8	1.4E-7
205-99-2	Benzo(b)fluoranthene	Y	Y	Y	C									1.3E-8	5.7E-8	3.3E-8	1.4E-7
207-08-9	Benzo(k)fluoranthene	Y	Y	Y	C									1.3E-8	5.7E-8	3.3E-8	1.4E-7
218-01-9	Chrysene	Y	Y	Y	C									1.3E-8	5.7E-8	3.3E-8	1.4E-7
53-70-3	Dibenzo(a,h)anthracene	Y	Y	Y	C									8.7E-9	3.8E-8	2.2E-8	9.6E-8
193-39-5	Indeno(1,2,3-cd)pyrene	Y	Y	Y	C									1.3E-8	5.7E-8	3.3E-8	1.4E-7
191-24-2	Benzo(g,h,i)perylene	Y	N	n/a										9.5E-9	3.8E-8	2.6E-8	9.6E-8
7440-41-7	Beryllium	Y	Y	Y	C	1.9E-5	8.2E-5			2.3E-5	1.0E-4	3.8E-4	1.7E-3	8.7E-8	3.8E-7	2.2E-7	9.6E-7
92-52-4	Biphenyl	Y	Y	Y	A												
7440-43-9	Cadmium	Y	Y	Y	C	2.9E-6	1.3E-5			2.3E-5	1.0E-4	3.8E-4	1.7E-3	8.0E-6	3.5E-5	2.0E-5	8.8E-5
75-15-0	Carbon Disulfide	Y	Y	Y	A												
7440-47-3	Chromium	Y	Y	Y	A	5.3E-5	2.3E-4			2.3E-5	1.0E-4	3.8E-4	1.7E-3	1.1E-5	4.5E-5	3.0E-5	1.1E-4
18540-29-9	Cr (VI)	Y	Y	Y	C												
7440-48-4	Cobalt	Y	Y	Y	A	2.4E-5	1.0E-4			2.3E-5	1.0E-4	3.8E-4	1.7E-3	6.6E-7	2.7E-6	1.8E-6	6.8E-6
592-01-8	Cyanide	Y	Y	Y	A							1.2E-3	5.3E-3				
106-46-7	Dichlorobenzene	Y	Y	Y	A									9.5E-6	3.8E-5	2.6E-5	9.6E-5
206-44-0	Fluoranthene	Y	N	n/a										2.4E-8	9.5E-8	6.5E-8	2.4E-7
86-73-7	Fluorene	Y	N	n/a										2.2E-8	8.9E-8	6.1E-8	2.3E-7
50-00-0	Formaldehyde	Y	Y	Y	C									5.5E-4	2.4E-3	1.4E-3	6.0E-3
110-54-3	Hexane	Y	Y	Y	A									0.014	0.057	0.039	0.145
7647-01-0	Hydrogen Chloride	Y	Y	Y	A												
7439-92-1	Lead	Y	N	n/a		4.7E-5	2.1E-4			2.3E-5	1.0E-4	3.8E-4	1.7E-3				
7439-96-5	Manganese	Y	Y	Y	A	1.8E-3	7.7E-3			2.3E-5	1.0E-4	3.8E-4	1.7E-3	3.0E-6	1.2E-5	8.2E-6	3.1E-5
7439-97-6	Mercury	Y	N	n/a		5.6E-6	2.5E-5			2.3E-5	1.0E-4	3.8E-4	1.7E-3	2.1E-6	8.3E-6	5.6E-6	2.1E-5
91-20-3	Naphthalene	Y	Y	Y	A									4.8E-6	1.9E-5	1.3E-5	4.9E-5
7440-02-0	Nickel	Y	Y	Y	C	1.2E-5	5.2E-5			2.3E-5	1.0E-4	3.8E-4	1.7E-3	1.5E-5	6.7E-5	3.9E-5	1.7E-4
85-01-8	Phenanthrene	Y	N	n/a										1.3E-7	5.4E-7	3.7E-7	1.4E-6
108-95-2	Phenol	Y	Y	Y	A												
7723-14-0	Phosphorus	Y	Y	Y	A	3.8E-3	0.017			2.3E-5	1.0E-4	3.8E-4	1.7E-3				
129-00-0	Pyrene	Y	N	n/a										4.0E-8	1.6E-7	1.1E-7	4.0E-7
7782-49-2	Selenium	Y	Y	Y	A	2.4E-6	1.0E-5			2.3E-5	1.0E-4	3.8E-4	1.7E-3	1.9E-7	7.6E-7	5.2E-7	1.9E-6
108-88-3	Toluene	Y	Y	Y	A									2.7E-5	1.1E-4	7.3E-5	2.7E-4
1330-20-7	Xylene	Y	Y	Y	A												
7429-90-5	Aluminum	N	Y	N	A	0.418	1.829			2.3E-5	1.0E-4	3.8E-4	1.7E-3				
7440-39-3	Barium	N	Y	N	A	4.7E-3	0.021			2.3E-5	1.0E-4	3.8E-4	1.7E-3	3.5E-5	1.4E-4	9.5E-5	3.5E-4
1317-65-3	Calcium Carbonate	N	Y	N	A	0.082	0.361			2.3E-5	1.0E-4	3.8E-4	1.7E-3				
1305-78-8	Calcium Oxide	N	Y	N	A												
7440-50-8	Copper	N	Y	N	A	2.9E-5	1.3E-4			2.3E-5	1.0E-4	3.8E-4	1.7E-3	6.7E-6	2.7E-5	1.8E-5	6.8E-5
110-82-7	Cyclohexane	N	Y	N	A												
7783-06-4	Hydrogen Sulfide	N	Y	N	A					0.900	3.942						
7439-89-6	Iron	N	Y	N	A	0.107	0.469			2.3E-5	1.0E-4	3.8E-4	1.7E-3				
7439-98-7	Molybdenum	N	Y	N	A	5.9E-6	2.6E-5			2.3E-5	1.0E-4	3.8E-4	1.7E-3	8.7E-6	3.5E-5	2.4E-5	8.8E-5
109-66-0	Pentane	N	Y	N	A									0.021	0.083	0.056	0.209
7440-22-4	Silver	N	Y	N	A	2.9E-6	1.3E-5			2.3E-5	1.0E-4	3.8E-4	1.7E-3				
7664-93-9	Sulfuric Acid	N	Y	N	A					2.030	8.891						
7440-28-0	Thallium	N	Y	N	A	5.9E-5	2.6E-4			2.3E-5	1.0E-4	3.8E-4	1.7E-3				
7440-61-1	Uranium	N	Y	N	A	5.9E-5	2.6E-4			2.3E-5	1.0E-4	3.8E-4	1.7E-3				
7440-62-2	Vanadium	N	Y	N	A	1.6E-4	7.2E-4			2.3E-5	1.0E-4	3.8E-4	1.7E-3	1.8E-5	7.3E-5	5.0E-5	1.8E-4
25551-13-7	Trimethyl benzene	N	Y	N	A												
7440-33-7	Tungsten	N	Y	N	A	5.9E-5	2.6E-4			2.3E-5	1.0E-4	3.8E-4	1.7E-3				
7440-66-6	Zinc	N	Y	N	A	2.1E-4	9.0E-4			2.3E-5	1.0E-4	3.8E-4	1.7E-3	2.3E-4	9.2E-4	6.3E-4	2.3E-3
HAP TOTAL						***9.8E-3***	***0.043***			***2.8E-4***	***1.2E-3***	***5.8E-3***	***0.025***	***0.015***	***0.060***	***0.041***	***0.152***
MERCURY TOTAL (exempt)										***2.3E-5***	***1.0E-4***	***3.8E-4***	***1.7E-3***			***5.6E-6***	***2.1E-5***
MERCURY TOTAL (non-exempt)						***5.6E-6***	***2.5E-5***							***2.1E-6***	***8.3E-6***		
TAP TOTAL (HAP-TAP addressed by NSPS/NESHAP)						***9.8E-3***	***0.043***			***2.3E-4***	***1.0E-3***	***5.0E-3***	***0.022***			***0.041***	***0.152***
TAP TOTAL (For EL Evaluation)						***0.612***	***2.682***			***2.930***	***12.835***	***4.6E-3***	***0.020***	***0.036***	***0.144***	***0.057***	***0.212***

TABLE A-W3. HAP/TAP Emissions and Exemptions

						0	0	1	1	0	0	0	0	0	0	0	0	0	0
180,000 T/day Emissions						**PROCESSING AND PRODUCTION - Continued**													
chk						*Lime Production*						*Aggregate Prod.*		*Concrete Production*					
						LS1-11,LSBM		LK,LS12,LCR,LS-L/U		LS1-L/U,MillS2-L/U,ACS1-4		PCSP1,PCSP2		CM		CS1L,CS1U,CS2L, CS2U		CA-L/U	
CAS	HAP/TAP	HAP	TAP			Limestone Crushers, Screens, Mill, Xfers		Lime Kiln, Kiln Feed, Lime Mill, Pebble Lime Silo		Lime Silos and Lime Mill Crushing		Portable Crushers, Screens, Xfers		Central Mixer		Cement Silo #1 and #2 L/U		Aggregate Bin	
	NSPS or NESHAP HAP/TAP -->			*Y*		*OOO*	*OOO*	*5A*	*5A*			*OOO*	*OOO*					*OOO*	*OOO*
	Non-Carcinogenic Acute (A) or Carcinogenic (C) -->				*A/C*	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr
106-99-0	1,3-Butadiene	Y	Y	Y	C														
91-57-6	2-Methylnaphthalene	Y	N	n/a															
56-49-5	3-Methylchloranthrene	Y	Y	Y	C														
57-97-6	7,12-Dimethylbenz(a)anthracene	Y	N	n/a															
83-32-9	Acenaphthene	Y	N	n/a															
208-96-8	Acenaphthylene	Y	N	n/a															
75-07-0	Acetaldehyde	Y	Y	Y	C														
107-02-8	Acrolein	Y	Y	Y	A														
120-12-7	Anthracene	Y	N	n/a															
7440-36-0	Antimony	Y	Y	Y	A	1.4E-5	4.8E-5	3.1E-6	1.2E-5	1.6E-6	5.1E-7	3.1E-6	1.4E-5					3.5E-6	8.6E-6
7440-38-2	Arsenic	Y	Y	Y	C	1.0E-4	4.4E-4	2.4E-5	1.1E-4	1.1E-6	4.7E-6	2.9E-5	1.3E-4	2.0E-6	8.9E-6	1.2E-7	5.1E-7	1.8E-5	7.9E-5
71-43-2	Benzene	Y	Y	Y	C														
50-32-8	Benzo(a)pyrene	Y	Y	Y	C														
56-55-3	Benz(a)anthracene	Y	Y	Y	C														
205-99-2	Benzo(b)fluoranthene	Y	Y	Y	C														
207-08-9	Benzo(k)fluoranthene	Y	Y	Y	C														
218-01-9	Chrysene	Y	Y	Y	C														
53-70-3	Dibenzo(a,h)anthracene	Y	Y	Y	C														
193-39-5	Indeno(1,2,3-cd)pyrene	Y	Y	Y	C														
191-24-2	Benzo(g,h,i)perylene	Y	N	n/a															
7440-41-7	Beryllium	Y	Y	Y	C	3.5E-6	1.5E-5	8.4E-7	3.7E-6	3.7E-8	1.6E-7	1.0E-6	4.4E-6			1.3E-8	5.8E-8	6.3E-7	2.8E-6
92-52-4	Biphenyl	Y	Y	Y	A														
7440-43-9	Cadmium	Y	Y	Y	C	1.1E-6	4.8E-6	2.6E-7	1.2E-6	1.2E-8	5.1E-8	3.1E-7	1.4E-6	4.9E-9	2.1E-8			2.0E-7	8.6E-7
75-15-0	Carbon Disulfide	Y	Y	Y	A														
7440-47-3	Chromium	Y	Y	Y	A	8.5E-5	2.9E-4	1.9E-5	6.9E-5	9.7E-6	3.0E-6	1.9E-5	8.2E-5	8.7E-7	3.8E-6	7.9E-7	3.5E-6	2.1E-5	5.2E-5
18540-29-9	Cr (VI)	Y	Y	Y	C									1.9E-7	8.1E-7	1.6E-7	7.0E-7		
7440-48-4	Cobalt	Y	Y	Y	A	2.3E-5	7.7E-5	5.0E-6	1.8E-5	2.6E-6	8.1E-7	5.0E-6	2.2E-5					5.5E-6	1.4E-5
592-01-8	Cyanide	Y	Y	Y	A														
106-46-7	Dichlorobenzene	Y	Y	Y	A														
206-44-0	Fluoranthene	Y	N	n/a															
86-73-7	Fluorene	Y	N	n/a															
50-00-0	Formaldehyde	Y	Y	Y	C														
110-54-3	Hexane	Y	Y	Y	A														
7647-01-0	Hydrogen Chloride	Y	Y	Y	A	0	0	0.986	3.666										
7439-92-1	Lead	Y	N	n/a		1.7E-5	5.8E-5	3.7E-6	1.4E-5	1.9E-6	6.1E-7	3.8E-6	1.6E-5	2.5E-7	1.1E-6	3.0E-7	1.3E-6	4.1E-6	1.0E-5
7439-96-5	Manganese	Y	Y	Y	A	1.3E-3	4.6E-3	2.9E-4	1.1E-3	1.5E-4	4.8E-5	3.0E-4	1.3E-3	2.6E-5	1.1E-4	3.2E-6	1.4E-5	3.3E-4	8.2E-4
7439-97-6	Mercury	Y	N	n/a		1.1E-7	3.9E-7	2.8E-4	1.0E-3	1.3E-8	4.1E-9	2.5E-8	1.1E-7					2.8E-8	6.9E-8
91-20-3	Naphthalene	Y	Y	Y	A														
7440-02-0	Nickel	Y	Y	Y	C	2.2E-5	9.6E-5	5.3E-6	2.3E-5	2.3E-7	1.0E-6	6.3E-6	2.7E-5	1.7E-6	7.4E-6	1.1E-6	5.0E-6	3.9E-6	1.7E-5
85-01-8	Phenanthrene	Y	N	n/a															
108-95-2	Phenol	Y	Y	Y	A														
7723-14-0	Phosphorus	Y	Y	Y	A	7.4E-4	2.5E-3	1.6E-4	6.0E-4	8.4E-5	2.6E-5	1.6E-4	7.1E-4	8.2E-6	3.6E-5			1.8E-4	4.5E-4
129-00-0	Pyrene	Y	N	n/a															
7782-49-2	Selenium	Y	Y	Y	A														
108-88-3	Toluene	Y	Y	Y	A														
1330-20-7	Xylene	Y	Y	Y	A														
7429-90-5	Aluminum	N	Y	N	A	0.128	0.436	0.028	0.104	0.015	4.6E-3	0.028	0.124					0.031	0.078
7440-39-3	Barium	N	Y	N	A	8.2E-4	2.8E-3	1.8E-4	6.7E-4	9.4E-5	2.9E-5	1.8E-4	7.9E-4					2.0E-4	5.0E-4
1317-65-3	Calcium Carbonate	N	Y	N	A	1.558	5.291	0.260	0.969			0.343	1.503						
1305-78-8	Calcium Oxide	N	Y	N	A			0.216	0.802	0.480	0.150								
7440-50-8	Copper	N	Y	N	A	2.8E-5	9.6E-5	6.2E-6	2.3E-5	3.2E-6	1.0E-6	6.3E-6	2.7E-5					6.9E-6	1.7E-5
110-82-7	Cyclohexane	N	Y	N	A														
7783-06-4	Hydrogen Sulfide	N	Y	N	A														
7439-89-6	Iron	N	Y	N	A	0.059	0.199	0.013	0.048	6.7E-3	2.1E-3	0.013	0.057					0.014	0.036
7439-98-7	Molybdenum	N	Y	N	A	2.8E-6	9.6E-6	6.2E-7	2.3E-6	3.2E-7	1.0E-7	6.3E-7	2.7E-6					6.9E-7	1.7E-6
109-66-0	Pentane	N	Y	N	A														
7440-22-4	Silver	N	Y	N	A	0	0												
7664-93-9	Sulfuric Acid	N	Y	N	A														
7440-28-0	Thallium	N	Y	N	A	2.8E-5	9.6E-5	6.2E-6	2.3E-5	3.2E-6	1.0E-6	6.3E-6	2.7E-5					6.9E-6	1.7E-5
7440-61-1	Uranium	N	Y	N	A	2.8E-5	9.6E-5	6.2E-6	2.3E-5	3.2E-6	1.0E-6	6.3E-6	2.7E-5					6.9E-6	1.7E-5
7440-62-2	Vanadium	N	Y	N	A	8.8E-5	3.0E-4	1.9E-5	7.1E-5	1.0E-5	3.1E-6	1.9E-5	8.5E-5					2.1E-5	5.3E-5
25551-13-7	Trimethyl benzene	N	Y	N	A														
7440-33-7	Tungsten	N	Y	N	A	2.8E-5	9.6E-5	6.2E-6	2.3E-5	3.2E-6	1.0E-6	6.3E-6	2.7E-5					6.9E-6	1.7E-5
7440-66-6	Zinc	N	Y	N	A	1.0E-4	3.5E-4	2.2E-5	8.3E-5	1.2E-5	3.6E-6	2.3E-5	9.9E-5					2.5E-5	6.2E-5
HAP TOTAL						***2.3E-3***	***8.1E-3***	***0.987***	***3.669***	***2.6E-4***	***8.5E-5***	***5.3E-4***	***2.3E-3***	***3.9E-5***	***1.7E-4***	***5.7E-6***	***2.5E-5***	***5.6E-4***	***1.4E-3***
MERCURY TOTAL (exempt)						***0***	***0***	***2.8E-4***	***1.0E-3***										
MERCURY TOTAL (non-exempt)						***1.1E-7***	***3.9E-7***			***1.3E-8***	***4.1E-9***	***2.5E-8***	***1.1E-7***					***2.8E-8***	***6.9E-8***
TAP TOTAL (HAP-TAP addressed by NSPS/NESHAP)						***2.3E-3***	***8.0E-3***	***0.986***	***3.668***			***5.2E-4***	***2.3E-3***					***5.6E-4***	***1.4E-3***
TAP TOTAL (For EL Evaluation)						***1.746***	***5.930***	***0.517***	***1.923***	***0.502***	***0.157***	***0.385***	***1.684***	***3.9E-5***	***1.7E-4***	***5.4E-6***	***2.4E-5***	***0.046***	***0.114***

TABLE A-W3. HAP/TAP Emissions and Exemptions

180,000 T/day Emissions						PROCESSING AND PRODUCTION - Continued						MINING and LEACHING - Totals									
chk						*HVAC*		*Emer. Power/Fire*		*Fuel Storage*		*HAP Total*		*Mercury Total*		*Mercury Total*		*TAP Total*		*TAP Total*	
						H1M,H2M,HM,HAC,HR,HA,HMO,HTS,HW		EDG1,EDG2,EDG3,EDFP		TG1,TG2				*Exempt*		*Non-Exempt*		*HAP-TAP addressed by NSPS/NESHAP*		*For EL Evaluation*	
CAS	HAP/TAP	HAP	TAP			Heaters		Emergency Generators and Fire Pump		Gasoline Fuel Tanks											
	NSPS or NESHAP HAP/TAP -->			*Y*				*4Z*	*4Z*	*6C*	*6C*										
	Non-Carcinogenic Acute (A) or Carcinogenic (C) -->				*A/C*	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr
106-99-0	1,3-Butadiene	Y	Y	Y	C			8.4E-7	3.7E-6			0	0					0	0	0	0
91-57-6	2-Methylnaphthalene	Y	N	n/a		4.3E-7	1.9E-6														
56-49-5	3-Methylchloranthrene	Y	Y	Y	C	3.2E-8	1.4E-7														
57-97-6	7,12-Dimethylbenz(a)anthracene	Y	N	n/a		2.9E-7	1.3E-6														
83-32-9	Acenaphthene	Y	N	n/a		3.2E-8	1.4E-7	5.6E-6	6.7E-6												
208-96-8	Acenaphthylene	Y	N	n/a		3.2E-8	1.4E-7	1.1E-5	1.3E-5												
75-07-0	Acetaldehyde	Y	Y	Y	C			2.5E-5	1.1E-4												
107-02-8	Acrolein	Y	Y	Y	A			1.6E-5	2.0E-5												
120-12-7	Anthracene	Y	N	n/a		4.3E-8	1.9E-7	1.6E-6	1.9E-6												
7440-36-0	Antimony	Y	Y	Y	A							0.019	0.082							0.019	0.082
7440-38-2	Arsenic	Y	Y	Y	C	3.6E-6	1.6E-5					0.544	2.381							0.544	2.381
71-43-2	Benzene	Y	Y	Y	C	3.8E-5	1.6E-4	2.7E-4	1.2E-3	7.0E-3	0.031										
50-32-8	Benzo(a)pyrene	Y	Y	Y	C	2.1E-8	9.4E-8	8.7E-8	3.8E-7												
56-55-3	Benz(a)anthracene	Y	Y	Y	C	3.2E-8	1.4E-7	2.4E-7	1.0E-6												
205-99-2	Benzo(b)fluoranthene	Y	Y	Y	C	3.2E-8	1.4E-7	3.6E-7	1.6E-6												
207-08-9	Benzo(k)fluoranthene	Y	Y	Y	C	3.2E-8	1.4E-7	7.3E-8	3.2E-7												
218-01-9	Chrysene	Y	Y	Y	C	3.2E-8	1.4E-7	5.0E-7	2.2E-6												
53-70-3	Dibenzo(a,h)anthracene	Y	Y	Y	C	2.1E-8	9.4E-8	1.2E-7	5.4E-7												
193-39-5	Indeno(1,2,3-cd)pyrene	Y	Y	Y	C	3.2E-8	1.4E-7	1.4E-7	6.2E-7												
191-24-2	Benzo(g,h,i)perylene	Y	N	n/a		2.1E-8	9.4E-8	6.9E-7	8.3E-7												
7440-41-7	Beryllium	Y	Y	Y	C	2.1E-7	9.4E-7					2.6E-3	0.011							2.6E-3	0.011
92-52-4	Biphenyl	Y	Y	Y	A					4.4E-5	1.9E-4										
7440-43-9	Cadmium	Y	Y	Y	C	2.0E-5	8.6E-5					4.1E-4	1.8E-3							4.1E-4	1.8E-3
75-15-0	Carbon Disulfide	Y	Y	Y	A							0.014	0.063							0.014	0.063
7440-47-3	Chromium	Y	Y	Y	A	2.5E-5	1.1E-4					7.3E-3	0.032							7.3E-3	0.032
18540-29-9	Cr (VI)	Y	Y	Y	C																
7440-48-4	Cobalt	Y	Y	Y	A	1.5E-6	6.6E-6					3.3E-3	0.014							3.3E-3	0.014
592-01-8	Cyanide	Y	Y	Y	A							0.453	1.983							0.453	1.983
106-46-7	Dichlorobenzene	Y	Y	Y	A	2.1E-5	9.4E-5														
206-44-0	Fluoranthene	Y	N	n/a		5.4E-8	2.4E-7	5.3E-6	6.4E-6												
86-73-7	Fluorene	Y	N	n/a		5.0E-8	2.2E-7	1.7E-5	2.1E-5												
50-00-0	Formaldehyde	Y	Y	Y	C	1.3E-3	5.9E-3	5.1E-5	2.2E-4												
110-54-3	Hexane	Y	Y	Y	A	0.032	0.141			0.031	0.137										
7647-01-0	Hydrogen Chloride	Y	Y	Y	A																
7439-92-1	Lead	Y	N	n/a								6.5E-3	0.029								
7439-96-5	Manganese	Y	Y	Y	A	6.8E-6	3.0E-5					0.244	1.067							0.244	1.067
7439-97-6	Mercury	Y	N	n/a		4.7E-6	2.0E-5					1.3E-3	5.7E-3	1.3E-3	5.7E-3	0	0	0	0	0	0
91-20-3	Naphthalene	Y	Y	Y	A	1.1E-5	4.8E-5	1.6E-4	1.9E-4	1.9E-3	8.5E-3	0	0					0	0	0	0
7440-02-0	Nickel	Y	Y	Y	C	3.8E-5	1.6E-4					1.6E-3	7.1E-3					0	0	1.6E-3	7.1E-3
85-01-8	Phenanthrene	Y	N	n/a		3.0E-7	1.3E-6	5.0E-5	6.0E-5			0	0					0	0	0	0
108-95-2	Phenol	Y	Y	Y	A					2.4E-4	1.1E-3	0	0					0	0	0	0
7723-14-0	Phosphorus	Y	Y	Y	A							0.530	2.320					0	0	0.530	2.320
129-00-0	Pyrene	Y	N	n/a		8.9E-8	3.9E-7	4.7E-6	5.7E-6			0	0					0	0	0	0
7782-49-2	Selenium	Y	Y	Y	A	4.3E-7	1.9E-6					3.3E-4	1.4E-3					0	0	3.3E-4	1.4E-3
108-88-3	Toluene	Y	Y	Y	A	6.1E-5	2.7E-4	3.6E-4	4.3E-4	0.032	0.138	0	0					0	0	0	0
1330-20-7	Xylene	Y	Y	Y	A			2.5E-4	3.0E-4	0.031	0.137	0	0					0	0	0	0
7429-90-5	Aluminum	N	Y	N	A							0	0					0	0	57.855	253
7440-39-3	Barium	N	Y	N	A	7.9E-5	3.4E-4					0	0					0	0	0.652	2.855
1317-65-3	Calcium Carbonate	N	Y	N	A							0	0					0	0	11.408	49.967
1305-78-8	Calcium Oxide	N	Y	N	A							0	0					0	0	0	0
7440-50-8	Copper	N	Y	N	A	1.5E-5	6.7E-5					0	0					0	0	4.1E-3	0.018
110-82-7	Cyclohexane	N	Y	N	A					1.0E-3	4.6E-3	0	0					0	0	0	0
7783-06-4	Hydrogen Sulfide	N	Y	N	A							0	0					0	0	0	0
7439-89-6	Iron	N	Y	N	A							0	0					0	0	14.831	64.958
7439-98-7	Molybdenum	N	Y	N	A	2.0E-5	8.6E-5					0	0					0	0	8.1E-4	3.6E-3
109-66-0	Pentane	N	Y	N	A	0.047	0.204					0	0					0	0	0	0
7440-22-4	Silver	N	Y	N	A							0	0					0	0	4.1E-4	1.8E-3
7664-93-9	Sulfuric Acid	N	Y	N	A							0	0					0	0	0	0
7440-28-0	Thallium	N	Y	N	A							0	0					0	0	8.1E-3	0.036
7440-61-1	Uranium	N	Y	N	A							0	0					0	0	8.1E-3	0.036
7440-62-2	Vanadium	N	Y	N	A	4.1E-5	1.8E-4					0	0					0	0	0.023	0.100
25551-13-7	Trimethyl benzene	N	Y	N	A					0.011	0.048	0	0					0	0	0	0
7440-33-7	Tungsten	N	Y	N	A							0	0					0	0	8.1E-3	0.036
7440-66-6	Zinc	N	Y	N	A	5.2E-4	2.3E-3					0	0					0	0	0.029	0.125
HAP TOTAL						*0.034*	*0.148*	*1.2E-3*	*2.6E-3*	*0.103*	*0.453*	*1.826*	*7.998*								
MERCURY TOTAL (exempt)														*1.3E-3*	*5.7E-3*						
MERCURY TOTAL (non-exempt)						*4.7E-6*	*2.0E-5*									*0*	*0*				
TAP TOTAL (HAP-TAP addressed by NSPS/NESHAP)								*1.1E-3*	*2.5E-3*	*0.103*	*0.453*							*0*	*0*		
TAP TOTAL (For EL Evaluation)						*0.081*	*0.355*			*0.012*	*0.052*									*86.645*	*380*

TABLE A-W3. HAP/TAP Emissions and Exemptions

180,000 T/day Emissions						PROCESSING AND PRODUCTION - Totals										ALL	ALL	ALL	TAP EL	
chk						*HAP Total*		*Mercury Total Exempt*		*Mercury Total Non-Exempt*		*TAP Total HAP-TAP addressed by NSPS/NESHAP*		*TAP Total For EL Evaluation*		*HAP*	*Hg Non-Exempt*	*TAP For EL Evaluation*	*TAP Emission Screening Level (EL)*	
CAS	HAP/TAP	HAP	TAP																	
	NSPS or NESHAP HAP/TAP -->			*Y*															Non-car	Carcin
	Non-Carcinogenic Acute (A) or Carcinogenic (C) -->				*A/C*	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	ton/yr	ton/yr	lb/hr	lb/hr	lb/hr
106-99-0	1,3-Butadiene	Y	Y	Y	C	8.4E-7	3.7E-6					8.4E-7	3.7E-6			3.7E-6		0	--	2.4E-5
91-57-6	2-Methylnaphthalene	Y	N	n/a		1.1E-6	4.6E-6									4.6E-6			--	--
56-49-5	3-Methylchloranthrene	Y	Y	Y	C	7.8E-8	3.4E-7					3.3E-8	1.4E-7	4.5E-8	2.0E-7	3.4E-7		4.5E-8	--	2.5E-6
57-97-6	7,12-Dimethylbenz(a)anthracene	Y	N	n/a		7.6E-7	3.0E-6									3.0E-6			--	--
83-32-9	Acenaphthene	Y	N	n/a		5.7E-6	7.1E-6									7.1E-6			--	--
208-96-8	Acenaphthylene	Y	N	n/a		1.1E-5	1.4E-5									1.4E-5			--	--
75-07-0	Acetaldehyde	Y	Y	Y	C	2.5E-5	1.1E-4					2.5E-5	1.1E-4			1.1E-4			--	3.0E-3
107-02-8	Acrolein	Y	Y	Y	A	1.6E-5	2.0E-5					1.6E-5	2.0E-5			2.0E-5			0.017	--
120-12-7	Anthracene	Y	N	n/a		1.7E-6	2.4E-6									2.4E-6			--	--
7440-36-0	Antimony	Y	Y	Y	A	5.7E-4	2.5E-3					5.7E-4	2.5E-3	1.6E-6	5.1E-7	0.085		0.019	0.033	--
7440-38-2	Arsenic	Y	Y	Y	C	4.5E-3	0.020					4.5E-3	0.020	8.2E-6	3.6E-5	2.400		0.544	--	1.5E-6
71-43-2	Benzene	Y	Y	Y	C	7.4E-3	0.032					7.3E-3	0.032	5.3E-5	2.3E-4	0.032		5.3E-5	--	8.0E-4
50-32-8	Benzo(a)pyrene	Y	Y	Y	C	1.4E-7	6.1E-7					1.1E-7	4.8E-7	3.0E-8	1.3E-7	6.1E-7				
56-55-3	Benz(a)anthracene	Y	Y	Y	C	3.1E-7	1.4E-6					2.7E-7	1.2E-6	4.5E-8	2.0E-7	1.4E-6				
205-99-2	Benzo(b)fluoranthene	Y	Y	Y	C	4.4E-7	1.9E-6					3.9E-7	1.7E-6	4.5E-8	2.0E-7	1.9E-6				
207-08-9	Benzo(k)fluoranthene	Y	Y	Y	C	1.5E-7	6.6E-7					1.1E-7	4.7E-7	4.5E-8	2.0E-7	6.6E-7		2.9E-7	--	2.0E-6
218-01-9	Chrysene	Y	Y	Y	C	5.8E-7	2.5E-6					5.3E-7	2.3E-6	4.5E-8	2.0E-7	2.5E-6				
53-70-3	Dibenzo(a,h)anthracene	Y	Y	Y	C	1.8E-7	7.7E-7					1.5E-7	6.4E-7	3.0E-8	1.3E-7	7.7E-7				
193-39-5	Indeno(1,2,3-cd)pyrene	Y	Y	Y	C	2.2E-7	9.6E-7					1.7E-7	7.6E-7	4.5E-8	2.0E-7	9.6E-7				
191-24-2	Benzo(g,h,i)perylene	Y	N	n/a		7.5E-7	1.1E-6									1.1E-6			--	--
7440-41-7	Beryllium	Y	Y	Y	C	4.3E-4	1.9E-3					4.3E-4	1.9E-3	3.5E-7	1.5E-6	0.013		2.6E-3	--	2.8E-5
92-52-4	Biphenyl	Y	Y	Y	A	4.4E-5	1.9E-4					4.4E-5	1.9E-4			1.9E-4			0.100	--
7440-43-9	Cadmium	Y	Y	Y	C	4.6E-4	2.0E-3					4.3E-4	1.9E-3	2.8E-5	1.2E-4	3.8E-3		4.4E-4	--	3.7E-6
75-15-0	Carbon Disulfide	Y	Y	Y	A											0.063		0.014	2.000	--
7440-47-3	Chromium	Y	Y	Y	A	6.8E-4	2.8E-3					6.3E-4	2.6E-3	4.8E-5	1.6E-4	0.035		7.4E-3	0.033	--
18540-29-9	Cr (VI)	Y	Y	Y	C	3.4E-7	1.5E-6							3.4E-7	1.5E-6	1.5E-6		3.4E-7	--	5.6E-7
7440-48-4	Cobalt	Y	Y	Y	A	4.7E-4	2.0E-3					4.7E-4	2.0E-3	4.8E-6	1.0E-5	0.016		3.3E-3	3.3E-3	--
592-01-8	Cyanide	Y	Y	Y	A	1.2E-3	5.3E-3					1.2E-3	5.3E-3			1.988		0.453	0.333	--
106-46-7	Dichlorobenzene	Y	Y	Y	A	5.7E-5	2.3E-4					2.6E-5	9.6E-5	3.1E-5	1.3E-4	2.3E-4		3.1E-5	30.000	--
206-44-0	Fluoranthene	Y	N	n/a		5.5E-6	7.0E-6									7.0E-6			--	--
86-73-7	Fluorene	Y	N	n/a		1.7E-5	2.1E-5									2.1E-5			--	--
50-00-0	Formaldehyde	Y	Y	Y	C	3.3E-3	0.015					1.4E-3	6.2E-3	1.9E-3	8.3E-3	0.015		1.9E-3	--	5.1E-4
110-54-3	Hexane	Y	Y	Y	A	0.117	0.480					0.070	0.281	0.046	0.198	0.480		0.046	12.000	--
7647-01-0	Hydrogen Chloride	Y	Y	Y	A	0.986	3.666					0.986	3.666			3.666			0.050	--
7439-92-1	Lead	Y	N	n/a		4.8E-4	2.1E-3									0.031			--	--
7439-96-5	Manganese	Y	Y	Y	A	4.6E-3	0.017					4.4E-3	0.017	1.9E-4	2.2E-4	1.085		0.244	0.067	--
7439-97-6	Mercury	Y	N	n/a		7.1E-4	2.9E-3	6.9E-4	2.8E-3	1.3E-5	5.4E-5					8.6E-3	5.4E-5		--	--
91-20-3	Naphthalene	Y	Y	Y	A	2.1E-3	8.8E-3					2.1E-3	8.7E-3	1.6E-5	6.7E-5	8.8E-3		1.6E-5	3.330	--
7440-02-0	Nickel	Y	Y	Y	C	5.5E-4	2.4E-3					4.9E-4	2.2E-3	5.6E-5	2.4E-4	9.5E-3		1.7E-3	--	2.7E-5
85-01-8	Phenanthrene	Y	N	n/a		5.1E-5	6.3E-5									6.3E-5			--	--
108-95-2	Phenol	Y	Y	Y	A	2.4E-4	1.1E-3					2.4E-4	1.1E-3			1.1E-3			1.270	--
7723-14-0	Phosphorus	Y	Y	Y	A	5.6E-3	0.023					5.5E-3	0.023	9.3E-5	6.2E-5	2.343		0.530	7.0E-3	--
129-00-0	Pyrene	Y	N	n/a		5.0E-6	6.6E-6									6.6E-6			--	--
7782-49-2	Selenium	Y	Y	Y	A	4.1E-4	1.8E-3					4.1E-4	1.8E-3	6.2E-7	2.6E-6	3.2E-3		3.3E-4	0.013	--
108-88-3	Toluene	Y	Y	Y	A	0.032	0.139					0.032	0.139	8.8E-5	3.7E-4	0.139		8.8E-5	25.000	--
1330-20-7	Xylene	Y	Y	Y	A	0.032	0.138					0.032	0.138			0.138			29.000	--
7429-90-5	Aluminum	N	Y	N	A									0.648	2.577			58.504	0.667	--
7440-39-3	Barium	N	Y	N	A									6.8E-3	0.028			0.659	0.033	--
1317-65-3	Calcium Carbonate	N	Y	N	A									2.244	8.125			13.652	0.667	--
1305-78-8	Calcium Oxide	N	Y	N	A									0.696	0.952			0.696	0.133	--
7440-50-8	Copper	N	Y	N	A									5.3E-4	2.2E-3			4.6E-3	0.067	--
110-82-7	Cyclohexane	N	Y	N	A									1.0E-3	4.6E-3			1.0E-3	70.000	--
7783-06-4	Hydrogen Sulfide	N	Y	N	A									0.900	3.942			0.900	0.933	--
7439-89-6	Iron	N	Y	N	A									0.213	0.812			15.043	0.067	--
7439-98-7	Molybdenum	N	Y	N	A									4.7E-4	2.0E-3			1.3E-3	0.333	--
109-66-0	Pentane	N	Y	N	A									0.123	0.495			0.123	118	--
7440-22-4	Silver	N	Y	N	A									4.1E-4	1.8E-3			8.2E-4	7.0E-3	--
7664-93-9	Sulfuric Acid	N	Y	N	A									2.030	8.891			2.030	0.067	--
7440-28-0	Thallium	N	Y	N	A									5.2E-4	2.2E-3			8.7E-3	7.0E-3	--
7440-61-1	Uranium	N	Y	N	A									5.2E-4	2.2E-3			8.7E-3	0.013	--
7440-62-2	Vanadium	N	Y	N	A									8.4E-4	3.5E-3			0.024	3.0E-3	--
25551-13-7	Trimethyl benzene	N	Y	N	A									0.011	0.048			0.011	8.200	--
7440-33-7	Tungsten	N	Y	N	A									5.2E-4	2.2E-3	0		8.7E-3	0.333	--
7440-66-6	Zinc	N	Y	N	A									2.2E-3	8.8E-3	0		0.031	0.667	--
HAP TOTAL						*1.200*	*4.566*									*12.564*				
MERCURY TOTAL (exempt)								*6.9E-4*	*2.8E-3*											
MERCURY TOTAL (non-exempt)										*1.3E-5*	*5.4E-5*						*5.4E-5*			
TAP TOTAL (HAP-TAP addressed by NSPS/NESHAP)												*1.150*	*4.353*							
TAP TOTAL (For EL Evaluation)														*6.928*	*26.109*			*93.573*		

Air Sciences Inc.	PROJECT TITLE: Stibnite Gold Project	BY: K. Lewis
	PROJECT NO: 335-20-3	PAGE: 1 OF: 19 SHEET: Calcs
AIR EMISSION CALCULATIONS	SUBJECT: HAP/TAP Emission Calculations	DATE: October 4, 2021

Model Scenario W3 T-RACT Emissions

Hazardous Air Pollutants (HAP)/Toxic Air Pollutants (TAP) Emissions Summary

		Emissions[1]									
		Fuel Combustion		Process/Prod/Leach		Mining		Total			
CAS	HAP/TAP	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	HAP	TAP
106-99-0	1,3-Butadiene	8.4E-07	3.7E-06	0	0	0	0	8.4E-07	3.7E-06	Y	Y
91-57-6	2-Methylnaphthalene	1.1E-06	4.6E-06	0	0	0	0	1.1E-06	4.6E-06	Y	N
56-49-5	3-Methylchloranthrene	7.8E-08	3.4E-07	0	0	0	0	7.8E-08	3.4E-07	Y	Y
57-97-6	7,12-Dimethylbenz(a)anthracene	7.6E-07	3.0E-06	0	0	0	0	7.6E-07	3.0E-06	Y	N
83-32-9	Acenaphthene	5.7E-06	7.1E-06	0	0	0	0	5.7E-06	7.1E-06	Y	N
208-96-8	Acenaphthylene	1.1E-05	1.4E-05	0	0	0	0	1.1E-05	1.4E-05	Y	N
75-07-0	Acetaldehyde	2.5E-05	1.1E-04	0	0	0	0	2.5E-05	1.1E-04	Y	Y
107-02-8	Acrolein	1.6E-05	2.0E-05	0	0	0	0	1.6E-05	2.0E-05	Y	Y
120-12-7	Anthracene	1.7E-06	2.4E-06	0	0	0	0	1.7E-06	2.4E-06	Y	N
7440-36-0	Antimony	0	0	5.7E-04	2.5E-03	1.3E-02	5.8E-02	1.4E-02	6.1E-02	Y	Y
7440-38-2	Arsenic	8.7E-06	3.8E-05	4.5E-03	2.0E-02	0.23	1.02	0.24	1.04	Y	Y
56-55-3	Benz(a)anthracene	3.1E-07	1.4E-06	0	0	0	0	3.1E-07	1.4E-06	Y	Y
71-43-2	Benzene	3.6E-04	1.6E-03	7.0E-03	3.1E-02	0	0	7.4E-03	3.2E-02	Y	Y
50-32-8	Benzo(a)pyrene	1.4E-07	6.1E-07	0	0	0	0	1.4E-07	6.1E-07	Y	Y
205-99-2	Benzo(b)fluoranthene	4.4E-07	1.9E-06	0	0	0	0	4.4E-07	1.9E-06	Y	Y
191-24-2	Benzo(g,h,i)perylene	7.5E-07	1.1E-06	0	0	0	0	7.5E-07	1.1E-06	Y	N
207-08-9	Benzo(k)fluoranthene	1.5E-07	6.6E-07	0	0	0	0	1.5E-07	6.6E-07	Y	Y
7440-41-7	Beryllium	5.2E-07	2.3E-06	4.3E-04	1.9E-03	1.9E-03	8.1E-03	2.3E-03	1.0E-02	Y	Y
92-52-4	Biphenyl	0	0	4.4E-05	1.9E-04	0	0	4.4E-05	1.9E-04	Y	Y
7440-43-9	Cadmium	4.8E-05	2.1E-04	4.1E-04	1.8E-03	2.9E-04	1.3E-03	7.5E-04	3.3E-03	Y	Y
75-15-0	Carbon Disulfide	0	0	1.4E-02	6.3E-02	0	0	1.4E-02	6.3E-02	Y	Y
7440-47-3	Chromium	6.6E-05	2.7E-04	6.1E-04	2.5E-03	5.2E-03	2.3E-02	5.9E-03	2.6E-02	Y	Y
18540-29-9	Cr (VI)	0	0	3.4E-07	1.5E-06	0	0	3.4E-07	1.5E-06	Y	Y
218-01-9	Chrysene	5.8E-07	2.5E-06	0	0	0	0	5.8E-07	2.5E-06	Y	Y
7440-48-4	Cobalt	4.0E-06	1.6E-05	4.7E-04	2.0E-03	2.3E-03	1.0E-02	2.8E-03	1.2E-02	Y	Y
592-01-8	Cyanide	0	0	0.45	1.99	0	0	0.45	1.99	Y	Y
53-70-3	Dibenzo(a,h)anthracene	1.8E-07	7.7E-07	0	0	0	0	1.8E-07	7.7E-07	Y	Y
106-46-7	Dichlorobenzene	5.7E-05	2.3E-04	0	0	0	0	5.7E-05	2.3E-04	Y	Y
206-44-0	Fluoranthene	5.5E-06	7.0E-06	0	0	0	0	5.5E-06	7.0E-06	Y	N
86-73-7	Fluorene	1.7E-05	2.1E-05	0	0	0	0	1.7E-05	2.1E-05	Y	N
50-00-0	Formaldehyde	3.3E-03	1.5E-02	0	0	0	0	3.3E-03	1.5E-02	Y	Y
110-54-3	Hexane	8.5E-02	0.34	3.1E-02	0.14	0	0	0.12	0.48	Y	Y
7647-01-0	Hydrogen Chloride	0	0	0.99	3.67	0	0	0.99	**3.67**	Y	Y
193-39-5	Indeno(1,2,3-cd)pyrene	2.2E-07	9.6E-07	0	0	0	0	2.2E-07	9.6E-07	Y	Y
7439-92-1	Lead	0	0	4.8E-04	2.1E-03	4.6E-03	2.0E-02	5.1E-03	2.2E-02	Y	N
7439-96-5	Manganese	1.8E-05	7.2E-05	4.6E-03	1.7E-02	0.17	0.76	0.18	0.78	Y	Y
7439-97-6	Mercury	1.2E-05	5.0E-05	6.9E-04	2.9E-03	1.2E-03	5.1E-03	1.9E-03	8.0E-03	Y	N
91-20-3	Naphthalene	1.9E-04	3.1E-04	1.9E-03	8.5E-03	0	0	2.1E-03	8.8E-03	Y	Y
7440-02-0	Nickel	9.1E-05	4.0E-04	4.6E-04	2.0E-03	1.2E-03	5.1E-03	1.7E-03	7.5E-03	Y	Y
85-01-8	Phenanthrene	5.1E-05	6.3E-05	0	0	0	0	5.1E-05	6.3E-05	Y	N
108-95-2	Phenol	0	0	2.4E-04	1.1E-03	0	0	2.4E-04	1.1E-03	Y	Y
7723-14-0	Phosphorus	0	0	5.6E-03	2.3E-02	0.38	1.65	0.38	1.67	Y	Y
129-00-0	Pyrene	5.0E-06	6.6E-06	0	0	0	0	5.0E-06	6.6E-06	Y	N
7782-49-2	Selenium	1.1E-06	4.6E-06	4.1E-04	1.8E-03	2.3E-04	1.0E-03	6.4E-04	2.8E-03	Y	Y
108-88-3	Toluene	5.2E-04	1.1E-03	3.2E-02	0.14	0	0	3.2E-02	0.14	Y	Y
1330-20-7	Xylene	2.5E-04	3.0E-04	3.1E-02	0.14	0	0	3.2E-02	0.14	Y	Y
Total HAP		9.0E-02	0.36	1.58	6.25	0.81	3.56	2.48	10.17		

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

	0.2155	0.8650	8.3307	31.6474	61.0803	267.5316	69.6264	300.0439
TRUE	0.2155	0.8650	8.3307	31.6474	61.0803	267.5316	69.6264	300.0439
	chk	chk	chk-15	chk	chk	chk	chk-14	chk

Hazardous Air Pollutants (HAP)/Toxic Air Pollutants (TAP) Emissions Summary - continued

		Emissions[1]									
		Fuel Combustion		Process/Prod/Leach		Mining		Total			
CAS	**Non-HAP TAP**	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	HAP	TAP
7429-90-5	Aluminum	0	0	0.65	2.58	41.11	180.04	41.75	182.62	N	Y
7440-39-3	Barium	2.1E-04	8.4E-04	6.6E-03	2.7E-02	0.46	2.03	0.47	2.06	N	Y
1317-65-3	Calcium Carbonate	0	0	2.24	8.12	8.11	35.50	10.35	43.63	N	Y
1305-78-8	Calcium Oxide	0	0	0.70	0.95	0	0	0.70	0.95	N	Y
7440-50-8	Copper	4.0E-05	1.6E-04	4.9E-04	2.1E-03	2.9E-03	1.3E-02	3.4E-03	1.5E-02	N	Y
110-82-7	Cyclohexane	0	0	1.0E-03	4.6E-03	0	0	1.0E-03	4.6E-03	N	Y
7783-06-4	Hydrogen Sulfide	0	0	0.90	3.94	0	0	0.90	3.94	N	Y
7439-89-6	Iron	0	0	0.21	0.81	10.54	46.15	10.75	46.96	N	Y
7439-98-7	Molybdenum	5.2E-05	2.1E-04	4.2E-04	1.8E-03	5.8E-04	2.5E-03	1.0E-03	4.6E-03	N	Y
109-66-0	Pentane	0.12	0.50	0	0	0	0	0.12	0.50	N	Y
7440-22-4	Silver	0	0	4.1E-04	1.8E-03	2.9E-04	1.3E-03	7.0E-04	3.1E-03	N	Y
7664-93-9	Sulfuric Acid	0	0	2.03	8.89	0	0	2.03	8.89	N	Y
7440-28-0	Thallium	0	0	5.2E-04	2.2E-03	5.8E-03	2.5E-02	6.3E-03	2.8E-02	N	Y
7440-61-1	Uranium	0	0	5.2E-04	2.2E-03	5.8E-03	2.5E-02	6.3E-03	2.8E-02	N	Y
7440-62-2	Vanadium	1.1E-04	4.4E-04	7.3E-04	3.0E-03	1.6E-02	7.1E-02	1.7E-02	7.4E-02	N	Y
25551-13-7	Trimethyl benzene	0	0	1.1E-02	4.8E-02	0	0	1.1E-02	4.8E-02	N	Y
7440-33-7	Tungsten	0	0	5.2E-04	2.2E-03	5.8E-03	2.5E-02	6.3E-03	2.8E-02	N	Y
7440-66-6	Zinc	1.4E-03	5.5E-03	8.0E-04	3.3E-03	2.0E-02	8.9E-02	2.2E-02	9.8E-02	N	Y
Total Non-HAP TAP		0.13	0.50	6.75	25.40	60.27	263.98	67.15	289.88		

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

Conversions

2,000 lb/ton
8,760 hr/yr
24 hr/day

PROPANE COMBUSTION

Source Data

Source ID	Description	MMBtu/day	MMBtu/yr
Lime Process Heating			
LKC	PFR Shaft Lime Kiln Combustion	529.0	163,935
Ore Process Heating			
ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	17.0	510
CKB	Carbon Regeneration Kiln (Burners)	54.1	19,754
PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	2.4	876
HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	120.0	43,800
Subtotal		193.5	64,940
HVAC			
H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	96.0	35,040
H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	96.0	35,040
HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	96.0	35,040
HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	6.0	2,190
HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	6.0	2,190
HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	6.0	2,190
HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	12.0	4,380
HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	48.0	17,520
HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	72.0	26,280
Subtotal		438.0	159,870

PROPANE COMBUSTION - CONTINUED

HAP/TAP Emission Factors and Emissions

O.Heat_pph O.Heat_tpy L.Heat_pph L.Heat_tpy HVAC_pph HVAC_tpy lb/hr ton/yr

		Emission Factor[2]		Emissions[1] Ore Proc Heat		Lime Proc Heat		HVAC		Total			
CAS	Pollutant	lb/MMscf	lb/MMBtu[3]	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	TAP	A/C
91-57-6	2-Methylnaphthalene	2.4E-05	2.35E-8	1.9E-07	7.6E-07	5.2E-07	1.9E-06	4.3E-07	1.9E-06	1.1E-06	4.6E-06	N	
56-49-5	3-Methylchloranthrene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
57-97-6	7,12-Dimethylbenz(a)ant	< 1.6E-05	1.57E-8	1.3E-07	5.1E-07	3.5E-07	1.3E-06	2.9E-07	1.3E-06	7.6E-07	3.0E-06	N	
83-32-9	Acenaphthene	< 1.8E-06	1.76E-9	1.4E-08	5.7E-08	3.9E-08	1.4E-07	3.2E-08	1.4E-07	8.5E-08	3.4E-07	N	
208-96-8	Acenaphthylene	< 1.8E-06	1.76E-9	1.4E-08	5.7E-08	3.9E-08	1.4E-07	3.2E-08	1.4E-07	8.5E-08	3.4E-07	N	
120-12-7	Anthracene	< 2.4E-06	2.35E-9	1.9E-08	7.6E-08	5.2E-08	1.9E-07	4.3E-08	1.9E-07	1.1E-07	4.6E-07	N	
7440-38-2	Arsenic	2.0E-04	1.96E-7	1.5E-06	6.4E-06	3.7E-06	1.6E-05	3.6E-06	1.6E-05	8.7E-06	3.8E-05	Y	C
56-55-3	Benz(a)anthracene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
71-43-2	Benzene	2.1E-03	2.06E-6	1.5E-05	6.7E-05	3.9E-05	1.7E-04	3.8E-05	1.6E-04	9.1E-05	4.0E-04	Y	C
50-32-8	Benzo(a)pyrene	< 1.2E-06	1.18E-9	8.7E-09	3.8E-08	2.2E-08	9.6E-08	2.1E-08	9.4E-08	5.2E-08	2.3E-07	Y	C
205-99-2	Benzo(b)fluoranthene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
191-24-2	Benzo(g,h,i)perylene	< 1.2E-06	1.18E-9	9.5E-09	3.8E-08	2.6E-08	9.6E-08	2.1E-08	9.4E-08	5.7E-08	2.3E-07	N	
207-08-9	Benzo(k)fluoranthene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
7440-41-7	Beryllium	< 1.2E-05	1.18E-8	8.7E-08	3.8E-07	2.2E-07	9.6E-07	2.1E-07	9.4E-07	5.2E-07	2.3E-06	Y	C
7440-43-9	Cadmium	1.1E-03	1.08E-6	8.0E-06	3.5E-05	2.0E-05	8.8E-05	2.0E-05	8.6E-05	4.8E-05	2.1E-04	Y	C
7440-47-3	Chromium	1.4E-03	1.37E-6	1.1E-05	4.5E-05	3.0E-05	1.1E-04	2.5E-05	1.1E-04	6.6E-05	2.7E-04	Y	A
218-01-9	Chrysene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
7440-48-4	Cobalt	8.4E-05	8.24E-8	6.6E-07	2.7E-06	1.8E-06	6.8E-06	1.5E-06	6.6E-06	4.0E-06	1.6E-05	Y	A
53-70-3	Dibenzo(a,h)anthracene	< 1.2E-06	1.18E-9	8.7E-09	3.8E-08	2.2E-08	9.6E-08	2.1E-08	9.4E-08	5.2E-08	2.3E-07	Y	C
106-46-7	Dichlorobenzene	1.2E-03	1.18E-6	9.5E-06	3.8E-05	2.6E-05	9.6E-05	2.1E-05	9.4E-05	5.7E-05	2.3E-04	Y	A
206-44-0	Fluoranthene	3.0E-06	2.94E-9	2.4E-08	9.5E-08	6.5E-08	2.4E-07	5.4E-08	2.4E-07	1.4E-07	5.7E-07	N	
86-73-7	Fluorene	2.8E-06	2.75E-9	2.2E-08	8.9E-08	6.1E-08	2.3E-07	5.0E-08	2.2E-07	1.3E-07	5.3E-07	N	
50-00-0	Formaldehyde	7.5E-02	7.35E-5	5.5E-04	2.4E-03	1.4E-03	6.0E-03	1.3E-03	5.9E-03	3.3E-03	1.4E-02	Y	C
110-54-3	Hexane	1.8E+00	1.76E-3	1.4E-02	5.7E-02	3.9E-02	1.4E-01	3.2E-02	1.4E-01	8.5E-02	3.4E-01	Y	A
193-39-5	Indeno(1,2,3-cd)pyrene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
7439-96-5	Manganese	3.8E-04	3.73E-7	3.0E-06	1.2E-05	8.2E-06	3.1E-05	6.8E-06	3.0E-05	1.8E-05	7.2E-05	Y	A
7439-97-6	Mercury	2.6E-04	2.55E-7	2.1E-06	8.3E-06	5.6E-06	2.1E-05	4.7E-06	2.0E-05	1.2E-05	5.0E-05	N	
91-20-3	Naphthalene	6.1E-04	5.98E-7	4.8E-06	1.9E-05	1.3E-05	4.9E-05	1.1E-05	4.8E-05	2.9E-05	1.2E-04	Y	A
7440-02-0	Nickel	2.1E-03	2.06E-6	1.5E-05	6.7E-05	3.9E-05	1.7E-04	3.8E-05	1.6E-04	9.1E-05	4.0E-04	Y	C
85-01-8	Phenanthrene	1.7E-05	1.67E-8	1.3E-07	5.4E-07	3.7E-07	1.4E-06	3.0E-07	1.3E-06	8.1E-07	3.2E-06	N	
129-00-0	Pyrene	5.0E-06	4.90E-9	4.0E-08	1.6E-07	1.1E-07	4.0E-07	8.9E-08	3.9E-07	2.4E-07	9.5E-07	N	
7782-49-2	Selenium	< 2.4E-05	2.35E-8	1.9E-07	7.6E-07	5.2E-07	1.9E-06	4.3E-07	1.9E-06	1.1E-06	4.6E-06	Y	A
108-88-3	Toluene	3.4E-03	3.33E-6	2.7E-05	1.1E-04	7.3E-05	2.7E-04	6.1E-05	2.7E-04	1.6E-04	6.5E-04	Y	A
109-66-0	Pentane	2.6E+00	2.55E-3	2.1E-02	8.3E-02	5.6E-02	2.1E-01	4.7E-02	2.0E-01	1.2E-01	5.0E-01	Y	A
7440-39-3	Barium	4.4E-03	4.31E-6	3.5E-05	1.4E-04	9.5E-05	3.5E-04	7.9E-05	3.4E-04	2.1E-04	8.4E-04	Y	A
7440-50-8	Copper	8.5E-04	8.33E-7	6.7E-06	2.7E-05	1.8E-05	6.8E-05	1.5E-05	6.7E-05	4.0E-05	1.6E-04	Y	A
7439-98-7	Molybdenum	1.1E-03	1.08E-6	8.7E-06	3.5E-05	2.4E-05	8.8E-05	2.0E-05	8.6E-05	5.2E-05	2.1E-04	Y	A
7440-62-2	Vanadium	2.3E-03	2.25E-6	1.8E-05	7.3E-05	5.0E-05	1.8E-04	4.1E-05	1.8E-04	1.1E-04	4.4E-04	Y	A
7440-66-6	Zinc	2.9E-02	2.84E-5	2.3E-04	9.2E-04	6.3E-04	2.3E-03	5.2E-04	2.3E-03	1.4E-03	5.5E-03	Y	A
Total				3.6E-02	1.4E-01	9.8E-02	3.6E-01	8.1E-02	3.5E-01	2.1E-01	8.6E-01		

(1) *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

(2) *AP-42, Table 1.4-3 & 1.4-4 (7/98) Natural Gas Combustion* 1.0766 1.0766

(3) *Natural Gas Higher Heating Value* 1,020 *MMBtu/MMscf* chk

Air Sciences Inc.	PROJECT TITLE: Stibnite Gold Project	BY: K. Lewis	
	PROJECT NO: 335-20-3	PAGE: 5	OF: 19 SHEET: Calcs
AIR EMISSION CALCULATIONS	SUBJECT: HAP/TAP Emission Calculations	DATE: October 4, 2021	

DIESEL COMBUSTION

Source Data

Source ID	Description	Power Rating kW	Power Rating hp	Operation hr/day	Operation hr/yr	Fuel Consumption[1] & [2] MMBtu/day	Fuel Consumption[1] & [2] MMBtu/yr
EDG1	Camp Emergency Generator	1,000	1,341	1	100	9.39	938.70
EDG2	Plant Emergency Generator #1	1,000	1,341	1	100	9.39	938.7
EDG3	Plant Emergency Generator #2	1,000	1,341	1	100	9.39	938.7
EDFP	Mill Fire Pump	200	268	1	100	1.88	187.7
Total						30.0	3,003.8

[1] *Based on brake specific fuel consumption for diesel generators* 7,000 *Btu/hp-hr* *AP-42 Tbl 3.3-1*

[2] *Heat Content of* 0.137 *MMBtu/gal* 1E+6 *Btu/MMBtu* 1.341 *hp/kW*

HAP/TAP Emission Factors and Emissions

lb/hr ton/yr

	Pollutant	Factor (lb/MMBtu) ≤600 hp[2]	Factor (lb/MMBtu) >600hp[3]	Emissions (≤600 hp) lb/hr	Emissions (≤600 hp) ton/yr	Emissions (>600 hp) lb/hr	Emissions (>600 hp) ton/yr	Total Emissions[1] lb/hr	Total Emissions[1] ton/yr	TAP	A/C
106-99-0	1,3-Butadiene	< 3.9E-05		8.4E-07	3.7E-06	0.0E+00	0.0E+00	8.4E-07	3.7E-06	Y	C
83-32-9	Acenaphthene	< 1.4E-06	4.7E-06	1.1E-07	1.3E-07	5.5E-06	6.6E-06	5.6E-06	6.7E-06	N	
208-96-8	Acenaphthylene	< 5.1E-06	9.2E-06	4.0E-07	4.7E-07	1.1E-05	1.3E-05	1.1E-05	1.3E-05	N	
75-07-0	Acetaldehyde	7.7E-04	2.5E-05	1.6E-05	7.2E-05	8.1E-06	3.5E-05	2.5E-05	1.1E-04	Y	C
107-02-8	Acrolein	< 9.3E-05	7.9E-06	7.2E-06	8.7E-06	9.2E-06	1.1E-05	1.6E-05	2.0E-05	Y	A
120-12-7	Anthracene	1.9E-06	1.2E-06	1.5E-07	1.8E-07	1.4E-06	1.7E-06	1.6E-06	1.9E-06	N	
56-55-3	Benz(a)anthracene	1.7E-06	6.2E-07	3.6E-08	1.6E-07	2.0E-07	8.8E-07	2.4E-07	1.0E-06	Y	C
71-43-2	Benzene	9.3E-04	7.8E-04	2.0E-05	8.8E-05	2.5E-04	1.1E-03	2.7E-04	1.2E-03	Y	C
50-32-8	Benzo(a)pyrene	< 1.9E-07	< 2.6E-07	4.0E-09	1.8E-08	8.3E-08	3.6E-07	8.7E-08	3.8E-07	Y	C
205-99-2	Benzo(b)fluoranthene	< 9.9E-08	< 1.1E-06	2.1E-09	9.3E-09	3.6E-07	1.6E-06	3.6E-07	1.6E-06	Y	C
191-24-2	Benzo(g,h,i)perylene	< 4.9E-07	< 5.6E-07	3.8E-08	4.6E-08	6.5E-07	7.8E-07	6.9E-07	8.3E-07	N	
207-08-9	Benzo(k)fluoranthene	< 1.6E-07	< 2.2E-07	3.3E-09	1.5E-08	7.0E-08	3.1E-07	7.3E-08	3.2E-07	Y	C
218-01-9	Chrysene	3.5E-07	1.5E-06	7.6E-09	3.3E-08	4.9E-07	2.2E-06	5.0E-07	2.2E-06	Y	C
53-70-3	Dibenzo(a,h)anthracene	< 5.8E-07	< 3.5E-07	1.2E-08	5.5E-08	1.1E-07	4.9E-07	1.2E-07	5.4E-07	Y	C
206-44-0	Fluoranthene	7.6E-06	4.0E-06	6.0E-07	7.1E-07	4.7E-06	5.7E-06	5.3E-06	6.4E-06	N	
86-73-7	Fluorene	2.9E-05	1.3E-05	2.3E-06	2.7E-06	1.5E-05	1.8E-05	1.7E-05	2.1E-05	N	
50-00-0	Formaldehyde	1.2E-03	7.9E-05	2.5E-05	1.1E-04	2.5E-05	1.1E-04	5.1E-05	2.2E-04	Y	C
193-39-5	Indeno(1,2,3-cd)pyrene	< 3.8E-07	< 4.1E-07	8.0E-09	3.5E-08	1.3E-07	5.8E-07	1.4E-07	6.2E-07	Y	C
91-20-3	Naphthalene	8.5E-05	1.3E-04	6.6E-06	8.0E-06	1.5E-04	1.8E-04	1.6E-04	1.9E-04	Y	A
85-01-8	Phenanthrene	2.9E-05	4.1E-05	2.3E-06	2.8E-06	4.8E-05	5.7E-05	5.0E-05	6.0E-05	N	
129-00-0	Pyrene	4.8E-06	3.7E-06	3.7E-07	4.5E-07	4.4E-06	5.2E-06	4.7E-06	5.7E-06	N	
108-88-3	Toluene	4.1E-04	2.8E-04	3.2E-05	3.8E-05	3.3E-04	4.0E-04	3.6E-04	4.3E-04	Y	A
1330-20-7	Xylene	2.9E-04	1.9E-04	2.2E-05	2.7E-05	2.3E-04	2.7E-04	2.5E-04	3.0E-04	Y	A
Total				1.4E-04	3.6E-04	1.1E-03	2.2E-03	1.2E-03	2.6E-03		

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

[2] *AP-42, Tab. 3.3-2, 10/96, diesel engines (≤ 600 hp)* chk chk

[3] *AP-42, Tabs. 3.4-3 & 3.4-4, 10/96, large diesel engines (> 600 hp)*

ORE PROCESSING

Source Data

Source ID	Description	PM Emissions lb/day	PM Emissions ton/yr
OC1	Loader Transfer of Ore to Grizzly	3.500	0.639
OC2	Grizzly to Apron Feeder	3.500	0.639
OC3	Apron Feeder to Dribble Conveyor	3.500	0.639
OC4	Apron Feeder to Vibrating Grizzly	3.500	0.639
OC5	Dribble Conveyor to Vibrating Grizzly	3.500	0.639
OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	3.500	0.639
OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	30.000	5.475
OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	3.500	0.639
OC9	Stockpile Transfers to Reclaim Conveyors	16.560	3.022
OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	16.560	3.022
OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	16.560	3.022
OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge C	33.120	6.044
OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	3.864	0.705
Total		141.164	25.762

HAP/TAP Emission Factors and Emissions

CAS No.	Pollutant	Concentration ppm[2]	Emissions[1] lb/hr	Emissions[1] ton/yr	TAP	A/C
7440-38-2	Arsenic	667	3.9E-03	1.7E-02	Y	C
7440-41-7	Beryllium	3.2	1.9E-05	8.2E-05	Y	C
7440-43-9	Cadmium	0.50	2.9E-06	1.3E-05	Y	C
7440-48-4	Cobalt	4	2.4E-05	1.0E-04	Y	A
7440-47-3	Chromium	9	5.3E-05	2.3E-04	Y	A
7439-97-6	Mercury [3]	0.96	5.6E-06	2.5E-05	N	
7439-96-5	Manganese	299	1.8E-03	7.7E-03	Y	A
7440-02-0	Nickel	2	1.2E-05	5.2E-05	Y	C
7439-92-1	Lead	8	4.7E-05	2.1E-04	N	
7440-36-0	Antimony	23	1.4E-04	5.9E-04	Y	A
7723-14-0	Phosphorus	650	3.8E-03	1.7E-02	Y	A
7782-49-2	Selenium [4]	0.40	2.4E-06	1.0E-05	Y	A
7440-22-4	Silver	0.50	2.9E-06	1.3E-05	Y	A
7429-90-5	Aluminum	71,000	4.2E-01	1.8E+00	Y	A
7440-39-3	Barium	800	4.7E-03	2.1E-02	Y	A
1317-65-3	Calcium Carbonate	14,000	8.2E-02	3.6E-01	Y	A
7440-50-8	Copper	5	2.9E-05	1.3E-04	Y	A
7439-89-6	Iron [4]	18,200	1.1E-01	4.7E-01	Y	A
7439-98-7	Molybdenum	1	5.9E-06	2.6E-05	Y	A
7440-28-0	Thallium	10	5.9E-05	2.6E-04	Y	A
7440-61-1	Uranium	10	5.9E-05	2.6E-04	Y	A
7440-62-2	Vanadium	28	1.6E-04	7.2E-04	Y	A
7440-33-7	Tungsten	10	5.9E-05	2.6E-04	Y	A
7440-66-6	Zinc	35	2.1E-04	9.0E-04	Y	A
Total			6.2E-01	2.7E+00		

(1) *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

(2) *(Midas Gold 2017c) Median concentration of 55,000 SGP samples.*

(3) *(Midas Gold 2018e) Median ore concentration of 151,000 SGP samples; resource block model.*

(4) *(Midas Gold 2020) Median concentration of 56,000 SGP samples for Fe and 1,500 SGP samples for Se.*

1E+6 parts/ppm

Air Sciences Inc.	PROJECT TITLE: Stibnite Gold Project	BY: K. Lewis
	PROJECT NO: 335-20-3	PAGE: 7 OF: 19 SHEET: Calcs
AIR EMISSION CALCULATIONS	SUBJECT: HAP/TAP Emission Calculations	DATE: October 4, 2021

ORE CONCETRATION AND REFINING

Source Data

Source ID	Description	Subpart 7E Allowable Limit lb/yr[1]	Oper. hr/yr	% of Subpart 7E for Controlled Systems %	Controlled Hg Emissions lb/hr	ton/yr	lb/yr
AC	Autoclave	213.4	8,760	[2]	0.000023	0.00010	0.20
EW,MR,MF,CKD	Refinery Sources (C. Kiln, EW, Retort, Furn	16.8		20% [3]	0.000384	0.00168	3.36
7439-97-6 Mercury	Total	230.2			0.000407	0.00178	3.56

[1] *Subpart 7E Limit - Ore Pretreatment Processes (CFR 2018b)*

$$\frac{84\ lb}{MMton} \times \frac{2{,}540{,}400\ ton}{yr} \times \frac{MMton}{1.0E{+}6\ ton} = \frac{213.4\ lb}{yr}$$

[1] *Subpart 7E Limit - Carbon Processes with Mercury Retorts*

$$\frac{0.8\ lb}{ton} \times \frac{21\ ton}{yr} = \frac{16.8\ lb}{yr}$$

[2] *Controlled SysCAD modeled emissions from Autoclave:* 0.0105 g/hr 2.3E-05 lb/hr 0.20 lb/yr (M3 2019)

[3] *Based on similar source (but with much higher ore Hg content) Hg reporting levels provided below:*

Goldstrike Refinery (2015 & 2016 Hg Reports) (NDEP 2015a) (NDEP 2016)

$$\frac{28.79\ lb}{yr} \times \frac{yr}{251.00\ ton} = \frac{0.11\ lb}{MMton} \times \frac{ton}{0.8\ lb} = 14.3\%$$

Twin Creeks Refinery (2015 & 2016 Hg Reports) (NDEP 2015a) (NDEP 2016)

$$\frac{31.27\ lb}{yr} \times \frac{yr}{142.77\ ton} = \frac{0.22\ lb}{MMton} \times \frac{ton}{0.8\ lb} = 27.4\%$$

HAP/TAP Emission Factors and Emission

AC_pph AC_tpy Refin_pph Refin_tpy lb/hr ton/yr

CAS No.	Pollutant	Emission Factor[1]	Autoclave lb/hr	Autoclave ton/yr	Refinery lb/hr	Refinery ton/yr	Total Emissions lb/hr	Total Emissions ton/yr	TAP	A/C
7440-38-2	Arsenic	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	C
7440-41-7	Beryllium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	C
7440-43-9	Cadmium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	C
7440-48-4	Cobalt	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-47-3	Chromium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7439-97-6	Mercury	see above	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	N	
7439-96-5	Manganese	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-02-0	Nickel	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	C
7439-92-1	Lead	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	N	
7440-36-0	Antimony	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7723-14-0	Phosphorus	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7782-49-2	Selenium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-22-4	Silver	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7429-90-5	Aluminum	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-39-3	Barium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
1317-65-3	Calcium Carbonate	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-50-8	Copper	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7439-89-6	Iron	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7439-98-7	Molybdenum	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-28-0	Thallium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-61-1	Uranium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-62-2	Vanadium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-33-7	Tungsten	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-66-6	Zinc	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
Total			5.5E-04	2.4E-03	9.2E-03	4.0E-02	9.8E-03	4.3E-02		

[1] *Hg is the most difficult metal to control due to it existing in both particulate and gaseous form. Therefore, all other metals are conservatively estimated to be equal to or less than the Hg emissions.*

0.0525 0.0525 chk

7664-93-9	Sulfuric Acid	Autoclave	2.03	8.89			2.03	8.89
7783-06-4	Hydrogen Sulfic	Autoclave	0.90	3.94			0.90	3.94
592-01-8	Cyanide	Point Sources - 5 EW Cells			0.0012	0.0053	0.00	0.01
Total			2.93	12.84	0.01	0.05	2.94	12.88

ORE CONCETRATION AND REFINING - CONTINUED

Source Data

Source ID	Description	Throughput ton/day	Throughput ton/yr	Operation hr/day	Operation hr/yr
AC	Autoclave	6,960	2,540,400	24	8,760

Autoclave HAP/TAP Emission Factors and Emission lb/hr ton/yr

CAS No.	Pollutant	Emission Factor		Emissions[1] lb/hr	Emissions[1] ton/yr
7664-93-9	Sulfuric Acid	0.007	lb/ton[2]	2.03	8.89
7783-06-4	Hydrogen Sulfide	0.9	lb/hr[3]	0.90	3.94

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

[2] *H2SO4 is based on Acidic Autoclave test data (APT 2010)*

[3] *H2S is based on Acidic Autoclave test data (APT 2013)*

LEACHING OPERATION

Cyanide (HCN) Source Data, Emission Factors, and Emissions

Source	II	Description	Dia. ft[1]	pH[1]	Free CN- g/m3[1]	T C[1]	pKa	a0	H	kG[2] m/s	Fa*Fw	g/s	lb/hr	ton/yr
TSF		***Fugitive Sources***												
TSF		Tailings Maint. Pond	76	7.75	1	3.74	9.803	0.9912	0.0025	1.89E-05	0.641	1.27E-05	0.0001	0.0004
MILLTA		CN Detox Tank 1	40	8.5	25	25	9.250	0.8490	0.0055	0.000311	0.688	0.002891	0.0229	0.101
MILLTA		CN Detox Tank 2	40	8.5	25	25	9.250	0.8490	0.0055	0.000311	0.688	0.002891	0.0229	0.101
MILLTA		CIP Leach Tank 1	52	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.668	0.001435	0.0114	0.050
MILLTA		CIP Leach Tank 2	52	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.668	0.001435	0.0114	0.050
MILLTA		CIP Leach Tank 3	52	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.668	0.001435	0.0114	0.050
MILLTA		CIP Leach Tank 4	52	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.668	0.001435	0.0114	0.050
MILLTA		CIL Tank 1	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA		CIL Tank 2	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA		CIL Tank 3	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA		CIL Tank 4	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA		CIL Tank 5	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA		CIL Tank 6	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA		CIP Tank 1	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
MILLTA		CIP Tank 2	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
MILLTA		CIP Tank 3	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
MILLTA		CIP Tank 4	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
MILLTA		CIP Tank 5	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
MILLTA		CIP Tank 6	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
			Acres[1]											
TSF		Tails, Aqueous Surface	110.222	7.75	1	3.74	9.803	0.9912	0.0025	1.89E-05	0.421	0.008845	0.0702	0.307
TSF		Tails, Wet Sediment	110.222							5.31E-08	0.421	0.009961	0.0791	0.346
TSF		Tails, Dry Sediment	110.222							2.33E-08	1	0.010375	0.0823	0.361
			330.666											
592-01-8		Cyanide Fugitive Sources - Subtotal											0.4527	1.983
75-15-0		Carbon Disulfide											0.01446	0.06332
		Point Sources												
EW		EW Cells	[3]										0.0006	0.003
EW		Preg/Barren Tanks	[3]										0.0006	0.003
592-01-8		Cyanide Point Sources - Subtotal											0.0012	0.0053
Total													0.454	1.988

[1] *(Midas Gold 2016)(M3 2017c)(M3 2017d)*

[2] *The emission factors and caculation methodology are from the EPA directed HCN study: (Card, T. 2009)(EPA 2009)(Schmidt 2010)*

[3] *(APT 2009)*

Carbon Disulfide Emissions from Xanthate Decomposition

CAS No.	Pollutant	Xanthate[1] ton/yr	Molar Decomp.[2]	CS_2 MW Ratio	Temperature Adj. Factor[3]	Emissions lb/hr	Emissions ton/yr
75-15-0	Carbon Disulfide	1,700	0.99%	0.376	1%	0.0145	0.063

	MW	
Xanthate (PAX)	202.37	$C6H11KOS_2$
Carbon disulfide	76.139	CS_2

[1] *(Midas Gold 2016) p. 12-11*

[2] *(Air Sciences 2020) molar decomposition of xanthate in solution to CS2 gas*

[3] *(Air Sciences 2020) based on the comparison of CS2 generation at 25C and 70C*

Conversions

8,760	hr/yr	453.5929	g/lb
2,000	lb/ton	3.28084	ft/m
4,046.86	m2/acre	3,600	s/hr

Wind adjustment factor Fw 1

LIME PRODUCTION

Source Data

Source ID	Description	Throughput ton/day	Throughput ton/yr	PM Emissions lb/day	PM Emissions ton/yr
LS1	Limestone transfer to Primary Crusher Hopper			3.39	0.48
LS2	Primary Crushing and Associated Transfers In and Out			6.10	0.86
LS3	Primary Screening and Associated Transfers In and Out			28.25	3.97
LS4	Secondary Crushing and Associated Transfers In and Out			6.10	0.86
LS5	Secondary Screening and Associated Transfers In and Out			28.25	3.97
LS6	Limestone transfer to Ball Mill Feed Bin			3.39	0.48
LS7	Limestone transfer to Ball Mill Feed Conveyor			3.39	0.48
LS8	Ball Mill Feed transfer to Ball Mill			3.39	0.48
LSBM	Limestone Ball Mill			45.65	6.42
LS9	Limestone transfer to Kiln Feed Bin			0.80	0.12
LS10	Limestone transfer to Lime Kiln Feed Conveyor			0.80	0.12
LS11	Fines Screening and Associated Transfers In and Out			6.68	1.03
Subtotal LS1-11				136.18	19.28
LS12	Kiln Feed transfer to PFR Shaft Lime Kiln			0.80	0.12
LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	169	52,377	21.97	3.40
Subtotal LS12,LK				22.77	3.53
Total				158.95	22.80

HAP/TAP Emission Factors and Emissions

LS_pph LS_tpy LS12_pph LS12_tpy LK_pph LK_tpy lb/hr ton/yr

CAS No.	Pollutant	Concentration ppm[2]	LS1-11,LSBM lb/hr	LS1-11,LSBM ton/yr	LS12 lb/hr	LS12 ton/yr	Lime Kiln lb/hr	Lime Kiln ton/yr	Emissions[1] lb/hr	Emissions[1] ton/yr	TAP	A/C
7440-38-2	Arsenic	23	1.01E-04	4.43E-04	6.51E-07	2.85E-06	1.79E-05	7.83E-05	1.20E-04	5.24E-04	Y	C
7440-41-7	Beryllium	0.8	3.52E-06	1.54E-05	2.27E-08	9.92E-08	6.22E-07	2.72E-06	4.17E-06	1.82E-05	Y	C
7440-43-9	Cadmium	0.25	1.10E-06	4.82E-06	7.08E-09	3.10E-08	1.94E-07	8.51E-07	1.30E-06	5.70E-06	Y	C
7440-48-4	Cobalt	4	2.27E-05	7.71E-05	1.34E-07	4.96E-07	3.66E-06	1.36E-05	2.65E-05	9.12E-05	Y	A
7440-47-3	Chromium	15	8.51E-05	2.89E-04	5.01E-07	1.86E-06	1.37E-05	5.11E-05	9.93E-05	3.42E-04	Y	A
7439-97-6	Mercury [3]	0.02	1.13E-07	3.86E-07	6.68E-10	2.48E-09	2.82E-04	1.05E-03	2.82E-04	1.05E-03	N	
7439-96-5	Manganese	236.5	1.34E-03	4.56E-03	7.89E-06	2.93E-05	2.16E-04	8.05E-04	1.57E-03	5.39E-03	Y	A
7440-02-0	Nickel	5	2.20E-05	9.64E-05	1.42E-07	6.20E-07	3.89E-06	1.70E-05	2.60E-05	1.14E-04	Y	C
7439-92-1	Lead	3	1.70E-05	5.78E-05	1.00E-07	3.72E-07	2.75E-06	1.02E-05	1.99E-05	6.84E-05	N	
7440-36-0	Antimony	2.5	1.42E-05	4.82E-05	8.34E-08	3.10E-07	2.29E-06	8.51E-06	1.66E-05	5.70E-05	Y	A
7723-14-0	Phosphorus	130	7.38E-04	2.51E-03	4.34E-06	1.61E-05	1.19E-04	4.43E-04	8.61E-04	2.96E-03	Y	A
7440-22-4	Silver	0	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	Y	A
7429-90-5	Aluminum	22600	1.28E-01	4.36E-01	7.54E-04	2.80E-03	2.07E-02	7.69E-02	1.50E-01	5.15E-01	Y	A
7440-39-3	Barium	145	8.23E-04	2.79E-03	4.84E-06	1.80E-05	1.33E-04	4.94E-04	9.60E-04	3.31E-03	Y	A
1317-65-3	Calcium Carbonate	274500	1.56E+00	5.29E+00	9.16E-03	3.40E-02	2.51E-01	9.35E-01	1.82E+00	6.26E+00	Y	A
7440-50-8	Copper	5	2.84E-05	9.64E-05	1.67E-07	6.20E-07	4.58E-06	1.70E-05	3.31E-05	1.14E-04	Y	A
7439-89-6	Iron	10350	5.87E-02	1.99E-01	3.45E-04	1.28E-03	9.47E-03	3.52E-02	6.85E-02	2.36E-01	Y	A
7439-98-7	Molybdenum	0.5	2.84E-06	9.64E-06	1.67E-08	6.20E-08	4.58E-07	1.70E-06	3.31E-06	1.14E-05	Y	A
7440-28-0	Thallium	5	2.84E-05	9.64E-05	1.67E-07	6.20E-07	4.58E-06	1.70E-05	3.31E-05	1.14E-04	Y	A
7440-61-1	Uranium	5	2.84E-05	9.64E-05	1.67E-07	6.20E-07	4.58E-06	1.70E-05	3.31E-05	1.14E-04	Y	A
7440-62-2	Vanadium	15.5	8.79E-05	2.99E-04	5.17E-07	1.92E-06	1.42E-05	5.28E-05	1.03E-04	3.53E-04	Y	A
7440-33-7	Tungsten	5	2.84E-05	9.64E-05	1.67E-07	6.20E-07	4.58E-06	1.70E-05	3.31E-05	1.14E-04	Y	A
7440-66-6	Zinc	18	1.02E-04	3.47E-04	6.01E-07	2.23E-06	1.65E-05	6.13E-05	1.19E-04	4.10E-04	Y	A
Subtotal			1.75E+00	5.94E+00	1.03E-02	3.82E-02	2.82E-01	1.05E+00	2.04E+00	7.03E+00	9.0667	9.0667
7647-01-0	Hydrogen Chloride	0.14 lb/ton product[4]					0.99	3.67	0.99	3.67		chk

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

[2] *(M3 2018) Median concentrations of SGP limestone material. Metals with medians below the detection limit (DL) are set to 1/2DL.*

[3] *Hg emissions from the Lime Kiln are conservatively estimated assuming 100% volatilization of all Hg in the limestone*

[4] *(EPA 1999b)*

1E+6 parts/ppm

LIME PRODUCTION - CONTINUED

Source Data

Source ID	Description	PM Emissions lb/day	PM Emissions ton/yr
LS1L	Mill Lime Silo #1 Loading	0.248	0.002
LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	1.200	0.011
MillS2L	Mill Lime Silo #2 Loading	0.248	0.002
MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	1.200	0.011
ACS1L	AC Lime Silo #1 Loading	0.990	0.009
ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.304	0.042
ACS2L	AC Lime Silo #2 Loading	0.990	0.009
ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.304	0.042
ACS3L	AC Lime Silo #3 Loading	0.990	0.009
ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.304	0.042
ACS4L	AC Lime Silo #4 Loading	0.495	0.004
ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	2.304	0.021
Subtotal - Mill & AC Lime Silos		15.576	0.203
LCR	Lime Mill Crushing and associated transfers In and Out	6.828	1.058
LSL	Pebble Lime Silo Loading via Bucket Elevator	0.149	0.023
LSU	Pebble Lime Silo discharge to Lime Slaker	0.015	0.002
Subtotal - Lime Mfg		6.991	1.083
Total		22.567	1.286

HAP/TAP Emission Factors and Emissions

CAS No.	Pollutant	Concentration ppm[2]	Mill and AC lb/hr	Mill and AC ton/yr	Lime Mfg lb/hr	Lime Mfg ton/yr	Emissions[1] lb/hr	Emissions[1] ton/yr	TAP	A/C
7440-38-2	Arsenic	23	1.06E-06	4.66E-06	5.69E-06	2.49E-05	6.75E-06	2.96E-05	Y	C
7440-41-7	Beryllium	0.8	3.70E-08	1.62E-07	1.98E-07	8.67E-07	2.35E-07	1.03E-06	Y	C
7440-43-9	Cadmium	0.25	1.16E-08	5.07E-08	6.18E-08	2.71E-07	7.34E-08	3.22E-07	Y	C
7440-48-4	Cobalt	4	2.60E-06	8.11E-07	1.17E-06	4.33E-06	3.76E-06	5.14E-06	Y	A
7440-47-3	Chromium	15	9.74E-06	3.04E-06	4.37E-06	1.63E-05	1.41E-05	1.93E-05	Y	A
7439-97-6	Mercury	0.02	1.30E-08	4.05E-09	5.83E-09	2.17E-08	1.88E-08	2.57E-08	N	
7439-96-5	Manganese	236.5	1.53E-04	4.79E-05	6.89E-05	2.56E-04	2.22E-04	3.04E-04	Y	A
7440-02-0	Nickel	5	2.31E-07	1.01E-06	1.24E-06	5.42E-06	1.47E-06	6.43E-06	Y	C
7439-92-1	Lead	3	1.95E-06	6.08E-07	8.74E-07	3.25E-06	2.82E-06	3.86E-06	N	
7440-36-0	Antimony	2.5	1.62E-06	5.07E-07	7.28E-07	2.71E-06	2.35E-06	3.22E-06	Y	A
7723-14-0	Phosphorus	130	8.44E-05	2.63E-05	3.79E-05	1.41E-04	1.22E-04	1.67E-04	Y	A
7440-22-4	Silver	0	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	Y	A
7429-90-5	Aluminum	22,600	1.47E-02	4.58E-03	6.58E-03	2.45E-02	2.13E-02	2.91E-02	Y	A
7440-39-3	Barium	145	9.41E-05	2.94E-05	4.22E-05	1.57E-04	1.36E-04	1.86E-04	Y	A
1305-78-8	Calcium Oxide	740,000 [3]	4.80E-01	1.50E-01	2.16E-01	8.02E-01	6.96E-01	9.52E-01	Y	A
7440-50-8	Copper	5	3.25E-06	1.01E-06	1.46E-06	5.42E-06	4.70E-06	6.43E-06	Y	A
7439-89-6	Iron	10350	6.72E-03	2.10E-03	3.01E-03	1.12E-02	9.73E-03	1.33E-02	Y	A
7439-98-7	Molybdenum	0.5	3.25E-07	1.01E-07	1.46E-07	5.42E-07	4.70E-07	6.43E-07	Y	A
7440-28-0	Thallium	5	3.25E-06	1.01E-06	1.46E-06	5.42E-06	4.70E-06	6.43E-06	Y	A
7440-61-1	Uranium	5	3.25E-06	1.01E-06	1.46E-06	5.42E-06	4.70E-06	6.43E-06	Y	A
7440-62-2	Vanadium	15.5	1.01E-05	3.14E-06	4.52E-06	1.68E-05	1.46E-05	1.99E-05	Y	A
7440-33-7	Tungsten	5	3.25E-06	1.01E-06	1.46E-06	5.42E-06	4.70E-06	6.43E-06	Y	A
7440-66-6	Zinc	18	1.17E-05	3.65E-06	5.24E-06	1.95E-05	1.69E-05	2.31E-05	Y	A
Total			5.02E-01	1.57E-01	2.25E-01	8.38E-01	7.27E-01	9.95E-01		

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

[2] *See LIME PRODUCTION, page 10*

[3] *(NLA 2007) 40% to 74% CaO in lime*

1E+6 parts/ppm

AGGREGATE PRODUCTION

Source Data

PM_ppd PM_tpy

Source ID	description Description	PM Emissions lb/day	ton/yr
PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conve	15.00	2.74
PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conve	15.00	2.74
Total		30.00	5.48

HAP/TAP Emission Factors and Emissions

lb/hr ton/yr

CAS No.	Pollutant	Concentration ppm[2]	Emissions[1] lb/hr	ton/yr	TAP	A/C
7440-38-2	Arsenic	23	2.88E-05	1.26E-04	Y	C
7440-41-7	Beryllium	0.8	1.00E-06	4.38E-06	Y	C
7440-43-9	Cadmium	0.25	3.13E-07	1.37E-06	Y	C
7440-48-4	Cobalt	4	5.00E-06	2.19E-05	Y	A
7440-47-3	Chromium	15	1.88E-05	8.21E-05	Y	A
7439-97-6	Mercury	0.02	2.50E-08	1.10E-07	N	
7439-96-5	Manganese	236.5	2.96E-04	1.29E-03	Y	A
7440-02-0	Nickel	5	6.25E-06	2.74E-05	Y	C
7439-92-1	Lead	3	3.75E-06	1.64E-05	N	
7440-36-0	Antimony	2.5	3.13E-06	1.37E-05	Y	A
7723-14-0	Phosphorus	130	1.63E-04	7.12E-04	Y	A
7440-22-4	Silver	0	0.00E+00	0.00E+00	Y	A
7429-90-5	Aluminum	22600	2.83E-02	1.24E-01	Y	A
7440-39-3	Barium	145	1.81E-04	7.94E-04	Y	A
1317-65-3	Calcium Carbonate	274500	3.43E-01	1.50E+00	Y	A
7440-50-8	Copper	5	6.25E-06	2.74E-05	Y	A
7439-89-6	Iron	10350	1.29E-02	5.67E-02	Y	A
7439-98-7	Molybdenum	0.5	6.25E-07	2.74E-06	Y	A
7440-28-0	Thallium	5	6.25E-06	2.74E-05	Y	A
7440-61-1	Uranium	5	6.25E-06	2.74E-05	Y	A
7440-62-2	Vanadium	15.5	1.94E-05	8.49E-05	Y	A
7440-33-7	Tungsten	5	6.25E-06	2.74E-05	Y	A
7440-66-6	Zinc	18	2.25E-05	9.86E-05	Y	A
Total			3.85E-01	1.69E+00		

(1) *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

(2) *See LIME PRODUCTION, page 10*

1E+6 parts/ppm

CONCRETE PRODUCTION

Source Data

Source ID	Description	Throughput ton/day	Throughput ton/yr
	description	TP_unit/day	TP_unit/yr
CS1L	Cement/Shotcrete Silo #1 Loading	164	60,000
CS1U	Cement/Shotcrete Silo #1 Unloading	164	60,000
CS2L	Cement/Shotcrete Silo #2 Loading	164	60,000
CS2U	Cement/Shotcrete Silo #2 Unloading	164	60,000
CM	Central Mixer Loading	164	60,000
	Subtotal Cement Silo Filling	658	240,000
	Subtotal Central Mix Batching	164	60,000

HAP/TAP Emission Factors and Emissions

CAS No.	HAP/TAP	Silo Fill lb/ton[2]	Central Mixer lb/ton[3]	Cement Silo L/U lb/hr	Cement Silo L/U ton/yr	Central Mix Batching lb/hr	Central Mix Batching ton/yr	Total Emissions[3] lb/hr	Total Emissions[3] ton/yr	TAP	A/C
		CF_pph		CF_tpy		CM_pph	CM_tpy	lb/hr	ton/yr		
7440-38-2	Arsenic	4.24E-09	2.96E-07	1.16E-7	5.09E-7	2.03E-6	8.88E-6	2.14E-6	9.39E-6	Y	C
7440-41-7	Beryllium	4.86E-10		1.33E-8	5.83E-8	--	--	1.33E-8	5.83E-8	Y	C
7440-43-9	Cadmium		7.10E-10	--	--	4.86E-9	2.13E-8	4.86E-9	2.13E-8	Y	C
7440-47-3	Chromium	2.90E-08	1.27E-07	7.95E-7	3.48E-6	8.70E-7	3.81E-6	1.66E-6	7.29E-6	Y	A
18540-29-9	Cr (VI)	5.80E-09	2.70E-08	1.59E-7	6.96E-7	1.85E-7	8.11E-7	3.44E-7	1.51E-6	Y	C
7439-92-1	Lead	1.09E-08	3.66E-08	2.99E-7	1.31E-6	2.51E-7	1.10E-6	5.49E-7	2.41E-6	N	
7439-96-5	Manganese	1.17E-07	3.78E-06	3.21E-6	1.40E-5	2.59E-5	1.13E-4	2.91E-5	1.27E-4	Y	A
7440-02-0	Nickel	4.18E-08	2.48E-07	1.15E-6	5.02E-6	1.70E-6	7.44E-6	2.84E-6	1.25E-5	Y	C
7723-14-0	Phosphorus		1.20E-06	--	--	8.22E-6	3.60E-5	8.22E-6	3.60E-5	Y	A
Total				5.73E-6	2.51E-5	3.91E-5	1.71E-4	4.49E-5	1.97E-4		

(1) *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

(2) *AP-42, Table 11.12-8, (06/06) Cement Silo Filing, Controlled.* 20% *Cr (VI), IDEQ email on 11/23/2020* 0.0002 0.0002

(3) *AP-42, Table 11.12-8, (06/06) Central Mix Batching, Controlled.* 21.29% *Cr (VI), IDEQ email on 11/23/2020* chk

Conversions

24 hr/day

CONCRETE PRODUCTION - CONTINUED

Source Data

PM_ppd PM_tpy

Source ID	description Description	PM Emissions lb/day	ton/yr
CAL	Aggregate Bin Loading	16.56	1.73
CAU	Aggregate Bin Unloading	16.56	1.73
Total		33.12	3.45

HAP/TAP Emission Factors and Emissions

lb/hr ton/yr

CAS No.	Pollutant	Concentration ppm[2]	Emissions[1] lb/hr	ton/yr	TAP	A/C
7440-38-2	Arsenic	23	1.81E-05	7.94E-05	Y	C
7440-41-7	Beryllium	0.8	6.30E-07	2.76E-06	Y	C
7440-43-9	Cadmium	0.25	1.97E-07	8.63E-07	Y	C
7440-48-4	Cobalt	4	5.52E-06	1.38E-05	Y	A
7440-47-3	Chromium	15	2.07E-05	5.18E-05	Y	A
7439-97-6	Mercury	0.02	2.76E-08	6.90E-08	N	
7439-96-5	Manganese	236.5	3.26E-04	8.16E-04	Y	A
7440-02-0	Nickel	5	3.94E-06	1.73E-05	Y	C
7439-92-1	Lead	3	4.14E-06	1.04E-05	N	
7440-36-0	Antimony	2.5	3.45E-06	8.63E-06	Y	A
7723-14-0	Phosphorus	130	1.79E-04	4.49E-04	Y	A
7440-22-4	Silver	0	0.00E+00	0.00E+00	Y	A
7429-90-5	Aluminum	22600	3.12E-02	7.80E-02	Y	A
7440-39-3	Barium	145	2.00E-04	5.00E-04	Y	A
7440-50-8	Copper	5	6.90E-06	1.73E-05	Y	A
7439-89-6	Iron	10350	1.43E-02	3.57E-02	Y	A
7439-98-7	Molybdenum	0.5	6.90E-07	1.73E-06	Y	A
7440-28-0	Thallium	5	6.90E-06	1.73E-05	Y	A
7440-61-1	Uranium	5	6.90E-06	1.73E-05	Y	A
7440-62-2	Vanadium	15.5	2.14E-05	5.35E-05	Y	A
7440-33-7	Tungsten	5	6.90E-06	1.73E-05	Y	A
7440-66-6	Zinc	18	2.48E-05	6.21E-05	Y	A
Total			4.63E-02	1.16E-01		

(1) *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

(2) *See LIME PRODUCTION, page 10*

1E+6 parts/ppm

FUEL STORAGE - GASOLINE

Source Data

Source ID	Description	VOC Emissions lb/day	VOC Emissions ton/yr
TG1	Mine Site Gasoline Tank #1	5.25	0.96
TG2	Mine Site Gasoline Tank #2	5.25	0.96
Total		10.49	1.91

HAP/TAP Emission Factors and Emissions

CAS No.	Pollutant	Concentration wt. %[2]	Emissions[1] lb/hr	Emissions[1] ton/yr	TAP	A/C
71-43-2	Benzene	1.608%	7.03E-03	3.08E-02	Y	C
92-52-4	Biphenyl	0.010%	4.37E-05	1.91E-04	Y	A
110-82-7	Cyclohexane	0.240%	1.05E-03	4.60E-03	Y	A
110-54-3	Hexane	7.138%	3.12E-02	1.37E-01	Y	A
91-20-3	Naphthalene	0.444%	1.94E-03	8.50E-03	Y	A
108-95-2	Phenol	0.055%	2.40E-04	1.05E-03	Y	A
108-88-3	Toluene	7.212%	3.15E-02	1.38E-01	Y	A
25551-13-7	Trimethyl benzene	2.500%	1.09E-02	4.79E-02	Y	A
1330-20-7	Xylene	7.170%	3.13E-02	1.37E-01	Y	A
Total			1.15E-01	5.05E-01		

(1) *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

(2) *(EPA 1999a)*

MINING FUGITIVE EMISSIONS

Dust Emissions

Source Data **Model Scenario** **W3** **T-RACT Emissions**

Operating schedule 365 day/yr

Clean rock cap (CR) >50% [1]

[1] *(Perpetua 2021h) Percent of VMTs on haul roads capped with CR*

Roads outside of the pits and DRSFs are capped with CR

Source ID	Description	PM Emissions lb/day	PM Emissions ton/yr
YPP	Yellow Pine Pit	--	--
HFP	Hangar Flats Pit	--	--
WEP	West End Pit	338.16	61.71
BT	Bradley Tailings	--	--
YPPBL	Yellow Pine Pit Blasting	--	--
HFPBL	Hangar Flats Pit Blasting	--	--
WEPBL	West End Pit Blasting	643.03	117.35
BTBL	Bradley Tailings Blasting	--	--
STKP	PC Stockpile	--	--
FDRSF	Fiddle DRSF	--	--
HFDRSF	Hangar Flats DRSF	152.12	27.76
YPDRSF	Yellow Pine DRSF	--	--
WEDRSF	West End DRSF	--	--
HR000	Haul Roads	12,723.41	2,322.02
TSF	Tailing Storage Facility	--	--
ACCRD	Access Roads	38.10	6.95
UGEXP	Scout Portal	0.008	0.002
Total		13,894.82	2,535.81
TSF, ACCRD, UGEXP		38.11	6.95 chk 2535.81

HAP/TAP Emission Factors

CAS No.	Pollutant	ORE Concentration ppm[1]	DR Concentration ppm[1]	CR Concentration ppm[3]	HRD Concentration ppm[4]	Borrow Concentration ppm[5]	AR Concentration ppm
7440-38-2	Arsenic	667	667	90	378.5	2.5	2.5
7440-41-7	Beryllium	3.2	3.2		3.2		3.2
7440-43-9	Cadmium	0.5	0.5		0.5		0.5
7440-48-4	Cobalt	4	4		4		4
7440-47-3	Chromium	9	9		9		9
7439-97-6	Mercury [2]	0.96	0.6		0.6		0.6
7439-96-5	Manganese	299	299		299		299
7440-02-0	Nickel	2	2		2		2
7439-92-1	Lead	8	8		8		8
7440-36-0	Antimony	23	23		23		23
7723-14-0	Phosphorus	650	650		650		650
7782-49-2	Selenium	0.4	0.4		0.4		0.4
7440-22-4	Silver	0.5	0.5		0.5		0.5
7429-90-5	Aluminum	71000	71000		71000		71000
7440-39-3	Barium	800	800		800		800
1317-65-3	Calcium Carbonate	14000	14000		14000		14000
7440-50-8	Copper	5	5		5		5
7439-89-6	Iron	18200	18200		18200		18200
7439-98-7	Molybdenum	1	1		1		1
7440-28-0	Thallium	10	10		10		10
7440-61-1	Uranium	10	10		10		10
7440-62-2	Vanadium	28	28		28		28
7440-33-7	Tungsten	10	10		10		10
7440-66-6	Zinc	35	35		35		35

[1] *(Midas Gold 2017c)* *Median concentration of 55,000 SGP samples.* *1E+6 parts/ppm*

[2] *(Midas Gold 2018e)* *Median ore and development rock (DR) concentrations of 151,000 samples; resource block model.*

[3] *(Perpetua 2021g)* *Median concentration of 265 SGP samples.*

[4] *HRD: haul road - emissions calculated based on 50% of the total VMT occuring on CR*

[5] *(ALS 2018)* *Median concentration of 8 SGP samples.*

DR DR DR DR DR DR DR DR ORE DR DR DR DR HRD DR/AR

MINING FUGITIVE EMISSIONS - CONTINUED **Model Scenario W3** DR **T-RACT Emissions**

HAP/TAP Emissions

Hourly [1] YPP_pph HFP_pph WEP_pph BT_pph YPPBL_pph HFPBL_pph WEPBL_pph BTBL_pph STKP_pph FDRSF_pph HFDRSF_pph YPDRSF_pph WEDRSF_pph HR000_pph CCRD, UGE lb/hr

CAS No.	Pollutant	YPP lb/hr	HFP lb/hr	WEP lb/hr	BT lb/hr	YPPBL lb/hr	HFPBL lb/hr	WEPBL lb/hr	BTBL lb/hr	STKP lb/hr	FDRSF lb/hr	HFDRSF lb/hr	YPDRSF lb/hr	WEDRSF lb/hr	HR000 lb/hr	TSF, ACCRD, UGEXP lb/hr	Total lb/hr
7440-38-2	Arsenic	0	0	9.4E-3	0	0	0	0.018	0	0	0	4.2E-3	0	0	0.201	4.2E-6	0.232
7440-41-7	Beryllium	0	0	4.5E-5	0	0	0	8.6E-5	0	0	0	2.0E-5	0	0	1.7E-3	5.1E-6	1.9E-3
7440-43-9	Cadmium	0	0	7.0E-6	0	0	0	1.3E-5	0	0	0	3.2E-6	0	0	2.7E-4	7.9E-7	2.9E-4
7440-48-4	Cobalt	0	0	5.6E-5	0	0	0	1.1E-4	0	0	0	2.5E-5	0	0	2.1E-3	6.4E-6	2.3E-3
7440-47-3	Chromium	0	0	1.3E-4	0	0	0	2.4E-4	0	0	0	5.7E-5	0	0	4.8E-3	1.4E-5	5.2E-3
7439-97-6	Mercury	0	0	8.5E-6	0	0	0	1.6E-5	0	0	0	3.8E-6	0	0	3.2E-4	9.5E-7	3.5E-4
7439-96-5	Manganese	0	0	4.2E-3	0	0	0	8.0E-3	0	0	0	1.9E-3	0	0	0.159	4.7E-4	0.173
7440-02-0	Nickel	0	0	2.8E-5	0	0	0	5.4E-5	0	0	0	1.3E-5	0	0	1.1E-3	3.2E-6	1.2E-3
7439-92-1	Lead	0	0	1.1E-4	0	0	0	2.1E-4	0	0	0	5.1E-5	0	0	4.2E-3	1.3E-5	4.6E-3
7440-36-0	Antimony	0	0	3.2E-4	0	0	0	6.2E-4	0	0	0	1.5E-4	0	0	0.012	3.7E-5	0.013
7723-14-0	Phosphorus	0	0	9.2E-3	0	0	0	0.017	0	0	0	4.1E-3	0	0	0.345	1.0E-3	0.376
7782-49-2	Selenium	0	0	5.6E-6	0	0	0	1.1E-5	0	0	0	2.5E-6	0	0	2.1E-4	6.4E-7	2.3E-4
7440-22-4	Silver	0	0	7.0E-6	0	0	0	1.3E-5	0	0	0	3.2E-6	0	0	2.7E-4	7.9E-7	2.9E-4
7429-90-5	Aluminum	0	0	1.000	0	0	0	1.902	0	0	0	0.450	0	0	37.640	0.113	41.106
7440-39-3	Barium	0	0	0.011	0	0	0	0.021	0	0	0	5.1E-3	0	0	0.424	1.3E-3	0.463
1317-65-3	Calcium Ca	0	0	0.197	0	0	0	0.375	0	0	0	0.089	0	0	7.422	0.022	8.105
7440-50-8	Copper	0	0	7.0E-5	0	0	0	1.3E-4	0	0	0	3.2E-5	0	0	2.7E-3	7.9E-6	2.9E-3
7439-89-6	Iron	0	0	0.256	0	0	0	0.488	0	0	0	0.115	0	0	9.649	0.029	10.537
7439-98-7	Molybdenu	0	0	1.4E-5	0	0	0	2.7E-5	0	0	0	6.3E-6	0	0	5.3E-4	1.6E-6	5.8E-4
7440-28-0	Thallium	0	0	1.4E-4	0	0	0	2.7E-4	0	0	0	6.3E-5	0	0	5.3E-3	1.6E-5	5.8E-3
7440-61-1	Uranium	0	0	1.4E-4	0	0	0	2.7E-4	0	0	0	6.3E-5	0	0	5.3E-3	1.6E-5	5.8E-3
7440-62-2	Vanadium	0	0	3.9E-4	0	0	0	7.5E-4	0	0	0	1.8E-4	0	0	0.015	4.4E-5	0.016
7440-33-7	Tungsten	0	0	1.4E-4	0	0	0	2.7E-4	0	0	0	6.3E-5	0	0	5.3E-3	1.6E-5	5.8E-3
7440-66-6	Zinc	0	0	4.9E-4	0	0	0	9.4E-4	0	0	0	2.2E-4	0	0	0.019	5.6E-5	0.020
Total		0	0	1.490	0	0	0	2.834	0	0	0	0.670	0	0	55.918	0.167	61.079

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.* chk 61.0794 61.0794

DR DR DR DR DR DR DR DR ORE DR DR DR DR HRD DR/AR

MINING FUGITIVE EMISSIONS - CONTINUED **Model Scenario W3** DR **T-RACT Emissions**

HAP/TAP Emissions

Annual

		YPP_tpy	HFP_tpy	WEP_tpy	BT_tpy	YPPBL_tpy	HFPBL_tpy	WEPBL_tpy	BTBL_tpy	STKP_tpy	FDRSF_tpy	HFDRSF_tpy	YPDRSF_tpy	WEDRSF_tpy	HR000_tpy	CCRD, UGE	ton/yr
		YPP	HFP	WEP	BT	YPPBL	HFPBL	WEPBL	BTBL	STKP	FDRSF	HFDRSF	YPDRSF	WEDRSF	HR000	TSF, ACCRD, UGEXP	Total
CAS No.	Pollutant	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr
7440-38-2	Arsenic	0	0	0.041	0	0	0	0.078	0	0	0	0.019	0	0	0.879	1.8E-5	1.017
7440-41-7	Beryllium	0	0	2.0E-4	0	0	0	3.8E-4	0	0	0	8.9E-5	0	0	7.4E-3	2.2E-5	8.1E-3
7440-43-9	Cadmium	0	0	3.1E-5	0	0	0	5.9E-5	0	0	0	1.4E-5	0	0	1.2E-3	3.5E-6	1.3E-3
7440-48-4	Cobalt	0	0	2.5E-4	0	0	0	4.7E-4	0	0	0	1.1E-4	0	0	9.3E-3	2.8E-5	0.010
7440-47-3	Chromium	0	0	5.6E-4	0	0	0	1.1E-3	0	0	0	2.5E-4	0	0	0.021	6.3E-5	0.023
7439-97-6	Mercury	0	0	3.7E-5	0	0	0	7.0E-5	0	0	0	1.7E-5	0	0	1.4E-3	4.2E-6	1.5E-3
7439-96-5	Manganese	0	0	0.018	0	0	0	0.035	0	0	0	8.3E-3	0	0	0.694	2.1E-3	0.758
7440-02-0	Nickel	0	0	1.2E-4	0	0	0	2.3E-4	0	0	0	5.6E-5	0	0	4.6E-3	1.4E-5	5.1E-3
7439-92-1	Lead	0	0	4.9E-4	0	0	0	9.4E-4	0	0	0	2.2E-4	0	0	0.019	5.6E-5	0.020
7440-36-0	Antimony	0	0	1.4E-3	0	0	0	2.7E-3	0	0	0	6.4E-4	0	0	0.053	1.6E-4	0.058
7723-14-0	Phosphorus	0	0	0.040	0	0	0	0.076	0	0	0	0.018	0	0	1.509	4.5E-3	1.648
7782-49-2	Selenium	0	0	2.5E-5	0	0	0	4.7E-5	0	0	0	1.1E-5	0	0	9.3E-4	2.8E-6	1.0E-3
7440-22-4	Silver	0	0	3.1E-5	0	0	0	5.9E-5	0	0	0	1.4E-5	0	0	1.2E-3	3.5E-6	1.3E-3
7429-90-5	Aluminum	0	0	4.382	0	0	0	8.332	0	0	0	1.971	0	0	165	0.494	180
7440-39-3	Barium	0	0	0.049	0	0	0	0.094	0	0	0	0.022	0	0	1.858	5.6E-3	2.029
1317-65-3	Calcium Ca	0	0	0.864	0	0	0	1.643	0	0	0	0.389	0	0	32.508	0.097	35.501
7440-50-8	Copper	0	0	3.1E-4	0	0	0	5.9E-4	0	0	0	1.4E-4	0	0	0.012	3.5E-5	0.013
7439-89-6	Iron	0	0	1.123	0	0	0	2.136	0	0	0	0.505	0	0	42.261	0.127	46.152
7439-98-7	Molybdenu	0	0	6.2E-5	0	0	0	1.2E-4	0	0	0	2.8E-5	0	0	2.3E-3	7.0E-6	2.5E-3
7440-28-0	Thallium	0	0	6.2E-4	0	0	0	1.2E-3	0	0	0	2.8E-4	0	0	0.023	7.0E-5	0.025
7440-61-1	Uranium	0	0	6.2E-4	0	0	0	1.2E-3	0	0	0	2.8E-4	0	0	0.023	7.0E-5	0.025
7440-62-2	Vanadium	0	0	1.7E-3	0	0	0	3.3E-3	0	0	0	7.8E-4	0	0	0.065	1.9E-4	0.071
7440-33-7	Tungsten	0	0	6.2E-4	0	0	0	1.2E-3	0	0	0	2.8E-4	0	0	0.023	7.0E-5	0.025
7440-66-6	Zinc	0	0	2.2E-3	0	0	0	4.1E-3	0	0	0	9.7E-4	0	0	0.081	2.4E-4	0.089
Total		0	0	6.527	0	0	0	12.412	0	0	0	2.936	0	0	245	0.731	268
															chk	267.5280	267.5280

MINING FUGITIVE EMISSIONS - CONTINUED

Mercury Evaporative Flux Emissions

Fugitive Mercury Flux and Emissions

			Area		Hg Flux	Emissions[1] lb/hr	ton/yr	lb/yr
CAS No.	Pollutant	Source	m^2	ha	$\mu g/m^2$-yr	lb/hr	ton/yr	lb/yr
		Stockpiles	52,623	5.3	556	7.37E-6	3.2E-5	6.5E-2
		Rock Dumps	2,063,990	206.4	76.2	3.96E-5	1.7E-4	0.35
		Tailings	1,338,158	133.8	2,144	7.22E-4	3.2E-3	6.32
		Pits	1,504,919	150.5	132.3	5.01E-5	2.2E-4	0.44
7439-97-6	Mercury					8.2E-4	3.6E-3	7.17

(1) *Hourly emissions based on:* 8,760 *hours per year of operation*

Fugitive Mercury Emission Factors

	Twin Creeks (TC)		Ore Hg Adjusted	Stibnite	
	Hg Flux (1)	Hg (2)	$\mu g/m^2/yr$	Hg Flux (3)	Hg (4)
Source	$\mu g/m^2$-yr	µg/g	TC	$\mu g/m^2$-yr	µg/g
Stockpiles	5,609	33	556	556	0.96
Rock Dumps	768	3.5	76.2	76.2	0.60
Tailings	21,621	33	2,144	2,144	0.96
Pits	1,334	9.5	132	132.3	0.60

(1) *(Eckley 2010)* *Table 1: Hg flux µg/m^2-yr*

(2) *(Eckley 2010)* *Table 1: Average Hg flux mg/g: " Stockpiles - high-grade stockpiles, Rock Dumps - waste rock dumps, Tailings - high-grade stockpiles as a surrogate; Pits - pit"*

(3) *(Eckley 2010)* *Figure 2: log(y) = m*log(x) + b*

y = Hg Flux (ng/m^2-d)
x = material Hg concentration (µg/g)]

Slope =	*Solar*	*TC*
	Low	*0.59*
	Medium	*0.6*
	High	*0.77*
	Average	*0.65*

(4) *(Midas Gold 2018e)*

Sample Calculation: m = log (y1/y2) / log(x1/x2)

m=	0.65	unitless
y1=	5,609	$\mu g/m^2$-yr
x1=	33	$\mu g/m^2$-yr
x2=	0.96	$\mu g/m^2$-yr
log(x1/x2)=	1.536243	unitless
log(y1/y2)=	1.003679	unitless
y1/y2=	10.08506	unitless
y2=	556.2	$\mu g/m^2$-yr

Conversions

2,000	lb/ton
10,000	m2/ha
453.593	g/lb

TABLE A-W3. HAP/TAP Emissions and Exemptions

T-RACT Emissions						MINING										LEACHING	
chk						*Mining*	*Model Scenario W3*									*CN Leach/PAX*	
						YPP,HFP,WEP,BT	YPPBL,HFPBL,WEPBL,BTBL		HR000		STKP, FDRSF, HFDRSF, YPDRSF, WEDRSF		TSF,ACCRD,UGEXP				
CAS	HAP/TAP	HAP	TAP			Pits		Blasting		Haul Roads		Stockpiles and DRFS		Tails, Access Road, Exploration		CN Leach and PAX	
	NSPS or NESHAP HAP/TAP -->			*Y*													
	Non-Carcinogenic Acute (A) or Carcinogenic (C) -->				A/C	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr
7440-38-2	Arsenic	Y	Y	Y	C	9.4E-3	0.041	0.018	0.078	0.201	0.879	4.2E-3	0.019	4.2E-6	1.8E-5		
7440-41-7	Beryllium	Y	Y	Y	C	4.5E-5	2.0E-4	8.6E-5	3.8E-4	1.7E-3	7.4E-3	2.0E-5	8.9E-5	5.1E-6	2.2E-5		
7440-43-9	Cadmium	Y	Y	Y	C	7.0E-6	3.1E-5	1.3E-5	5.9E-5	2.7E-4	1.2E-3	3.2E-6	1.4E-5	7.9E-7	3.5E-6		
50-00-0	Formaldehyde	Y	Y	Y	C												
7440-02-0	Nickel	Y	Y	Y	C	2.8E-5	1.2E-4	5.4E-5	2.3E-4	1.1E-3	4.6E-3	1.3E-5	5.6E-5	3.2E-6	1.4E-5		

TABLE A-W3. HAP/TAP Emissions and Exemptions

T-RACT Emissions						PROCESSING AND PRODUCTION											
chk						*Ore Processing*				*Ore Concentration and Refining*				*Process Heating*			
						OC1-13		PS		AC		EW,MR,MF,CKD		ACB, CKB, PV, HS		LKC	
CAS	HAP/TAP	HAP	TAP			Crushers & Xfers		Prill Silos		Autoclave		EW, Preg Tank, Retort, Furnace, Carbon Kiln		POX Boiler, C. Kiln Comb., Prop. Vap., Sol'n Heater		Lime Kiln Combustion	
	NSPS or NESHAP HAP/TAP -->			*Y*		*LL*	*LL*			*7E*	*7E*	*7E*	*7E*			*5A*	*5A*
	Non-Carcinogenic Acute (A) or Carcinogenic (C) -->				A/C	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr
7440-38-2	Arsenic	Y	Y	Y	C	3.9E-3	0.017			2.3E-5	1.0E-4	3.8E-4	1.7E-3	1.5E-6	6.4E-6	3.7E-6	1.6E-5
7440-41-7	Beryllium	Y	Y	Y	C	1.9E-5	8.2E-5			2.3E-5	1.0E-4	3.8E-4	1.7E-3	8.7E-8	3.8E-7	2.2E-7	9.6E-7
7440-43-9	Cadmium	Y	Y	Y	C	2.9E-6	1.3E-5			2.3E-5	1.0E-4	3.8E-4	1.7E-3	8.0E-6	3.5E-5	2.0E-5	8.8E-5
50-00-0	Formaldehyde	Y	Y	Y	C									5.5E-4	2.4E-3	1.4E-3	6.0E-3
7440-02-0	Nickel	Y	Y	Y	C	1.2E-5	5.2E-5			2.3E-5	1.0E-4	3.8E-4	1.7E-3	1.5E-5	6.7E-5	3.9E-5	1.7E-4

TABLE A-W3. HAP/TAP Emissions and Exemptions

T-RACT Emissions						PROCESSING AND PRODUCTION - Continued													
chk						*Lime Production*						*Aggregate Prod.*		*Concrete Production*					
						LS1-11,LSBM		LK,LS12,LCR,LS-L/U		LS1-L/U,MillS2-L/U,ACS1-4		PCSP1,PCSP2		CM		CS1L,CS1U,CS2L, CS2U		CA-L/U	
CAS	HAP/TAP	HAP	TAP			Limestone Crushers, Screens, Mill, Xfers		Lime Kiln, Kiln Feed, Lime Mill, Pebble Lime Silo		Lime Silos and Lime Mill Crushing		Portable Crushers, Screens, Xfers		Central Mixer		Cement Silo #1 and #2 L/U		Aggregate Bin	
	NSPS or NESHAP HAP/TAP -->			*Y*		*OOO*	*OOO*	*5A*	*5A*			*OOO*	*OOO*					*OOO*	*OOO*
	Non-Carcinogenic Acute (A) or Carcinogenic (C) -->				*A/C*	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr
7440-38-2	Arsenic	Y	Y	Y	C	1.0E-4	4.4E-4	2.4E-5	1.1E-4	1.1E-6	4.7E-6	2.9E-5	1.3E-4	2.0E-6	8.9E-6	1.2E-7	5.1E-7	1.8E-5	7.9E-5
7440-41-7	Beryllium	Y	Y	Y	C	3.5E-6	1.5E-5	8.4E-7	3.7E-6	3.7E-8	1.6E-7	1.0E-6	4.4E-6			1.3E-8	5.8E-8	6.3E-7	2.8E-6
7440-43-9	Cadmium	Y	Y	Y	C	1.1E-6	4.8E-6	2.6E-7	1.2E-6	1.2E-8	5.1E-8	3.1E-7	1.4E-6	4.9E-9	2.1E-8			2.0E-7	8.6E-7
50-00-0	Formaldehyde	Y	Y	Y	C														
7440-02-0	Nickel	Y	Y	Y	C	2.2E-5	9.6E-5	5.3E-6	2.3E-5	2.3E-7	1.0E-6	6.3E-6	2.7E-5	1.7E-6	7.4E-6	1.1E-6	5.0E-6	3.9E-6	1.7E-5

TABLE A-W3. HAP/TAP Emissions and Exemptions

T-RACT Emissions						PROCESSING AND PRODUCTION - Continued						MINING and LEACHING - Totals									
chk						*HVAC*		*Emer. Power/Fire*		*Fuel Storage*		*HAP Total*		*Mercury Total*		*Mercury Total*		*TAP Total*		*TAP Total*	
						H1M,H2M,HM,HAC,HR,HA,HMO,HTS,HW		EDG1,EDG2,EDG3,EDFP		TG1,TG2				*Exempt*		*Non-Exempt*		*HAP-TAP addressed by NSPS/NESHAP*		*For EL Evaluation*	
CAS	HAP/TAP	HAP	TAP			Heaters		Emergency Generators and Fire Pump		Gasoline Fuel Tanks											
	NSPS or NESHAP HAP/TAP -->			*Y*				*4Z*	*4Z*	*6C*	*6C*										
	Non-Carcinogenic Acute (A) or Carcinogenic (C) -->				*A/C*	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr
7440-38-2	Arsenic	Y	Y	Y	C	3.6E-6	1.6E-5					0.232	1.017							0.232	1.017
7440-41-7	Beryllium	Y	Y	Y	C	2.1E-7	9.4E-7					1.9E-3	8.1E-3							1.9E-3	8.1E-3
7440-43-9	Cadmium	Y	Y	Y	C	2.0E-5	8.6E-5					2.9E-4	1.3E-3							2.9E-4	1.3E-3
50-00-0	Formaldehyde	Y	Y	Y	C	1.3E-3	5.9E-3	5.1E-5	2.2E-4												
7440-02-0	Nickel	Y	Y	Y	C	3.8E-5	1.6E-4					1.2E-3	5.1E-3					0	0	1.2E-3	5.1E-3

TABLE A-W3. HAP/TAP Emissions and Exemptions

T-RACT Emissions						PROCESSING AND PRODUCTION - Totals										ALL	ALL	ALL	TAP EL	
chk						*HAP Total*		*Mercury Total Exempt*		*Mercury Total Non-Exempt*		*TAP Total HAP-TAP addressed by NSPS/NESHAP*		*TAP Total For EL Evaluation*		*HAP*	*Hg Non-Exempt*	*TAP For EL Evaluation*	*TAP Emission Screening Level (EL)*	
CAS	HAP/TAP	HAP	TAP																	
	NSPS or NESHAP HAP/TAP -->			*Y*															Non-car	Carcin
	Non-Carcinogenic Acute (A) or Carcinogenic (C) -->				*A/C*	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	ton/yr	ton/yr	lb/hr	lb/hr	lb/hr
7440-38-2	Arsenic	Y	Y	Y	C	4.5E-3	0.020					4.5E-3	0.020	8.2E-6	3.6E-5	1.037		0.232	--	1.5E-6
7440-41-7	Beryllium	Y	Y	Y	C	4.3E-4	1.9E-3					4.3E-4	1.9E-3	3.5E-7	1.5E-6	0.010		1.9E-3	--	2.8E-5
7440-43-9	Cadmium	Y	Y	Y	C	4.6E-4	2.0E-3					4.3E-4	1.9E-3	2.8E-5	1.2E-4	3.3E-3		3.2E-4	--	3.7E-6
50-00-0	Formaldehyde	Y	Y	Y	C	3.3E-3	0.015					1.4E-3	6.2E-3	1.9E-3	8.3E-3	0.015		1.9E-3	--	5.1E-4
7440-02-0	Nickel	Y	Y	Y	C	5.5E-4	2.4E-3					4.9E-4	2.2E-3	5.6E-5	2.4E-4	7.5E-3		1.2E-3	--	2.7E-5

Appendix B – Modeled Emissions per Modeling Scenario and Source

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Non-Carcinogenic TAP Modeling

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Carcinogenic TAP Modeling

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TABLE B-Y1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-Y1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-Y1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: Y1	YPP	Yellow Pine Pit	0	0.024	0.051	5.585	0.063	1.101
	HFP	Hangar Flats Pit	0	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	4.5E-3	9.7E-3	1.063	0.012	0.210
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.065	0.141	15.394	0.173	3.035
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.102**	**0.220**	**24.705**	**0.278**	**6.987**

TABLE B-Y1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-Y1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-Y1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: Y1	YPP	Yellow Pine Pit	0	1.432	0	7.9E-4	2.2E-3
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0.272	0	1.5E-4	4.2E-4
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	3.946	0	2.2E-3	6.1E-3
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**6.380**	**2.030**	**3.9E-3**	**0.010**

TABLE B-Y2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-Y2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-Y2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: Y2	YPP	Yellow Pine Pit	0	0.024	0.051	5.585	0.063	1.101
	HFP	Hangar Flats Pit	0	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	3.6E-3	7.9E-3	0.858	9.7E-3	0.169
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.096	0.208	22.711	0.256	4.478
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.131**	**0.285**	**31.817**	**0.358**	**8.390**

TABLE B-Y2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-Y2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-Y2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: Y2	YPP	Yellow Pine Pit	0	1.432	0	7.9E-4	2.2E-3
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0.220	0	1.2E-4	3.4E-4
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	5.822	0	3.2E-3	9.0E-3
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**8.203**	**2.030**	**4.9E-3**	**0.013**

TABLE B-Y3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-Y3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-Y3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: Y3	YPP	Yellow Pine Pit	0	0.024	0.051	5.585	0.063	1.101
	HFP	Hangar Flats Pit	0	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	3.6E-3	7.9E-3	0.858	9.7E-3	0.169
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.155	0.337	36.835	0.415	7.263
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.191**	**0.415**	**45.941**	**0.517**	**11.175**

TABLE B-Y3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-Y3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-Y3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: Y3	YPP	Yellow Pine Pit	0	1.432	0	7.9E-4	2.2E-3
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0.220	0	1.2E-4	3.4E-4
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	9.442	0	5.2E-3	0.015
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**11.823**	**2.030**	**6.9E-3**	**0.019**

TABLE B-H1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-H1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-H1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: H1	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0.024	0.051	5.585	0.063	1.101
	WEP	West End Pit	0	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	WEPBL	West End Pit Blasting	0	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	4.5E-3	9.7E-3	1.063	0.012	0.210
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.105	0.228	24.940	0.281	4.918
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.142**	**0.308**	**34.252**	**0.385**	**8.870**

TABLE B-H1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-H1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-H1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: H1	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	1.432	0	7.9E-4	2.2E-3
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0.272	0	1.5E-4	4.2E-4
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	6.393	0	3.5E-3	9.8E-3
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**8.827**	**2.030**	**5.2E-3**	**0.014**

TABLE B-H2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-H2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-H2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: H2	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0.024	0.051	5.585	0.063	1.101
	WEP	West End Pit	0	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	WEPBL	West End Pit Blasting	0	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	3.6E-3	7.9E-3	0.858	9.7E-3	0.169
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.157	0.342	37.334	0.421	7.362
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.193**	**0.419**	**46.440**	**0.523**	**11.273**

TABLE B-H2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-H2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-H2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: H2	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	1.432	0	7.9E-4	2.2E-3
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0.220	0	1.2E-4	3.4E-4
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	9.570	0	5.3E-3	0.015
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**11.951**	**2.030**	**7.0E-3**	**0.019**

TABLE B-H3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-H3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-H3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: H3	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0.024	0.051	5.585	0.063	1.101
	WEP	West End Pit	0	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	WEPBL	West End Pit Blasting	0	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	3.6E-3	7.9E-3	0.858	9.7E-3	0.169
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.096	0.209	22.854	0.258	4.506
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.132**	**0.287**	**31.960**	**0.360**	**8.418**

TABLE B-H3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-H3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-H3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: H3	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	1.432	0	7.9E-4	2.2E-3
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0.220	0	1.2E-4	3.4E-4
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	5.858	0	3.2E-3	9.0E-3
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**8.239**	**2.030**	**4.9E-3**	**0.013**

TABLE B-H4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-H4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-H4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: H4	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0.024	0.051	5.585	0.063	1.101
	WEP	West End Pit	0	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	WEPBL	West End Pit Blasting	0	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	3.6E-3	7.9E-3	0.858	9.7E-3	0.169
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.123	0.268	29.277	0.330	5.773
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.159**	**0.346**	**38.383**	**0.432**	**9.685**

TABLE B-H4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-H4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-H4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: H4	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	1.432	0	7.9E-4	2.2E-3
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0.220	0	1.2E-4	3.4E-4
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	7.505	0	4.1E-3	0.012
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**9.886**	**2.030**	**5.8E-3**	**0.016**

TABLE B-W1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-W1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-W1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: W1	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0	0
	WEP	West End Pit	0	0.024	0.051	5.585	0.063	1.101
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	4.5E-3	9.7E-3	1.063	0.012	0.210
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.090	0.196	21.435	0.242	4.227
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.127**	**0.276**	**30.746**	**0.346**	**8.179**

TABLE B-W1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-W1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-W1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: W1	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	1.432	0	7.9E-4	2.2E-3
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0.272	0	1.5E-4	4.2E-4
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	5.495	0	3.0E-3	8.5E-3
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**7.928**	**2.030**	**4.8E-3**	**0.013**

TABLE B-W2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-W2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-W2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: W2	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0	0
	WEP	West End Pit	0	0.024	0.051	5.585	0.063	1.101
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	3.6E-3	7.9E-3	0.858	9.7E-3	0.169
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.145	0.316	34.484	0.389	6.800
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.181**	**0.393**	**43.590**	**0.491**	**10.711**

TABLE B-W2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-W2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-W2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: W2	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	1.432	0	7.9E-4	2.2E-3
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0.220	0	1.2E-4	3.4E-4
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	8.840	0	4.9E-3	0.014
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**11.221**	**2.030**	**6.6E-3**	**0.018**

TABLE B-W3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-W3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-W3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: W3	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0	0
	WEP	West End Pit	0	0.024	0.051	5.585	0.063	1.101
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	3.6E-3	7.9E-3	0.858	9.7E-3	0.169
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.208	0.452	49.397	0.557	9.740
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.244**	**0.530**	**58.504**	**0.659**	**13.652**

TABLE B-W3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-W3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-W3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: W3	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	1.432	0	7.9E-4	2.2E-3
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0.220	0	1.2E-4	3.4E-4
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	12.662	0	7.0E-3	0.019
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**15.043**	**2.030**	**8.7E-3**	**0.024**

TABLE B-W4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-W4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-W4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: W4	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0	0
	WEP	West End Pit	0	0.024	0.051	5.585	0.063	1.101
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	3.6E-3	7.9E-3	0.858	9.7E-3	0.169
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.094	0.204	22.281	0.251	4.393
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.130**	**0.282**	**31.387**	**0.353**	**8.305**

TABLE B-W4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-W4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-W4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: W4	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	1.432	0	7.9E-4	2.2E-3
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0.220	0	1.2E-4	3.4E-4
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	5.711	0	3.1E-3	8.8E-3
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**8.092**	**2.030**	**4.8E-3**	**0.013**

TABLE B-W5. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-W5. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-W5. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: W5	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0	0
	WEP	West End Pit	0	0.024	0.051	5.585	0.063	1.101
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	3.6E-3	7.9E-3	0.858	9.7E-3	0.169
	HR000	Haul Roads	0	0.104	0.225	24.595	0.277	4.850
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.139**	**0.303**	**33.702**	**0.379**	**8.761**

TABLE B-W5. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-W5. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-W5. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: W5	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	1.432	0	7.9E-4	2.2E-3
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0.220	0	1.2E-4	3.4E-4
	HR000	Haul Roads	0	6.305	0	3.5E-3	9.7E-3
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**8.686**	**2.030**	**5.2E-3**	**0.014**

TABLE B-B1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-B1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-B1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: B1	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0	0
	BT	Bradley Tailings	0	0.023	0.051	5.567	0.063	1.098
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	STKP	PC Stockpile	0	4.5E-3	9.7E-3	1.063	0.012	0.210
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.120	0.260	28.394	0.320	5.599
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.156**	**0.339**	**37.687**	**0.424**	**9.547**

TABLE B-B1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-B1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-B1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: B1	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	1.427	0	7.8E-4	2.2E-3
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0.488	0	2.7E-4	7.5E-4
	STKP	PC Stockpile	0	0.272	0	1.5E-4	4.2E-4
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	7.278	0	4.0E-3	0.011
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**9.707**	**2.030**	**5.7E-3**	**0.015**

TABLE B-B2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-B2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-B2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: B2	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0	0
	BT	Bradley Tailings	0	0.023	0.051	5.567	0.063	1.098
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	STKP	PC Stockpile	0	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	3.6E-3	7.9E-3	0.858	9.7E-3	0.169
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.028	0.061	6.713	0.076	1.324
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.064**	**0.139**	**15.801**	**0.178**	**5.232**

TABLE B-B2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-B2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-B2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: B2	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	1.427	0	7.8E-4	2.2E-3
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0.488	0	2.7E-4	7.5E-4
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0.220	0	1.2E-4	3.4E-4
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	1.721	0	9.5E-4	2.6E-3
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**4.097**	**2.030**	**2.7E-3**	**6.8E-3**

TABLE B-Y1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-Y1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-Y1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: Y1	YPP	Yellow Pine Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	5.7E-3	2.7E-5	4.3E-6	0	1.7E-5
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.065	5.5E-4	8.5E-5	0	3.4E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.098**	**7.1E-4**	**1.4E-4**	**1.9E-3**	**5.0E-4**

TABLE B-Y2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-Y2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-Y2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: Y2	YPP	Yellow Pine Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	4.2E-3	2.0E-5	3.2E-6	0	1.3E-5
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.094	7.9E-4	1.2E-4	0	5.0E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.125**	**9.5E-4**	**1.8E-4**	**1.9E-3**	**6.5E-4**

TABLE B-Y3. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-Y3. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-Y3. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: Y3	YPP	Yellow Pine Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	4.2E-3	2.0E-5	3.2E-6	0	1.3E-5
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.150	1.3E-3	2.0E-4	0	7.9E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.182**	**1.4E-3**	**2.5E-4**	**1.9E-3**	**9.5E-4**

TABLE B-H1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-H1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-H1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: H1	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	5.7E-3	2.7E-5	4.3E-6	0	1.7E-5
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.103	8.7E-4	1.4E-4	0	5.4E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.136**	**1.0E-3**	**1.9E-4**	**1.9E-3**	**7.0E-4**

TABLE B-H2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-H2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-H2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: H2	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	4.2E-3	2.0E-5	3.2E-6	0	1.3E-5
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.152	1.3E-3	2.0E-4	0	8.1E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.184**	**1.4E-3**	**2.5E-4**	**1.9E-3**	**9.6E-4**

TABLE B-H3. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-H3. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-H3. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: H3	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	4.2E-3	2.0E-5	3.2E-6	0	1.3E-5
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.095	8.0E-4	1.2E-4	0	5.0E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.126**	**9.6E-4**	**1.8E-4**	**1.9E-3**	**6.5E-4**

TABLE B-H4. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-H4. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-H4. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: H4	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	4.2E-3	2.0E-5	3.2E-6	0	1.3E-5
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.120	1.0E-3	1.6E-4	0	6.4E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.152**	**1.2E-3**	**2.1E-4**	**1.9E-3**	**7.9E-4**

TABLE B-W1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-W1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-W1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: W1	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	5.7E-3	2.7E-5	4.3E-6	0	1.7E-5
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.089	7.5E-4	1.2E-4	0	4.7E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.122**	**9.1E-4**	**1.7E-4**	**1.9E-3**	**6.3E-4**

TABLE B-W2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-W2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-W2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: W2	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	4.2E-3	2.0E-5	3.2E-6	0	1.3E-5
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.141	1.2E-3	1.9E-4	0	7.5E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.173**	**1.3E-3**	**2.4E-4**	**1.9E-3**	**9.0E-4**

TABLE B-W3. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-W3. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-W3. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: W3	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	4.2E-3	2.0E-5	3.2E-6	0	1.3E-5
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.201	1.7E-3	2.7E-4	0	1.1E-3
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.232**	**1.9E-3**	**3.2E-4**	**1.9E-3**	**1.2E-3**

TABLE B-W4. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-W4. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-W4. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: W4	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	4.2E-3	2.0E-5	3.2E-6	0	1.3E-5
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.092	7.8E-4	1.2E-4	0	4.9E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.124**	**9.4E-4**	**1.7E-4**	**1.9E-3**	**6.4E-4**

TABLE B-W5. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-W5. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-W5. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: W5	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	4.2E-3	2.0E-5	3.2E-6	0	1.3E-5
	HR000	Haul Roads	0.101	8.6E-4	1.3E-4	0	5.4E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.133**	**1.0E-3**	**1.9E-4**	**1.9E-3**	**6.9E-4**

TABLE B-B1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-B1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-B1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: B1	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	9.2E-3	4.4E-5	6.9E-6	0	2.8E-5
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	STKP	PC Stockpile	5.7E-3	2.7E-5	4.3E-6	0	1.7E-5
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.117	9.9E-4	1.5E-4	0	6.2E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.149**	**1.1E-3**	**2.1E-4**	**1.9E-3**	**7.7E-4**

TABLE B-B2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-B2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-B2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: B2	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	9.2E-3	4.4E-5	6.9E-6	0	2.8E-5
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	4.2E-3	2.0E-5	3.2E-6	0	1.3E-5
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.030	2.5E-4	4.0E-5	0	1.6E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.061**	**4.1E-4**	**9.2E-5**	**1.9E-3**	**3.1E-4**

Appendix C – TAP Modeling Results

TABLE C. TAP Maximum Modeled Concentrations and AACs

	TAP Maximum Modeled Concentrations by Model Scenario																	
	Y1	Y2	Y3	H1	H2	H3	H4	W1 [2]	W2 [2]	W3 [2]	W4 [2]	W5 [3]	B1	B2	Max Scenario			Compl-
Pollutant	µg/m³	µg/m³	µg/m³	µg/m³	µg/m³	µg/m³	µg/m³	µg/m³	µg/m³	µg/m³	µg/m³	µg/m³	µg/m³	µg/m³	µg/m³	ID	AAC [4]	iance
Aluminum	1.13561	1.41646	1.13855	1.19028	1.28403	1.09010	1.17371	6.01079	5.27252	6.00999	4.97175	6.17075	1.17437	0.97352	6.17075	W5	500	Yes
Arsenic [1]	0.00030	0.00049	0.00029	0.00023	0.00053	0.00020	0.00021	0.00091	0.00095	0.00090	0.00087	N/A	0.00024	0.00012	0.00095	W2	0.0023	Yes
Barium	0.01279	0.01595	0.01282	0.01341	0.01446	0.01228	0.01322	0.06773	0.05941	0.06772	0.05602	0.06953	0.01323	0.01097	0.06953	W5	25	Yes
Beryllium [1]	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00001	0.00001	0.00001	0.00001	N/A	0.00000	0.00000	0.00001	W1	0.042	Yes
Cadmium [1]	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000	0.000002	0.000002	0.000002	0.000002	N/A	0.000000	0.000000	0.000002	W1	0.0056	Yes
Calcium Carbonate	0.34375	0.33431	0.37347	0.39124	0.38168	0.37132	0.38141	1.18652	1.04095	1.18637	0.98165	1.21807	0.39107	0.34851	1.21807	W5	500	Yes
Calcium Oxide	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	ALL	100	Yes
Cyanide	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	ALL	250	Yes
Formaldehyde [1]	0.00007	0.00007	0.00007	0.00007	0.00007	0.00007	0.00007	0.00007	0.00007	0.00007	0.00007	N/A	0.00007	0.00007	0.00007	ALL	0.77	Yes
Iron	0.29143	0.36343	0.29219	0.30525	0.32952	0.27957	0.30100	1.54079	1.35154	1.54058	1.27445	1.58179	0.30110	0.24962	1.58179	W5	50	Yes
Manganese	0.00477	0.00595	0.00478	0.00500	0.00538	0.00458	0.00493	0.02531	0.02220	0.02531	0.02094	0.02599	0.00494	0.00410	0.02599	W5	250	Yes
Nickel [1]	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00001	0.00001	0.00001	0.00001	N/A	0.00000	0.00000	0.00001	W1	0.42	Yes
Phosphorus	0.01036	0.01293	0.01039	0.01088	0.01169	0.00996	0.01073	0.05502	0.04827	0.05502	0.04551	0.05649	0.01074	0.00891	0.05649	W5	5	Yes
Sulfuric Acid	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	ALL	50	Yes
Thallium	0.00016	0.00020	0.00016	0.00017	0.00018	0.00016	0.00017	0.00085	0.00074	0.00085	0.00070	0.00087	0.00017	0.00014	0.00087	W5	5	Yes
Vanadium	0.00045	0.00056	0.00045	0.00047	0.00051	0.00043	0.00046	0.00237	0.00208	0.00237	0.00196	0.00243	0.00046	0.00039	0.00243	W5	2.5	Yes

[1] Carcinogenic TAP concentrations adjusted for 70-year exposure, as discussed in Section 3.4.4.

[2] Carcinogenic TAP concentrations adjusted for the West End pit LOM production limit, as discussed in Section 3.4.5.

[3] Modeling Scenario W5 is eliminated for carcinogenic TAP compliance, as discussed in Section 3.4.5.

[4] The AACs for carcinogenic pollutants are increased by a factor of ten per IDAPA 58.01.01.210.12(b); T-RACT adjustment.

Appendix D – Electronic Files

The electronic modeling files, emission inventory file, and Addendum references can be accessed via the following link:

https://drive.google.com/drive/folders/1o0-uNIu5DRds8hLShaD_0nPEBnlEJFCQ?usp=sharing

CERTIFICATE OF SERVICE

I hereby certify that on October 4, 2024, a true and correct copy of the foregoing EXPERT DECLARATION OF IAN H. VON LINDERN, P.E., Ph.D. was served on the following by electronic service:

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EX. NO. 303
L Schilling
DATE 10-17-24
ASSOCIATED REPORTING & VIDEO

TABLE C. TAP Maximum Modeled Concentrations and AACs

	TAP Maximum Modeled Concentrations by Model Scenario														Max Scenario			Compl-
Pollutant	Y1 µg/m³	Y2 µg/m³	Y3 µg/m³	H1 µg/m³	H2 µg/m³	H3 µg/m³	H4 µg/m³	W1 [2] µg/m³	W2 [2] µg/m³	W3 [2] µg/m³	W4 [2] µg/m³	W5 [3] µg/m³	B1 µg/m³	B2 µg/m³	µg/m³	ID	AAC [4]	iance
Aluminum	1.13561	1.41646	1.13855	1.19028	1.28403	1.09010	1.17371	6.01079	5.27252	6.00999	4.97175	6.17075	1.17437	0.97352	6.17075	W5	500	Yes
Arsenic [1]	0.00030	0.00049	0.00029	0.00023	0.00053	0.00020	0.00021	0.00091	0.00095	0.00090	0.00087	N/A	0.00024	0.00012	0.00095	W2	0.0023	Yes
Barium	0.01279	0.01595	0.01282	0.01341	0.01446	0.01228	0.01322	0.06773	0.05941	0.06772	0.05602	0.06953	0.01323	0.01097	0.06953	W5	25	Yes
Beryllium [1]	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00001	0.00001	0.00001	0.00001	N/A	0.00000	0.00000	0.00001	W1	0.042	Yes
Cadmium [1]	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000	0.000002	0.000002	0.000002	0.000002	N/A	0.000000	0.000000	0.000002	W1	0.0056	Yes
Calcium Carbonate	0.34375	0.33431	0.37347	0.39124	0.38168	0.37132	0.38141	1.18652	1.04095	1.18637	0.98165	1.21807	0.39107	0.34851	1.21807	W5	500	Yes
Calcium Oxide	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	ALL	100	Yes
Cyanide	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	ALL	250	Yes
Formaldehyde [1]	0.00007	0.00007	0.00007	0.00007	0.00007	0.00007	0.00007	0.00007	0.00007	0.00007	0.00007	N/A	0.00007	0.00007	0.00007	ALL	0.77	Yes
Iron	0.29143	0.36343	0.29219	0.30525	0.32952	0.27957	0.30100	1.54079	1.35154	1.54058	1.27445	1.58179	0.30110	0.24962	1.58179	W5	50	Yes
Manganese	0.00477	0.00595	0.00478	0.00500	0.00538	0.00458	0.00493	0.02531	0.02220	0.02531	0.02094	0.02599	0.00494	0.00410	0.02599	W5	250	Yes
Nickel [1]	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00001	0.00001	0.00001	0.00001	N/A	0.00000	0.00000	0.00001	W1	0.42	Yes
Phosphorus	0.01036	0.01293	0.01039	0.01088	0.01169	0.00996	0.01073	0.05502	0.04827	0.05502	0.04551	0.05649	0.01074	0.00891	0.05649	W5	5	Yes
Sulfuric Acid	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	ALL	50	Yes
Thallium	0.00016	0.00020	0.00016	0.00017	0.00018	0.00016	0.00017	0.00085	0.00074	0.00085	0.00070	0.00087	0.00017	0.00014	0.00087	W5	5	Yes
Vanadium	0.00045	0.00056	0.00045	0.00047	0.00051	0.00043	0.00046	0.00237	0.00208	0.00237	0.00196	0.00243	0.00046	0.00039	0.00243	W5	2.5	Yes

[1] Carcinogenic TAP concentrations adjusted for 70-year exposure, as discussed in Section 3.4.4.
[2] Carcinogenic TAP concentrations adjusted for the West End pit LOM production limit, as discussed in Section 3.4.5.
[3] Modeling Scenario W5 is eliminated for carcinogenic TAP compliance, as discussed in Section 3.4.5.
[4] The AACs for carcinogenic pollutants are increased by a factor of ten per IDAPA 58.01.01.210.12(b); T-RACT adjustment.

BEFORE THE OFFICE OF ADMINISTRATIVE HEARINGS
STATE OF IDAHO

IN THE MATTER OF AIR QUALITY PERMIT TO CONSTRUCT P-2019.0047	BEQ Case No. 0101-22-01
NEZ PERCE TRIBE, IDAHO CONSERVATION LEAGUE, and SAVE THE SOUTH FORK SALMON, Petitioners,	OAH Case No. 23-245-1
vs.	
DEPARTMENT OF ENVIRONMENTAL QUALITY, Respondent,	
and	
PERPETUA RESOURCES IDAHO, INC., Intervenor.	

HEARING DAY 2
Pages 249-512
October 18, 2024
Boise, Idaho
HEARING OFFICER DYLAN LAWRENCE

Reported by:
Rebecca Martin, CSR #1108, RPR, CRR

HEARING DAY 2

BE IT REMEMBERED that the administrative hearing was held at the offices of Veritext Legal Solutions, located at 1109 Main Street, Ste. 220, Boise, Idaho, before Rebecca Martin, Court Reporter and Notary Public in and for the State of Idaho, on Friday, the 18th day of October, 2024, commencing at the hour of 9:00 a.m. in the above-entitled matter.

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I N D E X
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P R O C E E D I N G S

THE HEARING OFFICER: So we're back on the record in the matter of Air Quality Permit to Construct P-2019.0047. It's BEQ Case Number 0101-22-01 and OAH Case Number 23-245-01.

I'm Dylan Lawrence, I'm the hearing officer in this matter. This is the second day of our hearing on the merits.

And before we proceed with the case, any preliminary things we need to discuss procedurally?

MS. HANCOCK: Nothing from us.

THE HEARING OFFICER: Okay. As I recall, we left off with Perpetua's case and it was going to be Mr. Lewis, so I'll turn it over to Ms. Hancock, and also we need to swear in the witness.

KEVIN LEWIS,

a witness having been first duly sworn to tell the truth, the whole truth and nothing but the truth, was examined and testified as follows:

EXAMINATION OF KEVIN LEWIS

BY MS. HANCOCK:

Q. Good morning, Mr. Lewis. Thanks for coming back for day two. Let's start with your

education.

Can you tell me about your educational background?

A. I have a BS in chemical engineering.

Q. When did you obtain that BS?

A. I graduated in 1990.

Q. And from which university?

A. University of Wisconsin-Madison.

Q. After you graduated from the University of Wisconsin, did you start working and using your chemical engineering degree?

A. Yeah. I spent -- my first job out of college was with the Wisconsin Department of Natural Resources, and there I worked in their air toxics program.

Q. How long did you work there?

A. That was two years.

Q. Were you an air quality expert at the end of those two years?

A. No. Two years at the agency is -- basically what you do is you take directions from your supervisors, and you get an introduction to what air quality is and an introduction to how the regulations work, but you're -- you're -- you know, you're just learning. I mean, I learned from my

supervisor, and I did some inspections. It's all pretty low-level stuff, but a great experience. It taught me that I'm actually pretty interested in this field.

Q. Okay. So not an expert, but enough to keep you in the field?

A. Not an expert.

Q. And then in 1993, you changed jobs.

What did you go do next?

A. I moved to Colorado. I actually looked for a job with the Colorado Department of Health, but oddly enough, that was the one year they weren't hiring. But I did find a job at a company called Air Sciences, and I've been there for -- you know, I'm still there. It's been 33 years.

Q. And what does Air Sciences do?

A. We're a consulting firm. It's a bit of a boutique company, just because all we do is air quality. There's 25, I think, now professional engineers and scientists, and we provide air quality consulting services, sometimes seven days a week, 52 weeks a year. It's just all we do.

Q. Okay. Very narrow specialty at Air Sciences?

A. Correct.

Q. What is your role at Air Sciences?
A. Well, I'm a consultant, as I said, and my -- I do a lot of different things, but I'd say my expertise is really in the gold mining industry and all the regulations that revolve around that, doing air quality analysis for gold mining, other mining as well, but in particular gold mining.
Q. Okay. How many mining projects do you believe that you've worked on over the course of your career?
A. Hundreds of air quality analyses for mining projects.
Q. And how many mining permits do you think that you've obtained of those different hundreds of analyses that you've performed?
A. Well, I'm just going to say it's also hundreds.
Q. Okay. And how many modeling -- how many models have you run for those hundreds of mining projects and permits that you've worked on?
A. Yeah. I mean, well, again -- I mean, depending on the mining project. The Stibnite gold-mining project was a minor source, but I also work on major sources that are mines, and every -- I mean, I say air quality analysis, but that can

require several different types of model -- models and multiple modeling runs and modeling analyses, and it's -- there's a -- you know, as Mr. Schilling mentioned in his testimony, there's the Federal National Ambient Air Quality Standards, so every project is modeled against those.

But every time you go to a different state, there will be different programs. In Idaho, it's -- they are toxic air pollutant programs, so countless.

Q. Okay. Is there anything unique about how mines work as opposed to other industries that you've done air quality analysis for?

A. Yeah. You know, every industry is obviously unique, but mining is clearly a special case. From a regulatory perspective, there's just going to be a variety of different regulations that apply to mining because they have a variety of different processes.

From a modeling perspective, it's -- I don't want to take too deep of a dive, but can I use that exhibit, point to it --

Q. Sure.

A. -- bring that in?

Q. Yeah.

A. Okay. You can see --

MS. HANCOCK: He's pointing to what is Figure 1 in his --

(Exhibit easel interruption.)

THE WITNESS: There goes the mine.

MS. HANCOCK: Just for the record, that was a joke.

Q. (BY MS. HANCOCK) The demonstrative that's blown up and that we're looking at, this is actually Figure 1 in your report; is that right?

And this is --

A. I think it's similar to that, sure.

Q. Okay.

A. Yeah -- oh, in my declaration?

Q. In your declaration.

A. Okay. Sorry. When you said "report," there's multiple reports that are done for this application, so that's...

MS. HANCOCK: Yeah. Exhibit 200 is his declaration, and this is Figure 1 in that declaration.

THE WITNESS: Okay. Thank you.

So in a mining operation, you can just see by looking at it, there's multiple locations where the emissions are coming from. It's spread

out, you know, over a large area.

It's classified as a stationary source, but there's very few things that are stationary at a mine, so it just makes it a little bit complicated from a regulatory perspective, but certainly from a modeling perspective, because you -- in modeling, it's not only the emissions that you're modeling. It's the location of those emissions, the initial dispersion characteristic of those emissions. Everything has to be characterized and carefully analyzed, then you can model it.

I'll compare it to just a factory that may have a couple of exhaust stacks. There, you're literally just modeling two points, and those emissions are very, I'll say, continuous and much less variability.

So that's a -- that would be considered a relatively easy -- I hate to use that word, but a relatively easy modeling analysis. This is a very complicated modeling analysis. I don't mean to say that it can't be done. I've done this hundreds and hundreds of times, but it does take quite a bit of effort.

Q. (BY MS. HANCOCK) Okay. And the

complexity is because instead of a single point of location in your factory example, you have multiple locations with the mine; is that right?

A. Multiple locations, multiple types of sources, all have their own initial dispersion characteristic, yes.

Q. And the emission source moves as opposed to a factory where it doesn't move?

A. Correct.

Q. Can you explain that?

A. So when you're modeling this -- and you can see there's the orange and there's the yellow areas, these are areas where the minerals are rich, and that's where you're going to be mining.

But you just don't mine from all of them the same amount at the same time. It will -- you know, as the mine develops, you might go from -- you might start out at the Yellow Pine Pit and then, you know, move over to the West End Pit, but it's not like, okay, today's Sunday, so let's move over to the West End Pit. It all has to be planned out and it has to be done in an organized way.

Q. Okay. And what is fugitive dust and how does that play into the uniqueness of mines?

A. So "fugitive sources" and "point

sources" are regulatory terms, and fugitive sources are basically emissions that would be impossible to just capture and funnel through a control device out through a stack. Those are the easiest things to model.

Fugitive sources are not that. They're just a little more complicated because they're spread out, complicated in terms of, you know, making sure that you're characterizing those correctly in a model.

Q. Okay. This takes somebody with some pretty significant expertise in order to take in all of these more complicated modeling scenarios that you're describing to capture the uniqueness about the mines?

A. It does. And Mr. Schilling, you know, testified to this about how it's -- you know, it's very complicated. You need a background education, you need years of experience in, you know, working with this stuff every single day. I mean, it's just -- you don't find too many air quality experts that also claim to be experts in water or hazardous waste. The field is just something that you have to focus on.

Q. When you say "the field," you mean air

quality?

A. Air quality, yes.

Q. So very technical in nature and it's really -- the expertise is needed in order to ensure that the information that you capture is accurate?

A. Yes. I mean, you better like the field because that's all you're doing all the time.

Q. And in addition to all of that, you have a regulatory overlay that you're operating within and you have to be familiar with those regulations as well?

A. Yes, you do. I mean, the regulatory landscape can be a little difficult to navigate. It's something that of course I've spent years doing and, you know, not only that, but working with EPA in rule development or working with state agencies and policy and rule development and, you know, methodologies for calculating emissions, you know, methods for, you know, how you demonstrate compliance once you have a permit, what's appropriate, what can be done.

Yeah, it's something that just really takes years to hone. That being said, under supervision, a lot of people can do pieces of this

work.

Q. Okay. And as somebody who has been working for Air Sciences for 33 years, you serve in different leadership roles and supervise and oversee more junior engineers that work under you as well; is that right?

A. Yeah. Yes, of course. I mean, maybe the best way to put it is I'll work with them, but they're really helping me because these analyses are very difficult. They take a lot of -- a lot of time and a lot of careful checking. So yeah, I direct the work, but it's clear that I need them more than they need me.

Q. I'm sure they'll be happy to hear that.

A. They've heard it before.

MS. HANCOCK: At this point I would like to move to qualify him as an expert in modeling air emissions, mining air permits, and as combined for modeling mining emissions for the purposes of obtaining air permits within the specific regulatory parameters.

THE HEARING OFFICER: Do we have any opposition to that request?

MS. THROWER: No.

MS. YOUNG: No.

THE HEARING OFFICER: Granted.

MR. HURLBUTT: Sorry, I just wanted to say I couldn't hear you very well, just FYI.

THE HEARING OFFICER: Oh. I wonder if that's an effect of our changing our audio source. Sorry.

But I was just asking if there was any opposition to the request to admit Mr. Lewis as an expert in mining and air permitting and modeling.

MR. HURLBUTT: No.

THE HEARING OFFICER: Okay.

All right. Request is granted.

MS. HANCOCK: Thank you.

Q. (BY MS. HANCOCK) Okay. So for purposes of why we're here today, can you tell me what your role was in the permit application and process that's led us here 'til today?

A. I was the lead and the manager of the whole process the entire time.

Q. And when you say you were the "lead and manager," were you involved in compiling the information in order to submit the initial application?

A. Yes.

Q. And did you perform the modeling that

was used to support that application?

A. Me and my team.

Q. Okay. And ultimately you were responsible for the substance of the application that your team helped you compile?

A. Yes.

Q. And what modeling work did you perform -- or maybe better said: Can you describe the modeling that you did?

A. So I'll just talk about the modeling that's relevant to this process, the arsenic modeling, if that's okay, or do you want me to talk about, you know, all the modeling?

Q. I think that we can assume for purposes of this record that you did a lot more work than what you're going to describe, so let's focus just on the arsenic modeling.

A. Okay. So the arsenic modeling -- I'll just go real quick, you know, from cradle to grave here. First, you have to characterize the emissions. That means you look at every source and every scenario and you come up with the emission calculations. Now, these emission calculations are going to be based on the "maximum design rate," is a term. You also have to take into consideration

inherent limits in the operation itself, and you will also take into consideration what the limits are going to be in the permit.

So you start with calculating all the emissions. Then you go to the next step where you are allocating those emissions across the area of the project and -- and so, again, I'm pointing to that figure there. You can see that some go here, some go there. On that, just real simply, the pits are sources of emissions, the haul roads are -- you know, connecting the pits, those are haul roads, are sources of emissions, and so on.

And once you've laid that out, then you characterize the type of the emission because the model requires what they call the initial dispersion characteristic of that emission. Again, we talked about fugitive and point source. Those are the big categories.

After that, you have to gather the meteorological data. So that was previously gathered by a meteorological tower that's, you know, near this location, and that gives you a lot of gigabytes of information of how the weather is there. That is an input to the model.

Another input of the model -- and I'm

just going to stop here. There's a lot more. But another important one is -- especially for this project, is the terrain. The terrain goes into the model. It matters whether it's flat terrain or what they'll call this complex terrain. You can see by the figure it's in a mountainous area, a very remote mountainous area. All that goes into the model.

Then you run the model, and what's important there is, you know, are you running a short-term model and trying to get short-term concentrations or are you running a long-term model and getting long-term concentrations. In this case, we're looking for long-term concentrations.

Then you -- I think I'll just stop there because now we're going to start getting into how you use those results. But I'll let you continue.

Q. Okay. I appreciate that.

How many different modeling -- modeling scenarios did you perform for this permit?

A. There's 14 modeling scenarios, and each scenario represents a possible worst-case mining operation. Again, if this was -- if this was just a factory, there would be one scenario because everything's in one location, and it all comes out

the same place.

But to characterize something as complex as a mine -- this is true for all mining modeling analyses. You have to look at, okay, what if they were modeling just in this pit and they were extracting nothing but ore. That ore would go to this location. That's one modeling scenario. Okay.

What if they were modeling from that same pit but, you know, for whatever reason they were just pulling out development rock to get to the ore. That would go to a development rock storage facility.

So you have all these different cases and -- you know, this is something that we worked with DEQ on of figuring out, okay, how do we capture all those different spatial differences in the modeling so that we can take those results and really be sure that we've characterized the mine correctly and characterized all the possibilities so we truly are getting the worst-case impacts out of the model.

Q. Okay. So 14 different scenarios that you were modeling, each one of which was using the worst-case mining scenarios -- or worst-case

scenarios that you could recreate for your modeling purposes; is that right?

A. There's a worst-case emissions scenario where you're looking at the production and there's a worst-case spatial scenario, and it's really the combination of those. Again, you're just looking for the maximum emission case and -- I'll call it the maximum spatial scenario.

But really what that means is that when emissions come from one location versus the next -- and, again, I'm going to use the figure that's up here, you can see -- I'm sure we'll talk about this later, but you can see the location of the West End Pit in relation to the boundary, and it doesn't take an expert to understand that, okay, those emissions -- and you can see the prevailing wind. The wind is coming from the south -- the southwest and going to the northeast. If emissions are coming from that orange West End Pit area, they're going to blow to the boundary and that's -- you know, that's not a large distance relative to everything else. You're going to see the highest impacts there.

There's a lot of -- a lot more things going on in the modeling, but in a nutshell, that's

kind of how it works. So that's why the spatial part matters.

Q. Okay. And in your different -- 14 different modeling scenarios using those worst-case emission scenarios and spatial worst-case scenarios, did you also apply layers of conservatism over -- in those modeling -- in that modeling as well?

A. That's -- I'm glad you brought that up.

So when you're doing these air quality analyses, there's a lot of steps, as I went through, and it takes a careful look. The emission calculations -- like anything else, you can calculate the emissions, but there can be a range to those emissions.

I don't want to say it's not an exact science because it is, but with -- when you're dealing with the environment, you tend to have, you know, a little bit of a range.

So it's very common -- I mean, it's absolutely common from one state agency to the next, that they'll do an analysis and they'll look at this, and they'll say, all right -- there can be a range here, so as we do -- as we go through each one of these steps, let's make sure that we're on

the conservative side of that range. That would be, in this case, the higher emissions side if we're talking about emissions.

So I've got some examples in my declaration. I'll just run through them real quick. In the emission calculations, when I worked with the permit engineer at that time, we looked at different emission factors for characterizing, say, haul roads, and there's factors that have been -- they're all developed from empirical data and studies, but they're, not surprisingly, not all the same.

In that case, it came down really to two factors, and then at the end of the day, DEQ makes these decisions, but -- and the decision was, let's use the higher factor, which I believe was roughly five times higher than the alternative factor.

Q. And this is just pertaining to the haul road dust?

A. Yeah. So now you do this, you know, a hundred different times with the hundred other sources.

Now, the model itself is a model that's created and approved by EPA. When they develop these models -- and they're just computer

simulations that are used to predict what this emission here is going to impact over here, they actually do studies -- field studies on these models. They'll have an emission source of a known quantity, and they'll look at the concentration downwind with the monitor, they'll compare that to the model, and they'll be able to assess how accurate that model is.

Now, that model, if it under-predicts, they will not approve it. They only approve it if it is predicting correctly and where it's -- where it's going to be biased, it's going to be biased on the over-prediction.

This particular model that we used, called AERMOD, in the way we used it for this particular type of source, with a lot of ground-level emission sources, is going to over-predict by, you know, one-and-a-half to three-and-change.

Q. And that's what you have in paragraph 21 of your declaration?

A. Yeah, I guess I could give the exact numbers. It was 21, you said?

Q. Yeah. Your declaration is Exhibit 200.

MS. HANCOCK: That's previously been

admitted in the hearing record, but we should just confirm that for -- in this portion of the transcript, if that's okay.

THE HEARING OFFICER: Yes. Can the court reporter confirm that we admitted that.

THE REPORTER: Yes, Exhibit 200 was admitted yesterday.

MS. HANCOCK: Thank you.

Q. (BY MS. HANCOCK) So in paragraph 21, you're saying that the conservatism model, as applied using AERMOD, over-predicted, in this case, the arsenic emissions by 1.41 to 3.21 times?

A. It over-predicts all emissions used in this type of application. The studies found it was between, yeah, 1.4 and 3.2. So that's another layer of conservatism.

Q. What other layers of conservatism did you apply? Can you give us other examples?

A. There's one more example in here I'll just run through real quick.

One of the larger sources of fugitive dust, and in this case fugitive dust that contains, you know, microscopic levels of arsenic metal in it, you know, are haul roads. And with the haul roads, there's a -- there's a work practice or a

mitigation technique, and this is required by the permit -- proposed by the applicant and then memorialized in the permit, to use a combination of chemical suppressants and watering to prevent dust emissions.

Now, there's -- there's EPA-published control efficiencies from studies they've conducted that tells you, you know, what kind of -- what level of mitigation you get for this type of source. And for chemical, they -- it ranges between 90 and 99 percent, roughly.

Again, we're -- DEQ is faced with a range and -- again, all agencies do this. This is just part of the process. They look at that and they say, okay, let's add a layer of conservatism here and use the 90 percent.

You get an added benefit by periodically watering the roads. So, you know, we used an additional 33 percent control to account for that. EPA's published numbers go up to 95 percent.

Q. Okay. So if I'm understanding you correctly, you're saying in your modeling for watering the dust, you input a value saying that it was 33 percent effective at controlling it when EPA says that the watering is actually somewhere

between 75 and 95 percent effective in controlling?

A. Correct.

Q. So you've used a lower number in order to inject an additional layer of conservatism in your modeling work?

A. That's true. In this case, a lower control efficiency means higher emissions.

Q. Okay. And of the 14 modeling scenarios, each one produces a result; is that right?

A. Yes.

Q. And what do you do with those results after you've run all 14 different worst-case conservative scenarios?

A. Well, in the context of the TAP rule, you take that result and what you're looking for from the model is the long-term average. In this case, the long-term average for the model is one year. It doesn't spit out a longer term, and Kevin -- Mr. Schilling talked about this in his declaration.

So now you have an annual average concentration, and you compare that -- in accordance with, you know, 586 and 210 of the rule, you compare that to the increment, and you -- if it's above, DEQ cannot issue that permit. If it's

below, they can. This case it was below, and they issued the permit.

Q. Okay. So of those 14 different scenarios, did you use the lowest one?

A. We used the highest one.

Q. Okay. So you took 14 worst-case scenarios with the layers of conservatism applied, and of those 14 results, you took the worst result, meaning the highest emission possible, and you compared that against the regulatory --

A. Increment.

Q. -- increment?

A. That's correct.

Q. Okay. I want to talk about those numbers now. So we understand that Perpetua opted to use the T-RACT controls, and you understand that that means that it has to -- that the results have to prove that the cancer risk presented by these emissions fall under the 1 in 100,000 limit; is that right?

A. That's correct.

Q. And that's the increment that you were referring to?

A. That's correct.

Q. Okay. And so of those modeling results,

how much of that 1-in-100,000 cancer risk did you calculate was being used by the -- out of the 14 modeling scenario results when you applied that worst-case result to that metric? What did you determine?

A. The result of that was that the excess cancer risk probabilities that would be caused by this project was 41 percent of that 1 in 100,000 allowable increment.

Q. And yesterday we looked at Exhibit 301 with Mr. Schilling. And you can look at this.

Are you familiar with Exhibit 301?

A. I am.

Q. Okay. And I think that's the third page in, on the chart there.

What is that number -- what does that chart show?

A. This table, right?

Q. Yeah. Table 6.1.2, there's a chart below that.

A. Okay. Table 6 shows that the arsenic concentration, the maximum model lifetime exposure concentration, was 0.0095 [sic]. The lifetime acceptable ambient air concentration under T-RACT was 0.0023 [sic], which the 0.0095 is 41.3 percent

of that incremental ambient air concentration -- acceptable ambient air concentration.

Q. Okay. And is that consistent with the calculations that you performed as well?

A. I did perform these calculations, and so did DEQ, that's how it always works, and yes.

Q. Okay. So in other words, that 41.3 percent, it means of that one in $100,000 -- or dollar, I don't know where that came from. Sorry.

Of that 1-in-100,000 cancer risk probability, based on your 14 modeling scenarios, worst-case scenarios with layers of conservatism, in the worst possible conditions, this mining operation is only going to come 41 percent of the way close to that 1-in-100,000 limit?

A. Yes.

Q. Okay. And is that using the five-year rolling average?

A. Yes.

Q. Okay. And that five-year -- let's talk about the production limits that are -- I'll take that back from you.

Let's talk about the production limits that are in the permit that we're talking about

today.

You're familiar with what those are; is that right?

A. I am.

Q. And you're familiar with them because through the iterative process with DEQ, you guys talked about those and you had -- on behalf of Perpetua had said: Those are conditions that Perpetua would agree to abide by in the constraints of this permit; is that right?

A. That's correct.

Q. Okay. And tell me what those conditions are, as you understand them.

A. Well, I think everybody understands what they are. So in condition 3.5 of the permit, there's two limits in there. I characterized one of them as a short-term limit, and that is 180,000 tons per day. Compliance demonstration with that is on a 24-hour basis.

In that same condition, there's another limit that's 135,000 tons per day, but that's over a five-year rolling average, so that's considered a long-term limit. That limit was established as part of the T-RACT analysis. You do the analysis, and you establish a limit in accordance with 210.

Condition 3.6 has two more limits. These are also long-term limits that came about as a result of T-RACT and the modeling, and those limits are 788.4 million tons for the facility as a whole, and for West End Pit in particular, it's 3- -- it's half that. It's 394.2 million tons --

Q. Okay. And so --

A. -- for the life of the project.

Sorry, keep going.

Q. No, I appreciate that. I cut you off there.

So the total amount that can be -- if we look at Figure 1, the total amount that can be taken out of all of the locations that are noted there, the West End Pit and all the non-West End Pit locations, is 788.4 million tons; is that right?

A. That's correct.

Q. And then just the orange -- what we have in orange there where it's West End Pit, that's 50 percent of the total limit is the maximum amount that can be taken out of the West End Pit; is that right?

A. That's correct.

Q. And so yesterday we heard an example,

the Halloween candy example.

In short, is it just no matter how much you take out of the West End Pit, it's deducted from the total 788-, and the remainder can be taken out of the remaining pits; is that right?

A. Yes, that's correct. And the example was very helpful.

Q. Okay. And then the 180,000 tons per day, that's the maximum in a 24-hour period that can be taken out of all of the mines in total; is that right?

A. That's correct.

Q. So regardless of which location you're in in the moment, you cannot take more than 180,000 tons a day out, but the operations have to operate in a manner to ensure that at the end of five years you have averaged no more than 135,000 tons a day?

A. That's correct.

And I just want to add that these are permit conditions that are driven by the T-RACT analysis and modeling. If anybody is wondering why are there short-term limits, why are there long-term limits, well, in modeling there's both short-term and long-term modeling.

Q. So it's consistent --

A. Yeah, sorry. So this is what you find in every permit, especially for mining.

Q. And there's been some implication that 100- -- using 135,000 tons a day for the five-year rolling average, which gets you to the 41.3 percent of that T-RACT amount, that that's somehow a way in which you can disguise or otherwise manipulate the numbers in order to come in under that 1-in-100,000 risk.

Is that the case?

A. No. There is -- there is no disguising, there's no manipulation. These are just air quality analyses, and there's -- there's a procedure and a process by how you do these.

The limits are driven, in this case, by modeling, and that's -- and that's very common, and those limits are reflected in the modeling, and that's how you demonstrate compliance with, in this case, the T-RACT rule. I'm starting to mix RACT and TAP, so forgive me.

Q. Did you ever calculate what the emissions would be if you operated at 180,000 tons a day for 12 months in a row? Did you ever look at that number to see how that stacks up against that 1-in-100,000 T-RACT limit?

A. You can do hypothetical calculations, but I think I need to make this point before we get into that.

When you -- when you're running the model -- and let's start with the 180,000 tons per day. That's a short-term maximum production rate, which results in short-term maximum emissions. You're trying to get a value out of the model that matches the standard. In this case, it's the National Ambient Air Quality Standard. So that's -- so you need that 24-hour average concentration model so it's comparable to the standard.

Now, there's been a lot of talk about this five-year rolling average and whether, you know -- what that means. But at the end of the day, what we're trying to get out of the model for comparison to the TAP rule is an exposure concentration that's on the same basis as the AACC. They're both -- they're both concentrations, they're both in terms of micrograms per cubic meter, but the basis of the AAC is lifetime.

There's no model that just says, okay, here's your lifetime number. The model can give you an annual average, but then you've got to --

that's on a different basis than the AACC.

So we saw those equations yesterday from Dr. Paden's testimony and Ms. Lopez's testimony. There's a -- to be able to compare the two, you have to take the model concentration and convert it to the same units and basis of the number you're comparing it to. You don't compare 5 pounds to 5 kilograms and say they're the same. That basis has to be the same.

So to get into your question, which I think is let's look at a what-if hypothetical scenario where the 135,000 ton per day over five-year average, if that permit limit didn't exist, right? Am I -- I think I'm on the right question here.

Q. Yeah.

A. Okay. So what would happen if that limit just went away and we had to model 180,000 tons per day? Well, I mean, you don't have to model it to know what the answer is. 180,000 is 33 percent more than 135,000, and so your impacts are going to be 33 percent higher. I mean, just doing it real simple. This is not -- this is not even a real case because these permit conditions exist and we're trying to keep everything on the

same basis, but just to go through it.

So if we're at 41 percent of the limit at 135,000, we're going to be 41 percent, increasing that by 33 percent, and that would take you to 55 percent.

Q. Okay.

A. It's still under the limit.

Q. Would you mind doing a --

A. It's very hypothetical.

Q. Would you mind doing it on the white paper, just so that we can see it?

A. Okay. Okay.

So we have --

Q. Can we put the 1 in 100,000 on the top? You got that one?

A. I will.

Q. Okay.

A. We have the increment. That's the 1 and the --

Q. You might have to keep your voice up, just so Bryan can hear on the TV.

A. Okay. I'm not going to write everything, but in the rule, there is a permissible or allowable increase. That's called the increment. And the increment is the excess cancer

risk probability. So that's what we're measuring against. In this case, I'm just going to call it 1 in 100,000.

Now, we did the modeling based on 135,000 -- so I'm just going to switch colors. This is tons per day. You take that and you do a very complicated modeling analysis and you get 0.00095. I'm just going to skip writing the units because we're just going to do the math here.

And this one is -- when you calculate the risk on this number, and that's using the unit risk factor or comparing it to the -- we did all these calculations yesterday, so I'm just going to write it down here. That's 41.3 percent of the permissible increase in excess cancer risk probability.

Q. Just so we're clear, that's also what Ms. Lopez testified, was a 1-in-240,000 risk.

A. Yeah. We can do a lot of calculations here, but yeah --

Q. I'm not trying to give you a new calculation --

A. Yeah, sure.

Q. -- I just want to make sure that what we're talking about is clear to everybody in the

room, that these are all the same numbers as what Ms. Lopez talked about.

A. Yeah, I prefer to work in the percentages because sometimes that's even confusing to me, that 1 in 240,000 is less than 1 in 100,000, but it just is.

Then we have -- then we have -- so this is a -- I'll put here that this is the five-year rolling.

Q. Okay.

A. Okay. Then we have a short-term limit of 180,000. This is also tons per day. And -- but this one is on a 24-hour basis. I mean, this is a great example of, you know, you just can't look at the tons per day and say, okay, I've got -- I know what the number is. You have to look at the entire bases of the number. Same with the micrograms per cubic meter.

This is going to be -- because emissions and impacts in the AERMOD, you know, model, they're just proportional. So if you double the emissions, you're going to double the impact.

In this case, we're clearly not doubling the emissions. The difference between these two numbers is 55 percent. So if I multiply -- I guess

I have to do it on my calculator here real quick so I don't mess up these numbers.

If I take 00095 and I increase that by 33 percent, then I get 00126. Okay. That's the 50 -- or 33 percent increase.

Now, under the T-RACT -- I guess I'll put this on red -- this 1 in 100,000 is analogous to -- you know, can be expressed as -- I'll just write "AACC" here. It can be expressed as 0.0023. Again, I'm not showing units or anything right now, which is difficult for an engineer to do, but we're just doing the math right now.

So now if you -- if you take this, divide it by this --

Q. When you say "this," what are -- just so our record is clear.

A. Yeah. Sorry.

You take the math exercise number that we're doing where we're ratioing this up to 180,000 and -- I mean, you can already see it's less than this.

Q. Less than the T-RACT number?

A. Less than the -- yeah, the AACC. And I'll just do the calculation so there's a number, .00126...

Now we are at 55 percent of the T-RACT AACC. All these numbers are on the same basis. These are your exposure concentrations. So you can actually compare them, you can divide them, you can add them. They're all on the same basis.

MS. HANCOCK: Okay. Thank you for that. We can take a pause for a second.

(A discussion was held off the record.)

(Exhibit No. 222 was marked.)

THE WITNESS: I would summarize that --

Q. (BY MS. HANCOCK) Hold on.

A. Okay. Go ahead.

Q. We just need to make sure we get everybody on the same page, so I don't want to move ahead.

A. No, that's absolutely fine.

MS. HANCOCK: Bryan, will you just give us a thumbs up when you got your copy of it?

MR. HURLBUTT: Got it. Thank you.

MS. HANCOCK: Okay.

Q. (BY MS. HANCOCK) Mr. Lewis, you were going to give us a summary of what the math was that you just demonstrated for us in Exhibit 222.

A. Yeah. I think what we're just trying to illustrate here is there's been a lot of discussion

about, you know, this five-year rolling average and the what-if, there's variability and what does that mean. And it just seems kind of -- it's really -- I don't want to say irrelevant, but a bit academic because there's just -- there's not just this permit condition in the permit. Probably there's around 2- to 300 conditions in there. You have to look at the whole thing.

I think I overheard Mr. Simon talking about how there's sideboards in the permit, and I think -- conditions, and I think that's a good way to explain this. It's the 135,000 tons per day has sideboards and, you know, other short-term limits that you have to demonstrate compliance with.

But again, the -- Dr. Paden touched on this in her testimony. What we're trying to get at here is the exposure concentration from the mine. The exposure concentration is on the same basis as the AACC, and one of those bases that's important here is it's a lifetime cancer risk calculation.

And so, honestly, as she said, the five-year rolling average of 135,000 tons per day is actually more representative than using something of a shorter averaging period --

Q. Okay. So let me make sure I'm

understanding, though.

So in Exhibit 222, while it might be just an academic exercise, what it really tells is us is it dispels the myth that is being presented here that somehow the five-year rolling average is a way to disguise whether or not this permit is going to allow Perpetua to exceed the T-RACT limits; is that right?

A. Yeah. That's just a complete mischaracterization of what's going on. I mean, a mis- -- I think it's more of a mischaracterization or a misunderstanding of what it is.

Q. Okay. So no matter what, this permit -- under this permit, Perpetua could never mine more than 180,000 tons a day; is that right?

A. That's also an inherent limit to the process itself, but it is a permit limit, so yes.

Q. Okay. And this calculation shows that even at its peak mining production, on any one given day, even if you strung it together every day for an entire year, it still wouldn't exceed the T-RACT control limit?

A. It still wouldn't exceed the increment -- the permissible increment.

Q. The cancer risk probability?

A. Yeah. Yeah. That doesn't change.
Q. Did you ever consider -- let me back up for a second.
You were instrumental in providing those permit conditions that would limit or restrain Perpetua's production limits on that daily average five-year rolling average and then total production; is that right?
A. Yes. In the application and in the process of reviewing the application and some interaction with the agency, you propose what your operational limits are going to be, and if those operational limits comply with all the applicable regulations, then they get memorialized in the permit.
Q. Why didn't you just put a duration limit in the permit itself? Why did -- in your iterative process with DEQ, why didn't you guys land on just a duration limit?
A. I think Mr. Schilling touched on this in his testimony, but there's -- there is -- there's two components when you're crafting permit conditions, and to be clear, it's the DEQ that is the final authority on what those conditions are going to be.

But one component is the analysis in calculations where you're figuring out, if this project operates at these limits, is it going to protect the increment, the excess cancer risk probability.

But then there's also a, you know, ongoing compliance component to those numbers and, you know, hypothetically you could say, all we really needed was the total production limit to do this, but you also have to have ongoing compliance.

So it's routine to say, okay, we're going to have, you know, a ton-per-day limit here and it's going to be on a 12-month rolling average or a five-year rolling average. You want to have -- you want to be able to assess and demonstrate compliance all through the life of the project, not just when you get to the end.

Q. And it's fair to say that with those production limits in place, you're able to ensure that Perpetua is never going to operate in a way that's going to exceed the cancer risk probabilities under T-RACT; is that right?

A. Correct.

MS. HANCOCK: Okay. I'd move to admit Exhibit 222.

THE HEARING OFFICER: Any objections?
MS. THROWER: No.
MS. YOUNG: No.
THE HEARING OFFICER: Bryan?
Bryan, can you hear us?
MS. HANCOCK: Any objection to 222?
MR. HURLBUTT: No, I have no objection.
THE HEARING OFFICER: Okay. It's admitted. Thank you.
(Exhibit No. 222 was admitted.)
MS. HANCOCK: Thank you.
At this point I have no further questions. Thank you for your time.
THE HEARING OFFICER: Okay. DEQ, any questions for Mr. Lewis?

EXAMINATION OF KEVIN LEWIS

BY MS. YOUNG:

Q. I had just, I think, one or two clarifying questions for you, Mr. Lewis.
When you were speaking earlier about the 14 modeling scenarios you performed, do you recall that?
A. I do.
Q. Do those 14 scenarios account for every

possible scenario; in other words, there's not another scenario that Perpetua might have undertaken that wasn't already included in that 14? I just wanted clarity on that.

A. It accounts for every possible scenario.

Q. Okay. When you did that modeling, you assumed that that scenario would be a permanent scenario, even though it's probably more of a short-term scenario given the phases of the mine; is that correct?

A. Short-term in terms of, yes, I mean, the mine could not do -- you know, let's call it scenario W2. It could not do that scenario every single day for 365 days and beyond.

But that scenario captures, you know, one of the four corners -- although there's 14 corners here -- that allows us to assess, okay, under every possible conceivable operating scenario at the limits in conditions 3.5 and 3.6, is there going to be any possibility that this mine could exceed the excess cancer risk probability increment? And the answer to that is a definitive no.

Q. Thank you.

And then, I'm sorry, your back was to me

when you were doing that calculation, and so I couldn't see it very well. So I'm sorry to make you repeat a couple of things, but could you just one more time, if you don't mind, tell me where you got that .00126 number?

A. So that is 0.00095 increased by 33 percent.

Q. And the 33 percent is the difference between the 135,000 and the 180,000; is that right?

A. That's correct.

MS. YOUNG: Okay. Thank you for that clarity. I don't have any additional questions.

THE HEARING OFFICER: Okay.

All right. How are you doing, Mr. Lewis?

THE WITNESS: You know, may I have a break?

THE HEARING OFFICER: Yes.

THE WITNESS: Sorry.

MS. YOUNG: I could also use a break.

THE WITNESS: Okay. Thank you.

THE HEARING OFFICER: 20 minutes?

MS. YOUNG: 20 minutes is great.

THE HEARING OFFICER: It's right at 10:00, so reconvene about 10:20.

(A recess was taken from 10:01 a.m. to 10:21 a.m.)

THE HEARING OFFICER: I believe we were going to proceed with cross-examination of Mr. Lewis.

Real quick, just so I know, how do you guys intend to allocate cross-examination?

MS. THROWER: Kind of the same as before. Bryan will go first, I'll follow up on -- yeah, I don't have -- I mean, yes.

THE HEARING OFFICER: Okay. Thanks.

MS. THROWER: He'll do most of everything that he wants, and then I'll...

THE HEARING OFFICER: Thank you.

EXAMINATION OF KEVIN LEWIS

BY MR. HURLBUTT:

Q. Mr. Lewis, can you hear me okay?

A. I can.

Q. I have a couple questions about the numbers in Exhibit 222, the whiteboard exhibit.

Is that still up and visible in the room?

A. It is.

Q. Okay. You found that the arsenic concentration from the Stibnite Gold Project to be 0.00095; is that right?

A. Yes.
Q. Does that include applying the 16/70 project-specific adjustment factor?
A. Well, it's not necessarily project-specific, but it includes taking the model output, which is an annual average concentration, and adjusting that so it's on the same basis as the AACC.
Q. So did you take the model output, multiply it by 16 divide by 70 to get that 00095 number?
A. Correct.
Q. Okay. Do you remember what the model output number is without the 16/70 adjustment?
A. I believe that number is in Dr. Paden's testimony and declaration.
Q. Yeah, I'll pull that up, actually.
Can you see, Mr. Lewis, this declaration of Dr. Paden that I pulled up?
A. Yes.
Q. Do you see this highlighted value in paragraph 9, 0.00416?
A. I do.
Q. Is that the model output number before the 16/70 adjustment?

A. Yes.
Q. Okay. And is that number, .00416, larger than the AACC value that you have up on the whiteboard?
A. It is not.
Q. It's not larger?
A. No.
Q. What's the AAC [sic] value on the whiteboard?
A. The AAC value on the whiteboard is 0.0023, and that's micrograms per cubic meter, and that represents a 1-in-100,000 risk over a 70-year lifetime exposure.
Q. I'm just asking if 0.0416 is larger than 0.0023.
Is it?
A. Well, it's not. You have to compare those two numbers on the same basis. You can't do a comparison of, you know, pounds and kilograms. So if I'm comparing those two numbers on the same basis, then the 0.00416 is not larger than the 0.0023.
Q. So you don't think that 0.00416 micrograms per meter cubed is a larger number than 0.023 -- sorry, 0.0023 micrograms per meter cubed?

A. I don't, because one number is on a -- is a 16-year exposure; the other number is a lifetime exposure. So, again -- I mean, this is just something they pound into chemical engineers. If you're going to compare two numbers, you're going to add two numbers together, you really have to have them on the same basis; otherwise, they're just not the same numbers. They're not comparable.

MR. HURLBUTT: Okay. Thank you, Mr. Lewis. I don't have any further questions.

EXAMINATION OF KEVIN LEWIS

BY MS. THROWER:

Q. Okay. Mr. Lewis, so you testified that the model spits out a long-term -- or a one-year average, let's call it a long-term average, right?

A. Yeah. When you're talking about model inputs, they categorize them in terms of short-term and long-term, and for the AERMOD model, a standard long-term averaging period is one year.

Q. Right.

And 0.00416 is what you're claiming that one-year model output is?

A. That was the output model -- the concentration from the outputted model.

Q. Okay. And how is that equivalent to the maximum -- so let me go back.

In Dr. Paden's declaration and Ms. Lopez's declaration, they both used these equations to calculate the cancer risk using the exposure concentration.

In those calculations, that was called the highest concentration. So in this case, it would be they were thinking they were using the highest concentration of arsenic to calculate cancer risk.

How does .00416 compare to the -- that highest concentration from your worst-case scenario? I guess, is that what the model spits out?

A. Sure. The 0.00416 is the annual average concentration out of the model based on the highest production rate.

Q. Okay. And the highest production rate is the W2 scenario or we've called it WEP2?

A. The highest production rate -- and since we're talking about the TAP rule -- okay. I don't want to mix this up with the max and that -- the highest production rate is 135,000 tons per day averaged over a five-year period. And all the

modeling scenarios are based on that production rate when I'm modeling or when DEQ is modeling for compliance of the TAP rule.

Q. Right. Thanks for clarifying that.

So this model output number, .00416, represents the highest production rate for one modeling scenario -- or you can say a mining production scenario?

A. For a mining production scenario and all the 14 mining production scenarios, correct.

Q. All 14 --

A. Uh-huh.

Q. -- this one number encompasses all 14 production scenarios?

A. Yes. There's -- yeah, that's the limit for all 14 modeling scenarios, 135,000 tons per day on a five-year rolling average. That was applied to all 14 modeling scenarios.

Q. Right.

But for each modeling scenario, you get a different annual average.

A. Correct.

Q. Okay. And so just to clarify, this .00416 is one output for one modeling scenario.

A. That's correct.

Q. Okay. So you're saying that that is the -- that is one output for one modeling scenario and that is an annual average for that modeling scenario?

A. Correct.

Q. Okay. So on Exhibit -- what is your chart?

THE HEARING OFFICER: 222.

MS. THROWER: 222?

THE HEARING OFFICER: Yes.

MS. THROWER: Thank you.

Q. (BY MS. THROWER) On Exhibit 222, you have the .00095 figure, and that is a five-year rolling average?

A. No.

Q. It's not?

A. No.

Q. What is that, then, and why do you have "5-year rolling" under that?

A. I have 5-year rolling under the 135,000 tons per day.

Q. Okay. But the 00095 is an annual average?

A. It's the annual average concentration of the model that's been adjusted to the same basis as

the AACC lifetime exposure concentration. So, I mean, if I can -- if I say "exposure concentration," that will encompass all the things I just said.

Q. So just to clarify, then, so if you take .0095 [sic], and I think Bryan -- sorry if I'm repeating this. I think Mr. Hurlbutt asked you this.

If you take .0095 and back out the 16/70 adjustment factor, you get .00416.

A. Right.

Q. And that is a maximum. That is not -- this number is not a five-year rolling average?

A. They're both maximums.

Q. They're both maximums? Okay.

A. They're just on different bases; one's on a one-year average, and the other one is on the basis of a 70-year lifetime average.

Q. Okay. Yeah, I understand that.

So I'm going to show you Exhibit 301 that we had entered into the record. So this is --

MS. HANCOCK: I don't think that's what I have as 301.

MS. THROWER: It's Table C?

MS. HANCOCK: I have that as 303.

MS. THROWER: Oh, I'm sorry. Okay.
THE WITNESS: That's okay.
MS. HANCOCK: Is that right?
MS. THROWER: Yeah. Sorry, I was --
MS. YOUNG: Yes, that's 303.
MS. THROWER: Thank you. I'm going to blame that on Mr. Hurlbutt for throwing an extra exhibit on me yesterday and then I skipped 302. I guess that's partially my fault.

So Exhibit 303 is also REC 6888.

Does everybody have that?

THE HEARING OFFICER: I've got one.

Q. (BY MS. THROWER) Can you just explain what this table is?

A. This table shows all the TAP pollutants that were modeled. So the first column under "Pollutant," it tells you what pollutant is. The second row is arsenic. Going across from left to right you have abbreviations for the 14 different modeling scenarios. Underneath each scenario, there's a -- there's a maximum modeled concentration.

Q. Okay. And can you find that 0.00095 number in this table?

A. Yes. It's under the column that says

"W2." W stands for West End Pit. It's the second row down. It's 0.00095. And it's also under the column on the right titled "Maximum Scenario."

Q. And I want to talk a little bit about this maximum scenario, or W2.

So this represents the worst-case scenario, maximum potential emissions from the mining operations; is that correct?

A. Yes.

Q. And in a lot of that worst-case scenario, were those emissions that were driven by the West End Pit, I gather, I mean, from your testimony with that map and everything?

A. The West -- you know, pound for pound, the West End Pit resulted in higher ambient air impacts.

Q. Okay. And just so everybody is -- can kind of figure out these modeling scenarios.

So in these modeling scenarios, Y1, Y2, Y3, do you recall if the ones labeled "W," W1, W2, W3, and W4 and W5, are those the ones that involve production from the West End Pit?

A. Correct.

Q. And the other ones do not?

A. Yeah. We've been referring to those as

the non-West End Pit scenarios.

Q. Right. Okay.

So do you remember if W2 scenario represents ore production from just the West End Pit or does it also represent ore production from the other pits?

A. Yeah, all these scenarios represent the production limits that limit emissions and permit conditions 3.5 and 3.6. So it --

Q. Okay. So this would be, then -- as the worst-case scenario, this would be 135,000 tons per day over a five-year rolling average, 180,000 tons per day over 24-hour time period of a hundred percent West End Pit production?

A. No.

Q. Okay. What else does it include?

A. It includes all the conditions of the permit, so condition 3.6 and condition 3.5.

Q. Right.

I guess I'm just focusing on just in terms of what pits are involved in this W2 scenario. I know there's all sorts of, you know, conditions. You mentioned the haul road dust conditions and controls. There's other emissions from other sources that are maybe constant through

the scenarios. But for this scenario, one of the differences between the non-West End Pit scenarios is obviously production from the West End Pit.

Do you recall, though, if W2 includes production from other pits or is it just accounting for a scenario where it would be a hundred percent West End Pit production?

A. No, it's 50 percent West End Pit production combined with the worst-case modeling from the non-West End permit -- non-West End Pit production.

MS. THROWER: Okay. So I'm going to show you Exhibit -- I think I'm on Exhibit 304.

Is that correct?

(Exhibit No. 304 was marked.)

Q. (BY MS. THROWER) Are you familiar with this exhibit?

A. Yes.

Q. And on the top, there's a Table C.

Does it look like the same table that was in Exhibit 303?

A. Yes.

Q. And can you remind us if -- or do you know where this exhibit is in terms of the documents that Perpetua produced?

A. Oh, yeah.
Q. Okay.
A. I produced this.
Q. Okay. Great.
And just for the record -- let's see. This is attached to Dr. von Lindern's declaration, which is Exhibit 302. It is attached as Exhibit L, and it is from the last page of Exhibit L where there are electronic modeling files, emissions inventory file, and the addendum references, and if you click on that link, you will come to some modeling files, and that's where this exhibit is from.
THE HEARING OFFICER: Which exhibit are we talking about now?
MS. THROWER: 304. The big sheet.
THE HEARING OFFICE: 304.
Q. (BY MS. THROWER) Mr. Lewis, under Table C, which we saw and is the same as Exhibit 303, there's some other -- you know, it looks like the same sort of table, except there are some other numbers.
So under the row and column for arsenic for W2, what is that number?
A. That number is 0.007. I'm rounding.

Q. Okay. So for the record, it's 0.00698 for those actually trying to follow this on the chart.

So what is the -- what does this table represent? Because that number is different from --

A. Yeah, sure. This table represents, again, modeling at 135,000 tons per day, and in this case, it's -- it's the annual average concentration that the model spits out. And it is not on a 70-year lifetime basis. And for this W2 scenario, the number I just mentioned, that is not including the permit condition that limits the West End Pit to 50 percent of the total.

Q. Okay.

A. This same number, you'll find also in Kevin Schilling's declaration and in his graph where he's illustrating the difference in impacts from the West End versus the non-West End Pit.

Q. Okay. So I want to go back and just clarify.

So .00698 does not include -- that's just the output from the model, and it does not include the 16/70 adjustment factor?

A. It doesn't include the permit condition that limits --

Q. Right. Yeah, I'll get to that.

A. Right. And it doesn't include the permit condition that limits West End Pit total production.

Q. Right.

And so as far as comparing the W2 in the chart in Table C above and the W2 in the spreadsheet below, the difference there is that the W2 above contains a 50 percent production limit and W2 below is a hundred percent --

A. Correct.

Q. -- production limit?

Okay. And then also, the difference between the W2 number above and the W2 number below is: Above, for the .0095, you have applied the 16/70 adjustment factor, and the number below, you have not, right? If you want to, like, mark those numbers.

A. Give me a second to think about what this number is.

Yes, that's correct.

Q. Okay. And so as far as comparing the W2 above and W2 below, if we backed out the 16/70

adjustment factor, we would -- for W2 above, we would be at that .00416.

A. Correct.

MS. THROWER: So the difference between -- so that's the difference between there. Okay.

Okay. I have no further questions.

THE HEARING OFFICER: Any redirect from Perpetua?

MS. HANCOCK: I just have a couple.

Still staying on this Exhibit 304 --

MS. THROWER: I'm sorry, I just never actually asked to admit Exhibit 304 into the record.

THE HEARING OFFICER: Oh, okay.

MS. HANCOCK: I think it's already part of the record with --

MS. THROWER: Well, yeah, I suppose I have it separated out. I mean, his exhibit's 302, but...

MS. HANCOCK: Right.

THE HEARING OFFICER: Any objection to admitting it separately as Exhibit 304?

Okay.

(Exhibit No. 304 was admitted.)

MS. THROWER: Thank you.

REDIRECT EXAMINATION OF KEVIN LEWIS

BY MS. HANCOCK:

Q. Mr. Lewis, Exhibit 304 that we just -- you were just talking about with petitioner's counsel, it's fair to say that everything on the bottom half of that chart is not reflective of the current permit conditions; is that right?

A. Correct.

Q. Okay. So it wouldn't be relevant to what we're talking about here?

A. It is not.

Q. Okay. And if we look at -- let me do this. Just maybe one other question. There's been some suggestion that there could be a 16-year limitation on the permit.

What are your thoughts on whether that would be an appropriate condition to add to the current permit?

A. Well, the 16-year is already effectively in the permit. When agencies, DEQ in particular in this case, when they're establishing permit conditions, these -- the purpose of these permit conditions is to limit the emissions, limit the emissions on the timeframe we're talking about, in this case the 70-year lifetime.

And so when you're calculating emissions -- in this case, the emissions are calculated from the production. So what you want to do in a permit is you want to limit the parameter that's directly -- that was directly used to calculate the emissions.

So in this case, the parameter is production, and so there's -- that production is split up between 135,000 tons per day and 788.4 million tons. The 16 years is calculated from those limits. So if we take -- if you take, you know, 788.4 million tons and you divide into that 135,000 tons a day, you arrive at 16. So 16 years is calculated.

16 years would not make a good metric for putting the permit. Years don't equal emissions. Production equals emissions. That's why it's permitted that way. This is how every agency does it.

I don't know, I guess I could say more about that, but I'll just say this last thing.

When you're modeling, you're always modeling the maximum. In this case, we're modeling production. We talked a little bit yesterday. Ms. Lopez had a great example on there about how,

you know, the hypothetical if it's half the production and it takes twice as long, it's -- it gives you the same answer.

But, again, here, there's a reason why DEQ permitted the way they did permit it, and there doesn't seem to be any logical reason why you would add a 16-year limit. I'll just say it again, the years don't make the emissions. The production makes the emissions.

Q. Okay. 16 years was just a way to ensure that you're calculating the correct emissions; is that right?

A. Well, 16 years is -- again, it's derived from the production limits in the permit and then used on the model output to convert that output from a contaminate concentration, or CA in that equation that we looked at yesterday, to the exposure concentration, EC, so then it can be compared to the permissible incremental increase in excess cancer risk probability.

Q. And if what we're here to do today, at least to talk about, is to ensure that the permit has proper conditions in place in order to ensure that we're not exceeding the cancer risk probability, it's the production limit that

accomplishes that; is that right?

A. That's 100 percent correct.

MS. HANCOCK: That's all I have.

THE HEARING OFFICER: Okay. Thank you.

EXAMINATION OF KEVIN LEWIS

BY THE HEARING OFFICER:

Q. I have a couple just follow-up questions, and you -- I know you've touched on them and I'm not asking you to repeat yourself, but I'm thinking ahead to my future self and drafting the opinion, and so having a couple of summaries will be helpful.

So one of the concerns the Board expressed when it remanded this back to me is they say: There need to be permit conditions that ensure the modeled 135,000-tons-per-day figure is not exceeded for some portion of the five-year rolling period.

Do you need me to repeat that or does that -- did you track with what I --

A. I totally tracked.

Q. Okay. What's your just overall response to that concern, if you can articulate it for me?

A. Yeah. I mean, there's -- the premise is

kind of a little bit off. I think that the simplest way to characterize it is that we have a lifetime exposure increment. And so five years is certainly less than a lifetime -- and I think Dr. Paden, you know, characterized it pretty well, that you're really looking for the lifetime exposure concentration. I mean, you do calculations, you run the model, you get the model output and, you know, if the model output gave you an output in kilograms per, you know, cubic kilometer, you'd have to convert it to micrograms per cubic meter. You just can't compare an apple and an orange.

And in this case, the comparison is done on a 70-year lifetime basis. So really, the -- you know, if the model could spit out the lifetime of that 16-year average, that's the correct one to use. But it doesn't. It spits out an annual average, and -- sorry, I didn't finish my sentence.

As Dr. Paden said, the five-year average is actually the better number to use because that one is a lot closer to the 70-year lifetime concentration that you're trying to get to. So it's kind of hard to answer the question directly because it's just kind of a little off because I

presume just their understanding of the -- you know, the increment is 70 years, other standards are one year, some standards are 24 hours, and they each have to be handled, you know, accordingly.

THE HEARING OFFICER: Right.

Okay. Thank you.

Anything else for Mr. Lewis?

Okay. Thank you.

Do we need to take a quick reshuffle break?

MS. HANCOCK: Yes, please.

THE HEARING OFFICER: How long do we think?

MS. HANCOCK: Two minutes.

THE HEARING OFFICER: I'll round up to five.

(A recess was taken from 10:51 a.m. to 10:57 a.m.)

THE HEARING OFFICER: Now turning it over to our Petitioners.

WILLIAM TIEDEMANN,

a witness having been first duly sworn to tell the truth, the whole truth and nothing but the truth, was examined and testified as follows:

EXAMINATION OF WILLIAM TIEDEMANN

BY MR. HURLBUTT:

Q. Good morning, Mr. Tiedemann.

Can you start by describing your relevant educational background?

A. Yes. I have a BS in mechanical engineering from Gonzaga University. I graduated in 2013.

Q. And what did you do for work after that?

A. I was employed for a company called Hawkin Industries, they manufactured large HVAC air handling units, as a production engineer. I was responsible for production of HVAC units as well as the facilities compliance for environmental regulations, including Clean Air Act permitting and hazardous waste management.

Q. Did you work at the Department of Environmental Quality after that?

A. I did. I worked as a permitting engineer for Department of Environmental Quality. There, I analyzed and/or developed dozens of permits, including Title V permits, PTC permits, exemption documentations as well, for a variety of facilities from food processors, gravel mining, concrete batch plants, landfills, among others.

Q. And those were all permits here in Idaho under the Air Rules; is that right?

A. Yes, those are permits here in Idaho.

Q. What did you do after you worked at DEQ?
A. DEQ? I worked at an environmental consulting firm called Brown and Caldwell as a senior environmental engineer. I worked with a variety of mostly private sector clients, permitting clients specifically, I was within the permitting and compliance division there, as well as did some additional work in site investigation and/or mediation. I worked with state, local, and federal regulations across a multitude of disciplines, Clean Air Act, Clean Water Act, Emergency Planning and Community Right-to-Know, Spill Prevention, Control, and Countermeasure as well as NEPA, cyanidation permitting, and a few others.
(Clarification by the court reporter.)
THE WITNESS: Cyanidation permitting.
I worked across, like I said, federal, state, local, including Idaho, Oregon, Washington, Texas, Minnesota, New Jersey, Massachusetts --
(Clarification by the court reporter.)
THE WITNESS: I worked across a variety of states, including Texas, Minnesota, New Jersey, and Massachusetts.
I worked across site investigation

remediation as well, including groundwater, surface water, baseline monitoring, abandoned mine site characterization, patrolling impacted sites, remediation action, and monitoring to access impacted sites. Within the Clean Air Act specifically, my scope of work included assessing clients who were a stationary source permitting compliance for a variety of industrial facilities primarily in Idaho and New Jersey.

Q. And what did you do for work after that?

A. After that, I joined the Idaho Conservation League as a regulatory conservation associate. In this role, I review and provide comments on environmental permits, including Clean Air Act permits, I participate in federal and state rulemakings, and I review Clean Water Act, Clean Air Act as well as other environmental act compliance and enforcement activities in a watchdog role, if you will.

Q. Mr. Tiedemann, have you reviewed the PTC in the statement of basis for the Stibnite Gold Project?

A. I have.

Q. Have you reviewed any of the graph versions of those documents?

A. I have as well.
Q. When were you reviewing those, and what for?
A. I have an initial introduction to this at Brown and Caldwell. They have assisted Perpetua with many different phases of permitting as well as acting as kind of a managing contractor on the Clean Air Act permitting. When the Perpetua first submitted an initial permit -- or application for permit, based on my experience at DEQ, I was asked to provide a preliminary assessment and provide informal comments on my opinions on that application.
Since then, since joining DEQ, perhaps -- or sorry, since joining ICL, perhaps some way through -- halfway through the permit development process, maybe the second draft permit, that's when I joined ICL and was involved in reviewing -- or started reviewing the permitting materials.
Q. And have you reviewed the declarations submitted by Dr. von Lindern, Lopez, Lewis, Schilling, and Paden in this case?
A. I have.
Q. Have you reviewed the Idaho Air Rules,

Mr. Tiedemann?

A. I have.

MR. HURLBUTT: I'd like to move that Mr. Tiedemann be admitted as an expert based on his knowledge, skill, experience, training, and education in mechanical engineering, air permitting, and environmental compliance.

THE HEARING OFFICER: Any objections to that request?

MS. HANCOCK: Yeah, we would object to that request for the reasons that are stated in our motion to strike his declaration. And then in addition to that, I don't believe that the two years at DEQ or the other time that -- in which that he's been performing these roles are too limited in nature to qualify him as an expert in this matter.

THE HEARING OFFICER: Okay. Any response, Mr. Hurlbutt or Ms. -- sorry, Thrower?

MR. HURLBUTT: I'll just -- under Idaho Rules of Evidence 702, people can be admitted if they have relevant knowledge, skill, and experience, like Mr. Tiedemann does, to help understand matters that are before the deciding officer, and I think he can help do that here.

And also under the OAH Rule 475, it's generally encouraging hearing officers to take evidence, not to exclude them, to frustrate the record. So I would argue that Mr. Tiedemann should be considered as a witness -- expert witness.

MS. HANCOCK: Okay. I think that -- if I can respond if that's okay.

THE HEARING OFFICER: Real quickly, please.

MS. HANCOCK: I think that he is appropriate to provide evidence for the record. I don't think that it has to be as an expert. His limited duration at DEQ for two years, just a short period of time after he came out of his educational facility in 2013. In addition, you know, he's -- he has since left DEQ in 2019. So after only spending two years there, it's been five years since he's had that relevant time period there, and even after just having such a limited amount of time, I don't believe that that qualifies him as an expert in any of this.

If we are going to even consider qualifying him as an expert, it should be narrowly tailored to his special interest groups, upon which he currently works -- or for whom he currently works.

THE HEARING OFFICER: All right. So I'm going to go ahead and -- I mean, I'm going to grant your request to treat him as expert witness for air permitting purposes and interpretation of the rules.

I'm going to rule on the motion to strike that's already been filed when I issue the opinion, and I'll deal with the objection formally at that time.

The other thing I'd note is that because I am the fact finder, even if I'm admitting him as an expert, I can take those arguments in in terms of weighing the evidence and credibility.

So does that make sense to everybody?

MS. HANCOCK: Thank you. It does.

THE HEARING OFFICER: Okay.

MR. HURLBUTT: Thank you.

Ms. Thrower, can you hand Mr. Tiedemann his expert declaration?

THE WITNESS: I have it.

Q. (BY MR. HURLBUTT) Oh, you got it. Okay.

Mr. Tiedemann, can you glance through that? Is that a true and correct copy of the declaration you filed in this matter, along with all exhibits attached to it?

A. It is.

Q. And, Mr. Tiedemann, let's talk for a minute about those exhibits.

How did you obtain the exhibits that are in your declaration?

A. I obtained these exhibits through somewhat of a tertiary process or ancillary process. Before this permit had been finalized or maybe perhaps shortly thereafter, I submitted a public records request to DEQ for documents, memos, notes related to interpretations of TAPs rules. I was provided a fairly limited subset of documents that would have come from DEQ's electronic, you know, online document -- their service, more or less. It was maybe five or six documents.

After the Schilling declaration was filed, I noticed there was attachments in his declaration that fit this description, you know, memos, response to comments, interpretation of the TAPs rule. Those documents, I had not previously received in my public records request. So I reached out to DEQ public records request officers noting such. I said, "It seems like there seems to be more records that fit this description in DEQ's possession."

They said, "Yes, in fact, we have a large box of hard-copy records that were" -- as I understood and they explained -- "retrieved from the state archives."

As I understand it, and as I worked at the time at DEQ, there's a certain timeframe in which hard-copy records may exist in the DEQ state office facility, but then they get transferred to a state repository.

So it was my understanding that they came from the state repository. And it was a -- essentially, it was a large banker's box of hundreds of documents that, as they described, were from and related to TAPs rulemaking.

Q. So are each of the exhibits to your declaration from those hard-copy documents --

A. They are.

Q. -- you produced?

Did you scan or copy those?

A. In the first instance I reviewed the document, an administrative assistant with DEQ scanned those documents and provided them to me.

In the second instance in which I reviewed those documents, DEQ legal staff instructed me to scan what I felt was appropriate

to them, they reviewed it, and then distributed it to all parties to this case, as I understand it.

Q. Okay. So each of these exhibits to your declaration is a document you got from this public records request to DEQ; is that right?

A. Yes.

Q. Okay. And they're true and correct copies of the documents you copied or scanned there --

A. They are.

MR. HURLBUTT: I'd like to mark Mr. Tiedemann's declaration as Exhibit 304. I think that's where we are, 304?

MS. THROWER: Bryan, I think we're at 305.

MR. HURLBUTT: Okay. 305?

THE HEARING OFFICER: Any objections?

MR. HURLBUTT: I'd like to introduce Mr. Tiedemann's declaration and all attachments.

THE HEARING OFFICER: Do we have any objection to that request?

MS. HANCOCK: Yeah, so we would object for the reasons that are stated in our amended motion to strike.

But in addition to that, even his attempt to authenticate the documents simply

authenticates the fact that he went through a public record request. It doesn't authenticate the underlying documents. Those documents are all contained hearsay. He can't provide the proper authentication to put them into the context to make sure that they're in the record in a way that would contextualize them to ensure that they're represented for what is actually the truth and veracity of what's contained in those documents, and so we would object on that basis.

We understand that you've previously ruled that the petitioners would have a chance to respond to our motion -- or our amended motion to strike in their briefing, so we would not object to the admission of his declaration with those caveats in place and preserving those objections until you can rule on that.

THE HEARING OFFICER: Okay. I mean, I'm going to go ahead and deny the objection, just because the rules of evidence in these proceedings are so, you know, liberal, and I believe the way they're worded is I can -- you know, if something looks to be -- I can sort of rely on something that looks reliable.

So I'm going to allow the admission of

the declaration and the exhibits.

(Exhibit No. 305 was admitted.)

Q. (BY MR. HURLBUTT) Mr. Tiedemann, in your declaration, you state that the AACCs are annual averages that must be met year over year.

Is that how you assessed TAPs compliance during your time working at DEQ?

A. It is.

Q. When you worked at DEQ, did you ever use a project-specific adjustment factor similar to the 16/70 adjustment that was used for the Stibnite Gold Project?

A. I did not.

Q. And when you worked at DEQ, did you ever use a rolling average, like the five-year rolling average used for the Stibnite Gold Project, to assess TAPs compliance?

A. Not with regards to anything in this way, no.

Q. Okay. I'm going to share some parts of the Air Rules. Bear with me here.

THE HEARING OFFICER: Bryan, real quickly, can you clarify which version of the rules you're pulling up?

MR. HURLBUTT: These are the 2022 rules.

THE HEARING OFFICER: Thank you.

Q. (BY MR. HURLBUTT) Let's look at Rule 161, Toxic Substances.

Mr. Tiedemann, will you read the highlighted part of that rule?

A. Any contaminate which is, by its nature, toxic to human or animal life or vegetation shall not be emitted in such quantities or concentration as to alone, or in combination with other contaminants, injure or unreasonably affect human or animal life or vegetation.

Q. What's your understanding of that provision, Mr. Tiedemann?

A. I took this to be what you might call in environmental regulations as a general duty clause. This gives broad discretion to DEQ to consider multiple factors to meet a higher, broad, very standard to, as it says, you know, protect human health, animal life, and vegetation.

Q. Okay. Moving on in the rules here.

MR. HURLBUTT: And I apologize if this is clunky. Thank you, everyone, again, for accommodating me not being there in person.

Q. (BY MR. HURLBUTT) Let's look at Section 203 now.

What's Section 203, Mr. Tiedemann?

MS. YOUNG: Mr. Hearing Officer, I'd just like to make an objection, and I understand if you want to preserve this for the record and rule on it later, but at this point Mr. Hurlbutt is asking the witness to go through the rules, and he doesn't currently work at DEQ and doesn't implement the rules, and he's not been qualified as a legal expert.

THE HEARING OFFICER: I'll note the objection for the record and evaluate it when I'm drafting the opinion --

MS. YOUNG: Thank you.

THE HEARING OFFICER: -- but I want to hear what he has to say.

MS. YOUNG: Thank you.

THE WITNESS: This gets a little more specific working down from that 161 general duty clause. It is even broader in that it talks about multiple types of pollutants, right, max under that 02 subsection, and then more specifically it talks about toxic air pollutants under that 03 section.

Q. (BY MR. HURLBUTT) And do you mind reading part 03 on toxic air pollutants?

A. Yes.

It says: Using the methods provided in Section 210, the emissions of toxic air pollutants from the stationary source or modification would not injure or unreasonably affect human or animal life or vegetation as required by Section 161. Compliance with all applicable toxic air pollutant carcinogen increments and toxic air pollutant noncarcinogen increments will also demonstrate pre-construction compliance with Section 161 with regards to the pollutants listed in Sections 585 and 586.

Q. Okay. Are you familiar with using the methods provided in Section 210 of the Air Rules?

A. I am.

Q. And generally, what's the first step in Section 210?

A. When it came to TAPs, the first method that we would generally look at is a comparison to what are the emission levels, ELs. Those are listed in Section 586 in a column. If you could demonstrate that your project's emissions on any worst case for an annual year were below the ELs for any pollutant, then your TAPs compliance was shown for that pollutant.

Some facilities were able to show all

potential TAPs, carcinogens, were below the ELs for any worst case year over year. In that case, they were -- no further compliance demonstration was needed. If there were pollutants whose emission levels were over in a pounds per hour, right, we're not talking concentration yet, in a pounds per hour, they were over the ELs, there would be additional TAPs compliance needed -- or demonstration needed.

Q. Okay. And so let me pull up under section rules here.

Okay. This is Section 210 and -- sorry, hold on a second here.

What's this Section 210.08?

A. This is Controlled Ambient Air Concentration demonstration. This -- as I referred to, you know, after, if you could not have a pollutant whose emissions were below the ELs, additional demonstration was needed. This was the most common additional demonstration and could also be called modeling, as we've talked a lot about already.

Q. Okay. And what's the method in this part of Section 210 that's used to check for TAPs compliance?

A. Right. That's going to be kind of under the (a) and (b) part, right? It says: Compare the source's or modification's controlled ambient air concentration at the point of compliance -- that's the fence line -- for the toxic air pollutant to applicable ambient concentration listed in Sections 585 or 586.

And then he goes on to say, right, that: If your fence-line concentration is less than the AACC, shown in 586, no further procedures for demonstrating pre-construction compliance will be required.

Your compliance was demonstrated. Nothing more was needed from TAPs, carcinogens, at least for 586.

Q. Okay. So if you couldn't show that, it's one option to use T-RACT?

A. It was.

Q. Okay. This is subsection (12) now in Section 210 on T-RACT Ambient Concentration For Carcinogens.

Are you familiar with this, Mr. Tiedemann?

A. I am.

Q. Do you want to read part (b), please?

A. Yes.

It says: Compare the source's or modification's approved T-RACT ambient concentration at the point of compliance for the toxic air pollutant the amount of the toxic air pollutant that would contribute an ambient air cancer risk probability of less than 1 in 100,000, which amount is equivalent to 10 times the applicable ambient air concentration listed in 586 -- Section 586.

Q. So based on your understanding, what's the method in Section 210 that would be used here for a T-RACT source to check compliance?

MS. HANCOCK: Excuse me. I would object to the extent that he's asking for a legal interpretation of the application of this provision. I don't believe that that's a proper expert testimony under any of the expert qualifications and offers that have been made with respect to this witness, who is an engineer and had done work in that air permitting process.

What he's asking for now is a legal interpretation of the statutory provisions that we're looking at here, and I don't believe that that's appropriate witness testimony.

MR. HURLBUTT: I'm asking for his practical understanding based on working as a permit writer and working in air compliance and dealing with technical terms that are in here.

MS. HANCOCK: It's a legal conclusion. It doesn't call for a witness testimony.

THE HEARING OFFICER: I'm going to deny the objection because I do think that there's a certain amount of groundwork that needs to be laid when we're dealing with these technical rules, and I think that's what Bryan is doing.

But I will also remind everybody that you're going to have an opportunity to file post-hearing statements and, to me, that's a better context to really, you know, do super detailed analysis of the rule language.

So, Mr. Hurlbutt, do what you need to do to lay the groundwork, but let's not get too bogged down in the rule language, which to me, that's what the post-hearing briefs will be helpful for.

MR. HURLBUTT: Okay. Thank you.

Q. (BY MR. HURLBUTT) So that question, again, Mr. Tiedemann: Based on your experience, what is the Section 210 method that is supposed to be used here to compare to check for TAPs

compliance?

A. Right. When I read that section and understood that section, and how I understood that to be implemented was most significantly highlighted by that parenthetical. We would take the ambient air fence-line concentration and we would compare it to the AAC in 586, but 10 times that amount. That would be the T-RACT AACC.

Q. Okay. This section (b), though, mentions that -- the cancer risk of 1 in 100,000, doesn't it?

A. It does.

Q. Does that serve a purpose?

A. I understood that to be background for understanding, saying that, you know, this is 10 times the AAC, that's what this means, but the instruction here was to, you know, compare the fence-line ambient air concentration to 10 times the AACC listed in 586.

Q. Okay. And then, Mr. Tiedemann, are you familiar with short-term source factor in Section 210.15?

A. I am.

Q. Could you just describe what that is?

A. That says for a source that will operate

for five years or less, there is another further adjustment to TAPs demonstration compliance, specifically another tenfold adjustment to the AACC or the EL.

Q. Okay. Mr. Tiedemann, are you aware of any other methods in Section 210 for adjusting the AACC based on a project's duration?

A. Based on a project's duration, no, I'm not aware.

Q. Okay. Mr. Tiedemann, will you turn to paragraph 29 of your declaration. And I apologize, it's the paragraph that follows what's properly labeled as 28, but there's -- for some reason it says "9" instead of "29."

A. I'm there.

Q. Okay. Here, you discuss what happens if someone's exposed to multiple sources when the AACCs are treated as annual limits that must be met by all sources year over year.

Can you explain that?

A. Yeah, this hypothetical gets to kind of an underlying goal of environmental regulation and mandates for agencies to protect all people generally at all times under broad conditions.

This gets to the fact that if you do

treat the AACC as annual year-over-year limits, that -- at their fence line, every facility who emits TAPs, carcinogens, would not be allowed to emit those carcinogens over the AACCs.

So this way somebody can live, recreate, commute, travel, you know, what have you, in any airspace, public airspace in Idaho, across the whole entire state, the whole air shed, as you might call it, and know that, you know, they could live next to one source right next to -- their house could be right next to a source, and theoretically and legally that source would not be allowed to emit an air concentration of a TAP, carcinogen TAP, above the AACC.

They could then move to another facility or they could daily recreate or commute past another facility and they could know the same is true, that, again, no matter what facility they're adjacent to, there is the same concentration of a carcinogen that they would be exposed to at the fence line, and then that carcinogen -- that amount, over 70 years, a lifetime, represents a certain risk, and that theoretically and legally, they would not be exposed to any additional excess cancer risk and AACC concentration.

Q. Mr. Tiedemann, what could happen if someone's exposed to multiple sources that have been granted adjustment factors based on their less-than-70-year duration?

A. Right.

MS. HANCOCK: I'd object. I think that's outside the scope of this witness's expertise.

THE HEARING OFFICER: Can you repeat the question, Mr. Hurlbutt?

MR. HURLBUTT: Yeah.

Q. (BY MR. HURLBUTT) What happens if someone's exposed to multiple sources if sources are allowed to use project-specific adjustment factors based on their duration?

MS. HANCOCK: This witness isn't a toxicologist, doesn't have any way to deal with exposure and cancer risk probabilities.

THE HEARING OFFICER: Right. I'm going to sustain the objection on that basis.

Q. (BY MR. HURLBUTT) Okay. Well, can you talk about the emissions that would result without talking about the cancer implications?

A. I believe I could.

Q. If someone -- so let me re-ask the question.

Setting aside cancer risk, what happens to people's exposure -- sorry, what happens -- can you describe potential exposure scenarios if there's multiple sources using project-specific adjustment factors?

MS. HANCOCK: I'll object to that question. I think, you know, we're talking about here -- and we have a very limited scope of what we're being remanded to talk about here. We're talking about one permit and one emission source. We're not talking about tangential or other non-related exposure sources or any kind of cumulative effect thereof.

MR. HURLBUTT: Well, Mr. Schilling testified yesterday that this was a significant change in the regulatory approach, and so I think to consider the implications of this one permit requires thinking a little more broadly than just what's happening here.

MS. YOUNG: I would object to that characterization of Mr. Schilling's testimony yesterday.

MS. HANCOCK: Join. Because that's not what he was talking about when he referred to one document early on in the permitting process where

he talked about there -- this being -- requiring some additional looks. He's still talking about just this permit.

Nonetheless, what we have been remanded to talk about by the Board in this hearing is very limited in nature and it all falls within the four corners of the permit that we're looking at here.

THE HEARING OFFICER: I'll note that objection for the record. I mean, I want to give Mr. Hurlbutt a chance to articulate and ask his question. I agree that -- I mean, the Board narrowly articulated three issues, but the other thing is their instruction to me was to create a "complete factual record."

And I'll, again, remind everybody, the rules of evidence in these proceedings are pretty forgiving, and I think -- I'd like an opportunity to maybe let them get some momentum with their questions and answers.

I'll note the objection for the record, I'll deal with it when I do the opinion, but I want to give Bryan a chance to articulate his question.

THE WITNESS: I think I properly understand the question at this point and would be prepared to answer.

If sources were legally allowed to -- or I guess precedent was created and the rules were interpreted to allow for a project-specific adjustment factor, you could have successive sources who do the same.

So someone could live, work, recreate, play adjacent to a facility that is using a project-specific adjustment factor and on a year-over-year basis, they have a fence-line concentration of an AACC that is over the T-RACT AACC. And then they could move, they could recreate, they could change jobs, commute differently, recreate differently, and they could then be adjacent to another facility that also uses the project-specific adjustment factor that, again, for on a year-over-year basis has fence-line ambient air concentrations above the T-RACT AACCs.

And this could, theoretically, continue indefinitely through someone's entire 70 years. So by the end of 70 years, the baseline -- or I guess the concentration of an AACC that they theoretically could have been exposed to beyond the fence line is -- could be calculated to now be greater than the T-RACT AACC.

Q. (BY MR. HURLBUTT) Mr. Tiedemann, I'm

going to pull up the Paden declaration.

Mr. Tiedemann, what do you understand this number to be that's highlighted, the 0.00416 micrograms per meter cubed?

A. I assume that to be there was a complex emissions scenario generated from many of the different factors that Mr. Lewis describes, including the application with a five-year rolling average.

When you take those numbers, those emissions, you plug them into the modeling software, they produce a fence-line concentration, and that concentration was .00416.

Q. Okay. And you agree that that's the number that came out of the models before applying the 16/70 adjustment factor?

A. Yes, I did. And I agree that is correct.

Q. Okay. And then, Mr. Tiedemann, do you remember what the AACC is for arsenic when adjusted by T-RACT?

A. Yes. It is 0.0023 micrograms per meter cubed.

Q. And, Mr. Tiedemann, based on your experience as an engineer and permitting, is .00416

a larger number than .0023?

A. Yes, it is. It is approximately 180 percent of .0023.

Q. Both of those numbers are micrograms per meter cubed?

A. Right. I think what you're getting to is a fair comparison. I believe that is a fair comparison; that is, that 4- -- .00416 represents an annual concentration. As I understood, the AACCs are an annual year-over-year concentration, .0043. I believe that is a fair comparison, yes. So I would considered that number larger.

Q. Thank you, Mr. Tiedemann.

So based on your understanding of the methods in Section 210 for checking TAPs compliance, would the Stibnite Gold Project apply?

A. Under the methods they have currently used, I don't believe so.

Q. Okay. That's if you didn't use the project-specific adjustment factor?

A. Right. If you did not use the project-specific adjustment factor.

Q. Let's turn to Exhibit B to your declaration --

A. Okay.

Q. -- which I can pull up.
A. I have a copy in front of me.
Q. What is that, Mr. Tiedemann?
A. This was a document that I found in the previously aforementioned DEQ rulemaking, TAPs rulemaking, kind of hard-copy documents. It appears to be --
THE HEARING OFFICER: Sorry, what is the REC number on that, Mr. Hurlbutt?
MR. HURLBUTT: Oh. It is REC 6086.
THE HEARING OFFICER: Thank you.
THE WITNESS: I understand it to be an e-mail from Mr. Curt Fransen, who was an Idaho Deputy AG at the time, to Mr. Tim Teater and Mr. Robert Wilkosz. They are -- they were, at the time, DEQ staffers within, you know, toxics and air permitting and were deeply involved in the TAPs rulemaking process. Their name appears on dozens -- hundreds of documents within the historic TAPs rulemaking record that I reviewed.
Q. (BY MR. HURLBUTT) Now, Mr. Tiedemann, will you read the language that I've pulled up here that is kind of marked by this arc at the end of the e-mail --
A. Yes. I believe that's starting on

"Other Questions"?

Other questions that seem to arise from simply allowing higher exposure where the length of exposure is shorter include the unknown or potential combined and synergistic effect of many short-term or remediation sources or other sources in the same area and the potential of serial (one after another) short-term or remediation sources. Lastly, how will the operational life of the source be determined. What if an applicant says they only intend to operate for five years (for whatever reason) so want the higher emission number to apply. There is incentive for facilities to argue they will be short-term. The specter of serial short-term sources arises. Perhaps the definition can be clarified so there's less wiggle room.

Q. In your opinion, Mr. Tiedemann, does using project-specific adjustment factor, like 16/70, raise concerns about serial short-term sources and combined sources?

MS. HANCOCK: Object to the form. This witness is not a toxicologist and can't opine on that.

THE HEARING OFFICER: Mr. Hurlbutt, can you restate your question?

Q. (BY MR. HURLBUTT) In your opinion, does using project-specific adjustment factors raise concerns about the amount of emissions that will come from combined sources and serial short-term sources?

MS. HANCOCK: I'd object. I don't think that this witness is qualified to opine on that.

THE HEARING OFFICER: I'm going to deny the objection and let him answer.

THE WITNESS: I do. I see a connection between the hypothetical that I previously explained and what Mr. Fransen is, you know, seemingly describing concern over. He's describing the specter of serial short-term sources, right? Short-term sources that are having some kind of adjustment to how their ACC is determined and complied and what happens when you allow serial -- many sources in a row over someone's lifetime presumably, right, to use such adjustments, how might that affect how ACCs -- or fence-line concentrations actually exist in the public air shed.

MR. HURLBUTT: Thank you, Mr. Tiedemann.

No further questions.

THE HEARING OFFICER: Ms. Thrower, were you

going to ask him any more questions?

MS. THROWER: No, I don't have any questions.

THE HEARING OFFICER: Okay. Let's do a time check. We're at about 11:35.

Does anybody need to break?

THE WITNESS: I could use a five-minute break just for bathroom and to fill some water.

THE HEARING OFFICER: Okay. Let's take a five-minute break, then.

(A recess was taken from 11:36 a.m. to 11:42 a.m.)

THE HEARING OFFICER: We'll go back on the record and we'll do cross-examination.

DEQ and Perpetua, have you an arrangement in terms of who goes first?

MS. YOUNG: Yeah. I'll be going first, and I think we have a number of different types of questions, so I'll start out, and then I know Ms. Hancock has other issues to cover.

THE HEARING OFFICER: Okay.

MS. YOUNG: Perfect. Thank you.

EXAMINATION OF WILLIAM TIEDEMANN

BY MS. YOUNG:

Q. Good afternoon, Mr. Tiedemann.

A. Good afternoon.
Q. I'd like to draw your attention to paragraph 4 of your declaration, and I believe it's stated again in paragraph 15, that you stated that when you were a permitting engineer with DEQ, you had developed "dozens of Clean Air Act air quality permits."
Do you see that in your declaration?
A. I do.
Q. Great.
Now, you specifically say you "developed" those permits, correct?
A. Yeah. That's what looks to be written here, yes.
Q. Perfect.
So according to Mr. Schilling's testimony yesterday, developing a permit involves considering a permit application, considering and calculating emission limits, crafting necessary permit conditions, potentially modeling, and then ultimately ensuring that compliance is achieved with relevant standards or increments.
Is that correct?
A. I think I could add some context there, that at DEQ at the time, and it may still likely be

the case, that -- and I think Mr. Schilling alluded to this, that there was somewhat a division of duties, that permit engineers were responsible for working with the applicant, receiving an application, verifying its completeness, probably most importantly verifying the emission inventory.

They would take in what the applicant proposed, saying: Here's what we're emitting, here's how we're going to do it, here's all those operational factors that, you know, Mr. Lewis testified to, and then that would be provided to the modeling staff, and the modeling staff were more -- were primarily involved in taking that emissions inventory, putting it into the model, right, that black box, and creating those fence-line concentrations.

They would develop a modeling memo that was a written result of their findings, and there was always -- at the beginning, there was important caveats, assumptions, saying, you know: I was given this emission inventory to me by a permit writer, you know, I have not in-depth -- to a different degree sometimes, but, you know, maybe I have not verified, you know, this is what was given to me. Other factors too that saying, you know, my

model was constrained by very important assumptions and if these assumptions are not met or memorialized in the permit, my model is not valid.

Q. Perfect. I appreciate that clarification.

So would processing a name change for a facility qualify as developing a permit?

A. It depends on your opinion, but it's possible.

Q. Based on the definition that you just provided of developing a permit wherein you emphasized that it was really important to verify emission inventory?

A. In that kind of form, that was more what we called an administrative amendment.

Q. Perfect.

What about processing a request to simply terminate a permit because the permittee was no longer, you know, in business, would that qualify as developing a permit?

A. Probably not alone, but it's exposure to different permits and would include a review of such permit.

Q. Okay. But it's not developing a permit, I think I heard you say?

A. Sure. Yes.
Q. Okay. Thanks.
You also go on to say that you were responsible for analyzing compliance with the TAPs requirements.
Is that correct?
A. As I explained before, that was a bit of a two-part, right? There was permit writers who would verify emissions and modelers who would verify concentrations, is a way to put it.
Q. Okay. Are you familiar with DEQ's internal permitting tracking system called AIMS? And that, just to refresh your memory, stands for Air Quality Information Management.
A. AIMS sounds somewhat unfamiliar. Perhaps it was developed after I left DEQ.
Q. I have Mr. Mike Simon sitting in the room.
Do you recognize him?
A. I do.
Q. He was your supervisor supervisor -- your supervisor's supervisor; is that correct?
A. He was.
Q. Okay. So if I had asked Mr. Simon to use the tracking system called AIMS to pool the

permits that you had worked on, that would include all of the permitting projects that you had, you know, been involved with when you were at DEQ.

Would that sound right to you?

A. It's possible. I don't know exactly how that software works, but it's also possible it maybe doesn't include exemptions. Exemption projects were where somebody submitted an application saying -- there's a process in the Idaho Rules for which if your emissions are below certain levels, it's considered below regulatory concern, and you could submit an exemption concurrence process that says, "Hey, we think we're exempted based on agreement rules. We're asking for your concurrence on that."

That would be akin to developing a permit in some ways. It would involve analyzing emissions, compliance to rules. So those may or may not be included in there. I'm unsure.

Q. Perfect.

So when you were at DEQ, you processed five exemptions; is that correct?

A. I do not specifically recall, but...

Q. And then when you were at DEQ, you developed 18 permits using that definition of

developed; isn't that correct?

A. That sounds within the ballpark.

Q. Perfect.

Of those 18 permits that you developed, only 10 involved some level of a TAPs analysis; isn't that correct?

A. I would have to review them specifically to be able to confirm that.

Q. Great.

But if I had asked Mr. Simon to pull that information for me, he would have been able to provide that to me, correct?

A. I believe -- right. If you looked at that individual permit, you could look at the statement of basis --

(Clarification by the court reporter.)

THE WITNESS: If you looked at the statement of basis, a copy of the permit, you would be able to determine what level of analysis went into that permit.

Q. (BY MS. YOUNG) Of those 10 permits that required a TAPs analysis, five of those were standardized, meaning the analysis had been done by a senior permit writer, and then the junior permit writer essentially, like, copied and pasted that

analysis into the permit; isn't that correct?

A. You'll have to add more context to what you mean by "standardized."

Q. So for general permits, for example, like, the -- I think you had mentioned earlier that you had developed some permits for concrete batch plants; is that correct?

A. Yes.

Q. So for a concrete batch plant, DEQ has developed a general permit.

Do you recall what a general permit is?

A. Yes. They refer to them as general permits.

Q. Can you describe that, just for the record?

A. A general permit was a permit in which you would see from sources that were somewhat common, that they -- one permit from one to another might share similar permitting conditions, but it might also have different ones.

Q. Sure.

So in the way that it's pretty standardized, the senior permit writer at DEQ knew what, in general, a concrete batch plant might have as far as emissions are concerned, what types of

TAPs might, you know, potentially be at play, they created a standardized analysis, and then a junior permit writer could essentially copy and paste or rely on that previously-put-together analysis of the TAPs and then place it into the permit for this new facility.

Does that sound accurate?

A. Not quite. You said the word "copy and paste." You would use an Excel spreadsheet in the case of a concrete batch plant. There was an Excel spreadsheet where you would have to take variables submitted from an applicant, you would have to look at those variables, is that reasonable? Does that seem right? Is that correct? You would use those variables to input into a spreadsheet and more or less that spreadsheet would create emission, you know, values.

Every time you did a concrete batch plant, you would carefully review that emissions worksheet to make sure you're using the correct variables, that the spreadsheet was working correctly as we understood it, and to analyze those emissions that were output to see how they complied with the rules.

Q. Great. Okay. I think that that's in

line with what I'm asking, so I appreciate that.

So out of the 10 projects where -- permit projects where you had to develop a permit that had some level of TAPs analysis, really only a handful required you to conduct your own analysis for TAPs compliance; isn't that correct?

A. I think there's qualifications that are important to add to that. I think from every permit --

Q. I'm sorry, I asked you a yes-or-no question, so just a yes-or-no answer would be great.

A. Can you repeat the question?

Q. Sure.

So out of the 10 projects where you developed a permit that required a TAPs analysis, only a handful of those 10 actually required you to perform any of your own analysis; isn't that correct?

A. I wouldn't be comfortable stating it quite like that, no.

Q. Sure. Thank you.

Let's see here. So of the permits -- of the 18 permits that you developed while you were a permit engineer at DEQ, how many of those permits

that you developed were for a mine?

A. I did not develop any permits for a mine.

Q. Okay. And were any of the permits that you developed for a project where the applicant provided you a known duration of the project?

A. There is a permit that I specifically recall -- I can't remember if I helped develop it or subsequently reviewed it at some point, where a concrete batch plant, I believe it was -- perhaps a rock crusher, said, "Hey, you know, we don't anticipate operating for more than five years. Can we apply that five-year exemption?"

In that case, I recall we said yes, there was a tenfold adjustment to either the EL or the AACC, but a permit condition was placed in the permit that said you could not operate for more than five years.

There were additional permits in which it could be reasonably concluded that there would be a limited duration, say, concrete batch plants, of those nature, that, you know, you're not going to probably operate a concrete batch plant for 70 years --

Q. I have a couple --

A. -- in one location.
Q. I'm sorry. Go ahead.
A. And in that case, while I think an engineer and applicant, you could reasonably conclude that it would not be, in no case did an applicant say, "Hey, you know, we're going to operate for less than 70 years. We'd like to apply a project-specific adjustment factor."
Q. Great.
For the one specific example you provided, they used -- they provided you a less-than-five-year duration under that explicit section in the rule that allows for less than five years' duration; isn't that correct?
A. Yes, they specifically identified that exemption and applied that, as the rule states.
Q. Perfect.
So nothing in between that 5 and 70 timeframe?
A. You're saying no permit ever used --
Q. No permit applicant asked you for -- you had testified earlier that, you know, you've never applied any sort of project-specific adjustment, and I'm just asking: Beyond the one example that relies on this specific section of the rule, if a

permit applicant ever came to you and asked for some sort of adjustment based on the fact they knew exactly how long they would be operating.

A. Right. That was not understood as a tool at the time that could be used, and no one asked.

Q. So no one asked?

A. Correct.

Q. Thank you.

Let's see here. You had testified earlier regarding Section 210.08 of the rules.

MS. YOUNG: I don't know if maybe we could bring those -- bring that section up.

Sorry, Michael, I should have given you a heads-up there.

MR. SIMON: No worries. 210.08?

MS. YOUNG: Yeah.

Q. (BY MS. YOUNG) I'll give you a second to review Section 210.08 of the rules.

A. Okay. I am there.

Q. Perfect.

Despite what you testified to earlier, nowhere in Section 210.08 does it include the term "annual concentration"; is that correct?

A. Correct. I do not see the word "annual"

in here.

Q. Okay. Just wanted that piece of clarification.

Okay. And you worked at DEQ for 20 months, correct?

A. That sounds reasonable. That sounds -- as I recall, yeah.

Q. Perfect.

I want to move on to the exhibits that you attached in your declaration. It might be helpful if you have those in front of you.

You reference and attach documents that are purportedly from DEQ's 1990s rulemaking for TAPs; isn't that correct?

A. That document -- or that box of documents contained documents that covered technically multiple rulemakings.

Q. Okay. Perfect.

A. They were conducted over generally the span of 1990 to 1995.

Q. Okay. And you testified earlier that you obtained those documents through a public records request to DEQ, right?

A. I was -- essentially, yeah, I was allowed to view them under a public records

request, correct, in the DEQ state office.

Q. Okay. You came to DEQ and you physically reviewed those documents?

A. I did.

Q. And when you came to DEQ, wasn't it made clear to you that those documents were not a part of the official rulemaking record?

A. It was not. They were described to me as, "Here is a box of documents that" -- as the administrative assistant relayed -- "that came from the state archives. I believe" -- she said, "I believe the DEQ AGs compiled this record."

Q. Michael Short, the DAG at DEQ, didn't tell you these were not part of the official rulemaking record?

A. The first time I reviewed the document, I did not speak to Mr. Michael Short.

Q. The second time?

A. The second time, we did, yes.

Q. Perfect.

Are you aware that documents that are part of the official rulemaking record are stamped with essentially a Bates number or a record number?

A. I'm generally familiar with there's a process to do such.

Q. Do we see any of those record numbers along the bottom or at any part of these records that you've attached to your exhibit?

A. As what you described, no, I do not.

THE HEARING OFFICER: Ms. Young, real quick, can you give me a REC range for the documents you're referring to right now? I apologize to interrupt.

MR. SIMON: The documents she's referring to are the attachments to the declaration.

THE HEARING OFFICER: But don't they still have REC numbers on them?

MS. YOUNG: They do, and unfortunately, the copy in front of me does not.

MS. THROWER: Just a second, Mr. Hearing Officer.

MR. SIMON: Yeah, no, mine is unstamped. Sorry.

MS. THROWER: It starts with Exhibit A, but it's REC 6071, and I think it goes for --

THE HEARING OFFICER: Okay. So we're talking about --

MS. THROWER: You found them?

THE HEARING OFFICER: Yeah. Got it.

MS. YOUNG: Thank you.

Q. (BY MS. YOUNG) When you came in to DEQ, do you know approximately how many documents you reviewed?

A. There was a large banker's box -- a standard-size banker's box full of documents and there's two additional large manila folders. I did not specifically count them, but it was hundreds, if not -- you know, multiple hundreds, perhaps a size of a thousand.

Q. Perfect.

You took copies of several of these documents, correct?

A. Yes, the first time I was provided specific copies.

MS. THROWER: I'm sorry to interrupt, but Bryan just said he's kicked off the Zoom.

Can we please just pause to try to let him reconnect?

Sorry, Ms. Young.

MS. YOUNG: That's fine, yeah.

(A discussion was held off the record.)

(The record was read from page 367, lines 1-14.)

Q. (BY MS. YOUNG) So you reviewed and copied documents from this large file box and the file folders, and then ultimately you only attached

22 pages to your declaration, is that correct, of these documents?

A. I believe 22 sounds about right.

Q. Okay. So you didn't include everything you reviewed?

A. I did not include all upwards of a thousand pages.

Q. Okay. And again, the box from archives you took copies from was not DEQ's official record, right?

A. I guess I don't know if I'm qualified to say official record or not. As I understood it from my practical experience, this was a group of documents that DEQ deemed was important to save for a record of the TAPs rulemaking.

Q. Were they stamped?

A. They were not stamped.

Q. Perfect.

In your declaration in paragraph 9, you said you reviewed the historic TAPs rulemaking record which includes hundreds of separate documents, correct?

A. Yes. And I guess based on your light of the official record, I guess my term for that is "the documents that I reviewed," that's what I have

called them.

Q. Okay. So you attached six documents from the unofficial record from a file folder box that included several different rulemaking records, correct?

A. Yes. They were all related to TAPs rulemaking.

Q. And in the same paragraph 9, you stated that the documents capture the 1991 to 1995 time period, correct?

A. Generally, yes. There could be some documents that were stamped slightly, you know, dates before or after, but that is generally the time period.

Q. Okay. So Exhibit D was completely undated, correct? We can look at it if that's helpful.

A. Right. This document was provided as you see it here in the box.

Q. As to Exhibit D, since we're here, you have no idea who wrote this, correct?

A. That's not accurate. I see --

Q. Let me rephrase the question.

You can assume who wrote the document, correct?

A. I can use context clues, based on my review of the hundreds of documents, to make a best reasonable guess on who I believe wrote this document and who it was to.

Q. The hundreds of documents that you didn't include as attachments to this exhibit, correct?

A. Nope, I did not include all the documents, that's correct.

Q. Let's see here.

Can you say with any, you know, definitive certainty, you know, if there was a response to this document?

A. I cannot. There was many documents in there. That's something I specifically looked for.

Q. You can't say with any definitive certainty that there were, you know, correspondence that preceded this record as well, correct?

A. Right. I do feel confident in saying that there was not additional documents that were characterized outside of this -- the sentiments that were conveyed in here.

Q. Okay. So let's see.

Isn't it true that the rule wasn't finalized until 1994?

A. There is a complicated process in which rules go from negotiated rulemaking to ultimately finally approved by a legislature in place. That sounds like that's probably correct, and as a lawyer, I assume you know it to be correct.

Q. I'm familiar with the rulemaking process. Thank you.

Four of the documents you attached were from 1992, those would be Exhibits A, B, C, and E, two years before the rule was finalized, correct?

A. That's correct. It's not unusual for rulemakings to precede for multiple years before they are ultimately finalized, especially considering very complex topics.

Q. Absolutely.

So in the vein of what you just said, isn't it true that in these complicated rulemaking processes, they can involve many different conversations, sometimes in rulemaking meetings, sometimes in correspondence, and they can go on for years?

Isn't that right?

A. That's possible, yes.

Q. So in 1992, the rule would still be in fairly early iterations, correct?

A. I guess early is somewhat could be -- opinions --

MR. HURLBUTT: I'm going to object. This is speculative, calling on him to speculate.

MS. YOUNG: I can strike the question.

THE HEARING OFFICER: Okay.

Q. (BY MS. YOUNG) Let's see here.

Regarding the e-mails contained in Exhibit B and C --

MS. YOUNG: If you don't mind pulling those up, Michael --

THE WITNESS: Got it. Yes.

Q. (BY MS. YOUNG) Perfect. Thank you.

These are not identified as any official position of the agency, correct?

A. It depends on what you want to classify as an official position.

Q. Sure.

A. Agency position could be communicated through guidance, it can be communicated through memo, it can be communicated through rule.

Q. Is this guidance, memo, or rule?

A. As DEQ would formally call them, it does not meet -- no, it's not guidance.

Q. Perfect.

Doesn't this e-mail demonstrate that when DEQ is engaged in any project, including a rulemaking, that oftentimes ideas are circulated and discussed, including through e-mail?

A. Sure. That would be -- that could happen in any rulemaking.

Q. Perfect.

But we have no way of telling from this e-mail string if there were additional e-mails that occurred, you know, maybe even on this same string, after this e-mail was sent, correct?

A. I guess all I can speculate on is what I found in that box of documents, and I did not find anything, right, that appeared to be a specific response or continuation of this, at least what was in the documents of this e-mail chain.

Q. Perfect.

I think I know the answer to this question, but did you personally participate in the TAPs rulemaking in the early '90s?

A. I did not.

Q. Yesterday Mr. Schilling testified that he has over 20 years of experience at DEQ and he's developed over hundreds of permits.

Do you recall that testimony?

A. I do.

Q. Are you aware that earlier in this contested case Mr. Mike Simon was qualified as an expert witness in this proceeding and he has over 30 years of experience at DEQ?

A. I believe that's true, based on the case record.

Q. Okay. And your testimony is that you're the person with the best knowledge and interpretation of how the TAPs rules should be implemented?

A. No, I think it's a mischaracterization. I'm simply using my expertise and my experience at DEQ to review historic plots of rulemakings. In my experience in rulemakings and environmental law, these kinds of documents are obviously very significant and important for reading between the lines, quote-unquote, right? How do you ultimately interpret the rules, how do you implement them.

Based on that experience, I found these documents -- I would consider them, you know, invaluable to helping answer that question. Whether other people want to make different conclusions based on their experience, they're free to do so.

Q. Based on their, you know, experience of combined 50 years?

A. Whatever their experience might be, yes.

Q. Okay. I don't have any other questions for -- actually, I had one question that popped into my mind -- I apologize -- related to: Earlier when we were talking about these standardized, you know, TAPs analyses that would go into a general permit condition and you were describing the Excel spreadsheet, do you recall?

A. Are you talking for the concrete batch plants?

Q. Yeah, yeah, for example.

A. For example, yes.

Q. Did you develop the Excel spreadsheet that you would have been inputting the numbers into?

A. No, that was previously developed.

MS. YOUNG: Okay. Now I'm done. Thank you.

THE HEARING OFFICER: Okay. Thank you, Ms. Young.

Is now a good time to break for lunch? It's about 12:11.

MS. YOUNG: That would be great.

(A recess was taken from 12:12 p.m. to 1:17 p.m.)

THE HEARING OFFICER: All right. So we're back on the record, and I believe it's Perpetua's turn for cross of Mr. Tiedemann.

Are you ready to proceed, Ms. Hancock?

MS. HANCOCK: Do we need to do anything to start the recording?

(A discussion was held off the record.)

THE HEARING OFFICER: We're back on the record, and I believe it was Perpetua's turn for cross of Mr. Tiedemann.

Are we ready to proceed?

MS. HANCOCK: Yes. Thank you.

EXAMINATION OF WILLIAM TIEDEMANN

BY MS. HANCOCK:

Q. Good afternoon, Mr. Tiedemann.

Did you have a chance to get some lunch and refuel?

A. I did.

Q. Okay. Good.

I want to turn your attention to Dr. Paden's declaration --

MS. HANCOCK: Is it Exhibit 101?

MS. YOUNG: It would have been Exhibit 101, yes.

Q. (BY MS. HANCOCK) If we can pull that up, we'll look at paragraph 9 again.

You're familiar with that?

A. I think so.

Q. That's the paragraph in which you testified that you believe that the risk presented -- or maybe you tell me if this is correct.

Did you testify that the risk presented by the permit was 180 percent of the T-RACT controls under your calculation?

A. I guess we'd have to check with the court reporter, but I think I specifically said that basically .00416 would be 180 percent of the T-RACT AAC .0023.

Q. Okay. So you weren't trying to say that that's what the permit production would emit. You're just saying that if you calculated the calculations in paragraph 9 using .00416, that that would be 180 percent of the T-RACT limit?

A. I think I was -- probably more specifically, I was attempting to use a concentration that was arrived at by DEQ/Perpetua before 16/70 adjustment was applied and comparing that to the T-RACT AACC.

Q. Is it your opinion that that's the number that reflects the emissions that would come out of the mine using all the conditions that are currently in the permit?

A. So I think there is some gray area, some uncertainty, on exactly timeframes matter, right? We've testified that there was a five-year rolling average on that -- that went into the calculation of this number. There was perhaps uncertainty about which exact pits were contributing to this number, was it multiple pits or just the West End Pit.

So I can't say for certain because, again, I think there was disagreement and maybe not full information to determine whether this is the true maximum annual year-over-year average that you would, but I do feel confident in saying if you did not use the five-year rolling average and you only analyzed emissions from the West End Pit, you quite likely would see a number that is higher than .00416.

I know if you did not use the five-year average, right, I can fairly reasonably say I'd be confident that even if you didn't use five-year rolling average, you would also be higher than

.00416, but to say that 100 percent, I'd have to do some math.

Q. Okay. You didn't do those calculations, did you?

A. The ones I just referred to, the ones I would need to do?

Q. Correct.

A. No, those were never done. I believe Mr. von Lindern will address that more.

Q. I'm sorry, you speak fast, so I wasn't sure I heard what your answer was.

Did you do those calculations?

A. My understanding is there may not be enough information from what the public can see to make that calculation.

Q. Okay. What information would you need to do that calculation?

A. I'll defer to Mr. von Lindern to best be able to answer that question.

Q. Is it fair to say that as you sit here today, you don't know?

A. With the current information I have in my hands, I could not confidently say specifically.

Q. Okay. And you understand that this number, .00416, that Dr. Paden has in paragraph 9

is a calculation based on an emission -- on a production level that would be 24/7 365 days a year for 70 years continuous running?

A. I believe you said 70 years, but we're talking about a lifetime of 16, but perhaps I'm misunderstanding your question.

Q. Yeah.

Do you understand that the calculation of .00416 is based on the 70-year exposure here that's noted in paragraph 9?

A. I understand it to use a five-year rolling average of emissions -- of a specific emission scenario.

Q. For 70 years?

A. For 70 years? The way you're stating that -- I don't quite understand when you say that exactly myself until I can better understand your question.

Q. Okay. Is it fair to say that you don't know if her calculation in paragraph 9 is based on an exposure duration of over 70 years?

A. I think obviously there's quite a bit of debate about whether this exposure is over 70 years. I understand that emission calculation is related to a 16-year life operation with a

five-year rolling average employed.

Q. Do you have an opinion as to whether the duration of the exposure matters for purposes of determining cancer risk probabilities?

A. Similar to Mr. Schilling, I am not a toxicologist, but I have experience and am familiar with concepts related to it. If you'd like me to opine on that based on that experience, I can.

Q. Sure.

A. Okay. Do you mind restating the question for me?

Q. Sure.

Do you have an opinion as to whether the exposure duration matters for purposes of assessing cancer risk probabilities?

A. It is an important factor, yes.

Q. In fact, in your Exhibit A to your declaration -- do you have that?

A. I do.

Q. And you had referenced this as one of the documents that was in -- that was relied upon -- or in the record from DEQ; is that right?

A. Yes.

Q. And this was dated August 13th of 1992?

A. That's what I see.

Q. And what do you understand this document to be?

A. I understand that this is a letter to Ms. Joan Cloonan. She is a member of the Idaho Association of Commerce and Industry. They were a stakeholder that was particularly involved in the rulemaking process throughout the, you know, early '90s into 1995.

Q. Why did you include this document in your declaration?

A. I included this document because on page 2, basically "Explanation of additions and changes," there are important explanations that are relevant to this case.

Q. And did you use these explanations as a way to help understand what the URFs were or how they were applied in this matter?

A. I did not use this document as it refers to URFs. There's not particular discussion, as I recall, that is most relevant to URFs.

Q. Okay. What about for the T-RACT controls?

A. For T-RACT controls? You're saying the --

Q. Or the T-RACT limits that we've looked

at.

A. The T-RACT limits.

I would have to double-check, but I do not believe this document opines on T-RACT.

Q. Were you using this for helping you to understand Section 210?

A. I believe it is relevant as far as 210 speaks to how to do a TAPs compliance demonstration.

Q. Okay. And if you turn to the third page in -- you said the second page was what you were referring to; is that right?

A. It goes on for a little bit. I guess I'll quote the REC 6072. That is primarily with some onto REC 6073.

Q. Okay. If we look at the top of 6073, this is from the prior page under the title "Environmental remediation."

Do you see that?

A. Environmental remediation or short-term remediation adjustment factors.

Q. Okay. On 6073, it says, at the top there: That the adjustment factors were arrived at in the following way: For remediation sources, five years divided by 70 years equals 0.070.

Do you see that?

A. I do.

Q. And then it goes on to say: This is roughly equivalent to a risk of 1 in 10,000, actually a bit less, and we have chosen not to make this a sliding calculation, i.e., 4 out of 70, 3 of 70, et cetera. This was done for reasons alluded to in the section above on the environmental remediation sources.

Do you see that?

A. I do.

Q. And did you read that before you issued your declaration in this matter?

A. I did.

Q. Okay. You understood, then, that that Section 210 subsection (15) for that five years or less was calculated as making an adjustment for the duration of exposure; is that right?

A. I think perhaps the second paragraph just below is a little bit more relevant and what I found to be more relevant in relating to the five-year adjustment.

Q. How about answering the question that I asked first, though?

A. I believe it informs that question.

Can you state your question again for me, please?

Q. Yeah.

You can see there in that paragraph that they're doing a calculation of 5 divided by 70; is that right?

A. That's what they say.

Q. And based on your expert opinion, would you agree that that was them doing an exposure calculation of five years as compared to the 70-year total exposure?

A. As I understand T-RACT now and as I understood it as a permit writer, it was an acquiescence of risk, that we allow -- we accept going from a 1-in-a-million risk to -- or the basis of -- you know, forming this -- the basis of this decision is going from 1-in-a-million risk to 1-in-a-100,000 risk, and that it was deemed as a fair tradeoff considering industry and public health.

Q. And in order to make that acquiescence, they did the math of 5 divided by 70; is that right?

A. There is some indication that they are saying that, referencing, you know, 1 in 10,000,

that's equivalent to 1 in 10,000.

Q. Well, it's not just a reference, right? They actually say it. It says: 5 years divided by 70 years.

Do you see that?

A. I do.

Q. Okay. You understand that that's where they calculated that acquiescence?

A. I believe this is a factor, but it's not the sole factor.

Q. You said you worked for Brown and Caldwell?

A. I did.

Q. What is Brown and Caldwell?

A. Brown and Caldwell is a national environmental consulting firm.

Q. What did you do there?

A. I worked within the permitting compliance division as a senior engineer. In broad terms, I helped private entities comply with environmental law.

Q. Did you work on this project when you were at Brown and Caldwell?

A. As I alluded to earlier, I was given a copy of an initial -- I believe, perhaps the first

application that was submitted -- or that was to be submitted, perhaps it hadn't been submitted yet, to DEQ from Air Sciences. I was asked, based on my experience, to take a look at that and provide some thoughts to other co-workers on the project.

Q. Was Jessica your boss at the time?

A. She was.

Q. You actually reviewed the second iteration of Air Sciences, which is Mr. Lewis's company; is that right -- of their PTC application?

A. I believe it was Air Sciences, yes, that's...

Q. And you reviewed the second iteration of that application, didn't you?

A. It sounds like you know that to be the second iteration, so I believe that's -- you are correct.

Q. Does that sound accurate with what you can recall?

A. That sounds accurate.

Q. Okay. And you never said that you saw anything impermissible in any of that submission, did you?

A. I had certain -- impermissible.

I had certain opinions on ways that the

application could be improved, but I do not recall specifically if -- you know, if this issue had yet come into that permit as far as 16/70 or five years over -- or five-year rolling average.

Q. A calculation actually was in that version, wasn't it?

A. If it's in there, I believe you.

Q. You never raised any concerns with that calculation when you worked at Brown and Caldwell?

A. No. But again, I was asked to perform a cursory review. It wasn't in-depth and it wasn't evaluating all issues for compliance.

Q. Because you were kind of low man on the totem pole?

A. I was asked to review that based on my experience with air permitting.

Q. And did you also do a financial assurance review?

A. Of the Stibnite Gold Project?

Q. Yeah.

A. That does not -- perhaps I did, but maybe you can refresh my memory.

Q. Okay. Did you at some point while you were at Brown and Caldwell ask to not be assigned to any more mining matters while you worked there?

A. I don't know if I specifically recall that.

Q. Did you tell your boss, Jessica, that you felt that you had a moral dilemma working on mining projects because you disagreed with them in general?

A. At some point in time I might have conveyed some of the complexities and the environmental pros and cons that relate to mining, yes.

Q. Do you feel like you do have your own personal, moral, and ethical concerns with allowing mining projects to proceed?

A. I think my feelings are in line with ICL. ICL understands, and I understand, mining is a critical part to modern society. I use many things that mining made possible. I understand that.

But as I said, it can be true, other things can be true, and that mining should be conducted to the full letter of the law -- or in compliance with the environmental law, and it should be done as environmentally responsible as possible, and our organization strives to protect and understand and advocate for that balance.

Q. I appreciate that.

Mr. Tiedemann, do you have a moral and ethical concern with mining projects in general?

A. I think that's too vague. Every mining project is different. As an expert in this case, I'm simply reviewing what I see to be presented. That's not within the scope of my review. If you'd like me to expand further, like I said, my sentiments are in line with how I just described ICL.

Q. Just to be clear, while you worked at Brown and Caldwell, you never raised any objections to the Perpetua mining permit application, did you?

A. "Objections" could be somewhat subjective, but I did have -- I identified certain issues with the permit that I believed could be issues, yes.

Q. Can you tell me what those were?

A. One of the issues, as I recall, was perhaps some of the lack of detail and finality against the ultimate emissions equipment that will be used at the mine. There's a balance usually that has to go with people need their permits before they can purchase their equipment, but you might not know exactly what your emissions are

until you purchase that equipment. That's a common conundrum, if you will, in permitting.

And I expressed that perhaps they were -- there is -- there was some liability in that this far ahead their emission scenarios could change whether they have or have not was laid out in the permitting record.

Q. Then after your departure from Brown and Caldwell, you understand now, based on your review of the record, that those details were completed?

A. I think there are still details of this permit, obviously, that Petitioners' parties believe are not completed or are not sufficiently completed.

Q. And while you specifically remember raising those equipment detail concerns, you don't have, as you sit here today, any recollection of raising any concerns with using the 16/70 calculations; is that right?

A. Like I said, I performed a pretty cursory review of more big-picture issues with an application. I was not individually looking over every emission spreadsheet. That would take quite a bit of time for which I was not afforded to look at this. This was something to take a quick look

at, but there's no client to bill here in this case, so please be judicious with your time.

MS. HANCOCK: Thanks. I have no further questions.

THE HEARING OFFICER: Any redirect from Petitioners?

MR. HURLBUTT: I couldn't hear you, Dylan. Sorry.

THE HEARING OFFICER: Sorry. Any redirect from the petitioners?

MR. HURLBUTT: I don't have any redirect. Thank you.

THE HEARING OFFICER: Ms. Thrower?

MS. THROWER: No. No, thank you.

THE HEARING OFFICER: Okay. Anything else from Mr. Tiedemann?

Okay. Thank you.

MS. THROWER: Mr. Hearing Officer, I'm just going to do a quick switchover here. Dr. von Lindern is our next witness and he is soft-spoken, so he just asked me to be across from him so he wasn't facing this way so you could hear him.

THE HEARING OFFICER: All right.

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IAN VON LINDERN,

a witness having been first duly sworn to tell the truth, the whole truth and nothing but the truth, was examined and testified as follows:

EXAMINATION OF IAN VON LINDERN

BY MS. THROWER:

Q. Good afternoon, Dr. von Lindern. You got your water. Great.

A. I may need more.

Q. If you need more, just let me know, and we can take a break and there's some right behind you.

THE WITNESS: I do have a low voice. Just signal me if I need to speak up.

THE HEARING OFFICER: Okay.

Q. (BY MS. THROWER) Can you please state your name and spell your last name for the record?

A. My name is Ian von Lindern. Last name is v-o-n with a small V, space, L-i-n-d-e-r-n.

Q. And are you testifying for the petitioners today?

A. Yes, I am.

Q. Okay. What's your general area of expertise?

A. Environmental science and engineering with a specialty in exposure and risk assessment.

Q. Can you please describe your educational background?

A. Well, I grew up in Idaho public schools, and then I have a chemical engineering degree from Carnegie Mellon University in Pittsburgh, Pennsylvania. I have a Master's Degree in Air Pollution Public Health and a Doctoral Degree in Environmental Science and Engineering from Yale University in New Haven, Connecticut.

Q. And can you describe your professional background?

A. Well, my first job after my master's degree was with DEQ's predecessor, known then as the Department of Environmental and Community Services. I was the third air pollution control engineer that the agency hired, and my responsibilities included everything north of Salmon River.

Q. Okay. How many years were you with that agency -- or approximately the date?

A. 48 months, I believe.

Q. Okay. And then what were your duties while you were there?

A. To implement the Clean Air Act in northern Idaho with the major industries. I did the permits, the inspections, the enforcement. There weren't many of us. There were fewer people in DEQ than there are in this room right now.

But I was responsible for North Idaho, as I said, and that included the mining district in Silver Valley and the Bunker Hill smelting complex, which was the largest lead and zinc smelter complex in the United States at the time, and pulp and paper mills in Lewiston.

Q. Okay. And you said you were there for 48 months.

Did the agency change over or did you go somewhere else?

A. I moved on. While I was there, there was a major incident at smelter and several thousand children were poisoned and it ended up being the worst lead poisoning event in the United States at the time.

Q. Is that in the Silver Valley that you just mentioned?

A. That's in the Silver Valley.

And I -- at a very young age, I was not in a situation like Mr. Lewis. I was thrown in the

fire immediately, and I designed and implemented one of the largest lead poisoning investigations ever undertaken at the time in collaboration with the Centers for Disease Control in Atlanta.

Q. You mentioned the Bunker Hill Superfund site.

Did you work on that while you were there?

A. I've worked on the Bunker Hill with DEQ for 42 years, 42 years of continuous work with DEQ.

Q. Okay. And then --

A. That involved that site the entire time.

Q. Okay. And then after that work, you said you moved on.

So what happened next? Where did you go next?

A. I began to be involved in international mining issues, smelting issues. I was on an advisory board for the Centers for Disease Control in the mid-2000s, and I was asked to go with Centers for Disease Control to a site in western Africa that -- where several hundred children had died of lead poisoning associated with gold mining. And I ended up staying there for four or five years implementing a cleanup program, a health response

program, that emulated the work that we did at Bunker Hill. And based on that experience, my wife and I sold our company and started a nonprofit that works overseas in communities that are affected by mining pollution.

Q. Okay. So that work in Africa was with, you mentioned, Terragraphics Environmental Engineering? That was with your company -- that's your company?

A. We originally went as our company, Terragraphics, which Terragraphics was the lead Superfund contractor for DEQ for 32 years.

Q. Okay. It was under Terragraphics that you continued to work on the Bunker Hill site for DEQ?

A. Yes.

Q. Okay.

A. I worked for DEQ as a -- the history on that site was I worked as an employee for the 48 months. I was also sent on an assignment on loan to the Environmental Protection Agency because the work that was done at Bunker Hill was one of the three main studies on which the National Ambient Air Quality Standards for lead is based.

So I was on assignment with EPA to

develop the national ambient air quality standard.

When I finished that, I had an invitation to go back to graduate school. I went as -- on fellowship. That was for state employees. And I -- the conditions were that I was to work for two years for DEQ for each year that they sent me to school.

While I was there, the Air Quality Bureau was disbanded. The State decided they weren't going to regulate air quality anymore and they handed it back to EPA. So there was no Air Quality Bureau for a couple of years here in DEQ's predecessor.

When I finished my doctorate, I was hired by EPA to do permits for Idaho on their behalf, and I did that for two years.

In 1983, we revisited the Silver Valley, again, working for IDHW at that time, and we repeated the earlier lead studies of the 1970s. We found that there were still children suffering lead poisoning in the Valley at that time, and that was the impetus for the Superfund site.

And as it became a Superfund site, I was hired by DEQ to be project manager for that CERCLA action, and I spent the next 28 years in that

position. This is the first time I've ever been on this side of the table against DEQ. I don't like that position, but I'm here.

Q. So you've been around -- or you were around when the TAPs rules were being negotiated, rulemaking.

Did you have any involvement in that process?

A. Yes.

Q. Okay. Can you explain what that was?

A. Well, at that time, on the CERCLA site, we had implemented Superfund risk assessment guidance on numerous occasions on the Superfund site, and Orville Grane, the manager of the Air Quality Bureau at that time, asked me to sit in on the TAPs because a big part of what they didn't want to do at TAPs was Superfund risk assessment. So they wanted my advice on how you could implement a TAPs program that -- as Kevin pointed out when he was here as well, that was -- minimize the regulatory burden on the regulating community but still provided health-protective -- was health-protective for the public and was simple to implement.

Q. Okay. I want to go back to this

nonprofit that you talked about a bit that is in your declaration.

You call that TIFO, right, T-I-F-O?

A. We say TIFO.

Q. TIFO. Excuse me.

A. We were going to call it TGIF, but they wouldn't let us do that.

Q. What does TIFO do?

A. We work with communities in poor countries who have -- we help them to live as safely as they can in mining communities. We had the genesis of this when we were still Terragraphics and we were working on the site in Nigeria. We collaborated with an organization, M decins Sans Fronti res, it's known as Doctors Without Borders in this country, and we implemented a joint environmental and health response program; they did the medical part, we did the environmental part.

And when we started the nonprofit, we worked -- we continued to work with them. We're an environmental arm -- collaborator with M decins Sans Fronti res. We've done about eight or ten projects now.

Q. Do you do any projects in the US?

A. Yes. We consider Native American tribes international government, and we work with them in the same way that we work with poor countries overseas.

Q. Okay. And who exactly hires you or asks for help or who are your clients when you do work under your nonprofit?

A. Well, we're a nonprofit, so --

Q. That's why I said, "who asks for your help," maybe not quite hires you, but for --

A. Well, our main access to these projects is through M decins Sans Fronti res. They work in a number of communities in the world that are mining-related, particularly those that are -- that have drug-resistant tuberculosis problems. They run clinics because a lot of miners around the world have drug-resistant tuberculosis. So they're operating 15, 20 different sites in the world where they maintain medical services for those communities.

Often they find other problems associated with pollution in those communities and they ask us to come and work on that.

Q. And under your nonprofit, have you worked on any projects that are similar to the

Stibnite Gold Project?

A. Absolutely.

Q. Can you describe those?

A. I worked on a project in Kyrgyzstan that was the former Soviet Union's largest antimony and mercury facility. It's now abandoned. The mercury facility continues to operate, the antimony one does not, and there are high incidence of noncommunicable disease in those communities related to a number of factors. Several of those factors are associated with the pollution that they live with.

The mines are trying to continue to operate. They are the only source of livelihood in those communities. We are not anti-mining. We try to work with the governments and the mining companies to make it as safe as possible for the people that live in those communities. We don't go anywhere where we're not invited by the Ministry of Health and those programs, and we collaborate with the Ministry of Health for those countries.

Q. Okay. I'm going to -- I guess Exhibit -- your declaration has already been offered as an exhibit. I believe it was Exhibit 302. We'll just go ahead and pull that up

right now. But I just wanted to go to Attachment A where you have your CV.

You list a host of special appointments and memberships there -- it's Attachment A. There you go. I'm just letting you look at that, just so you can have a recollection of that. There's several there.

Are there any in particular that you want to point out that you find particularly relevant to you as a testifying expert here in this proceeding?

A. I mentioned before that I went on loan to EPA in the early '70s to work on a national ambient air quality standard. As a result of that, in 1975, I began to serve on the Environmental Protection Agency's Science Advisory Board and Clean Air Science Advisory Committee. I was never a permanent member of that. I was always a consulting member. But I had 20, 30 different assignments over the years working with EPA, developing guidance and regulation.

Q. How many years --

A. That board serves as an oversight of the EPA's scientific applications of -- applications of science during regulation.

Q. How many years have you been on this board for EPA?

A. I think I set the record. I was on it from 1975 to 2018.

Q. I won't fact check you on that.

Okay. And you also list -- are there any other appointments that you want to mention or is that -- that sounds like your most major one there?

A. Probably the one most relevant to this, other than I've been on several CDC advisory committees as well. The one that got me into the international work was one of them.

Q. Okay. And you also list several publications that you authored in your CV.

Can you describe some of the topics of those publications?

A. Most of my publications are about heavy metals poisoning in mining communities.

Q. Okay.

A. Particularly lead. Lead is my expertise. But we also deal with a suite of other metals that always accompanies lead in those sites.

Q. Okay. You mentioned that this is the first time you've been on the other side of DEQ, so

it sounds like you've been in some other judicial or administrative proceedings?

A. Oh, yes. I did Superfund for 28 years. I've been around.

Q. Okay. So --

A. Superfund is as big a lawsuit as it is an environmental investigation, so I spent plenty of time representing DEQ in negotiations, testifying on their behalf.

Q. And did you testify as an expert?

A. Yes.

Q. Did you provide expert reports?

A. Yes.

Q. Do you remember if you were qualified as an expert in those proceedings?

A. In this proceeding?

Q. No, in those former proceedings.

A. Oh, yes.

MS. THROWER: I request that we qualify Dr. von Lindern as an expert in this proceeding.

THE HEARING OFFICER: Can you specify for what sort of purpose?

MS. THROWER: Yeah. For his expertise in environmental engineering and risk assessment and his expertise in -- specifically in air quality and

Clean Air Act compliance.

THE HEARING OFFICER: Okay. Do I have any objections to that request?

MS. HANCOCK: Can I ask a -- can I voir dire the witness in aid of an objection?

THE HEARING OFFICER: When it's your turn for questioning or right now?

MS. HANCOCK: Just right now for purposes of objecting to his qualifications as an expert.

THE HEARING OFFICER: Yeah, go ahead.

MS. HANCOCK: Dr. von Lindern, are you a toxicologist?

THE WITNESS: No.

MS. HANCOCK: I have no objection to him being qualified as a chemical engineer, but with the clarification that he's not a toxicologist and not qualified as a toxicologist.

THE HEARING OFFICER: Okay.

MS. THROWER: But he does have extensive experience in risk assessment. So I didn't say for toxicology, but he has done extensive risk assessment work.

THE HEARING OFFICER: Right. Okay.

MS. HANCOCK: Risk assessment to the extent that he's a chemical engineer, I have no objection.

But again, not risk assessment with respect to being a toxicologist.

THE WITNESS: May I elaborate?

THE HEARING OFFICER: Go ahead.

THE WITNESS: I have an expertise in risk assessment. I've done hundreds of risk assessments. Risk assessments have particular steps in them: Characterize the site, develop an exposure profile, you compare those to existing standards and scientific criteria. I have managed many of those projects. There's a point in those projects when my personal expertise requires assistance from others.

THE HEARING OFFICER: Right.

THE WITNESS: I can take, with comfort, risk assessment process through to the intake of the materials into the body and the absorption of the body, which is the transition point from exposure assessment towards the kinds of expertise that toxicologists have.

I have training in advanced toxicology, but at that point in the process, I would ask and engage other experts --

THE HEARING OFFICER: You would turn it over to toxicologists?

THE WITNESS: -- and it's not -- it's in this process which I've managed. I think we've heard some testimony about it before. You can't do this by yourself.

THE HEARING OFFICER: Right.

THE WITNESS: You need other experts in different fields.

THE HEARING OFFICER: But you're not --

THE WITNESS: I'm not a certified toxicologist. I have a lot of knowledge in toxicology, and I know whether I got a good toxicologist working for me or not.

THE HEARING OFFICER: Right. Okay.

But, Ms. Thrower, you're not trying to get him qualified as an expert -- as a toxicologist specifically, correct?

MS. THROWER: Correct.

THE HEARING OFFICER: Okay. So then, yeah, I mean, I approve the acceptance of Dr. von Lindern as an expert for the items enumerated by Ms. Thrower, but specifically not including a formal toxicology opinion.

Does that make sense?

MS. THROWER: Yeah, to the extent, I guess it depends on how much of the toxicology field you

want to stretch back to risk assessment or something --

THE HEARING OFFICER: Right.

MS. THROWER: -- so, you know --

THE WITNESS: It's a little of a flexible area. I know where to cut myself off, and there are issues of toxicology I feel quite competent in.

THE HEARING OFFICER: Okay. I mean, I think we can proceed and, again, I have the ability to sort of evaluate and weigh evidence and credibility when I render a decision. So I would suggest we just proceed.

MS. THROWER: Okay. Thank you.

Q. (BY MS. THROWER) So when is the first time you were involved in reviewing any portion of this permit or the draft permit for the Stibnite Gold Project?

A. Maybe I could lay out how I --

Q. How you got involved?

A. -- got involved in this project.

Q. Sure. Sure.

A. My wife over here was an ICL board member, and ICL was invited to -- by Perpetua -- Midas at that time, I think -- to tour the site and listen to their proposal for the site. I attended

that with her, and I became intrigued with the site because we were working in Kyrgyzstan in the same kind of ores and the same kind of facilities that they were talking about building.

In fact, it was really interesting to me because the way Stibnite was in World War II was the way the place was that I was working in Kyrgyzstan. So that was my interest. I began to ask around. I know quite a few people in regional EPA and DEQ and others that work professionally in this field and I began to inquire about this project.

I became quite interested in this project for the first permit that was publicly released.

Q. And to clarify, you mean the first draft permit?

A. First draft permit, yes.

Q. Okay. And so did you comment on that draft permit?

A. I understood from colleagues that I'd spoken to that DEQ was proposing a major change in policy and strategy with that permit. And I attended the first hearing. It was my first Zoom hearing. It was during COVID. And during the

discussions of that hearing it was -- it became evident that that first permit was going to exempt 99 percent of all arsenic from any regulation, and that would have been a horrific situation, so I commented extensively on that. And, fortunately, DEQ came around and decided to begin to regulate it under TAPs, and I've been involved in following that process since.

Q. So the first permit didn't have -- you said there was a change in policy, but did the first permit have anything to do with the 16/70 adjustment factor that we're talking about here?

A. No need for it. It said they could emit all the arsenic that they wanted without any restrictions whatsoever.

Q. How would they have accomplished that or what were they --

A. They tried to run an exemption for gold mines through it, and it doesn't specifically address arsenic, and they made the contention that because that didn't specifically address arsenic, then nobody cares.

That's just not the case. It's not the way the NESHAP rule was implemented, and it's not how anyone else has implemented it. And when DEQ

seriously evaluated it, they required then that the arsenic be regulated under TAPs, and we're still here today trying to get that done properly.

Q. Okay.

Okay. I'm going to go back to Exhibit 302. This is your declaration.

You're familiar with the contents of that declaration, correct?

A. Oh, I had a few Biden moments here and there at my age, but yes, I'm familiar with it.

MS. HANCOCK: Oh, ouch.

MS. THROWER: Dr. von Lindern's declaration was offered as Exhibit 302, but I don't believe it's been formally admitted, so I'd like to request that we admit -- move to admit Exhibit 302 with the attachments into the record.

THE HEARING OFFICER: Any objections?

MS. HANCOCK: We would just reserve --

MR. HURLBUTT: No.

MS. HANCOCK: Oh. Sorry.

MR. HURLBUTT: Go ahead.

MS. HANCOCK: We would just reserve all of our objections in the motion to strike that we filed already.

THE HEARING OFFICER: Okay. Yeah. Approved

subject to the motion to strike.

MS. THROWER: Thank you.

(Exhibit No. 302 was admitted.)

Q. (BY MS. THROWER) So let's walk you through the declaration.

What do you understand that your assignment was in drafting this declaration?

A. My assignment was to review the final order of the Board, the respondent's declarations, and give an expert opinion to assist the hearing officer in establishing the facts that the Board is requesting.

Q. Okay. So I want to go one by one through the opinions that you state in this declaration, but let's first just go to paragraph 17. There are several opinions that you make.

Can you just please state what those opinions are?

A. Those are the Board's opinions.

Q. Oh, there should be -- maybe I have the wrong paragraph. I don't want the Board's opinions, but I want yours.

A. Well, mine --

Q. Oh, yeah, I have an electronic copy.

Maybe I need to go up a little bit higher.

A. Oh, no. I'm sorry, I misspoke. Those are my opinions of the Board's opinions.

Q. Okay. Can you go ahead --

A. I structured them the same -- tried to structure them the same way as...

Q. Okay. Can you just go ahead and read through those, please?

A. DEQ's application of the 16/70 Stibnite Gold Project-specific adjustment factor underestimates cancer risk and is inappropriate science and public policy;

(b) is: Ambient air arsenic concentrations and cancer risk are underestimated by the use of five-year rolling average;

(c) is: Ambient arsenic concentrations and cancer risk are underestimated by improper application of the non-WEP emissions scenario;

(d) is: The combined application of the SGP 16/70, five-year rolling average, and non-WEP project-specific adjustment factors increase cancer risk and negate the health protectiveness of the TAPs rule; and

(e) is: DEQ's SGP project-specific adjustment factors represent a significant change

in the regulation carcinogenic risk in Idaho that increases both cancer risk and regulatory burden.

Q. Thank you.

I want to go to your first opinion, which you said was: The application of the 16/70 project-specific adjustment factor is inappropriate science and public health policy.

We'll go through, you know, the basis of your opinion and how you came to that conclusion.

Again, I just want to touch on the -- your involvement in development of the TAP rules. You discussed your involvement, what you were asked to do, and you said some of the recollection of some of the issues was -- I mean, that generally everybody wanted an easy-to-use rule for industry that was not burdensome and -- but was protective of public health.

As far as the TAPs rule, as written as you understand, do you think the rule achieved that result?

A. Yes, I think the TAPs rules worked pretty well for the last 30 years.

Q. Okay. There's --

A. I think -- at the time that it was put together, as I mentioned, the regional EPA, and

particularly the State of Washington, was encouraging the adoption of a much more rigorous -- much more -- one that would have a lot more regulatory burden than the one that we ended up with because it would have required risk assessment as a stip.

Q. Okay. Instead of --

A. It was a main -- one of the main objectives of developing the TAPs -- these rules was to avoid risk assessment.

Q. Okay. I want to explore -- there's been a little bit of testimony about the AACC as being an increment.

Can you explain what your understanding is of the AAC being an "increment" and what that means in this -- in the TAPs regulation -- or the TAPs rule?

A. Well, the rule is incremental, as several people have testified here. It only looks at the particular source. It doesn't look at past, present, future sources or other factors. So the AAC -- AACC is the -- AACC is the cornerstone of the rule, and annual compliance with it is the cornerstone of the rule, as opposed to some of the opinions that we've had here previously.

Q. Okay. And I believe this term has come up. I think your first figure in your declaration had been shown under somebody's testimony. That's Figure 1 on page 11 of your declaration.

A. Yes.

Q. I just want to go through this term, "margin of safety."

What do you mean by "margin of safety"?

A. The margin of safety is what protects the public from excessive risk by -- it's accomplished by a very strict interpretation of the rule so that an individual who is exposed will have some comfort in knowing that the exposure that they will get from this source is not going to cause them to have excessive exposure or risk.

Q. Okay.

A. Margin -- I should -- maybe I should point out a couple things. "Margin of safety" is my term. It's not -- you're not going to find it in the regulation, and that's because this particular figure is --

THE WITNESS: I don't know -- no offense, but the other day you said you didn't have --

THE HEARING OFFICER: The STEM background.

THE WITNESS: -- the STEM gene. Well, I

have the STEM gene and it's a little bit of a curse because it's hard to explain what we do.

THE HEARING OFFICER: Right.

THE WITNESS: It's all hard for all scientists, so -- after many years of risk communication, to try to put these things together so that they're understandable.

Margin of safety is not in the rules, but the margin of safety is what we depend on to keep the public safe.

Q. (BY MS. THROWER) Okay. So maybe you could go through Figure 1 and kind of explain what the different color lines are and the gray part, and I guess you kind of explained what the green part is, but --

A. I would point out, yesterday I heard this characterized as "the von Lindern method." It's my method of explaining it, but what I'm explaining is exactly how TAPs has been implemented for the last 30 years. This has been DEQ's method since it was implemented.

The cornerstone of it is that diagonal line. That diagonal line is based on the one-year maximum annual concentration. That is the cornerstone of the standard.

And the 70 years is the lifetime risk, of course, but I prefer not to put it in years. I prefer to put it in age because when you're an engineer, you think a lot about the life of your project. When you're a risk assessor, you should be thinking about the life of the receptor, the life of the people who were going to breathe this air.

So that at the beginning of a project, you think most about someone who is going to be conceived at that time, and they're going to live that 70 years, and the way that TAPs is implemented right now, they get to get -- they're going to accumulate 1/70 of that allowable risk each year.

I think I could have saved Ms. Lopez a lot of trouble the other day. The 1 in 7 million, you could get by just dividing the -- 10 to the minus 5th by 70. You can do one -- you pile up 1-in-7-million risk every year for 70 years and when you're done, you're at the -- you've used it up. That's the way TAPs is implemented.

Q. And that's what this figure is showing?

A. That's what this figure shows. It also shows that the most vulnerable ages you have the greatest margin of safety where you need it as

young people. That's the "age 2" arrow that's on the left side. I put the 16 years on there because that's what this project's about. 16 years also corresponds with adolescence. Humans are most sensitive to cancer from birth to adolescence, fetus to adolescence.

So it does afford a good deal of safety to the population in those vulnerable age groups. By the time you get to my age, a little more exposure doesn't matter much at all, so that's -- that's for the older folks. When we get toward the end of our exposure life, it's not as important.

The gray part is that accumulation of risk during the lives of the receptors, not the life of the project.

Q. Okay. Thank you, Dr. von Lindern.

A. The red line at the top --

Q. I'm sorry.

A. I forgot the red line at the top.

Q. Sure.

A. That is the allowable risk level. This particular graph is for the 1 times to the minus 5th. That's for T-RACT.

Q. So that's the T-RACT risk level on the top?

A. So just in case I haven't been very articulate, you start with nothing. After 70 years, you would have your full exposure. That's the way TAPs has been implemented as far as you hear from Kevin every other project that's been done in Idaho to date.

Q. Okay. And Ms. Lopez's testimony, she said under EPA guidance, it was okay to do this exposure adjustment -- exposure duration adjustment, which we say would concentrate 70 years of cumulative risk that's shown on your Figure 1 here, into, you know, however many years you're adjusting that project, whether it be six years or 16 years or something like that.

I want to move to your Figure Number 2. And I think Bryan is going to try and to put those up on the screen if that's helpful for anyone.

Does Figure 2 illustrate the impact to the margin of safety if we concentrate the cumulative risk over 70 years into a shorter term of the project? I believe in this figure, you used six years, but it would be the same concept if you had used 16, correct?

A. I used six years because my understanding of Kevin's and Ms. Lewis's

declarations was that --

Q. I'm sorry to interrupt you, Dr. von Lindern, but by "Kevin," you mean Kevin Schilling?

A. Kevin Schilling. We have a long history.

I understand from their interpretation that you could apply this risk factor to as low as 6 over 70. This project is proposing 16 over 70, but there is a relief for less than -- short-term projects for less than five years. I think everybody agrees that it wasn't proper to put 70 years of life at five, but for some reason, they didn't believe it's proper to put in 70 in six years, so that's why I gave this particular sample -- example.

Q. Okay.

A. Well, that shows that by age 6, a child will have had experienced its entire allowable full-time cancer risk, and that's -- that is not good. That is bad.

Q. And that's for a six-year project.

What would be the case with a 16-year project?

A. They would have completely used their entire lifetime exposure by the end of adolescence.

That's not as bad as doing it to a 6-year-old, but it's still pretty bad.

Q. Okay.

A. That means that individual has to live the rest of their life with a full boat -- pan that Kevin talked about, it's going to be full for the rest of their lives.

Q. And that's Kevin Schilling?

A. Kevin Schilling.

Q. Okay. And in her testimony yesterday, Ms. Lopez pointed out a statement from page 10 of Appendix A of the EPA's 2005 Guidelines for Carcinogen Risk Assessment.

MS. THROWER: This was the exhibit that we did not have an electronic copy, but you provided -- and I was hoping you could help me with the exhibit number. But you provided us paper copies of this?

I don't remember what this was. I think it was your exhibit.

MR. FOSTER: 221.

MS. THROWER: 221?

Q. (BY MS. THROWER) Dr. von Lindern, I'm going to hand you a document that's been marked Exhibit 221, which is the EPA's 2005 Guidelines for

Carcinogen Risk Assessment.

And I apologize, I guess we're just going to have to flip through pages. I'll try and stop and make sure everybody sees the page we're on.

So she used this guidance to justify that it was okay to concentrate 70 years -- or to -- excuse me. She used this guidance to justify -- or support the 16/70 adjustment factor applied to the modeled arsenic concentration.

So specifically she pointed out to a statement on -- in Appendix A, page 10. And that statement, there was a -- she talked about that paragraph, but specifically there was a sentence in there that says: This assumes that a high dose of such an agent received over a shorter period of time is equivalent to a low-dose spread over a lifetime.

Do you remember that testimony?

A. Yes, I do.

Q. Okay. What is your opinion of her conclusion that: Based on this guidance, applying the exposure duration adjustment to this project to assess cancer risk was appropriate?

A. I think it's inaccurate. I don't think

this document supports that.

Q. Okay. Are there particular areas of this document that you can lead us through --

A. Yes.

Q. -- where you think does not support that?

A. If you look at the introduction.

Q. Okay. Can you just state the page number on the bottom?

A. 1-1.

Q. 1-1? Okay.

Would you like to read some statements where you feel is contrary to the -- what Ms. Lopez testified to?

A. All of EPA's guidelines should be consulted when conducting a risk assessment in order to ensure that the information from studies on carcinogenesis and other health effects are considered together in the overall risk.

Further down the page: The developmental guidelines discuss hazards to children that may result from exposures during preconception and prenatal or postnatal development to sexual maturity. Similar guidelines exist for reproductive toxicant risk assessments and for

neurotoxicity assessment. The overall characterization of risk is conducted within the context of broader policies and guidance, such as Executive Order 1345 [sic], "Protection of Children from Environmental Health Risks and Safety Risks."

Q. Okay. And are there any other statements in that document that --

A. Yes.

Q. -- you'd like to read?

A. Yeah.

Q. So what page are you about to look at there?

A. 3-26.

Q. 3-26. Okay.

Go ahead and read or explain the portion.

A. Well, this is the same sentence that she cited in the appendix.

MS. HANCOCK: Hold on one second. I gotta get to that page. 3-26?

Okay.

Q. (BY MS. THROWER) Okay. Go ahead, Dr. von Lindern.

A. Ms. Lopez cited the sentence that is: The assumption is made that a high dose of

carcinogen received over a short period of time is equivalent to a corresponding low-dose spread over a lifetime.

The next sentence says: This approach becomes more problematic as the exposures in question become more intense but less frequent, especially when there's evidence that the agent has shown a dose-rate effects (US EPA 1986a).

If you turn to the next page, bottom of the page, into the last paragraph: In contrast, for a susceptible life stage, higher risks can be expected from exposures during only a portion of the lifetime, but everyone in the population may pass through these life stages. Effects of exposures during a susceptible period are not equivalent to the effects of exposures at other times; consequently, it is useful to estimate the risk attributable to exposures during each period.

On the facing page, 3-28, third bullet: In addition, the concern that dose-averaging generally used for assessing less-than-lifetime exposure is more likely to understate than overstate risk, contributes to the suggestion that the alternative approaches should be considered for assessing risks from less-than-lifetime exposures

that occur during childhood.

Q. Okay. So based on your review of that document and those passages that you read to us, what is your opinion of applying the exposure duration adjustment to this project to assess cancer risk? Was that appropriate?

A. It's horribly dangerous, and I think -- you know, I understood her response to (b). I think -- as I understood the question, you asked her if she thought it was all right, and she said it was allowable within EPA's guidelines.

I've served on 20 -- at least 20 science advisory committees, and a purpose of many of those is to review these kinds of documents. I've worked with the agency for almost 50 years now. I don't think I could find a single person in EPA that would admit that you should -- you should completely consume the lifetime exposure in -- to have a 7-year-old face the rest of their life with a life with a full boat of exposure.

Q. Okay. I want to go back to -- oh, I'm sorry, did I --

A. No, I just -- I'm obviously concerned that I've heard that, and I want to point out, I don't know anybody at EPA that would say that.

Q. Okay. I want to go back -- and you don't need to necessarily look at this page, but on page 1-1, the statement that you read referenced other -- or all of EPA's guidelines, that all of EPA's guidelines should be considered.

Do you know of any of those other EPA guidelines that might be appropriate to consider?

A. Yes, there's one in my exhibits.

Q. Okay. And is that in Exhibit D?

A. Yes.

Q. Okay. I believe that starts at REC 6279.

MS. THROWER: Is that right? Oh, I forget that I have an electronic copy. I'm a paper person too a lot times.

Okay. Is everybody on the right page? It should be a document entitled "Supplemental Guidance for Assessing Susceptibility from Early-Life Stage Exposure to Carcinogens."

THE HEARING OFFICER: Yeah. If you give me the right REC number, I'm there.

MS. THROWER: Oh, yeah. It's 6270.

THE HEARING OFFICER: Okay.

MS. THROWER: I'm sorry. I think I said -79, but that's -- yeah.

Q. (BY MS. THROWER) Okay. So, Dr. von Lindern, are there some particular things in that guidance that you wanted to point out that are --

MS. HANCOCK: 6279?

MS. THROWER: 6270 is the start of the exhibit. It's the title page.

MS. HANCOCK: Do you know what the PDF number is?

MS. THROWER: 171.

Q. (BY MS. THROWER) Okay. So, Dr. von Lindern, I think there are a couple passages from this guidance that you wanted to point out, and one of them is on page 1 of the document, also REC 6279, if I got that right.

Can you go ahead and read from that document?

A. This is the introduction, the first page, what the document is about: Cancer risk to children in the context of the U.S. EPA's cancer guidelines includes both early-life exposures that may result in the occurrence of cancer during childhood and early-life exposures that may contribute to cancers later in life.

The National Research Council recommended the "EPA should assess risk to infants

and children whenever it appears that their risk may be greater than that of adults." This document focuses on cancer risk from early-life exposure compared with those exposures that occur later in life. Evaluating childhood cancer and childhood exposures resulting in cancer later in life are related, but separable, issues.

Q. Okay. Thank you.

I think there's another passage you wanted to read from page 4, REC 6282.

A. The last sentence: However, susceptibility differences with respect to early life stages are not taken into consideration because cancer slope factors are based upon effects observed following exposures to adult humans or sexually mature animals.

Q. You mentioned a term in there, "cancer slope factors."

What is that?

A. Well, the universe factor is one example of them.

Q. The universe factor that we've been talking about today?

A. That we're talking about today, yes.

This is -- this is particularly

important because we've heard all this -- all this talk about 70-year life. That URF is based on a 70-year life. That doesn't mean that the risk is the same across that. It's the average across that life.

When you begin to break that into segments, then you have to look at the specific dose relationships within those segments. So it is not applicable.

Q. It's not applicable just to early life stages?

A. To do these 16/70 is equivalent to -- it's called dose-averaging, and dose-averaging isn't appropriate to apply to these kind of standards.

Q. And I believe there might be one more passage that you wanted to read through there on page 30, REC 63- --

A. I should read the rest of the last one.

Q. Sure. Go ahead.

A. Since a much larger database exists for chemicals, including [sic] cancer in adult humans or sexually mature animals, it is necessary to determine whether adjustments of such adult-based cancer slopes would be appropriate when assessing

cancer risk associated with exposures in early life.

Q. Thank you.

I think you actually got your thumb on it there.

A. Did I hit it? 32?

Q. Do you have page --

A. 30.

Q. Oh, 30. Okay. And, again, this is REC 6282 [sic], and if you could just take a moment to make sure everybody is turned to that page.

THE HEARING OFFICER: Sorry, what page again?

MS. THROWER: It's page 30 of that document, but it's REC 6308.

THE HEARING OFFICER: Okay. Got it.

MS. THROWER: I'm sorry, I think I misspoke earlier.

Q. (BY MS. THROWER) Okay. Go ahead, Dr. von Lindern.

A. Children, in general, are expected to have some exposures that differ from those of adults, either higher or lower, due to differences in size, physiology, and behavior. For example, children are generally assumed to eat more food and

drink more water relative to their body weights than adults. Children's normal activities, such as putting their hands into their mouths or playing on the ground, can result in exposures to contaminants that adults do not encounter. Moreover, children and adults exposed to the same concentrations of an agent in food, water, or air may receive different, higher or lower, internal doses due to the differences, for example, in intake, metabolism, or absorption rates. Children are less likely than adults to be exposed to certain products used in industrial settings and often have more limited diets than adults. When assessing risks, if the data are available and relevant, it is important to include exposure that is measured or modeled for all life stages, including exposures during childhood and adulthood.

Q. So I think what I'm getting, and I will probably put this in terms of -- in very nonscientific terms, but what I'm getting from this guidance and the passages you read from this guidance and also from the previous 2005 EPA guidance, that risk assessment is a lot more than just dose-averaging, just a 16/70 adjustment factor, and it is inappropriate to just use that to

calculate cancer risk; is that correct?

A. Risk assessment is a complex multi-faceted undertaking. It's not pulling one equation out of one document and claiming that that justifies what this project seems to think it justifies. It would require comprehensive evaluation of other potential sources, age, susceptible populations, a myriad of considerations to --

Q. And that --

A. To eliminate that safety factor -- that margin of safety. That margin of safety is built to accommodate all of those things that you would ordinarily have to consider in a risk assessment.

So if you were to start to adopt this dose-averaging business, you would be obliged to do a really sophisticated risk assessment to justify doing that to the people of Idaho, not pull out one -- you know, they're pulling one equation out of a Superfund document to begin with, they're citing one sentence out of an appendix of a document that says: Don't do this.

It's irritating, frankly. Sorry.

Q. And so you had mentioned that Idaho, in development of the TAPs rules, had tried to avoid

this whole risk assessment thing. But I think you had mentioned that State of Washington does use a risk assessment in their permitting process?

A. State of Washington mandates it.

Q. They mandate it.

And so do they have -- are you familiar with their rules?

A. Yes.

Q. And do they specify what sorts of factors you need to consider in a risk assessment?

A. They have a very precise guidance called an HIA, Health Impact Assessment, that they require. They have -- the first tier of their law is quite similar to ours. They calculate the one-year maximum exposure. They compare it to -- they don't call theirs AACC. It escapes me right now exactly what they call it, but it's the same thing, and if it's -- if it exceeds, then they're required to do a risk assessment before they can move into the other steps, before they can -- before they can get relief.

In Idaho, we have a very strict standard. We don't require risk assessment, and you can move immediately into the two levels of relief. One is a short-term exemption that you can

get a factor of 10 relief for a less-than-five-year project. The other is T-RACT.

There are no other -- there are no other exceptions. You get relief for the five-year or you get relief for T-RACT. You don't get T-RACT, which gives you a tenfold reduction in exposure, and then come and ask for more by trying to apply these techniques.

Q. And if you could turn to Exhibit C of your declaration.

A. Yes.

Q. Is that an example of Washington's guidelines on how they do their permitting?

A. This is their guidance document for their equivalent of the TAPs rule.

Q. I want to go back to Figure 2. Sorry I keep having you flip pages.

A. Yes.

Q. Now, you've read the Board of Environmental Quality's final order, and I believe you've reviewed the transcript of their meeting as well, the May 1st meeting --

A. Yes.

Q. -- as well?

Does Figure 2 illustrate your

interpretation of what McMillan was concerned about and that he expressed at the Board's May 1st hearing?

MS. HANCOCK: I'd object to this. I mean, he can't talk about what somebody else was talking about. He can talk about what he's doing, but I just don't think --

MS. THROWER: I just asked if it's his interpretation.

MS. HANCOCK: I'm just making my objection for the record.

THE HEARING OFFICER: All right. I'm going to overrule the objection and allow the question.

Q. (BY MS. THROWER) You can answer, Dr. von Lindern.

A. I agree with Dr. McMillan. I think he was right. Application of this will increase risk of cancer. I don't think there's any doubt about that.

Q. We talked about the TAPs rule being an increment, that it doesn't consider other sources outside of the source that it's looking at.

I want you to go to Figure 3 of your declaration.

A. Yes.

Q. Actually, go ahead and explain what you're showing here on Figure 3.

A. It'll take a little background for that.

There is a class of carcinogens that they've been discussed, I think in some of the earlier testimony, that have a carcinogen that has a mutagenic mode of action, and that's a particular problem for early life stages.

EPA has looked extensively at that, and they recommend, and in fact they almost require, that you do age-adjusted risk factors for assessing risk -- for estimating risk for early life stages.

Q. Can I stop you there?

But is arsenic a mutagenic carcinogen?

A. EPA does not classify it as a mutagenic carcinogen.

Q. Okay. So --

A. There is an asterisk there, of course.

Q. Okay. What is that asterisk?

A. There's probably -- well, certainly in metals and metalloids, arsenic is the most difficult metalloid to deal with. There's a lot of chemistry reasons why that's so. But the mechanisms of arsenic cancer are not well understood and have not been well understood for a

long time.

Arsenic does act as a mutagen in combination with other carcinogens and other stressors, they call them. So EPA does not classify it as a mutagen, but it leaves it up to the discretion of the risk assessors and the risk managers as to whether to treat it as mutagenic.

The State of California, on the other hand, says you must treat it as a mutagenic carcinogen, so -- or mode of action.

Q. What about Idaho?

A. I don't know that in the context of TAPs Idaho has ever done a risk assessment, so I don't know what they say. This would be the first one.

Q. So --

A. And this is not one.

Q. So under the TAPs rules, as you believe they should be applied and have been applied 'til now, it wouldn't matter whether it's mutagenic or not because the TAPs rules provide this margin of safety?

A. It's close. It's close. The margin of safety -- it can be very comfortable with the margin of safety for the carcinogens that don't exhibit that characteristic. Those that do, margin

of safety works, but barely. We didn't anticipate this issue in the 1990s. This issue came up about 2005 to treat risk assessment for the mutagenic MOAs differently --

Q. Okay.

A. -- and fortunately, our margin of safety was able to accommodate that for one project. You pile two projects on and it can't make it. You can pile two or three projects on, on the other carcinogens, and still be safe under our margin of safety, but...

Q. Okay. So Figure 3, then, is showing basically what somebody's cancer risk would be if you treated arsenic as a mutagenic carcinogen. And you have some lines there.

Can you go ahead and explain what those lines are?

A. The red line's the standard. That's the tracked 10 to the minus 5th standard.

The blue line is if you did a six-year project with a mutagenic MOA. In that case, you know, it's bad enough that with a regular carcinogen, you're doing the full-time exposure by age 6. With this one, you're doing it by age 1 because the first two years -- first two years, as

EPA recommends you treat it, are equivalent to 20 years with the other -- with the nonmutagenic.

You multiply the first two years by 10, you multiply up to age 16 by 3. So you've really expended everything by adolescence in that case.

Q. Okay.

A. But in the case of the six-year project, you don't even get to be 2 years old before you have a full lifetime cumulative exposure.

Q. And you mentioned project upon project upon project can amplify that, and that the incremental nature of TAPs doesn't consider future projects; however, its margin of safety kind of helps with that when you're looking at, you know, compliance and permitting on a regional basis.

So does Figure 4 -- if we could go to Figure 4, does that kind of explain that concept of what happens if you have one project that has an adjustment factor and then you get another one and then you get another one?

Can you explain Figure 4?

A. Yes. The left side down in the lower corner of Figure 4 is Figure 2. And remember back on Figure 2 at age 6 that child has its full lifetime cumulative exposure.

In this state, it's an incremental standard. DEQ is not allowed to consider past exposures. The next project gets another full boat of lifetime exposure. By -- in this example, by age 12, you're twice the amount. By age 18, you're three times your total cumulative lifetime exposure.

I think Kevin Schilling did a good job yesterday on explaining how DEQ would treat that. If it's a new project, he has to approve it, he has to allow this to happen. If it's a modified project, there may be some consideration as to how you can do it. But if the first project already ate up all the exposure, I don't know how you can modify it in a way that doesn't increase risk further.

Q. Right.

And so --

A. We really need that margin of safety in this state if we're going to stay incremental.

Q. Right.

So each project gets that increment of cancer risk, regardless of what project --

A. Yes.

Q. -- goes before it or what projects are

after it?

Okay. Did you want to say anything more about that figure?

A. I could point out it has a little error on it.

Q. Sure. Sure. Since you've pointed that out, yeah.

A. Yeah. And the top line should be all the way up to 3. The text is correct --

Q. To 3 --

A. -- but the top line stops a little short.

Q. To 3.00E-05.

A. I have to talk to my graphics department about that.

THE HEARING OFFICER: I was going to do a quick time check. I might need a break pretty soon. I just wanted to see how that might jive with what you have going on.

MS. THROWER: Yeah -- well, if we can -- I think if we can go through one more figure, that would get sort of through this part, and we'll move on to his second opinion, and the other opinions will go a lot faster.

THE HEARING OFFICER: So then take a break

after this next figure?

MS. THROWER: Yeah. Would that be okay?

THE HEARING OFFICER: Yes.

Ms. Young, are you okay?

MS. YOUNG: Yeah.

MS. HANCOCK: I'm just curious how much longer we have with this witness on direct so that we can plan our day accordingly.

MS. THROWER: Yeah, it's about 3:00. I mean, we've got -- well, so the other opinions will go much faster. This one had lots of figures associated with it and everything. I don't remember what time I started.

THE REPORTER: You started at 1:38.

MS. THROWER: 1:38? Okay.

MS. HANCOCK: So we've been going about an hour-and-a-half already with this witness.

MS. THROWER: Well, we have 'til 5:00, right? I mean, the hard --

MS. HANCOCK: We have redirect as well.

MS. YOUNG: I understand that.

MS. HANCOCK: And a rebuttal case.

MS. YOUNG: The other opinions, we'll go through them a lot faster. This one was --

MS. HANCOCK: Do you have an estimate how

much long your have with this witness?

MS. THROWER: I don't know, maybe we can get through this in another half hour or something?

MS. HANCOCK: And you finish him at that point?

MS. THROWER: Yeah.

MS. YOUNG: We could take a break at the end of that.

MS. HANCOCK: I mean, we still have cross of him and then we have -- you know, if we do a 20-minute break, I'm just concerned we're not leaving time for a rebuttal case and we're going to obviously need some time for that.

MS. THROWER: I won't object to going past 5:00 if you need time to.

MS. HANCOCK: I just think that we're exceeding what we had agreed to on these witnesses on the original --

MS. THROWER: I don't think those were hard limits.

MS. HANCOCK: Let me finish what I'm saying, please.

I feel like we've all worked really hard to make sure that we kept our witnesses within the correct time parameter, so I want to make sure

we're being fair to all the parties.

MS. THROWER: Okay. Well, I'm happy to have my witness here for the full amount of time you need for cross.

I think right now we're wasting time.

MS. HANCOCK: I guess I'm looking to Dylan. My conversation is with him, not with you.

THE HEARING OFFICER: Okay. So what would you like me to do? What is the request?

MS. HANCOCK: My request is that you put some time constraints on this to make sure we can all put in our case by the end of the day. We've managed our witnesses and our case to ensure that we've complied with the time limits and we've gone way beyond on this witness already.

MS. THROWER: Well, I think we've kept in the general timeframe and we've got through three witnesses yesterday --

MS. HANCOCK: Because we honored our time constraints.

MS. THROWER: Kevin Schilling took a little bit longer, I believe, than two hours. But we got through half of the witnesses yesterday. We're going to get through half of the witnesses today.

I mean, I don't think -- you know, you

could cut us off and I'll object that we didn't get to present our case.

THE HEARING OFFICER: So, again, just going back to something I said earlier, we gotta remember that -- I mean, from my perspective, the Board, you know, they use that phrase, like, "full development of the record." So I mean, I don't want people to feel like they didn't get enough time. So if we need to -- you know, if we find ourselves and we're at the end of the day and we need to do a follow-up Zoom to tie up some loose ends or whatever, you know, then we can do that.

But, you know, I really don't want to create a situation and create a potential reversible error by not -- you know, by not giving people the time they think they need.

MS. HANCOCK: Yeah, I appreciate that. I just -- we came into this with your guidance about time and we've managed our witnesses in the way we put in direct in a way to honor that scheduling order that you put out, and so I'm just saying -- I'm just asking that we have all parties do the same.

THE HEARING OFFICER: Okay.

MS. THROWER: Do you have a --

THE HEARING OFFICER: I have not been tracking the time. I don't have the bandwidth to do that and pay attention to all the testimony.

Do we have a way to update on time allocations?

THE REPORTER: Yes. But I can't talk and be on the record at the same time.

MS. THROWER: Can we just get through one more graph and we'll take a break and we can figure that issue out?

THE HEARING OFFICER: Yeah, let's do that.

MS. THROWER: Thank you.

Q. (BY MS. THROWER) Dr. von Lindern, can you please go to Figure 5a in your declaration? It's page 22.

A. Yes.

Q. And can you go ahead and explain this figure?

A. This is the same as the previous figure, the same situation, if it were implemented under the current TAPs rule.

We saw in the previous figure that after the third project, the individual would have three times the cumulative -- lifetime cumulative allowable exposure.

The line down at the bottom using the margin of safety in implementing three six-year projects in a row show that the risk would be 2 times 10 to the minus 6. The allowable is 1 times 10 to the minus 5th. So it would have consumed probably 20 percent of their lifetime exposure.

So under the current TAPs, they would have used 20 percent of their lifetime allowable exposure. Under this new operation, they would have three times their lifetime allowable exposure.

Q. Okay. And, Dr. von Lindern, what do you conclude about the impacts to public health if you use this sort of 16/70 adjustment factor?

A. I think it's -- it's unacceptable. It's -- I think the whole philosophy that a source is entitled to consume the entire lifetime exposure of its neighbors is not good public policy or good science for me and -- try to implement that in this state where it's an incremental exposure. An incremental source analysis means they can do it over and over again. These TAPs rules are not available -- are not able to accommodate this right now.

Maybe if the legislature wanted to redo it all and put particular risk assessment burden on

the regulatory community and they did it in the way that Washington and many other states did, they could consider this, but boy, it doesn't fit in Idaho right now. This is not good policy, not good for public health, and not good science.

MS. THROWER: Okay. Thank you, Dr. von Lindern.

I think this will be a good time to take a break.

THE HEARING OFFICER: Okay. How long? Ms. Young, do we need a 20-minute?

MS. YOUNG: 15.

THE HEARING OFFICER: 15?

MS. YOUNG: Let's go 15.

THE HEARING OFFICER: Okay. So it's right at 3:00, so we'll reconvene at 3:15.

(A recess was taken from 3:00 p.m. to 3:19 p.m.)

THE HEARING OFFICER: Please proceed, Ms. Thrower.

Q. (BY MS. THROWER) Dr. von Lindern, we're going to move on to the second opinion that you expressed in your declaration, and that was that: The ambient air arsenic concentrations and cancer risk are underestimated for the Stibnite Gold Project by using a five-year rolling average.

In your opinion, how does using a five-year rolling average to calculate emissions differ from the emission calculations that are required under the tax rules?

A. As I said before, I think a cornerstone of the TAPs rule is a maximum one-year annual average ambient carcinogen concentration. It's critical that they calculate that and it's critical that we use that to maintain the margin of safety that's required to make this rule health-protective.

That is not a five-year average. It's not an average of multiple different sources that might operate over the time period. It is the single one-year maximum. That's the value that has to be calculated.

Now, the five-year average is a five-year average in my role, but it's a five-year average. So any calculation that they've presented is a five-year average. I don't think they've disputed that. It's written up there.

But in terms of averaging -- that ends up -- the five-year -- using the five-year emission average ends up calculating a five-year average exposure. So that's averaging exposure over

another time period other than one year.

It's the same as the 16/70. It's just another form of dose-averaging. So it's the same problem. All the problems we've talked about so far with 16/70 are just accelerated by putting the five-year average on the front of it. It's disguised as an input to a model, but it is actually the same averaging risk over time period, so it just makes the 16/70 worse. That just does it at the front end.

Q. Were you ever able to obtain this maximum annual average, as you discussed, the actual just one-year maximum average from DEQ?

A. No.

Q. Okay. And were you able to estimate it from the information in, you know, all of their application?

A. I made my best estimate of it that -- the information that was available.

Q. Okay.

A. Frankly, the calculations aren't very transparent. It's very difficult to work back through those spreadsheets and figure out what's going on with their calculations.

Q. Is one of those pieces of information

you used to try and estimate the maximum annual average, was that in the TAP addendum?

A. Yes.

Q. Okay. Can you turn to -- this is Figure 3 of Perpetua's TAP addendum, it's REC 6695, and it is in Exhibit L of your declaration. It might be the other binder.

Again, it's REC 6695. It's probably that last pink tab or close to it.

MS. THROWER: Bryan, could you pull that one up real quick, by chance? Sorry to put you on the spot there.

MR. HURLBUTT: Yeah. Sorry, what's the REC number for it?

MS. THROWER: I think I said 6695.

Okay. I got it for Dr. von Lindern anyway, if you can't find it really quickly. As long as everyone else has it.

Mr. Hearing Officer, do you have --

THE HEARING OFFICER: Oh, sorry, are you waiting on me? Yeah, I'm there.

MS. THROWER: I just wanted to make sure you were ready. I apologize.

Q. (BY MS. THROWER) Can you please walk us through how you estimated the maximum annual

average using this figure?

A. Well, I interpreted this figure to show the maximum five-year rolling average by year. So I interpreted this as there are five years within each one of these bars, five-year average, and that as they roll through this, they take one off one end and add one to the other end. And I used what's called a peak-to-mean-ratio calculation -- it's pretty common in air pollution, it was very common in the early days before there were commuters -- to look at what the highest concentration was compared to the mean of all the concentrations in the series, and I estimated that the peak is about 1.8 times the mean in this series of figures, and if that -- that's true, then you can multiply the estimated five-year average by 1.8 to get the best shot you can out of one-year average.

Q. Okay. So your conclusion here is that the five-year rolling average is underestimated by 1.8 times of what you -- or -- sorry, let me start over.

The maximum annual average, your estimated maximum annual average, is 1.8 times higher than what their five-year rolling average

was calculated?

A. That's half right.

Q. Okay. Clarify my attempt to --

A. They also added another dose-averaging on the other end of this, so...

Q. Okay. We'll get --

A. The five-year -- because of the five-year, you should multiply by 1.8 to work your way toward the maximum one-year.

Q. And by underestimating the maximum average concentration, you would thereby underestimate cancer risk if you put it into any of these cancer risk equations; is that correct?

A. You're just doing another element of the 16/70. 16/70 dilutes the exposure by about 78 percent. This dilutes it another 40 percent.

Q. Okay. Thank you.

And let's move on to that third dose-averaging issue that you started to mention.

So this goes to your opinion 3, and you conclude that: The ambient air arsenic concentration and cancer risk are underestimated by improper application of non-WEP scenarios.

That's W-E-P.

So what do you mean by that?

A. The five-year rolling average that we just talked about is input to the model that predicts concentrations. So that's a dose-averaging step in the input.

The output comes out and then they do another dose-averaging exercise where they take the worst-case scenario and they dilute it by combining it with other scenarios. Mr. Lewis, so far, has best described that as the 50 percent WEP and the 50 percent non-WEP combination at the end.

Q. Okay. And when Mr. Lewis was testifying on cross, I had shown him Exhibit 302, which was this big chart that I printed out, and this was one of the electronic files that were attached to the TAP addendum.

Could you explain what happened using that spreadsheet?

A. Yes. I believe they identified the W2 scenario -- that's the West End Pit operating at the alleged maximum, as the -- as the highest emission rate, and consequently, the highest concentration that would be estimated through the modeling.

And the result of that modeling was that .00698 figure that we see in the second lower --

Q. Right.

So in the space that intersects between the row for arsenic and the column for W2; is that right?

A. Yeah.

So W2 was the -- as far as I understand, is the maximum, and it would be that W2 year that would -- that should be reflected as the maximum to calculate the one-year standard. You can't do it because they use the five-year standard for the input. But this identifies the maximum year that should have been used in the calculation.

This step was then to take -- this gets hard because it's an average of the average of the average of the average. But it's the average of Y1 through H4, which each are five-year rolling averages, as I understand, to begin with, and it averages that with W2. And that's where that .00416, whatever that number was that the toxicologists used -- risk assessors used.

Q. Dr. Paden and Ms. Lopez, correct?

A. Yes.

Q. Okay. So --

A. It was really difficult to figure that out.

Q. How did you figure that out? Did you run a computer model or --

A. I asked Kevin's boss if I could sit down with Kevin and Pal, I believe was the modeler's name, and they steered me through it. I think you could have done it yesterday if you had been inclined.

Q. Okay. So just to recap: So you found that arsenic emissions calculated for the W2 model were calculated by averaging a five-year rolling average, WEP2 scenario, with the average of seven five-year rolling non-WEP scenarios before applying the 16/70 adjustment factor to get that 0.00416 number that went into Dr. Paden and Ms. Lopez' corresponding cancer risk calculations?

A. I don't want to ask her to read that back, but assuming you have the right number of averages in there, yes, that describes it.

Q. Did you make an assessment of how averaging the non-WEP and WEP scenarios alone impacted your estimated annual -- maximum annual average?

A. The five-year reduced it by 45 percent, the non-WEP by 41 percent, and the 16/70 by 78 percent.

Q. Okay. And --
A. Those all multiply together for the total dose-averaging that was accomplished for this project.
Q. Okay. And Figure 6, does that sort of give us a visual of what was going on here? Can you explain Figure 6?
A. That's my best effort to try and reconstruct it, yes.
Q. Okay. So just briefly kind of go through the -- what the bars represent.
A. Well, the bars -- the first bar represents what should have been calculated under the tabs.
Q. And that's the maximum annual average of the worst-case scenario --
A. This is the risk associated with the maximum -- single -- this is the risk associated with the -- applying the maximum one-year annual average ambient carcinogenic concentration over 70 years.
Q. Okay. And in that figure, what excess cancer risk do you see there?
A. Over 5 times 10 to the minus 5th.
Q. Okay. And the next --

A. It's five times the criteria.
Q. The criteria, the 1 times 10 to the minus 5th, you have depicted on Figure 6 as the orange line; is that correct?
A. Yes, that's the T-RACT acceptable risk.
Q. I didn't ignore the orange line on this one. It's right in the middle, so easy.
Okay. So the next bar graph that has "five year" under it, what is that?
A. That's how much they reduced that estimate by applying the five-year rolling average.
Q. Okay. And it reduced the excess cancer risks to what level?
A. 3 times 10 to the minus 5th.
Q. And the next bar graph that says "non-WEP" under it, what is that?
A. Non-WEP gets them down to around 1.8 times 10 to the minus 5th.
Q. So that bar represents applying the five-year rolling average as well as the WEP and non-WEP averaging?
A. Yes.
Q. Okay. That last bar graph, "16/70"?
A. 16/70. Project-specific adjustment factor is what allegedly gets them into compliance

by diluting it another 78 percent.

Q. Okay. So if you were to accept Dr. Paden's and Ms. Lopez's methodology for calculating excess cancer risk, how confident would you be in the results that the project will not exceed 1-in-100,000 excess cancer risk, knowing that their calculations were based on the average of the average of the seven five-year rolling averages for non-WEP modeling scenarios and the five-year rolling average of the WEP2 modeling scenarios and underpredicted by your calculations the maximum -- this isn't going anywhere.

Okay. How confident are you -- based on these dose adjustment factors, as you call them, how confident are you in Dr. Paden's and Ms. Lopez's conclusions that this project will not exceed the T-RACT cancer risk -- excess cancer risk of 1 in 100,000?

A. Their calculation was made at the third bar. They applied the fourth bar, although -- although whoever did this put the fourth bar in there too, so...

But they were given the concentration at the end of the non-WEP dilution, and then they applied the 16/70 afterwards. If you --

Q. Okay. But --
A. If you back that out, like we did here, to do the proper TAPs calculation, they're way over.
Q. Right.
So what they used for their highest concentration in their equations was that bar that's labeled "non-WEP"?
A. Yes.
Q. Whereas they should have used the bar labeled "max" or --
A. If this was applied correctly, they should have used the bar on the left.
Q. Right. For -- that's your estimated max, anyway?
A. Yes.
Q. Okay.
Okay. I just want to go to your last figure, Figure 7.
Can you explain that figure?
A. This is another way of unraveling the dilution and risk averaging that's gone on, dose-averaging, and this actually does look at the 16 years as opposed to 70 years.
Q. Okay. So all these graphs, then, all

these scenarios represented in this graph still have the 16/70 adjustment factor applied?

A. Yeah. It's put back in the format of Figures 1, 2, et cetera.

Q. Okay.

A. And the lower line is what they maintain is their concentration. That's the 41.3 percent that we've been talking about quite a bit of using it up. The line above that is if you remove the five-year rolling average. And the line above that is if you were to remove both the five-year rolling average and the non-WEP.

Q. So this basically corresponds to those bars that you had in your previous figure?

A. Yes.

Q. Okay. Mr. von Lindern, I'm going to ask you to just -- just to make a conclusion based on your analysis here.

But before I do that, is there anything else that we skipped over that you wanted to add in terms of your analysis and everything in your declaration that we didn't get to or that I didn't get to?

A. No. I'm anxious to finish, unless the hearing officer would like to hear more.

Q. Well, unfortunately, when I'm done, you're not finished yet.

A. Oh.

Q. So unless the hearing officer has any questions, I'll go ahead and ask you if you could just make a conclusion based on your analysis that we discussed here today about whether this project, this permit, complies with the TAPs rules and complies with the intent of the TAPs rules in terms of protecting the public health from these sorts of emission sources.

A. My biggest conclusion is this precedent could be horrible for the state in terms of increased cancer risk, in terms of regulatory burden. This project is not acceptable in any way, shape, or form because it takes advantage of the TAPs rule and uses up that margin of safety.

That margin of safety is what guarantees Idaho industry that they don't have to do sophisticated risk assessments to get a permit. This is no way a sophisticated risk assessment. It's one single calculation done by people who were handed the number and were involved in developing the exposure.

So if you're going to be a risk

assessor, you gotta be involved from the beginning through the end. You just don't take a number at the end and do a 30-minute calculation.

So if this philosophy of dose-averaging were deemed, for some reason, to be acceptable, along with that would become the obligation to do really sophisticated analyses and spend a lot of time and trouble to get a permit. I don't -- I just don't think Idaho's been there, and I don't think they want to go there.

So the precedent bothers me the most, both from the fact it's a rule that has worked for a long time and because it increases cancer risk.

MS. THROWER: All right. Thank you.

THE HEARING OFFICER: Okay. Does that conclude direct?

MS. THROWER: Yes.

THE HEARING OFFICER: Anything else before we go onto cross-examination?

MS. THROWER: Nothing from me.

THE HEARING OFFICER: Pardon? I didn't catch that, Ms. Thrower.

MS. THROWER: Nothing from me.

THE HEARING OFFICER: Okay. Mr. Hurlbutt, anything from you?

MR. HURLBUTT: No. Thank you.
THE HEARING OFFICER: Okay. Proceed with cross.
MS. HANCOCK: Thank you.

EXAMINATION OF IAN VON LINDERN

BY MS. HANCOCK:

Q. Dr. von Lindern, I'm going to be as brief as I can be. Let's take a look at Exhibit 304. That's the large spreadsheet.

Did you look at the arsenic levels that were modeled at the top half of that page?

A. Yes.

Q. Do you know what those reflect?

A. I recognize the 00095 as the final exposure that was used in the alleged risk assessment.

Q. Okay. Did you understand that the top half of this Exhibit 304 was the calculations that were performed once all of the permit conditions were taken into account?

A. I don't know the answer to that because I think these were done before the permit conditions. So I don't know.

Q. Okay. Have you read the permit

conditions?

A. Yes.

Q. Do you know how many there are?

A. No.

Q. Did you hear Mr. Lewis's characterization of them, that there's hundreds of conditions in there?

A. No.

Q. Okay.

A. I don't -- I don't doubt it, but I don't remember hundreds.

Q. Did you calculate what the effect of the conditions were that are in the permit on the emissions in doing your analysis?

A. I used these data, so if they're in there, I did, yes.

Q. Do you know if they're in there?

A. I don't doubt you. I've not gone through each one of them and looked. I'll accept that they are, yes.

Q. Okay. In the bottom half of this page where you were looking at arsenic at W2 as being .00698, do you see that?

A. Yes.

Q. Do you know if the conditions that are

in the permit are reflected in that number?

A. I'll accept that they are. If you assert they are, I'll accept they are.

Q. I'm not saying that they are.

I'm asking you: Do you know if they are?

A. No.

Q. Okay. If I were to tell you that one of the conditions, for example, the limitation on the production that can come out of the West End Pit, were not factored into this calculation, would that be important for you to know in order to determine if that number is an accurate reflection of the risk that you're calculating in your declaration?

A. Tell me that again.

Q. Yeah.

What if that .00698 number doesn't include the 50 percent production limit on the West End permit -- on the West End Pit, what would that do to your analysis?

A. Nothing.

Q. Nothing?

Because it doesn't matter to you if there's a production limit on the West End Pit?

A. It matters to me what the one-year

annual average is.

Q. So is it your testimony that a 50 percent production limit on the West End Pit would have no impact on the one-year average?

A. No.

Q. If there was a 50 percent production limit on the West End Pit, would that affect the one-year average under your calculations?

A. No. Maybe I don't understand the question.

My understanding of this is this is the maximum five-year average concentration for the way the facility is intended to be run.

Q. So does that mean that you assume that all the conditions are calculated in there as well?

A. All the conditions?

Q. All the production limitations.

Do you assume that those are also calculated in that number as well?

A. I would hope so.

Q. Do you know if they are?

A. I assume they are.

Q. Does that mean that you don't know one way or the other?

A. No. I assume there are because these

calculations are meaningless if they're not.

Q. Do you know when these calculations were performed on the bottom half of this page?

A. No.

Q. Okay. Could they have been performed before the production limits were put in place?

A. I don't think so because -- I don't think so because Kevin is the one that led me through them after the permit, so that's --

Q. If Kevin wouldn't --

A. I assume that he was leading me through the permit conditions because we were discussing the permit, so...

Q. When you say "Kevin," are you referring to --

A. Kevin Schilling, yes.

Q. -- Mr. Schilling?

A. Yes.

And I asked his boss if his boss is all right with me sitting down with him and having him explain it to me.

Q. Okay. Were you able to recreate those numbers on your own?

A. Oh, hell no.

Q. Do you know what makes up those numbers?

MS. THROWER: Can you be a little more specific about which numbers? Because he testified to what he thought made up one of the --

MS. HANCOCK: I'm just asking my question.

Q. (BY MS. HANCOCK) Do you understand my question?

A. No.

Q. Okay. The number that you're looking at in W2 on the bottom half of that page, .00698 -- do you see that?

A. Yes.

Q. Do you know what makes up that number?

A. I know what it's supposed to be.

Q. Do you know what it is?

A. It is the estimated five-year average ambient concentration for that scenario.

Q. Do you know if that takes into account the production limits that are in the permit?

A. Yeah. I gave you my answer. I don't think -- I don't think DEQ would explain it to me in any other way.

Q. And you had mentioned earlier, when we asked you about being a toxicologist, you said you're not a toxicologist, but that sometimes you rely -- you know when you need to bring a

toxicologist in; is that right?

A. Yes.

Q. Okay. Do you have toxicologists that are on staff with you?

A. Yes.

Q. And where are you employed?

A. I have a nonprofit and I have a toxicologist associated with us.

Q. Okay. And why isn't your toxicologist here today?

A. We don't think the testimony needs to extend to there. We could bring him in if you want.

Q. You don't believe that --

A. I can give you his qualifications if you'd like.

Q. You don't believe that your report requires analysis by a toxicologist; is that fair?

A. I have consulted with a toxicologist about my report, yes.

Q. But you don't need a toxicologist to be able to explain your report; is that fair?

A. Yes.

Q. Okay. And by "report," I mean your declaration in Exhibit 302, right?

A. Do I need a toxicologist for this? I don't think so, no.
Q. Okay. Did you say that your wife was on the board for the Idaho Conservation League?
A. Yes.
Q. Okay. Do you know how long she's been on the board for the Idaho Conservation League?
A. Nine years. She's not now. It was earlier. But she served a nine-year term.
Q. When did her term expire?
A. She's over there.
Q. Do you know?
A. Probably three years ago?
Q. Okay. And your Clean Air Act experience, that was back in the 1970s and 1980s; is that right?
A. No.
Q. When you said you worked on the Clean Air Act --
A. I've worked on the Clean Air Act through 2016.
Q. When you worked on the Clean Air Act in northern Idaho, that was in the 1970s and 1980s?
A. I was employed by DEQ to implement the Clean Air Act in those times. The Clean Air Act

comes up in almost every risk assessment I've done for the last 35, 40 years.

Q. And after that, you spent the majority of your career working on the Superfund site?

A. Yes.

Q. Based on your scientific expertise, do you believe that the duration of exposure to any carcinogen will affect the risk that's posed by that carcinogen?

A. Oh, yes.

Q. Can we take a look at your expert report in Exhibit Figure -- I said "report." I'm sorry -- your expert declaration, Exhibit 302. And I'm at Figure 1 on page 11.

And I think when you were explaining this, you said you could use it as years, but you like to use it in ages because it helps you understand the effect of the carcinogen on certain age groups; is that right?

A. Yeah. Yeah, I said it's a perspective. You take the perspective of the receptor or the perspective of the emitter, and what we care about is age.

Q. Okay. And I want to make sure I understand this figure correctly.

What is the dark blue line, the one that goes diagonally?

A. That is the risk that accumulates each year if you implement the TAPs correctly.

Q. So if I take year 1 plus 2, I'll get to year 3; is that right?

A. Almost all the testimony we've heard today is 1 and 2 equals 3, yeah.

Q. When you nod, it doesn't reflect on the record, so is that a yes?

A. Do that math for me again.

Q. Yeah.

A. 1 and 1 was 3?

Q. If I take year 1 plus year 2, that gives me the line at year 3 because it's the cumulative effect; is that right?

A. Yeah. 1 plus 1 is 2 --

Q. And 2 plus 1 is 3?

A. -- the next one would be 3, yeah.

Q. Okay. So I'm just making sure that I'm understanding what that blue line is.

So if I take the dosage in year 1, and I add the dosage in year 2, I will get to the total dosage that you've been exposed to by year 3; is that right?

A. Yeah.
Q. Are there --
A. You would get the dose that you've been exposed to by the end of year 2.
Q. Okay. So I'm just trying to say that the exposure, the more you're exposed -- the longer you're exposed to the carcinogen, the greater the risk; is that right?
A. Yes. It accumulates.
Q. So if you go -- if we go from year 1 to year 2, and we add how much you're exposed to in year 1, we add it to how much you're exposed to in year 2, then we keep tracking up that line; is that right?
A. That's right.
Q. And so if the total production limit life of mine is 16 years, we can see where that would be if we track that line for 16 years or age 16; is that right?
A. Yes. Yes.
Q. If there's no more emittance from the project, and therefore no more exposure, there's nothing to add to it for the following year, is there?
A. No.

Q. Okay. So then we would just -- we would just stop at year 16 and say that's how much you've been exposed to based on that -- those years of exposure; is that right?

A. That's right.

Q. Okay. I think you said this earlier, but I just want to make sure the record is clear.

You did say that the word "margin of safety" is nowhere in any of the rules under the T-RACT rules; is that right?

A. Yes, that's my term to help explain this.

Q. Okay. That's something that you believe should be added above and beyond to make sure that we're protecting the population at whole?

A. Yes. That's -- that's the key to why TAPs is health-protective, because there is this margin of safety to accommodate all the things that you don't address in risk assessment.

Q. And I wrote in my notes that you said, "We really need that margin of safety in this state if we're going to stay incremental."

Is that right?

A. Yes.

Q. And so you feel passionately about that

that's something that should be factored in, even though it's nowhere in the rules?

A. What factored in?

Q. The margin of safety.

A. It's inherent in the rules. It's not factored in. It's inherent.

Q. When you say "inherent," meaning it's already built into the AACCs?

A. Yes.

Q. Okay. I think you said this earlier too, but you agree that under the EPA, the EPA does not consider arsenic to have a mutagenic mode of action; is that right?

A. EPA does not list arsenic as a mutagenic in IRIS. The EPA says it does -- that the mode of action is not clearly understood and that there is evidence that arsenic does act as a mutagenic in concert with other factors and other carcinogens. So they leave the option to the risk assessors, in this case to the states, to decide whether they should treat it as a mutagenic or not.

Q. It's fair --

A. Some states treat it as a mutagenic, others don't.

Q. It's fair to say you believe it should

be treated as a mutagenic --

A. Oh, yes.

Q. Let me make sure my question is on the record.

It's fair to say that you believe arsenic should be treated as having a mutagenic mode of action; is that right?

A. Yeah. No, that's not right, but there's a big caveat.

Q. Okay.

A. And it has to do with an understanding of arsenic exposure. It takes a little while to explain. I don't want to burn up your time. But with these metals and metalloids that are emitted from mining operations, there's a significant risk associated with the airborne exposures.

That risk is often more from the dust that accumulates around the sites, and the children, particularly, consume that dust. And their total burden of the metals is a combination of what they breathe and what they eat, and they eat a lot when they're young because they get all this stuff on their hands, they put them in their mouths, and if you were to do a real legitimate risk assessment here, you would analyze the effect

of the deposited dust as well as what's inhaled.

And when you do that, you will find out that most often, if not almost all the time, the amount of arsenic that is ingested becomes the risk driver in a risk assessment.

Q. Do the --

A. It's not what's inhaled. Inhaled is bad enough on its own, and that's everything we've talked about today, is only the inhalation rate.

But for children, it would be oral cancers and noncarcinogenic effects that would drive -- would probably be the risk driver for this facility if you really did a legitimate risk assessment.

Q. It's fair to say that ingesting --

A. I need to add to that.

Q. Oh, sorry.

A. So when you do those analyses, there are very significant age-specific intake factors. So you end up doing very much the same thing that's required for a mutagenic, is you multiply the effects of younger ages to account for the potential of oral and noncarcinogenic risks.

Q. And I think when you talked about this earlier, you referenced a 2005 report that talks

about the ingestion --

A. A 2005 report, yes.

Q. And it suggests that there's a difference between the risk associated with ingesting arsenic as opposed to just the inhalation risk; is that right?

A. There's additional risk, yes. Sometimes it's more significant than the inhalation. But it's due to the same material that passed through the air.

For example, the lead standard, which I was involved in, it's not an inhalation standard. It's an air standard. But it's not about inhalation. It's about the total effect of lead that comes through the air, and they regulate the amount of lead that's in the air as a result of all of the exposure pathways.

No difference with arsenic. Exactly the same if you're going to do an arsenic -- a true arsenic risk assessment. That's like the State of Washington would require if they were evaluating what was being done here.

Q. And in the two decades since that 2005 report, EPA has never updated any of its tables to suggest that arsenic should be characterized as

having a mutagenic mode of action; is that correct?

A. No, this is one of the most controversial things going on in EPA. Everybody yells at them they should have done it 10, 12 years ago, and they're reluctant to do it.

Q. I understand that that's where you think they should go. I just need you to answer the question that I've asked, which is: In the two decades since that report, EPA has not characterized arsenic as having a mutagenic mode of action; is that right?

A. No, they don't list it in IRIS as a mutagenic. They recommend that you take a hard look at whether to do age-specific risk adjustments, though. In fact, you wouldn't do an arsenic evaluation without doing age-specific --

Q. Do the --

A. -- risk.

Q. Are you done? Sorry.

A. You would not responsibly conduct a comprehensive arsenic evaluation when it's airborne dust that doesn't include those age-specific adjustments to the risk.

Q. Do the URFs take into account sub-susceptible population groups, like children

and pregnant women?

A. Every cancer.

Q. And that would include those sub-susceptible groups, like children and pregnant women as well; is that right?

A. Yes. But they're averaged over 70 years, and if you're going to start breaking up in -- that 70-year line into segments, EPA is pretty specific about you need to do life-stage evaluations.

Q. And you --

A. You only apply that if you're looking at a 70-year. If you're going to break it into the 16/70 type stuff, you gotta look at the age-specific stages. That's what's so distressing about this. That's the dumping everything in a 7-year old. That's not right. That's wrong.

Q. Throughout your report, you use the -- you bold the term repeatedly "maximum one-year annual average ambient air carcinogen concentration."

A. Yes.

Q. What's that quote from?

A. That's how you should interpret 586, which says "annual averages."

Q. Is that language in 586?
A. No.
MS. HANCOCK: That's all I have. Thank you.
THE HEARING OFFICER: Okay. Anything else for the current witness?
MS. THROWER: I have just a couple questions.
THE HEARING OFFICER: Okay.
MS. THROWER: I think, Ms. Young, you said you ceded your time to Ms. Hancock, right? You don't have any?
MS. YOUNG: I don't have any additional questions, no.
MS. THROWER: Okay.

REDIRECT EXAMINATION OF IAN VON LINDERN

BY MS. THROWER:

Q. Dr. von Lindern, Ms. Hancock referred to hundreds of permit conditions in this permit, correct?
A. Yes.
Q. Have we been talking about hundreds of permit conditions in the last two days?
A. We've talked about three, four, five. I've read the permit completely probably five times. Three times it's been submitted in earlier

versions that got sent back. There's a lot of permit conditions in there.

Q. But --

A. Not as many as in Nevada. Their permits for these facilities are, like, this thick as opposed to Idaho, but...

Q. But a majority --

A. But I don't know how many. I've never counted them up.

Q. But a majority in the permit, the ones that we haven't been talking about in the last two days, don't impact your calculations of the maximum -- your estimated maximum annual average or your WEP/non-WEP averaging calculations?

A. No. My assumption on these is that we were reviewing the permit. That's what we were doing. We were reviewing the PTC. I don't think it's -- I didn't understand and I couldn't get from the statement of basis how this was done. I sat down with DEQ and they explained it to me. I hope they were explaining the permit to me.

MS. THROWER: Okay. Thank you. I have no further questions.

THE HEARING OFFICER: Okay. Anything else for this witness?

Okay. Thank you.

THE WITNESS: Thank you.

THE HEARING OFFICER: So that concludes the petitioners' case, correct?

MS. THROWER: That's correct.

THE HEARING OFFICER: Okay. So I believe there's going to be some redirect from Perpetua and/or DEQ?

MS. HANCOCK: Yes. We'll have Theresa Lopez.

THE HEARING OFFICER: Okay. Do you want to go right into it?

MS. HANCOCK: I think so.

THE HEARING OFFICER: Okay.

MS. HANCOCK: Maybe just, like, a couple-minute transition?

THE HEARING OFFICER: Okay. We'll go off the record.

(A recess was taken from 4:08 p.m. to 4:19 p.m.)

THE HEARING OFFICER: We'll go back on the record.

We're doing redirect of Mr. Lewis, correct?

MS. HANCOCK: We're putting on a rebuttal to --

THE HEARING OFFICER: Okay. Sorry I used the wrong term.

MS. HANCOCK: -- the petitioners' testimony.

THE HEARING OFFICER: I understand that because he was sworn in earlier today, that carries forward. We don't need to re-swear him. So you may proceed.

MS. HANCOCK: Thank you.

EXAMINATION OF KEVIN LEWIS

BY MS. HANCOCK:

Q. Good afternoon, Mr. Lewis.

You were here when we sat through Dr. von Lindern's testimony; is that right?

A. Yes.

Q. And we were looking at his Exhibit 302.

MS. HANCOCK: Mr. Foster, if you would pull that up.

Q. (BY MS. HANCOCK) And I'm on page 30 of that report, which is the Figure 6.

Have you had a chance to listen to Dr. von Lindern's testimony and to analyze what he had written in his declaration for calculating what he has modeled in Figure 6?

A. Yes, I have.

Q. And do you have any thoughts on that?
A. Yes, I do.
Q. What are they?
A. Okay. So I guess I'll walk through these bars, but I'll just go to the end of the discussion.
I do agree with the orange line. That represents the T-RACT 1-in-100,000 risk. And I also agree with the last bar, which is the -- which represents the excess cancer risk probability from the project when you take into account all the permit conditions.
Q. And that's where it's labeled as "16/70"; is that right?
A. Yes. That's the same results that DEQ came up with, the same results that I came up with.
Q. And it appears that Dr. von Lindern came up with those results as well.
If you apply the same methodology, it's approximately 41 percent of the 1 in 100,000 T-RACT; is that right?
A. That's correct.
Q. Okay.
A. So one more big-picture item. The other three bars, you know, starting with the first,

second, and third bars, there's an issue with those because those bars are based on an annual average of one year, and they haven't been -- they're the contaminant concentration. They haven't been adjusted to the 70-year lifetime, the form of the increment. So it's a little off to have them on here when you're comparing them to the orange line.

But that's a big-picture statement. Let me just go through those bars one at a time.

So the first one is labeled "Max." And there's a problem with this one. It just has an erroneous calculation. And after listening to the testimony, I was -- I suspected this was the case, but I confirmed it after listening to Dr. von Lindern's testimony.

In his testimony, he takes us to Figure 3 from the TAP report. I believe it's Exhibit F in his --

Q. Just one second.

MS. HANCOCK: Mr. Foster, can we go to page 596 of 792? And then if you have the record number that we can -- 596, yeah. If you have the record number by chance. 6695.

THE WITNESS: Let's start at the top, if I may.

Q. (BY MS. HANCOCK) Yeah, he was just grabbing the record number.

A. So this is one of the pages out of the TAP report that we submitted at the request of DEQ, and just to give you a little context, the green bars represent a potential analysis and the 14 scenarios that we modeled, 14 worst-case scenarios.

The blue bars are the actual emission. So we've got potential emissions in the green bars and we've got actual emissions with the blue bars. What I mean by "actual emissions" are the predicted actual emissions of the mine. You don't permit on actual emissions. You permit it on, you know, maximum potential emissions.

But just as a data point, if you will, one of the analysis that DEQ wanted us to perform was, okay, before we get too far into this, let's just get a benchmark, you know, what's going to be the actual impact from this source, and there's -- you know, there's 16 blue bars, and that represents the 16 years of operation.

So I'm going to go back to the green bars. I think, Dr. von Lindern -- well, he said as much, so I guess I know at this point. I think he assumed that those green bars, instead of different

modeling scenarios, they represented different years of operation. When we were talking about this, he was talking about the five-year rolling average.

And you can see, those bars -- if you were to average any one of these five bars, then that highest bar that's labeled "0.232 pounds per hour of arsenic," you wouldn't -- you would assume that that wasn't modeled, and maybe some average, you know, five-bar average, I'll say, was modeled instead, and that's where the 1.8 factor comes from.

In fact, the -- each one of these bars was modeled as a -- one of the operating scenarios, and the bar that says "0.232" was that emission rate. That maximum emission rate was also modeled.

Q. So if we go back to page 11 -- I'm sorry, back to page 30.

A. That's Figure 1. So six more down. Oh, Wade's doing this, sorry.

Yeah, so we just have to disregard the first bar. It's erroneous.

The next two bars, I'll just say quickly, those are -- those numbers, I recognize. I think it was Exhibit 304. These are numbers that

come out of the model. But you have to understand that, you know, for instance, this bar number 2 labeled "Five Year," that does not take into account the T-RACT permit conditions. It doesn't take into account the permit condition that limits the West End Pit to 50 percent production. It doesn't take into the -- it doesn't take into consideration the lifetime limit.

So in effect, it just assumes that you have a hundred percent of production going through the West End Pit for 365 days a year for 70 years in a row.

The next bar is similar. That one, again, though, is --

Q. When you say "the next bar," the one that's labeled "non-WEP"?

A. Yeah. Yeah. Thank you.

The non-WEP bar is -- this assumes that you have a hundred percent production for 365 days, albeit now it's split between the West End Pit and the non-West End Pit, but occurring for 70 years. So this one also ignores the life-of-mine limits that restrict that operation and those emissions and that exposure to 16 years.

Q. In other words, that non-WEP, that

doesn't take into account the total production limit in the permit of 788.4 million tons?

A. It does not.

Q. Okay.

A. Then, you know, disclosing with the last bar, that one -- that bar is correct. It takes into account all the permit conditions, the concentration is expressed in the same form as the excess cancer risk probability rule, the lifetime cancer risk, and then it's -- and it's correctly portrayed here against the 1-in-100,000 incremental threshold.

MS. HANCOCK: Okay. Thank you so much for that, Mr. Lewis.

I have no further questions for him.

THE HEARING OFFICER: DEQ, anything?

MS. YOUNG: No.

THE HEARING OFFICER: Petitioners?

MS. THROWER: Okay. Yeah, I have a question.

EXAMINATION OF KEVIN LEWIS

BY MS. THROWER:

Q. So going back to Figure 3 in the TAP addendum that Ms. Hancock had just pulled up a

little bit, you said those bars represent different modeling scenarios, correct?

I can hand you this --

A. Yeah, can we --

MS. HANCOCK: Mr. Foster, can you pull that exhibit back up and we'll go to page 596 again.

Thank you.

Q. (BY MS. THROWER) Okay. So you said that the different bars represent different modeling scenarios.

A. The green bars represent different modeling scenarios. There's 14 of those. The blue bars represent 16 years of actual operation and actual emissions, not potential.

Q. Okay. So one single blue bar for a single operating scenario is a -- that's a compilation of 16 total years of emissions for that operating scenario?

A. Let me --

Q. I'm sorry, I --

A. -- try again.

Q. I'm not understanding.

A. The purpose of this graph was really to show, you know, how the analysis was done conservatively. You can look at the actual

emissions, that's fine. But when you're trying to do this permit analysis, when you're working towards writing a permit and making sure you comply with all applicable requirements, in this case the TAP rule, you're going to have some conservative assumptions.

And so, you know, the green bars are obviously a lot higher than the blue bars. The green bars represent 16 years of actual operations and actual predicted emissions. It hasn't been built yet, so I'm going to say actual predicted emissions.

Q. Okay. I'm sorry, can I just stop you there just to clarify?

A. Yeah.

Q. So you said the green bars are 16 years of potential emissions?

A. The blue bars are 16 years of actual predicted emissions.

Q. So each bar is all 16 years of emissions added together. So if I wanted to say -- if I wanted to go to this and I can look at the top of, you know, one of those blue bars, I could say that that is the total amount of arsenic that this project is going to emit for its entire life?

A. Each blue bar is what the -- I mean, they're expressed in pounds per hour. But each blue bar represents -- that represents a year. So the very first bar is year 1. That will be the arsenic emissions. The very last blue bar is year 16, and that will be the arsenic emissions.

Again, I don't want to distract what the blue bars, but the green bars are what we have been talking about all day.

Q. So what operating scenario is depicted here?

A. All 14 in the green bars. There's 14 of them. And, you know --

UNIDENTIFIED SPEAKER: Is it an average?

THE WITNESS: If you look at the label of the X axis, it just says, you know, "modeling scenario" and "MODPRO2." That just means actual emissions that were modeled in MODPRO2. Life of mine years. And I didn't put a number of years at the bottom because it really has two labels; one would be modeling scenario for the green bars and the blue bars would be years of operation.

Q. (BY MS. THROWER) Okay. Thank you.

A. Okay. You're welcome.

I don't know, do we -- if we go --

scroll down or do I just stop here?

MS. HANCOCK: There's no question, so you --

MS. THROWER: Yeah. No.

MS. HANCOCK: Do you have any further questions?

MS. THROWER: No, I don't. Nothing further.

Bryan, do you have any further questions?

MR. HURLBUTT: No. Thank you.

MS. HANCOCK: That's all we have for Mr. Lewis.

THE HEARING OFFICER: All right.

Okay. Thank you, Mr. Lewis.

Now, Ms. Lopez?

I understand we'll re-swear the witness since apparently her agreement yesterday doesn't carry forward today.

THERESA LOPEZ,

a witness having been first duly sworn to tell the truth, the whole truth and nothing but the truth, was examined and testified as follows:

EXAMINATION OF THERESA LOPEZ

BY MS. HANCOCK:

Q. Good afternoon, Ms. Lopez. Thank you

for coming back on the stand with us.

You had an opportunity to listen to the testimony today; is that right?

A. Yes.

Q. And in particular, the testimony from Dr. von Lindern, you heard his testimony?

A. Yes.

Q. I want to first just give you an open forum to allow you to kind of react to what you heard if you want to give us any general thoughts.

A. Sure.

I think that Dr. von Lindern's characterization of the risk assessment that both Dr. Paden and I performed was completely inaccurate and indicates that he does not understand toxicology.

Q. Can you tell me how it was inaccurate? Which aspects in particular strike you as the strongest?

(Indiscernible Zoom interruption.)

MS. HANCOCK: I'm sorry?

MR. HURLBUTT: That wasn't me. I don't know.

Q. (BY MS. HANCOCK) Go ahead.

A. Yeah. I think his assertion that

children were not considered and that this is pushing a dose down, or dose-averaging, were all incorrect. I'd like to, I guess, introduce or show everyone where the additional guidance is from the guidance documents that he read from, which, by the way, I do not disagree with.

Q. Okay. And what's the exhibit number that we marked that one?

A. 210.

Q. Okay. And can you tell us what Exhibit 210 is?

MS. HANCOCK: Mr. Foster, if you could bring that up as well, please.

THE WITNESS: Yes. This is additional guidance from U.S. EPA. It's called the Regional Screening Levels - User's Guide. This is where EPA calculates risk-based concentrations using their IURs, which in Idaho are called URFs.

Q. (BY MS. HANCOCK) What do you use this document for?

A. This provides risk-based screening levels that are based on the exposure duration of a potential receptor, in this case the assumed residential. They also assume industrial and they give you a different set of numbers. And they use

the lifetime in each of these calculations for carcinogens.

Q. Okay. Meaning this is what helps you understand what's all packed into those numbers?

A. Yes, it does.

Q. Okay. And then where would we go in this document to look at the guidance that you're -- is most relevant for your testimony today?

A. I think the first place to go would be page -- I'm sorry, it doesn't have a page number, but it's Section 5.17.

Q. If you just give everybody a second to get to that section.

A. It's way at the end of the document --

THE HEARING OFFICER: There's a document this long without page numbers.

MS. HANCOCK: It has less than a third left to the back.

THE HEARING OFFICER: What was the section again? Sorry.

MS. HANCOCK: 5.17.

THE WITNESS: It's the last page before all the charts.

MS. HANCOCK: The last page before all the

charts.

THE HEARING OFFICER: I'll just look at it on the screen. No, wait. I got it. Yep.

MS. HANCOCK: 5.17.

THE WITNESS: Okay. I'll just read directly from it and everyone can see it on the screen.

Q. (BY MS. HANCOCK) If you can read slowly, just remembering that there's a court reporter taking it down.

A. Sure.

Some of the cancer-causing analytes in this tool operate by a mutagenic mode of action for carcinogenesis. There is reason to surmise that some chemicals with a mutagenic mode of action, which would be expected to cause irreversible damage to DNA, would exhibit a greater effect in early-life versus later-life exposure. Cancer risk to children in the context of the U.S. Environmental Protection Agency's cancer guidelines -- and then there's a citation -- includes both early-life exposures that may result in the occurrence of cancer during childhood and early-life exposures that may contribute to cancers later in life. In keeping with this guidance, separate cancer risk equations are presented for

mutagenics.

I'm not going to read the rest of it because everyone can. But if you turn to the next page, scroll down a little bit, it says: The below table lists the chemicals considered to be carcinogenic by mutagenic mode of action for the purposes of the RSLs. Also provided in the table is a link as to why.

This table includes all of the chemicals that EPA considers to have a mutagenic mode of action, thereby requiring an age and life-stage adjustment factor, and arsenic is not in this list.

Q. So I think one of the gaps that we have in our kind of storytelling here is: Can you make the connection between that sensitive subpopulation group and mutagenic modes of action in chemicals, why do we keep asking about this and why is this important for this proceeding?

A. Dr. von Lindern implied in his statements that this was somehow overlooked or not considered, and that is a failure of the risk assessment that Dr. Paden and I performed separately.

It is not. It is not how arsenic is considered by EPA, and it is not required to adjust

for this. I understand he has a policy preference that he would like it to be for every chemical, but it is not scientifically justified, and that is what EPA has decided. They have provided their list of chemicals for which this adjustment must be done. And if said adjustment were to be done, you can page up -- again, I'm sorry there's no page numbers -- to Section 4.1.3.3.

MS. HANCOCK: Okay. Give us one second to get there.

THE HEARING OFFICER: To clarify, I wasn't blaming anybody in the room for the lack of page numbers.

Q. (BY MS. HANCOCK) 4.1.3.3?

A. Uh-huh. It's in the top there of the document.

MS. HANCOCK: Yes. He searched for it.

THE WITNESS: If one were to include this in a risk assessment, as required by that list of mutagens, you can see that the adjustment factor comes in to the exposure duration, which is, in this case, in the denominator of the equation.

Q. (BY MS. HANCOCK) Tell me what that means in layman's terms.

A. What that means is two things: That if

it was required, we would have done it; and secondly, that exposure duration and lifetime that you can see in the top in the numerator of this equation are always considered in a risk assessment.

Q. Okay. So if this was -- if arsenic had a mutagenic mode of action, you would have performed an additional calculation?

A. Yes.

Q. And if you would have performed this additional calculation, you still would have taken into account an exposure duration?

A. Yes.

Q. But because it doesn't have a mutagenic mode of action, which means you don't have to take the additional calculation steps to account for those sensitive subpopulation groups because it's already factored into the URF, you didn't do this additional calculation; is that right?

A. The sensitive subpopulations are included in the IUR. This is an additional step that's required for mutagenic mode of action carcinogens to account for the early life-stage exposures. That is not required for arsenic.

Q. Are there any other aspects of Dr. von

Lindern's testimony that you'd like to address today?

A. Yes.

Dr. von Lindern spent a lot of time discussing how his risk assessment and toxicological training or experience came from his work on a Superfund site that was focused on lead.

I would -- again, in this same document, if you went to Section 5.2, titled "Lead."

Q. Okay. One moment.

A. I'd like to point out that lead is not handled the same as any other chemical that EPA assesses by risk assessment. The statement from EPA is that: EPA has no consensus on RFD or SFO for inorganic lead, so it is not possible to calculate SLs using the same methodology used for other chemicals. EPA considers lead to be a special case because of the difficulty in identifying a level of exposure or dose below which adverse effects are unlikely, which is needed to develop an RfD.

And just to clarify, an RfD is a reference dose, and it refers to noncarcinogenic effects.

Q. Any other specific elements of his

testimony that you'd like to address?

A. Dr. von Lindern's assertions that somehow the five-year rolling average does not account for the correct exposure is also troubling.

If a one-year exposure is to be used to compare to the AACC, he's ignoring the fact that there's still a 70-year lifetime that needs to be accounted for in that one-year average.

So if you picked an average concentration of .00416 micrograms per cubic meter, which is the one that we've all been talking about, and you wanted to correctly compare it to the AACC, the correct equation would be to divide it by 70 to account for lifetime of exposure and then compare it to the AACC.

Q. And we heard his testimony when we were looking at his Figure 1 where he admitted that his Figure 1 and a cumulative risk grows with the number of years of exposure.

Do you recall him testifying about that?

A. Yes. We could bring his figure back up. I think the diagonal line discussion --

Q. It's on page 11 of his report.

A. Since arsenic is not a carcinogen that has a mutagenic mode of action, that's why that

line is diagonal. If it were a mutagenic mode of action, the beginning of that line would be far more steep, and then it would become more diagonal up to the corner starting after age 16.

Q. Because at that point --

A. At that point they don't adjust for life-stage exposures anymore. That is done in the exposure duration, and as Dr. von Lindern testified, this is the correct application and the correct reflection of the IUR that includes sensitive subpopulations.

Q. And so if this is the correct modeling of it, with the orange line being the 1-in-100,000 T-RACT risk, and as he testified, we can go to what is noted on here as "CR age 16," and that's tracking the risk exposure based on the emission levels in Perpetua's permit, where would the line go after that based on Perpetua's permit?

A. I believe he's modeling .0023, the AACC, but in either case, at 16 years of exposure, the line becomes completely horizontal and runs off the edge of the diagram.

Q. Meaning it wouldn't continue to increase because there would be no additional exposure amount after those 16 years?

A. Correct.

Q. Throughout Dr. von Lindern's report, he had bolded a sentence or a portion of a sentence that said: Maximum one-year annual average ambient air carcinogen concentration.

He very genuinely admitted that that language does not come from any of the rules, but that's how he would interpret it.

Do you believe that that is a correct interpretation of the rules as you've read them?

A. No. That's his interpretation of the rules.

Q. What would be concerning about the way in which he uses the "maximum one-year annual average ambient air carcinogen concentration"?

A. By continuing to state that he's denying the existence of a numerator in this equation -- I'm sorry, of a denominator in this equation, which is a 70-year lifetime.

Q. Anything further you'd like to add?

A. No.

MS. HANCOCK: Okay. That's all I have. Thank you.

THE HEARING OFFICER: Okay. Thank you.

Petitioners?

MS. THROWER: No, I don't have anything.
Bryan?
MR. HURLBUTT: No, I don't have anything. Thank you.
THE HEARING OFFICER: Okay.
Anything else -- or thank you, Ms. Lopez. Sorry.
MS. HANCOCK: Thank you so much, Ms. Lopez.
THE HEARING OFFICER: Petitioners, anything else that we need to talk about or discuss?
MS. THROWER: I don't think so.
THE HEARING OFFICER: Okay.
DEQ?
MS. YOUNG: No, nothing from DEQ.
THE HEARING OFFICER: Perpetua?
MS. HANCOCK: Nothing from Perpetua. Thank you.
THE HEARING OFFICER: Okay. Well, so this sounds like it concludes our hearing. As you might imagine, I'm not ready to render a decision. So the next step, as I recall, is the parties have 21 days to file their post-hearing statements, and I very much look forward to receiving those and -- yeah.
Thank you to everybody for all the

witnesses and all of the attorneys and all the hard work that went into this. This was very helpful for me. I will understand this at one point. I promise.

Thank you. We can go off the record.

(The hearing concluded at 4:49 p.m.)

* * *

REPORTER'S CERTIFICATE

STATE OF IDAHO)
) ss.
COUNTY OF ADA)

I, REBECCA MARTIN, Certified Shorthand Reporter and Notary Public in and for the State of Idaho, do hereby certify:

That said hearing was taken down by me in shorthand at the time and place therein named and thereafter reduced to text under my direction, and that the foregoing transcript contains a full, true and verbatim record of said hearing.

I further certify that I have no interest in the event of the action.

WITNESS my hand and seal this 29th day of October, 2024.



REBECCA MARTIN
RPR and Notary
Public in and for the
State of Idaho

My Commission Expires: 08-27-2030

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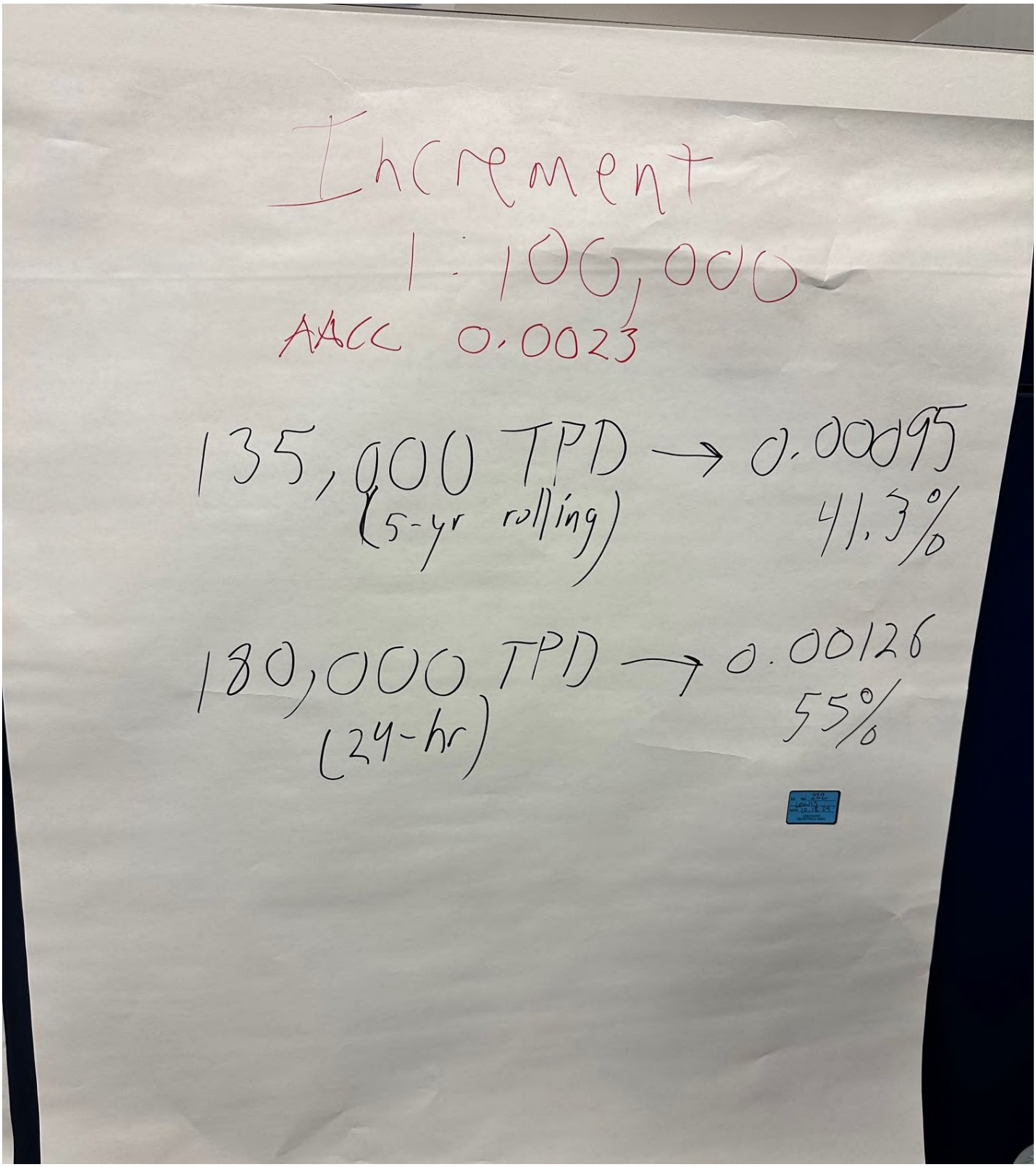
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1:100,000
AAQC 0.0023
135,000 TPD → 0.00095
(5-yr rolling)
41.3%
180,000 TPD → 0.00126
(24-hr)
55%

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BEFORE THE BOARD OF ENVIRONMENTAL QUALITY
STATE OF IDAHO

IN THE MATTER OF AIR QUALITY PERMIT TO CONSTRUCT P-2019.0047	)	Agency Case No. 0101-22-01
	)	OAH Case No. 23-245-01
NEZ PERCE TRIBE, IDAHO CONSERVATION LEAGUE, and SAVE THE SOUTH FORK SALMON	)	**EXPERT DECLARATION OF IAN H. VON LINDERN, P.E., Ph.D.**
Petitioners,	)	
v.	)	
IDAHO DEPARTMENT OF ENVIRONMENTAL QUALITY,	)	
Respondent,	)	
and	)	
PERPETUA RESOURCES IDAHO, INC.	)	
Intervenor-Respondent.	)	

EXHIBIT
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I, Ian H. von Lindern, P.E., Ph.D., hereby declare under penalty of perjury and pursuant to the law of the State of Idaho that the foregoing is true and correct:

QUALIFICATIONS

Name and Affiliation

1. My name is Ian von Lindern. I reside in Moscow, Idaho. I am a licensed Professional Engineer in Chemical Engineering in Idaho (License # 3044). I have practiced in the disciplines of Environmental Engineering and Risk Assessment in Idaho for the last 50 years. I was President and Principal Scientist for TerraGraphics Environmental Engineering with offices in Moscow, Kellogg, and Boise, Idaho for 30 years, retiring in 2016. TerraGraphics was the Idaho Department of Environmental Quality's (DEQ) prime consultant for the Bunker Hill Superfund Site (BHSF) and I was Project Manager and lead risk assessor for both the BHSF and the Coeur d'Alene Basin Superfund Sites from 1984 to 2014.

2. Since retiring from the consulting business, I co-founded the non-profit humanitarian organization TerraGraphics International Foundation (TIFO) and have continued to work in mining-related health and safety issues in low-income countries. TIFO's mission is to assist mining and mineral processing communities to operate as safely as practicable while maintaining essential economic activities. In that regard, we support scientifically sound and transparent analyses of the environmental and human health issues faced by mining communities, and the development of local solutions implemented within community socio-economic and cultural capabilities. Under my direction in the last ten years, TIFO has conducted and completed site characterization, risk assessment, and risk mitigation projects in

Russia, China, Peru, Dominican Republic, Senegal, Nigeria, Kyrgyzstan, Uzbekistan, and the Duck Valley Shoshone Paiute Reservation in Idaho and Nevada.

Education and Experience

3. I hold a B.S. degree in Chemical Engineering from Carnegie-Mellon University, Pittsburgh, Pennsylvania and Masters and Ph.D. degrees in Environmental Science and Engineering from Yale University, New Haven Connecticut, specializing in air pollution and public health. I have served on numerous advisory committees and the U.S. Environmental Protection Agency's (EPA) Science Advisory Board and Clean Air Science Advisory Committee on several occasions from 1975 to 2018, advising on topics relating to exposure and risk assessment in childhood heavy metal poisoning. During that tenure, I directed more than 30 major environmental health investigations at mining and smelting sites, both nationally and internationally. A current C.V. is attached.[1]

Relevant Projects and Assignments

4. I was the Regional Environmental Engineer for DEQ's predecessor agencies in both the Coeur d'Alene and Twin Falls offices. In that capacity, I processed air quality permits for the Agency for several years at the major mining and smelting operations in the State during the 1970s, and early 1980s, including the Bunker Hill Mining and Metallurgical Complex, the last U.S. operational antimony smelter at Big Creek, Idaho, and numerous mining operations in North and Central Idaho. I designed and directed the implementation of the Silver Valley Lead Health Study that investigated and provided emergency response to the childhood lead poisoning epidemic in the Coeur d'Alene mining district in the 1970-80s.

[1] Exhibit A.

5. I have particular experience with implementing EPA risk assessment guidance in Idaho. Beginning in 1984, DEQ's predecessor, Idaho Department of Health and Welfare-Division of Environment (IDHW-DOE) was the lead agency implementing the Risk Assessment and Cleanup Management Plan developed for the populated areas of the Bunker Hill Superfund Site (BHSS). The BHSS was the U.S. second largest Superfund site, and IDHW-DOE was among the first health/environmental agencies to implement the EPA Risk Assessment Guidance for Superfund (RAGS) in the late 1980s.

6. As Project Manager, I was responsible for developing and implementing the risk assessment/risk management protocols, and cleanup plan for the BHSS in collaboration with several State, federal, tribal, local governments, and industry. The project was monitored and collaboratively developed by several entities including EPA Regions VIII and X, the EPA National Center for Environmental Assessment (NCEA), EPA Headquarters, the Coeur d'Alene Tribe, the Panhandle Health District, and the States of Montana and Washington. I also served on a sub-committee of the EPA Science Advisory Board evaluating the consistency of heavy metals regulation across EPA Program Offices in the early 1990s.

7. Based on that experience, IDHW-DOE requested that I participate on the advisory committee regarding development of the toxic air pollutant (TAP) rules for the State. As a result, I had a diverse perspective in the development of the TAPS rules that afforded reasonable health protectiveness while relieving the regulators and industry of the burden of the risk assessment and risk management protocols evolving at the time. I continued as DEQ BHSS lead risk assessor until 2014.

8. In my most relevant recent experience, I am working with the international humanitarian organization Médecins Sans Frontières (MSF, or Doctors Without Borders) assisting the Kyrgyz Republic Ministry of Health in developing health protective strategies to reopen both mercury and antimony smelters in Batken, Kyrgyzstan. These facilities were among the largest mercury and antimony producers in the former Soviet Union and are essential to the regional economy.

9. TIFO is currently engaged with MSF, the U.S. Department of State, the Massachusetts College of Pharmacy and Health Sciences, and the Kyrgyz Ministry of Health in conducting risk assessment and risk mitigation activities in active and abandoned Kyrgyz antimony and mercury mining communities. Biological monitoring of the local populations indicates many children and reproductive aged women have arsenic and antimony blood and urine levels exceeding international norms. The principal source of metals contamination are mining-related fugitive dusts contaminating the community water, soil, air, and food sources.

10. I am the lead risk assessor for these projects and have produced several major reports in the last five years. The project is currently engaged in implementing medical, environmental, public health advocacy and educational interventions to reduce exposures and health risks. As such, I have considerable insight and experience with the issues associated with the proposed antimony-gold operation at Stibnite.

11. Over the past five years, I have monitored the development of the U.S. Forest Service Draft Environmental Impact Statement (DEIS) for the Stibnite Gold Project (SGP) and have reviewed and submitted comments regarding the several revisions of the Draft Permit to Construct (PTC) and associated support documents. As a result, I am familiar with the many

related issues, and particularly those related to contaminants of potential human health and environmental toxicity concerns.

ASSIGNMENT

12. My understanding is that the Board of Environmental Quality has remanded the PTC to the Hearing Officer for additional consideration of DEQ's analyses of ambient air arsenic and carcinogenic risk issues. The Petitioners in this case have requested that I provide an expert opinion regarding the Board of Environmental Quality conclusions and the Respondent's and Intervenor-Respondent's Declarations. I understand the purpose of my opinion is to assist the Hearing Officer regarding additional factual evidence on the ambient air concentration analysis performed by DEQ for the PTC analysis.

DOCUMENTS REVIEWED

13. For this assignment, I have reviewed the transcript of the May 1, 2024 special meeting of the Idaho Board of Environmental Quality in the matter of Air Quality Permit to Construct Issued to Perpetua Resources Idaho, Inc. (agency case number 11 0101-22-01)[2], the May 9, 2024 FINAL ORDER FROM THE BOARD, Case Docket No. 010-22-01 OAH Case No. 23-245-01 (Final Order in the Matter of Air Quality Permit to Construct P-2019.0045)[3], the subsequent May 23, 2024 Memorandum in Support of Joint Motion for Reconsideration and/or Clarification of Final Order,[4] the subsequent June 12, 2024, ORDER ON PETITIONS FOR RECONSIDERATION AND/OR CLARIFICATION OF FINAL ORDER[5], and the July 8, 2024 Scheduling Order.[6]

[2] TR 0156.
[3] REC 3695.
[4] REC 3731.
[5] REC 3835.
[6] REC 3867.

14. I have also reviewed the two DEQ Respondent Declarations and attached materials: EXPERT DECLARATION OF KEVIN SCHILLING and EXPERT DECLARATION OF NORKA E. PADEN, Ph.D., two Perpetua Intervenor-Respondent Declarations and attached materials: EXPERT DECLARATION OF KEVIN LEWIS and EXPERT DECLARATION OF THERESA LOPEZ, and the Petitioner Declaration and attached materials: DECLARATION OF WILL TIEDEMANN.

SUMMARY OF CONCLUSIONS

15. I have reviewed Idaho Board of Environmental Quality's Final Order and understand and agree with the Board's conclusions that:

a. DEQ Did Not Act Reasonably and in Accordance with Law When it Analyzed the Ambient Arsenic Air Concentrations for the SGP;

b. DEQ did not Act Reasonably in Using a Five-Year Rolling Average for T-RACT that was not Properly Supported by Permit Conditions;

c. There was Insufficient Evidence to Support the T-RACT Analysis Limiting the Non-West End Pit Production Limit; and

d. DEQ Did Not Act Reasonably and in Accordance with Law When it Applied the 16/70 Calculation to the Ambient Arsenic Air Concentration Analysis.

16. I have reviewed the transcript of the May 1, 2024 special meeting of the Idaho Board of Environmental Quality. I also concur with Vice Chair McMillan's testimony that:

> . . . DEQ has misinterpreted how the acceptable ambient concentration for carcinogens, the AACC, must be applied if it is to comply with our air quality rules.
>
> … DEQ's creation and application of a project-specific adjustment factor is not supported by Idaho's air quality rules.

> … the creation of a project-specific adjustment factor suggests that there is a significant ignorance about cancer, carcinogens, and carcinogenesis.
>
> … the short-sighted project-specific adjustment factor to the Stibnite Gold Project, DEQ created a misleading risk analysis that greatly underestimates the actual cancer risk.[7]

17. This report supports the Board of Environmental Quality's findings in the Final Order and concludes that:

a. DEQ's application of the 16/70 SGP Project-specific adjustment factor underestimates cancer risk and is inappropriate science and public health policy;

b. Ambient air arsenic concentrations and cancer risk are underestimated for the SGP by use of 5-year rolling average in the air quality modeling input factors;

c. Ambient air arsenic concentrations and cancer risk are underestimated for the SGP by improper application of the non-WEP emissions scenario;

d. The combined application the SGP 16/70, 5-year rolling average, and non-WEP Project-specific adjustment factors increase cancer risk and negate the health protectiveness of the TAPs rule; and

e. DEQ's SGP Project-specific adjustment factors represent a significant change in the regulation of carcinogenic risk in Idaho that increases both cancer risk and regulatory burden.

[7] TR 0159.

OPINIONS

A. DEQ's application of the 16/70 Project-specific adjustment factor is inappropriate science and public health policy.

18. DEQ has failed to properly implement Section 586 and T-RACT for the SGP PTC by introducing a 16/70 SGP Project-specific adjustment factor to allocate the full 70-year lifetime allowable cancer risk to the 16-year Life of Mine (LOM). The calculation averages the risk resulting from SGP emissions over the life of the receptor. This adjustment allows the SGP to emit as much as 70 years of allowable carcinogenic emissions in 16 years. This type of "adjustment factor," also known as risk amortization or cancer dose-averaging, undermines both the health protectiveness and the regulatory certainty of the TAPs rule. In the context of the existing TAPs rule, as applied the last 30 years, using the 16/70 Project-specific adjustment factor is an incorrect interpretation and represents unsound science and public health policy.

19. Specifically, DEQ misinterprets the purpose and function of the **maximum one-year annual average ambient air carcinogen concentration** in implementing the TAPs rule. It is important to review the development of the TAPs rule in understanding the strategy represented by this one-year annual standard. The Schilling Declaration asserts that the TAPs rule was developed nearly thirty years ago to accommodate DEQ's predecessor agency IDHW-DOE and the regulated communities' request to adopt rules that are: 1) are reasonably protective of public health, but still afford flexibility to facilities and projects; 2) are relatively easy to understand and implement; and 3) do not require excessive expenditure of time and resources by DEQ and the permittee during the permitting process.[8]

[8] Schilling Decl. ¶ 13.

20. I was invited by the IDHW-DOE Air Quality Bureau to engage in development of those rules at that time in an advisory committee role based on my previous experience outlined above. My recollection is that much of the IDHW-DOE's and regulated industries' initial experience with risk assessment analyses was in implementing Risk Assessment Guidance for Superfund at CERCLA sites.[9] Both IDHW-DOE and the regulated community were supportive of avoiding the onerous burden of incorporating similar risk assessment and risk management protocols into Idaho's TAPa rule. In short, after considerable effort, IDHW-DOE was successful in developing the Section 586[10] and T-RACT[11] rule with a strategy that simultaneously avoids requiring PTC applicants to submit risk assessment and risk management protocols, yet is protective of human health.

21. The resultant TAPs Section 586 and T-RACT rules are highly prescriptive. Strict adherence to the rules is requisite to simultaneously afford regulatory certainty and simplicity for the regulated community and provide health protectiveness to the public. The key aspects of the simple, yet protective, rules are: 1) the incremental nature of the rule relieves industry and DEQ of the burden of assessing multiple sources and exposures, and greatly simplifies the permitting process; and 2) a significant **margin of safety (MOS)** is provided to ensure surrounding communities are not subjected to industry-generated ambient air TAP concentrations exceeding health-based risk criteria.

22. The purpose and function of the MOS is to protect the community from those other sources and exposures, risk cofactors, and uncertainties that would otherwise be evaluated in comprehensive risk assessment and health impact analyses. The DEQ and the regulated

[9] Exhibit B. U.S. EPA, *The Risk Assessment Guidelines of 1986* (Aug. 1987).
[10] IDAPA 58.01.01.586.
[11] IDAPA 58.01.01.210.12.

community have successfully employed these TAPs rule in a productive and protective manner since the 1990s.

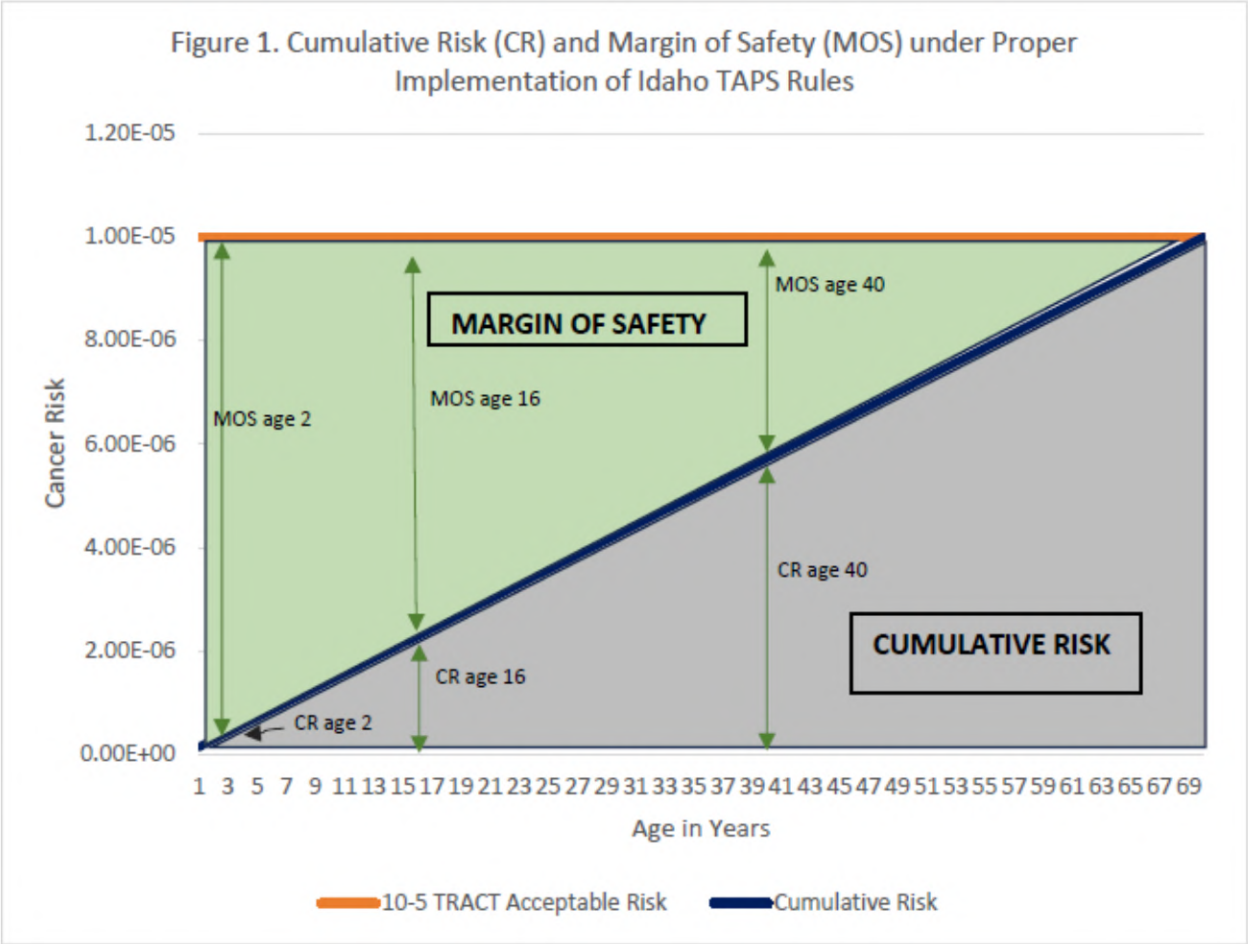
23. This prescriptive strategy specifically depends on protecting the public air space against the potential one-year annual maximum TAP emissions scenario throughout the life of the project. The one-year maximum emissions scenario is used to estimate **the maximum one-year annual average ambient air carcinogen concentration**. Ensuring that the maximum one-year annual ambient air carcinogen concentration does not exceed the acceptable ambient concentration for carcinogens (AACC) at the critical receptor location ensures that no receptor will be exposed to greater than the AACC by the incremental TAPs source for any year. The AACC is provided in Section 586 and is the ambient air concentration determined by dividing $1x10^{-5}$ lifetime risk by the Unit Risk Factor (URF). The URF is the lifetime cancer risk per 1.0 $\mu g/mg^3$ ambient air. Section 586 defines the AACC as an annual average.[12]

24. Ensuring that the criteria is achieved every year of the project guarantees the MOS will protect the individual receptors from other potential sources of the carcinogen that are not addressed in the incremental PTC analysis. Applying these criteria and MOS collectively to all individual sources assures that these health protections extend statewide.

25. Figure 1 illustrates the MOS and the cumulative lifetime risk at the critical receptor expected under the prescribed TAPS Section 586 maximum annual ambient concentration. The vertical axis is the carcinogenic risk. The horizontal axis represents the critical receptor's age commencing at the introduction of the incremental TAPs source. The

[12] *See* IDAPA 58.01.01.586 ("The AACC in this section are annual averages.").

maximum allowable lifetime risk is shown as the horizontal line at the top of the Figure ($1x10^{-5}$ T-RACT risk in this example).



26. If the TAPs rule is properly implemented, the cumulative incremental risk is shown by the diagonal line proceeding from birth to age 70 years (i.e., risk is allowed to accumulate at an annual rate of $(1x10^{-5})/70$ per year, or (AACC*URF/70) under T-RACT. The gray area below the diagonal line represents the portion of allowable lifetime risk accumulating from the incremental source. Risk increases proportional to the receptor age and the individual will have received the full allowable lifetime T-RACT exposure, and have a 10^{-5} carcinogenic risk burden at age 70-years.

27. The green area above the diagonal line represents the margin of safety (MOS) for the receptor to accommodate other contaminant exposures, risk cofactors, or uncertainties that might increase cancer risk from sources other than the incremental emissions regulated under TAPs Section 586 and T-RACT. Specifically, the large MOS safely accommodates those risk considerations that would otherwise be addressed in onerous risk and health assessment protocols. In this manner Idaho's TAPs compliance strategy purposefully, but safely, avoids requiring risk analyses.

28. The strategy also extends maximum protection to those population sub-groups most sensitive to carcinogenesis. Important life-stages of the receptor are indicated by the vertical lines at ages 0-2 years for infants and toddlers, ages 3-16 for children and adolescents, ages 17- 40 for reproductive-aged women and the fetus, and ages 41-70 years for older adults. This Idaho TAPs rule strategy affords minimal cumulative risk and maximal MOS protection during early life stages and pregnancy, acceptable risk levels during most of adulthood, with lesser protection at advanced ages when incremental cancer risk has limited effect on lifetime cumulative risk.

29. In the case of arsenic under the T-RACT criteria, the allowed annual rate of risk accumulation is a direct function of the .0023µg/m^3 T-RACT AACC multiplied by URL/70. As a result, contrary to Respondents' assertions, the AACC functions as an annual standard as historically applied in the TAPs rule. DEQ's and Perpetua's Declarations contend the Section 586 comparison of average annual ambient air arsenic concentration should utilize the average 70-year concentration, as opposed to basing health protectiveness on the worst-case **maximum one-year annual average ambient air carcinogen concentration** that is the foundation of the

MOS. Using the 70-year basis proposed by DEQ and Perpetua allows Perpetua to emit a lifetime of allowable emissions in 16 years, and undermines the health protectiveness of the rule and increases cancer risk.

30. The origin of DEQ's policy change can be found in the Lewis and Schilling Declarations. The initial Draft PTC offered by DEQ for public review exempted 99% of proposed allowable arsenic emissions from regulation and TAPs compliance because mining fugitive dust was not considered. Following subsequent public hearing testimony, DEQ required that Perpetua consider haul road dust arsenic emission under Section 586 TAPs rule.[13] As Schilling asserts, when subsequently required to consider the massive arsenic emissions, Perpetua informed DEQ that compliance with either the 10^{-6} AACC or the 10^{-5} T-RACT AACC limits were not achievable.[14] Any calculations or analyses to support these conclusions have never been disclosed.

31. According to Schilling, DEQ then suggested the ad hoc SGP 16/70 Project-specific adjustment factor, or dose-averaging approach, to avoid the annual one-year average constraints of the TAPs rule.

> Rather than revise the analytical approach to provide a less conservative assessment of impacts, I proposed that compliance with carcinogenic TAP increments could be based on cumulative cancer risk of the limited-duration project rather than the worst-case annual impact for a project of limited duration.[15]

32. The SGP 16/70 Project-specific Adjustment Factor was introduced in the TAPs Modeling Addendum, Section 4.3 AACC Adjustment for the Operational Life of the Mine.

[13] Lewis Decl. ¶ 18.
[14] Schilling Decl. ¶ 22.
[15] Schilling Decl. ¶ 22.

> [Perpetua] indicated the maximum life-of-mine will be 16 years. Life-time exposures to carcinogenic TAPs were refined by multiplying the maximum modeled annual impact by a ratio of 16/70.[16]

33. In defending this policy change, Schilling asserts that DEQ's position that the short-term factor of 10 applied to the allowable AACC when a project will have a duration of less than 5 years, shows that an adjustment in the exposure concentration is appropriate.[17] He further asserts that:

> . . . DEQ determined it would not be appropriate to subject individuals to a lifetime allowable cancer risk within a duration of less than 5 years. Therefore, the adjustment was capped at 10, rather than using a higher value or values calculated from exposure durations of 5 years of less (e.g., 70 years/5 years = 14 or 70 years/2 years = 35). These short-term projects were most commonly remediation and pilot-scale projects having a duration of up to several years.[18]

34. Schilling refers to IDHW-DOE's explicit 1992 interpretation,[19] also noted by Lopez,[20] that:

> For short term sources (usually less than five years in duration), such as remediation projects, a probability of greater than one in a million risk (over 70 years) will generally be acceptable to account for the decreased term of exposure. It is not acceptable however, for exposed individuals to receive a full 70-year exposure during the life of a short-term project. (Idaho DEQ 1992).[21]

35. In my opinion, nothing in the 1992 IDHW-DOE document suggests that an "adjustment factor" can be applied to any project with a life greater than 5 years, as the Schilling and Lopez Declarations imply is the modified DEQ policy. I am not aware of any quantitative

[16] REC 0698.
[17] Schilling Decl. ¶ 19.
[18] Schilling Decl. ¶ 19.
[19] Schilling Decl. ¶ 19.
[20] Lopez Decl., Memo. in Supp. of Decl. at 11.
[21] REC 3780.

"adjustment factor" connection between the 5-year project lifetime and the 70-year lifetime cancer risk basis. I believe that it is more accurate to describe the short-term factor of 10 as reflecting the order of magnitude increase in allowable risk from 10^{-6} to 10^{-5} criteria. This order-of-magnitude relief in allowable risk levels is commonly justified in cancer risk mitigation protocols throughout State and federal jurisdictions in various programs for various reasons, such as the Washington State protocols.[22]

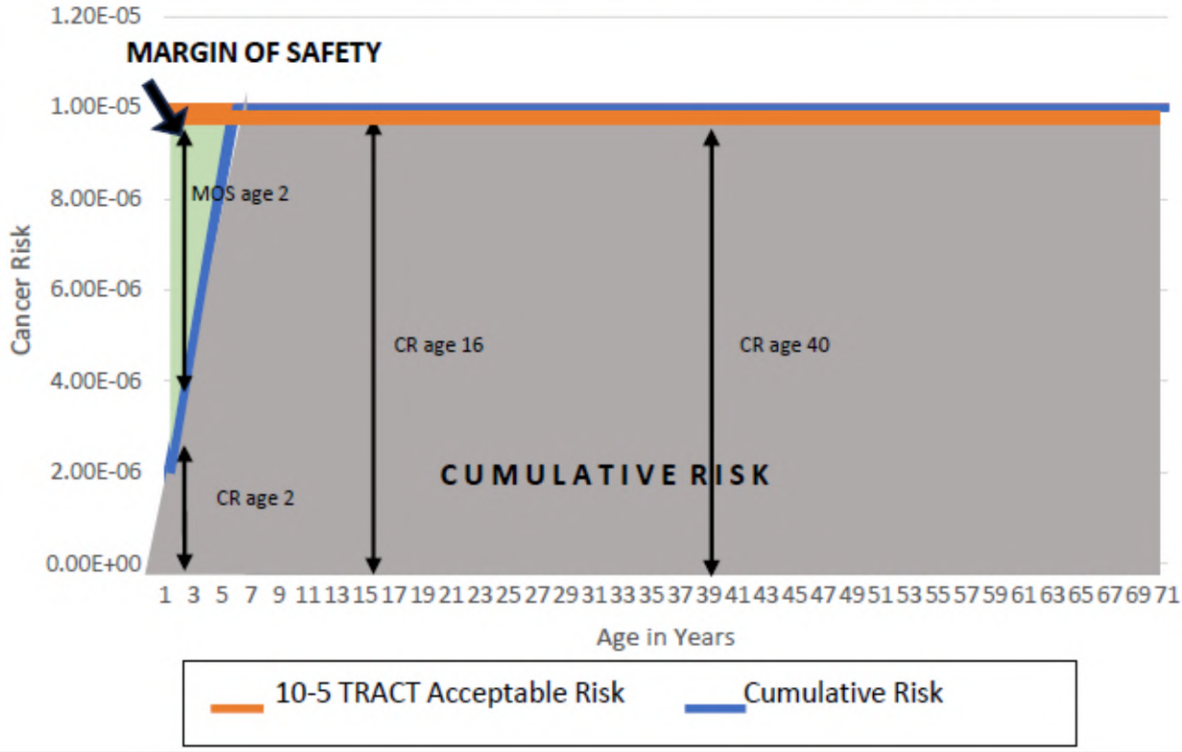
36. According to Schilling and Lopez, DEQ's modified policy implies that the SGP Project-specific adjustment factor can be applied to any carcinogenic source with a duration greater than five years. This shortsighted conclusion is incorrect, unprecedented, and not supported by EPA guidelines. The new policy is poor science and undermines the health protective strategy of regulating TAPs that has successfully been applied for the last thirty years.

37. Consider the extreme case of DEQ permitting a six-year (>5 yr.) life facility to emit sufficient carcinogens to expose individuals to the full 70-year lifetime acceptable risk in six years. The alleged allowable maximum annual ambient concentration would be 70/6 = 11.7 times the AACC, (or 117 times the AACC if T-RACT applied, (i.e. 1.17×10^{-4} cancer risk if applied for 70 years). DEQ's misinterpretation would allow emissions and consequent exposures of more than two orders of magnitude greater risk than the AACC (1.2×10^{-4} equivalent risk) for six years. At year 7 (or 10% of the receptor's assumed lifetime), the six-year-old child will have accumulated, and carry the lifetime burden, of a one-in-one hundred thousand cancer risk (10^{-5}). This risk burden will accompany the individual for the following six decades (> 90%) of the receptor's expected lifetime.

[22] Exhibit C. Washington State Department of Ecology, *Guidance Document First, Second, and Third Tier Review of Toxic Air Pollution Sources (Chapter 173-460 WAC)* (2010).

38. The effect of this dangerous scenario is illustrated in Figure 2. The MOS afforded this childhood receptor occurs briefly in the first six years of life. For the remainder of the receptor's lifetime, any additional arsenic exposure, from any source at any time, would immediately cause the cumulative lifetime exposure to exceed the unacceptable $>10^{-5}$ risk. The receptor would be challenged to avoid any additional arsenic exposures for the remainder of life.

Figure 2. Cumulative Risk (CR) and Margin of Safety (MOS) using the Project-specific (6/70) Adjustment Factor for a 6-year project



39. The ad hoc introduction of risk averaging by DEQ through a 6/70 adjustment factor, as depicted in Figure 2, would allow a six-year project to concentrate 70 years of emissions and lifetime cancer risk into both the 6-year life of the project and receptor child's first

six years of life. This scenario undermines the health protectiveness originally incorporated in Section 586, particularly with respect to neo-natal, pediatric, and adolescent cancers.

40. In justifying the use of the 16/70 Project-specific adjustment factor, the Respondents continually assert that the Unit Risk Factor (URF) is an average based on a 70-year lifetime. However, carcinogenic potency and cancer risk accumulation differ for various stages of life. The cancer dose varies based on contaminant intake and absorption rates and physiological factors such as body weight and organ development. Considering early life exposures, warrants additional examples of the inappropriateness of introducing the SGP 16/70 Project-specific adjustment factor. Pregnant women, the fetus, and pre-school children accumulate dose and risk at the highest rates and are especially vulnerable to disease due to age and developmental factors. Body weight, absorption, and hormonal considerations can make older children and adolescents more susceptible to childhood cancers.

41. DEQ's assertion that the SGP 16/70 Project-specific adjustment factor is health protective implies that it is permissible to subject these sensitive subpopulations to the equivalent $>10^{-4}$ risk levels from conceptus to school age because it will average out over the remainder of the child's life.

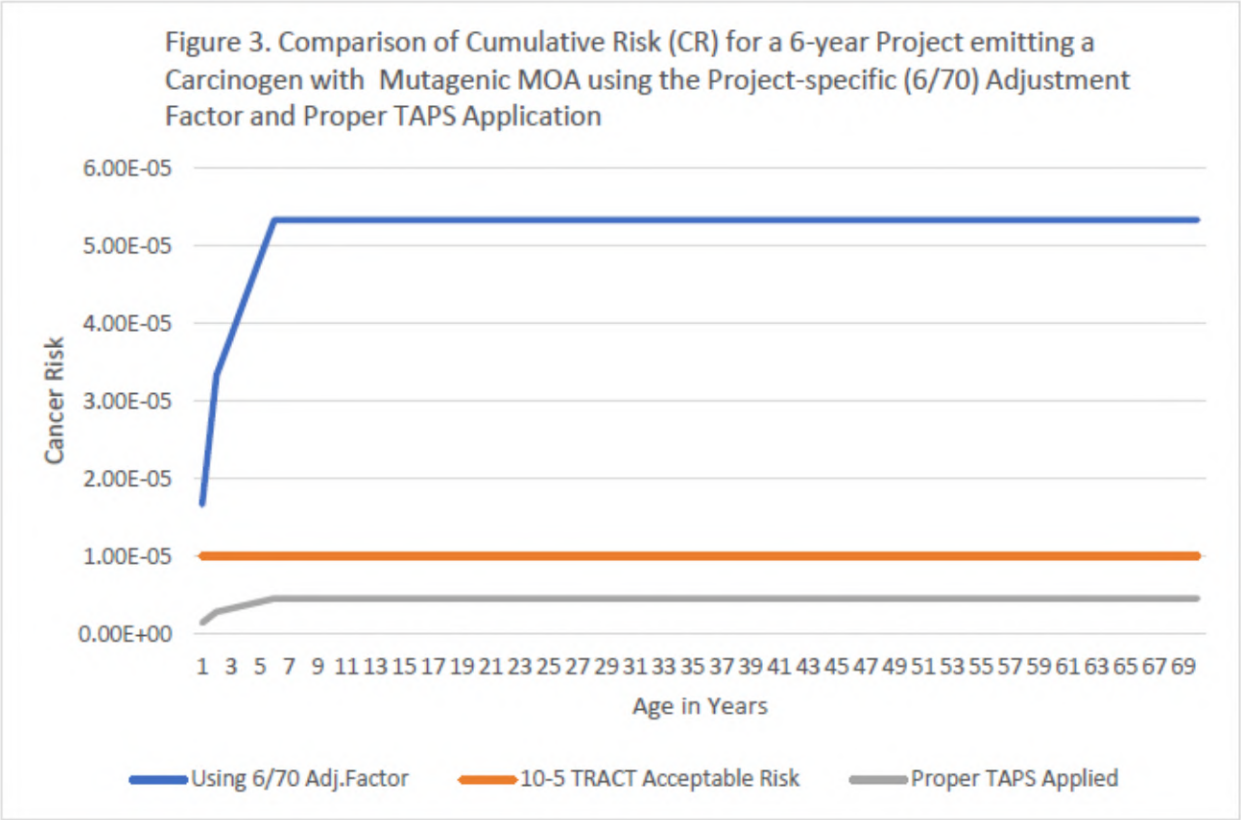
42. The SGP 16/70 Project-specific adjustment factor is a classic example of dose-averaging. The practice of averaging cancer risk over a receptor's lifetime progressively developed as an issue in the risk analyses applied to contaminated hazardous waste sites during the 1990s, and early 2000s. The EPA comprehensively considered the application of

dose-averaging or risk amortization in the Science Advisory Board (SAB) review *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens.*[23]

43. The excessive risk associated with early life-stage carcinogenic dose accumulation has long been recognized by most health authorities and specific protections were incorporated in EPA Risk Assessment Guidance for Superfund (RAGS) policy in 2009. The EPA recommends a quantitative adjustment of the toxicity value to account for early life susceptibility. This guidance recommends a 10-fold adjustment for exposures during the first 2 years of life; 3-fold adjustment for exposures from ages 2 to <16 years of age for carcinogens exhibiting mutagenic mode of action (MOA).[24]

44. Figure 3 shows lifetime cumulative risk were DEQ to apply the ad hoc 6/70 adjustment factor to a carcinogen exhibiting mutagenic MOA for the 6-year project life scenario (blue line). Applying the recommended age-specific adjustment factor shows that DEQs interpretation allowing dose-averaging over the 70-year lifetime would result in the allowable full lifetime exposure occurring by age 2 years, and the child's lifetime cumulative exposure will be $5.3x10^{-5}$ by age 6 (i.e., 53 times the one-in-one million criteria). These lifetime cumulative risks acquired by infants and toddlers, prior to adolescence far exceed EPA acceptable carcinogenic risk policy.

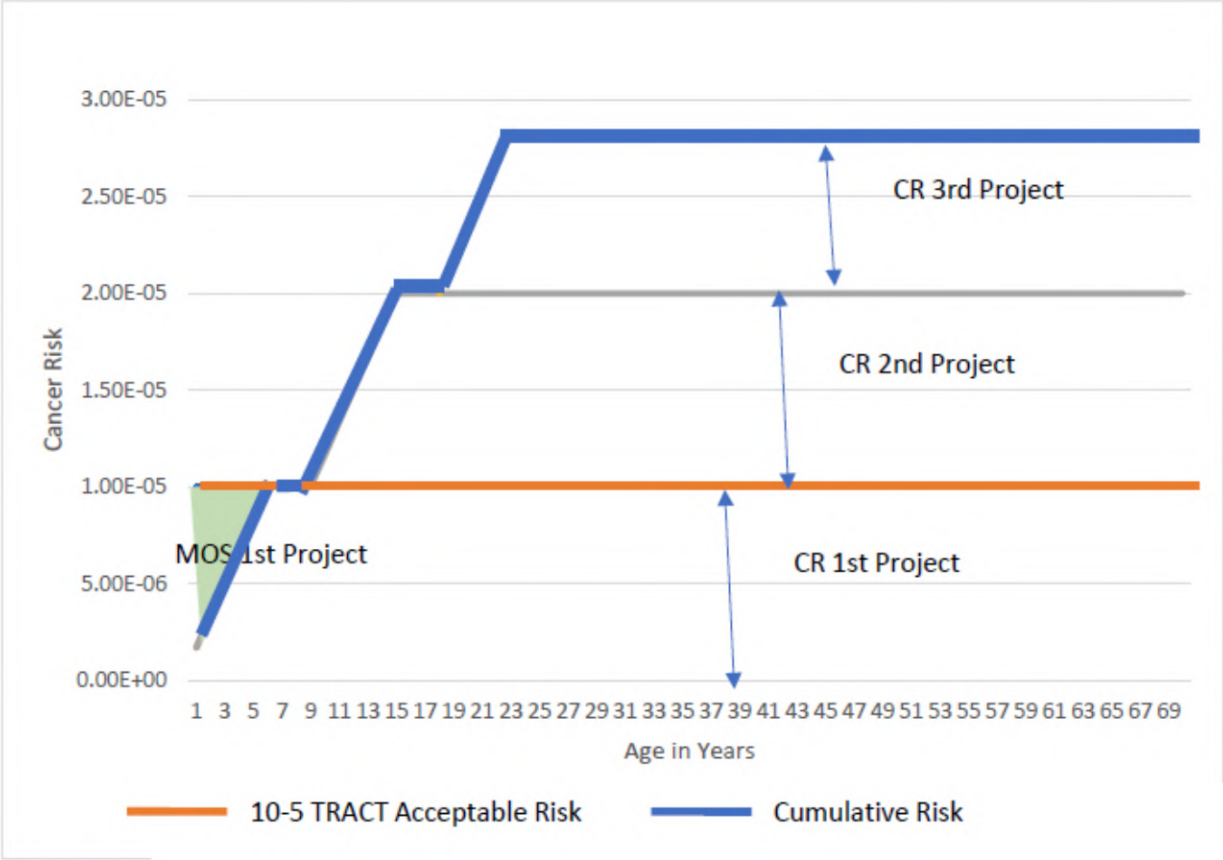
[23] Exhibit D. U.S. EPA, *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* (2005).
[24] Exhibit E. U.S. EPA, *Risk Assessment Guidance for Superfund. Vol. I: Human Health Evaluation Manual (Part F, Supplemental Guidance for Inhalation Risk Assessment* (Jan. 2009).



45. Conversely, proper application of the TAPs rule using the **maximum one-year annual average ambient air carcinogen concentration** is shown by the lower cumulative risk line (gray line). Proper implementation of the TAPs rule would result in 4.6×10^{-6} cumulative cancer risk at age six years, as shown in Figure 3. These results demonstrate that application of a 6/70 adjustment factor for a six-year facility increases a six-year-old child's cancer risk by 12 times over that were the TAPs rules applied under the past policy.

46. As another example, consider the case of two additional 6-year projects being implemented near the source represented in Figure 2 at years 9 and18 in this child's life. Figure 4 shows the child already exposed to the full lifetime allowable cancer $1x10^{-5}$ risk by age 6, will have double ($2x10^{-5}$) the acceptable risk level by adolescence, and will carry three times the allowable lifetime cumulative risk burden ($3x10^{-5}$) through the reproductive stage of life.

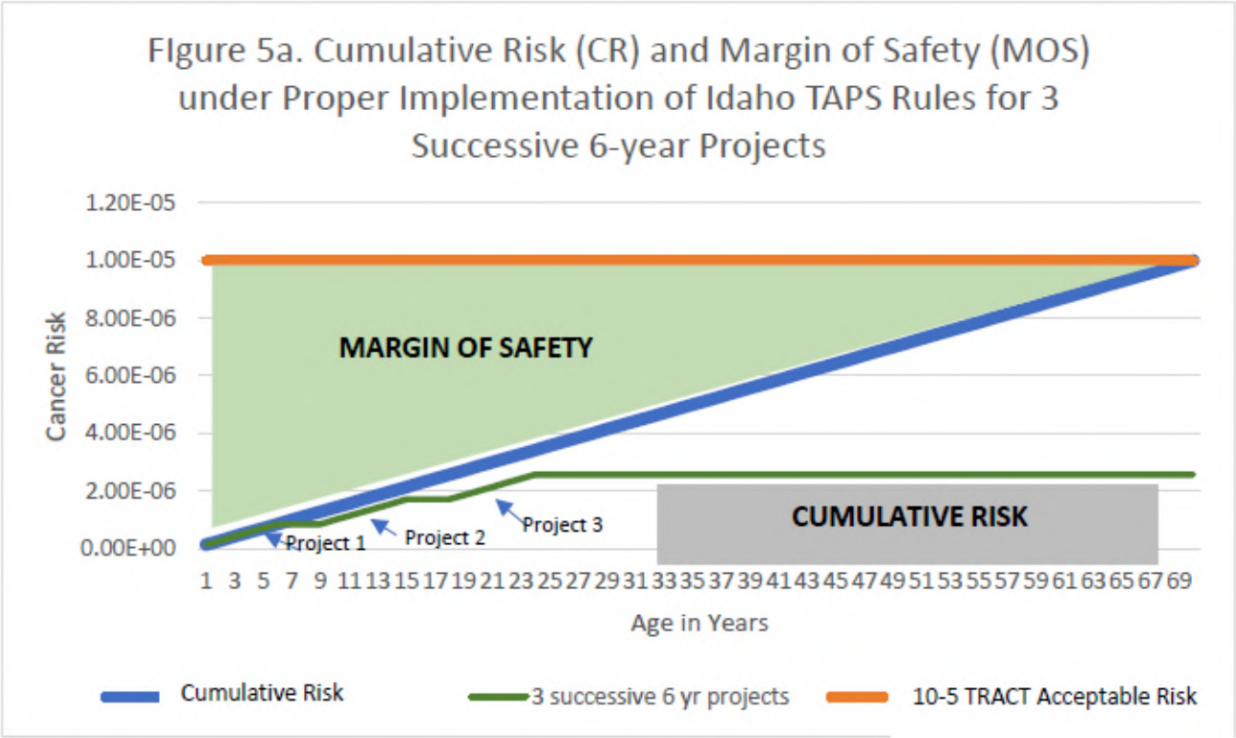
Figure 4. Cumulative Risk using the Project-specific (6/70) Adjustment Factors for 3 Successive 6-year Projects



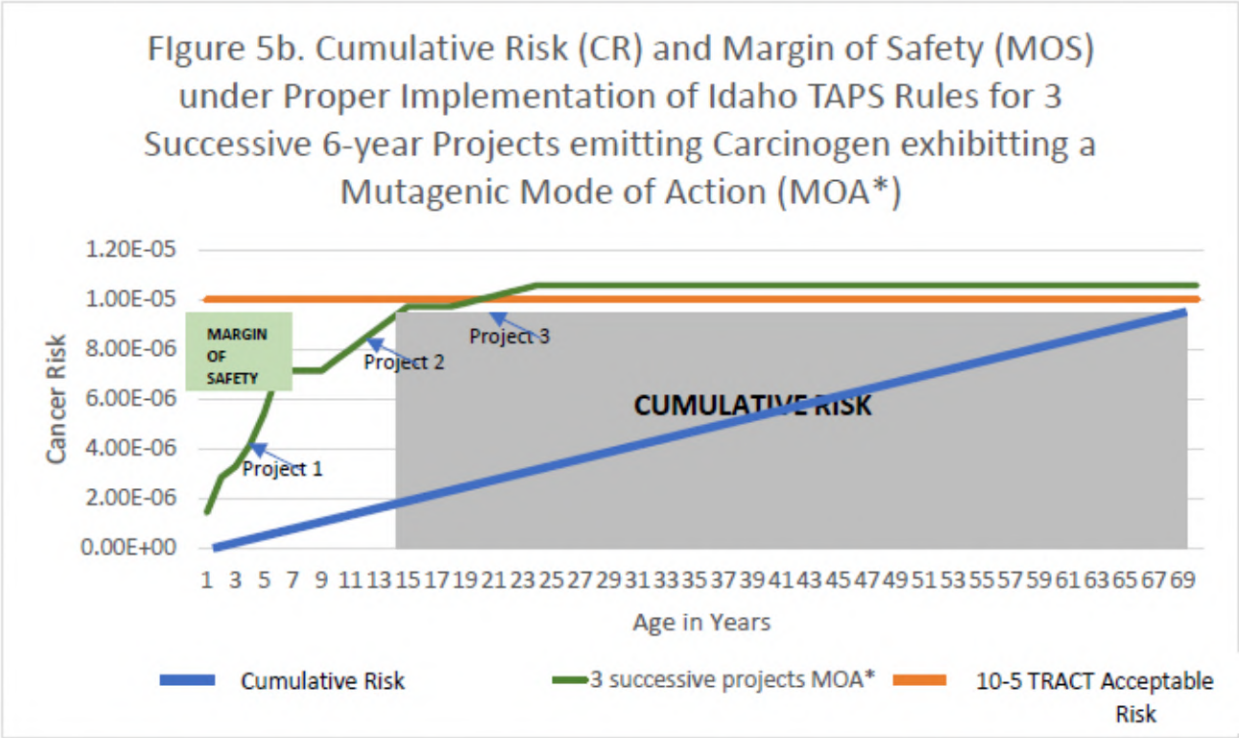
47. Consider the three sequential 6-year projects implemented under the new (6/16) adjustment factor emitting a carcinogen exhibiting mutagenic MOA. In this scenario, the three projects would increase individual cancer risk to >$1x10^{-5}$ lifetime allowable risk by age 2, to $5.3x10^{-5}$ for a 6-year-old child, $8.3x10^{-5}$ for a 16- year old adolescent, and $9.3x10^{-5}$ for a 24-year old adult. These are dangerous and unacceptable risks at vulnerable life stages.

48. Under Section 586, DEQ must consider these new projects incrementally. Thus, it would not account for the cumulative lifetime exposures associated with the earlier projects in a new source PTC application, and are not allowed to consider risk associated with those earlier projects. At Stibnite, for example, should SGP apply to open another pit at the mine, DEQ would be required to ignore the cumulative lifetime risk and cancer burden imposed by the proposed SGP 16-year LOM scenario.

49. Figures 5a and 5b demonstrate the same three sequential project scenarios under the proper implementation of the current TAPs rules using the **maximum one-year annual average ambient air carcinogen concentration** that incorporates the MOS to accommodate additional sources. Figure 5a shows the cumulative risk from all three projects for a carcinogen not exhibiting mutagenic MOA. In this case, a child growing up in the community would be protected from excess cancer risk through all life stages even though DEQ would not consider the earlier exposure in applying Section 586. The lifetime risk accrued by the individual is $2.6x10^{-6}$ as opposed to $3.0x10^{-5}$ in the earlier example. Allowing use of the 6/70 adjustment factor increases lifetime cancer risk by 12 times..



50. Figure 5b shows the cumulative risk for proper implementation of the current TAPs rule for three sequential 6-year projects emitting a carcinogen exhibiting mutagenic MOA. In this example, the MOS is successfully protective throughout childhood and adolescence, with the cumulative risk exceeding the 10^{-5} risk level at age 21. These examples illustrate the effectiveness of the MOS in accommodating additional sources and risk cofactors. The TAPs rule is health protective if properly implemented. Applying risk averaging through the use of the 16/70 Project-specific adjustment factors eliminates the MOS and substantially increases cancer risk, especially considering the incremental nature of the rule.



51. Figures 5a and 5b also demonstrate DEQ's shortsightedness in applying unprecedented cancer dose-averaging methods through the SGP 16/70 Project-specific adjustment factor. The inappropriate averaging is allegedly justified by ad hoc risk assessment calculations and risk management protocols that undermine both the simplicity and the health protectiveness of the TAPs rule. The MOS is compromised, the public is no longer secure, and the regulated industry is now obliged to include cancer risk and health impact assessments in TAPs PTC applications to support the assertions of health protectiveness.

52. There are no provisions in the Air Rules to allow manipulation of the required **maximum one-year annual average ambient air carcinogen concentration** or the **AACC,** or to submit risk calculations. The Respondents assert that because there are no specific prohibitions, using the SGP 16/70 Project-specific adjustment factor is permissible. DEQ did not

require any risk assessment justification during the PTC process, but only provided extremely limited risk analyses in post hoc declarations following the Special Board Hearing.[25]

53. In justifying the SGP Project-specific 16/70 adjustment factor, both the DEQ and Perpetua refer to the EPA Risk Assessment Guidance for Superfund (RAGS) risk assessment protocols eschewed by the agency for the last thirty years to support the ad hoc exposure averaging calculations. As noted in the Tiedeman Declaration, IDHW-DOE specifically avoided RAGS waste site remediation short-term risk protocols in developing the TAPS.[26]

54. The Board of DEQ Vice Chairman McMillan explicitly expressed concerns with this issue, indicating his belief that DEQ's creation and application of a Project-specific adjustment factor cannot be supported by Idaho's Air Rules and that DEQ has misinterpreted how the AACC must be applied if it is to comply with the those rules.

55. Vice Chairman McMillan further indicated that DEQ's application of what he called the "short-sighted" Project-specific adjustment factor to the Stibnite Gold Project created a misleading risk analysis that greatly underestimates the actual cancer risk. In his view:

> The Idaho rules are not ambiguous. There is an acceptable risk associated with the AACC standard. There is an acceptable risk associated with DEQ-approved T-RACT projects, and there is an acceptable risk associated with the short-term project that is five years or less. There are no other acceptable risks identified in Idaho's air quality rules.[27]

I agree with Dr. McMillan's statement.

[25] *See* Schilling Decl.; Paden Decl.; Lewis Decl.; Lopez Decl.
[26] Tiedemann Decl. ¶¶ 26-27.
[27] TR 0160.

B. Ambient air arsenic concentrations and cancer risk are underestimated for the SGP by using a 5-year rolling average in the air quality modeling input factors.

56. Another ad hoc SGP Project-specific adjustment factor DEQ applied to the exposure estimates (prior to implementing the 16/70 Project-specific adjustment factor) was a 5-year rolling average adjustment factor to the emissions rates used as input to the refined modeling. This disguised risk averaging technique results in the models predicting a five-year average ambient air carcinogen concentration rather than the **maximum one-year annual average ambient air carcinogen concentration** required under Section 586 and T-RACT, further undermining the health protectiveness of the TAPs rule.

57. The 5-year rolling average adjustment factor was introduced in the TAPS Modeling Addendum Section 4.2 -TAP Emission Averaging Period. In Section 4.2, DEQ asserts:

> Annual average emissions of carcinogenic TAPs are typically used in the dispersion model to estimate maximum annual impacts. PRI refined the analyses by using source-specific emission rates that are representative of a 5-year averaging period. This approach is appropriate because carcinogenic impacts are of concern from a long-term exposure basis.[28]

58. DEQ erroneously substitutes the 5-year rolling average emissions for the maximum one-year potential emissions required under Section 586 and T-RACT. Section 586 requires the prescribed maximum one-year annual average to be estimated by refined modeling of ambient concentrations based on maximum one-year potential emission rates, or PTE. The PTE should reflect the source configuration and operational scenario that would yield the maximum annual one-year ambient air arsenic concentration. This concentration is then

[28] REC 0698.

compared to the 10^{-6} AACC. If the 10^{-6} AACC is exceeded, the applicant may apply for 10-fold relief under TRACT.

59. DEQ has never disclosed this comparison. In response to public comments critical of DEQ for not calculating nor presenting the required AACC comparisons, DEQ provided the following rationale:

> The comparison offered, comparing maximum annual impacts to the T-RACT adjusted AACC, is irrelevant. Compliance with TAPs rules was demonstrated through a refined analysis, so there is no utility in focusing on results from a more conservative, less refined analysis.[29]

DEQ misinterprets the purpose the comparison and undermines the health protective strategy of the TAPS Rules as implemented in the past.

60. Instead, DEQ substituted the 5-year rolling average for the required maximum one-year emission rate. There is no provision in the TAPs rule for altering or adjusting the predicted maximum one-year annual average. This erroneous substitution significantly reduces the MOS inherent in proper allocation of the one-year maximum emission rates. To be health protective, the prescriptive Section 586 rule explicitly (not typically) requires predicting the **maximum one-year annual average contaminant concentration** using prescribed emissions estimates, and assuring that concentration is not exceeded during the life of the facility.

61. DEQ has never disclosed the required **maximum one-year ambient annual average arsenic concentration.** It is not possible from the available information provided by DEQ to determine how this 5-year rolling average compares to the maximum one-year emission rate that should have been used. I have estimated the underprediction by examining the ratio of

[29] REC 0693.

peak to mean 5-year rolling average emission rates presented in Figure 3 of Perpetua's TAP Addendum.[30] This figure shows estimated potential 5-year rolling average emissions for an alleged 16-year MODPRO2 operations plan. The estimated mean 5-year rolling average from this figure was calculated to be 0.132 lb/hr. Comparing this value to the maximum 0.232 lb/hr value suggests the peak to mean ratio for the alleged T-RACT PTE is approximately 1.8 (0.232 lb/hr / 0.132 lb/hr).

62. Because this Project-specific 5-year rolling average adjustment factor is inherently applied to the emissions input to the refined models, a 1.8 underprediction factor would translate directly to the estimated receptor point ambient air carcinogen estimates. As a result, the maximum one-year annual concentration in the model output is likely underpredicted by a factor of 1.8. The best estimate of the **maximum one-year annual ambient air arsenic concentration** for the modeled scenarios is 0.0125 $\mu g/m^3$ (1.8 x 0.00698 $\mu g/m^3$) for the WEP2.[31]

63. DEQ's application of the 5-year rolling average adjustment factor reduces the **maximum one-year annual ambient air arsenic concentration** and the associated cancer risk by 45%.

C. Ambient air arsenic concentrations and cancer risk are underestimated for the SGP by improper application of the non-WEP emissions scenarios.

64. A third SGP Project-specific adjustment, the non-WEP adjustment factor, was applied to model predicted ambient air concentrations. This is a second disguised dose-averaging step combining eight different 5-year rolling average scenarios, reducing the alleged WEP2

[30] Exhibit L. at 26.
[31] Exhibit L at PDF 224.

maximum annual average an additional 41%. DEQ averaged the maximum WEP2 scenario 5-year average arsenic concentration predicted by the model (i.e. 0.00698 μg/m^3) with the average of the seven model predicted non-WEP 5-year average concentrations (0.00134 μg/m^3). These alleged annual averages are actually an average of 5-year averages as these were predicted by the already diluted 5-year rolling average emissions input to the refined modeling. This non-WEP multi-averaging adjustment factor dilutes the ambient air carcinogenic concentration by an additional 41%, yielding the 0.00416 μg/m^3 alleged incremental annual ambient arsenic concentration. Paden and Lopez use this value to assert compliance with EPA cancer risk policies in subsequent risk calculations.[32]

65. DEQ and Perpetua assert this additional dose-averaging step is justified because no one scenario will apply throughout the 16-year LOM operation. In the context of properly applying the TAPs rule, the non-WEP adjustment factor is irrelevant. DEQ's obligation is to identify the emission scenario that produces the **maximum one-year annual average ambient air carcinogen concentration**. That value is the maximum WEP2 scenario, and would not consider non-WEP scenarios unless the non-WEP emissions sources were operating contemporaneously during the WEP2 emission maximum year. In that case, any non-WEP scenario operating in the same year as the WEP2 maximum configuration would add to, not dilute, the critical receptor maximum ambient air concentration.

66. DEQs applying the SGP Project-specific non-WEP adjustment factor effectively converts the 5-year alleged annual average value (0.00698 μg/m^3) to an arbitrary 0.00416 μg/m^3 16-year LOM average carcinogenic concentration. A variety of combinations of the different

[32] *See* Paden Decl. XXX; Lopez Decl. XXX.

modeling scenarios, based on alleged operations plans could have been combined to manipulate this multi-averaged hybrid LOM ambient air carcinogenic exposure estimate (e.g. 3-year rolling average and 70% non-WEP contribution).

67. The final effect of DEQ's application of an arbitrary multi-averaging non-WEP adjustment factor can be estimated by comparing the WEP2 and non-WEP average ambient air carcinogen estimates (i.e., (0.00698 $\mu g/m^3$ / 0.00416 $\mu g/m^3$), or by a factor of 1.7. Applying the non-WEP Project specific adjustment factor underpredicts the required **maximum one-year annual average ambient air carcinogen concentration** and associated cancer risk by an additional 41%.

D. The combined application of the SGP 16/70 Project-specific adjustment factor, the 5-year rolling average adjustment factor, and the non-WEP adjustment factor increase cancer risk and negate the health protectiveness of the TAPs rule.

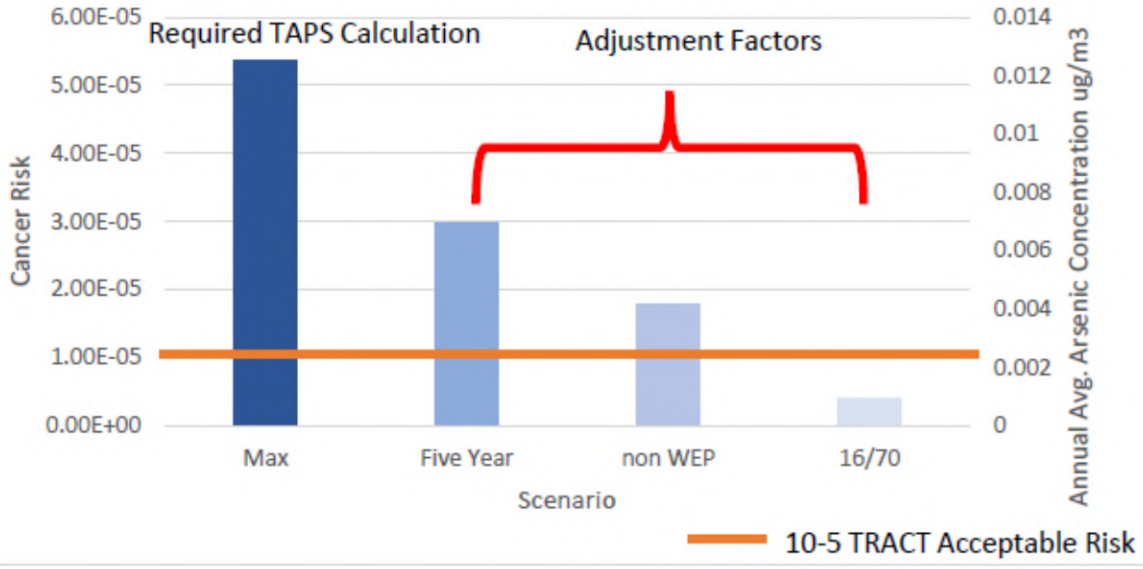
68. The conclusions in the DEQ Board's Final Order correctly identified the three Project-specific adjustment factors that undermine the health protectiveness of the TAPs rule for carcinogenic risk. The Board correctly concluded that application of these adjustment factors underestimates cancer risk. DEQ applied the: 1) 5-year rolling average; 2) non-WEP; and 3) SGP 16/70 LOM adjustment factors sequentially to the input and the output of the predictive air quality model. As a result, the dilution effects are multiplicative, rather than additive.

69. In summary, DEQ diluted the (0.0125 $\mu g/m^3$) maximum one-year annual average ambient air carcinogen concentration by 45% to 0.00698 $\mu g/m^3$ by applying the 5-year rolling average. DEQ further diluted 5-year average concentration by 41% to a value of 0.00416 $\mu g/m^3$ by applying the non-WEP adjustment factor, which is diluted an additional 78% to a value of 0.00095 $\mu g/m^3$ by applying the 16/70 SGP Project-specific adjustment factor. In total, DEQ

diluted the required **maximum one-year annual average ambient air carcinogen concentration** by 93%, or a factor of 13 times before calculating the corresponding cancer risk.

70. The risk levels associated with these exposures were similarly underpredicted as follows: the risk for estimated **maximum one-year annual average ambient air carcinogen concentration** of $5.3X10^{-5}$ was (1) diluted to $3x10^{-5}$ by applying the 5-year rolling average adjustment factor; (2) diluted to $1.8x10^{-5}$ by applying the non-WEP adjustment factor; and (3) to the alleged compliance $4x10^{-6}$ by applying the SGP 16/70 Project-specific adjustment factor. These results are shown in Figure 6. DEQs sequential application of the three SGP Project-specific adjustment factors underpredict cancer risk by 13 times, as these carcinogenic risk levels are employed in properly implementing the TAPs rule.

Figure 6. Effect of DEQs Application of the Project-specfic Adjustment Factors Compared to Required TAPS Calculation



71. These analyses confirm Vice-chairman McMillan's observation in the Special Hearing:

> The PTC proposes to allow 16 years higher daily carcinogen doses and disguises such doses using a non-rules-based mathematics.[33]

E. DEQ's SGP Project-specific adjustment factors represent a significant change in the regulation of carcinogenic risk in Idaho that increases both cancer risk and regulatory burden.

72. As DEQ admits,[34] cancer dose-averaging has seldom, if ever, been used in TAPs carcinogenic risk compliance evaluations for a stationary source under the Clean Air Act in Idaho. Although there is a history of using cancer dose-averaging in risk assessment and risk management protocols for short-term remediation projects at contaminated sites, applying it to the SGP PTC is unprecedented. In implementing the SGP 16/70 Project-specific adjustment factor, DEQ has deviated from the long-held prescribed TAPs rule protocol of guaranteeing the **maximum one-year annual average carcinogen concentration** will not exceed the AACC or T-RACT AACC for each year of the Project. This thirty-year health protective strategy has provided the public comfort that cancer risk exposures are within acceptable limits both near the source and Statewide.

73. Should application of risk averaging become precedent through acceptance of the SGP Project-specific adjustment factors, the conservative MOS inherent in the TAPs rule is significantly reduced. This major change in health protective strategy should simultaneously require PTC applications to include a comprehensive health risk assessment to consider other

[33] TR 0160.
[34] REC 1201.

potential sources otherwise inherently addressed in the MOS. Providing such evidence would be incumbent upon both the PTC applicants and DEQ.

74. These health and risk assessments would require new applicants to consider other past, present, and future sources that did, or may, expend significant portions of the critical receptor's lifetime allowable risk. A simple review of Washington State's required Health Impact Assessment (HIA) points out the numerous shortcomings in the ad hoc alleged risk analyses offered by the Respondents. The HIA requires specified emissions calculations, approved air dispersion modeling, AACC screening, risk assessment, hazard identification, exposure estimates considering other sources and exposure routes, dose-response criteria, non-carcinogenic risk characterization, uncertainty analysis, discussion of acceptability of risk, and a risk management analysis employing modified emission control strategies.[35]

75. DEQ has no history utilizing risk assessment to support TAPs rule applications, nor do the Idaho TAPs regulations offer any guidance for conducting health risk analyses. No comprehensive analyses, nor discussion related to risk and health assessment, are found in the Statement of Basis for the SGP PTC.[36] No comprehensive assessment of health and risk issues associated with application of the SGP Project-specific adjustment factors were required in Perpetua's application.

76. Additionally, from a regulatory standpoint, other Idaho air permit applicants may seek similar preferential relief. No facility plans for a 70-year life. The 70-year basis is an artifact of cancer risk analyses protocols, not a facility design criterion. Every facility ever to apply for a

[35] Exhibit C at 26.
[36] *See* REC 0410.

PTC that did not opt for short-term relief (less than 5 years) likely anticipated a project life of less than 70 years of operation. Will DEQ offer SGP-equivalent project-specific adjustment factor relief and require comprehensive Health Impact Analyses for 6/70, 10/70, 16/70, 20/70, 25/70, 30/70-year alleged project life, as Schilling Declaration suggests?[37] Will DEQ approve incremental emissions from a new source impacting the same critical receptor location that has already expended its lifetime allowable risk, as demonstrated in Figures 4 and 5, above? Will DEQ approve additional emissions from the same location after the original permit has exhausted the critical receptor lifetime allowable risk? Will DEQ require, and provide guidelines, for risk and health assessments to support the preferential relief?

77. These questions demonstrate the short-sightedness of DEQ's acquiescence to Perpetua in allowing dose-averaging concepts to be applied to the Section 586 TAPs rule. Proper application of the rule inherently precludes risk averaging to maintain health protectiveness, without requiring applicants to address the issues without guidance. The regulatory burden placed on future applicants by this modified policy is potentially immense.

78. Allowing Perpetua and the SGP to concentrate a lifetime of carcinogenic emissions and allowable risk in a shorter exposure period defined by the LOM introduces numerous issues and uncertainties that can appropriately be considered only in comprehensive risk assessment analyses.

79. There are numerous examples of inadequacies of the risk calculations offered by the Respondents. Among the more important are those related to the SGP Project-specific adjustment factors concentrating emissions and carcinogenic risk in childhood and adolescent

[37] *See* Schilling Decl. ¶ 19.

life stages. Environment Canada conducted an extensive review of the development and incorporation of life stage cumulative risk assessment, and particularly dose-averaging.[38]

80. This document provides an understandable and concise review of the several issues surrounding dose-averaging, and risk amortization in applying cumulative risk assessment to short-term exposure scenarios. The report also evaluates and describes how various U.S. and Canadian health agencies had implemented risk amortization policy in the preceding decade. Environment Canada's conclusions reflect earlier EPA's determinations that dose averaging generally underestimates risk for fetus, infant, toddler, school children and adolescents; can be appropriate for healthy adults; and overstates risk late in life.[39] Idaho's current TAPs rule MOS appropriately accommodates both these conclusions if properly implemented as illustrated in Figure 1, above.

81. Environment Canada's conclusion with regard to threshold carcinogens is most pertinent to consideration of the SGP 16/70 Project-specific adjustment factor. Environment Canada states:

> Without a sound basis for doing so (i.e. it cannot be a default assumption), **the human health risk assessor should not simply mathematically spread out a short-term dose over a long period and conclude that the short-term dose is toxicologically equivalent to a lower dose over the long period. In short, CSD recommends that the exposure be averaged over the total actual exposure period and compared with the appropriate TRV.** A scientific rationale is required to support any proposed amortization (dose averaging beyond actual exposure period) to ensure that short-term risks are not underestimated. This analysis needs to be done on a chemical-specific basis.[40] (emphasis added)

[38] Exhibit F. Environment Canada, *Interim Guidance on Human Health Risk Assessment for Short-Term Exposure to Carcinogens at Contaminated Sites* (2015).
[39] Exhibit F; Exhibit E.
[40] Exhibit F at 18.

82. TRV is the equivalent of the Idaho AACC. For the past 30 years Idaho has implemented the TAPs rule as Environment Canada recommends, providing a health-protective MOS that appropriately protects children, adolescents, and pregnancies. DEQ now proposes to endorse dose averaging through the three SGP Project-specific adjustment factors, increasing both cancer risk for these vulnerable populations and regulatory burden for PTC applicants.

83. Two examples of relevance to the SGP Project-specific adjustment factors demonstrate the inadequacy of the risk calculations offered by Paden and Lopez. A comprehensive HIA addressing arsenic at mining sites would address 1) Mode of Action (MOA); and 2) non-carcinogenic risk as these relate to critical life stages.

84. **MOA Considerations**: As the Lopez Declaration notes, arsenic is not considered a carcinogen exhibiting mutagenic MOA by the EPA at this time. Current EPA guidance does not specifically recommend applying the age-dependent adjustment factors to the arsenic inhalation URF. Current EPA policy requires life-stage adjustment for known mutagenic MOA carcinogens but leaves it to the risk assessment and risk managers' discretion whether to apply age-adjustments for carcinogens with unclear MOAs.[41] Some jurisdictions recommend applying age dependent adjustment factors to carcinogens for which the MOA is not definitive.[42] A comprehensive risk assessment would inform the risk management decision-makers that there is evidence suggesting arsenic, in combination with other co-stressors, has shown mutagenic

[41] Exhibit D.
[42] Exhibit G, California EPA, OEHHA, *Technical Support Document for Cancer Potency Factors: Methodologies for derivation, listing of available values, and adjustments to allow for early life stage exposures* (May 2009) at 3.

MOA.[43,44] A comprehensive risk assessment would inform the risk management decision-makers that there is evidence suggesting arsenic, in combination with other co-stressors, has shown mutagenic MOA.

85. **Non-carcinogenic Risk.** Environment Canada notes specific examples of non-carcinogenic arsenic health effects that can become the risk driver after applying age-specific exposure, absorption, and dose accumulation adjustments at contaminated sites where children may ingest, in addition to inhaling, arsenic laden dusts.[45]

86. Allocating a lifetime of allowable arsenic intake to children in 6 or 16 years, raises numerous non-carcinogenic concerns not mentioned in the Respondents' limited risk analyses.

87. The largest source of arsenic at the SGP are haul road fugitive dusts. Application of the SGP Project-specific adjustment factor allows the SGP to increase annual emission rates from haul roads by four to ten times more than that allowed under proper implementation of the TAPs rule.

88. This concentration of emissions in early childhood, not only increases ambient air arsenic concentrations, but more than quadruples the rate of arsenic laden dust deposition. It is well-known, in Idaho, nationally and internationally, that incidental ingestion of mining-related fugitive dusts is the major childhood exposure route for heavy metals in mining communities. Numerous DEQ risk assessments for abandoned mine sites in Idaho, including several at the

[43] Exhibit H, Environmental Health Perspectives, *Low-dose Arsenic: In Search of a Risk Threshold*, 122:5 (May 2014).
[44] Exhibit I. Speer, R.M., *et. al.*, *Arsenic and cancer: evidence and mechanisms*, Adv. Pharmacol. 96:151-202 (2023).
[45] Exhibit F at 18.

Bunker Hill and Coeur d'Alene Basin Superfund Site, have historically involved fugitive dusts from mining sites.[46, 47]

89. The EPA and DEQ Superfund regulators routinely apply age-dependent adjustment factors similar to those required for carcinogens that exhibit mutagenic MOAs.[48] There has been no consideration of non-carcinogenic risk for the SGP. Figures 3 and 5, above, demonstrate there is no need to assess other potential sources or non-carcinogenic risk if the TAPs rule is implemented properly using the **maximum one-year annual average carcinogen concentration**. Dust deposition would occur at rates anticipated under proper application of the TAPs rule. As a result, properly complying with the cancer risk criteria is also protective of non-carcinogenic risk.

90. The Paden and Lopez Declarations contain extremely limited risk calculations. Both Respondents use the inappropriately derived dose-averaged ambient concentration of 0.00095 $\mu g/m^3$ to calculate an alleged $4x10^{-6}$ cumulative cancer risk and assert compliance with EPA risk assessment policy. Both Respondents refer to the same EPA formulae found in Superfund guidance and simply compare the same long-term 70-year average value to the same range of alleged EPA allowable risk levels. Neither considers pertinent risk co-factors, vulnerable life stages, other potential sources, or a variety of other considerations inherent in the Idaho TAPs compliance strategy or MOS noted above. Neither mentions nor indicates understanding of the incremental nature of the TAPs Rule.

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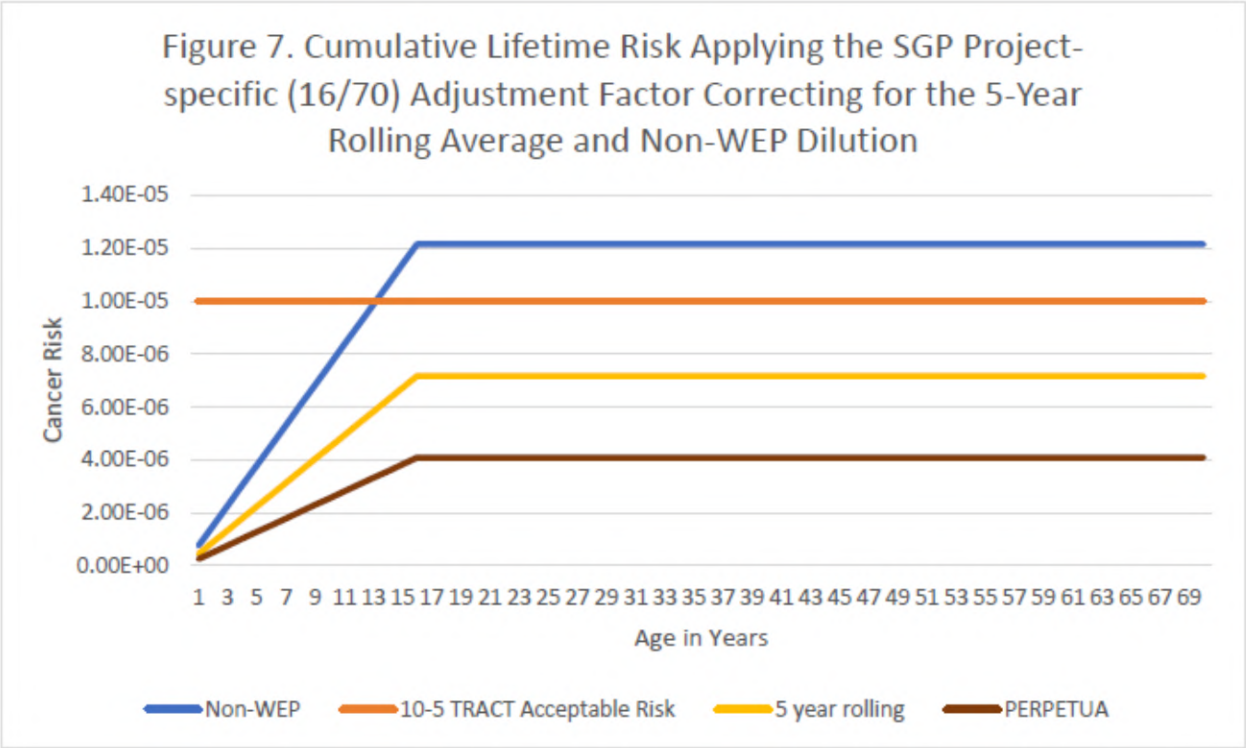
[46] Exhibit J. von Linder, I.H., *et. al.*, *Estimating Children's Soil/Dust Ingestion Rates through Retrospective Analyses of Blood Lead Biomonitoring from the Bunker Hill Superfund Site in Idaho*, Envtl. Health Perspectives, 124:9, 1462-1470 (2016).
[47] Exhibit K. U.S. EPA, *Estimation of Age-specific Soil and Dust Ingestion Rates for U.S. Children: Update to the Default Values for the Integrated Exposure Uptake Biokinetic Model for Lead in U.S. Children* (2021).
[48] Exhibit K.

91. Were the proper TAPs analysis conducted, the cumulative risk for long-term operations would be 5.1 $x10^{-5}$, as noted above. Figure 6, above, illustrated the sequential application of the three SGP Project-specific adjustment factors applied by DEQ (i.e., 5-year rolling average,, non-WEP sources, and 16/70 lifetime adjustment). The final 16/70 exposure dilution yields a cancer risk of $4.1x10^{-6}$. DEQ and the Respondents allege that 40% of the full lifetime allowable exposure is expended by the 16 years of SGP operations.

92. The $5.1x10^{-5}$ carcinogenic risk calculated for the SGP as TAPs requires does assume a 70-year basis. Figure 7 shows the application of the proper **maximum one-year annual average ambient air carcinogen concentration** (0.0125 $\mu g/m^3$) applied to the same 16-year LOM formulae used by the Respondents. After correcting for the 5-year rolling average and non-WEP adjustment factors disguised risk averaging steps, the cumulative risk after the16-year LOM is 1.2 x 10^{-5}.



93. This cumulative risk exceeds the allowable risk criteria by 20% using DEQ and Perpetua's calculation. Figure 7 also illustrates the effect of the serial application of SGP Project-specific 5-year rolling average and non-WEP Project-specific adjustment factors on cumulative cancer risk from the critical receptor viewpoint. Removing these dilution adjustments shows the individual receptor will experience a full lifetime allowable carcinogenic $1x10^{-5}$ equivalent exposure by year 13.

94. This opinion concludes that DEQs use of the ad hoc SGP Project-specific adjustment factors undermines the health protectiveness of the TAPs rule. The TAPs rule was specifically developed to avoid requiring risk assessment analyses by providing an inherent margin of safety (MOS). These SGP Project-specific adjustment factors facilitate cancer dose-averaging risk calculations that allow the SGP to significantly increase arsenic emissions

based on short-term Life of Mine (LOM) assumptions, but to nevertheless average the risk associated with those increased emission over 70-years.

95. This transfer of risk from the mine to the receptor's lifetime significantly reduces the MOS and negates the health protectiveness of the TAPs rule. The TAPs rule simply offers 10-fold increases in allowable risk, or emissions, for either 1) short-term projects of less than 5 years, or 2) T-RACT based relief based on available technology.

96. There is neither a provision, nor a need, for risk assessment if the TAPs Rules are properly implemented based on annual compliance with **maximum one-year annual average ambient air carcinogen concentration**. This application of the TAPs rule has served Idaho well for three decades. This policy change allowing risk averaging through the SGP Project-specific adjustment factors not only undermines the health protectiveness of the individual applicant source, but also the Statewide strategy that keeps all Idahoans safe with minimal regulatory burden.

DATED: October 4, 2024



Ian H. Von Lindern, P.E., Ph.D.

Exhibit A

Ian H. von Lindern, Ph.D., P.E.

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Education

Ph.D., Environmental Science and Engineering, Yale University, 1980
M.F.S., Biometeorology and Atmospheric Studies, Yale University, 1973
B.S., Chemical Engineering, Carnegie-Mellon University, 1971

Professional & Technical Certifications

Professional Engineer, Idaho # 3044 ChE (1975)

Professional Experience

Ian von Lindern is co-founder of TerraGraphics International Foundation (TIFO), a non-profit humanitarian environmental response organization. He served as Chief Executive Officer and Principal Scientist of TerraGraphics Environmental Engineering Inc. from 1984-2014. Under his direction, TerraGraphics developed into a one-hundred person multidisciplinary environmental firm, specializing in the design and management of complex projects including site characterization, risk assessment, hazardous waste remediation, engineering design, GIS and database, and remediation oversight. He has 46 years of national and international engineering and scientific experience that includes a variety of environmental assessments; studies in air, water, and soil pollution; toxic and hazardous materials investigations; remedial and cleanup plans; human health risk assessments; and application of statistical analysis techniques to multidisciplinary environmental problems. He has directed more than 40 major health/environmental projects including primary and secondary smelters, used battery processors, landfills, uranium mill tailings, and organic chemical waste sites in the U.S. He has designed and implemented international health risk assessment/remediation projects in countries with high levels of childhood morbidity and mortality including Russia, China, Peru, Bangladesh, Dominican Republic, Senegal, Nigeria, and Kyrgyzstan.

As a Principal Scientist at TIFO, Dr. von Lindern works with marginalized mining and recycling communities around the world to address pollution-related health and environmental issues. Projects are implemented at the local level acknowledging diverse ethnic, religious, socio-economic, and geographic backgrounds to protect future generations and maintain livelihoods in vulnerable communities. TIFO's mission focuses on building environmental health capacity in both the host countries and the next generation of US scientists by sponsoring and directing collaborative projects, pairing US and local professionals and students; and encouraging programmatic research publications summarizing project outcomes and lessons learned. Since 2010, TIFO has partnered with Médecins Sans Frontières (MSF, Doctors Without Borders) in implementing joint medical, public health and environmental responses. TIFO's recent projects are evolving into a global juxtaposition of simultaneously assisting indigenous and disadvantaged communities in both the US and poor/middle income countries responding to the exponential demand for gold and green-energy technologies in the US, central Asia and west Africa. These projects offer promise of reviving a specialty metals industry in the US and providing subsistence incomes for poor populations suffering from climate-related loss of traditional agricultural and pastoral support systems. Conversely, there is the potential for catastrophic health and environmental damages. US efforts involve rigorous technical analysis of sophisticated regulatory environmental impact and permit applications, conveying that to uninformed communities, and advocating for the highest levels of environmental responsibility. Responses in poor countries involve identifying and implementing protective measures achievable within the socio-economic, political and economic capacity of the community. International projects often involve developing practicable community, family, and individual worker level health interventions, as governments often lack the resources and capacity to effectively regulate industry in either the artisanal or formal sectors.

Dr. von Lindern has served as an EPA Science Advisory Board and Clean Air Scientific Advisory Committee (CASAC) Subcommittee Member on several occasions, including: EPA Criteria Assessment Committee for Lead in the Ambient Air (1975-1977), and subsequent CASAC NAAQS lead reviews (1982-1986, 2006-2008); Review Subcommittee Assessing the Use of the Biokinetic Model for Lead Absorption in Children at RCRA/CERCLA Sites (1988); Subcommittee Assessing the Consistency of Lead Health Regulations in U.S. EPA Programs (1992); SAB Review Subcommittee for Urban Soil Lead Abatement Demonstration Project (1993); the Ad Hoc All-Ages Lead Model (AALM) Review (2005-2007, 2019-2020); External Peer Review of EPA's Draft Report – Proposed Modeling Approaches for a Health-Based Benchmark for Lead in Drinking Water (2017).

Project Experience
Example Consulting Projects Directed by Dr. von Lindern

Bunker Hill Mining and Metallurgical Complex/Coeur d'Alene Basin Superfund Site, Idaho, 1974–2016

Dr. von Lindern has worked for the State of Idaho on various projects involving the Bunker Hill/Coeur d'Alene Basin Superfund Site for more than 40 years, both as the lead Risk Assessor and as TerraGraphics Project Manager for the State of Idaho CERCLA activities. In 1974, as an Environmental Engineer for the State of Idaho, he directed the field study of lead intoxication in children surrounding the Bunker Hill smelter. As the state oversight contractor for more than 20 years, his duties have included initial contact with local leaders, assisting IDEQ in Cooperative Agreement and PRP negotiations, legislative committee presentations, moderating Task Force meetings, reviewing PRP and EPA activities, and developing the risk management strategy and site-specific cleanup criteria. He has a number of peer-reviewed publications on the reduction of childhood blood lead levels and remedial activities at this site. He also represented the IDEQ at the National Academy of Sciences (NAS) review of this Project in Washington D.C. (Superfund and Mining Megasites Lessons Learned from the Coeur d'Alene River Basin, (NRC 2005)).

Washington State Department of Justice – Natural Resources Division Litigation Support and Expert Witness, Northeastern Washington State, December 2009– December 2012

Dr. von Lindern provided expert witness testimony and reports for numerous enforcement and civil environmental liability lawsuits and litigation at sites throughout the United States. He was Principal-in-Charge for a contract with the Washington State Attorney General Office, Natural Resources Division, regarding potential mining contamination in northeastern Washington state. He and other TerraGraphics personnel researched and visited numerous abandoned mine sites and collected samples to assess metal contamination. Dr. von Lindern provided his expert opinion to the client for litigation support.

Trail of the Coeur d'Alenes and Bayhorse Ghost Town Remediation and Idaho State Parks and Recreation (IDPR) Development

The Bayhorse Mine property is a well-known "ghost town" near Challis, Idaho with substantial historic value. After completion of an ASTM Phase I ESA and All Appropriate Inquiry standards, the IDPR was considering the site for development as a State of Idaho Park and wanted to ensure the site was suitable for such use. Dr. von Lindern led the team that completed the assessment of human health risk and water quality concerns for the purchase of the Bayhorse Mine property. After the assessment, IDPR successfully acquired the Bayhorse Mine properties for converting the "ghost town" and associated abandoned mine holdings into a cultural, historical, and adventure recreation park.

The Park design mimics innovative risk management strategies used at the Trail of the Coeur d'Alenes State Park in northern Idaho. Dr. von Lindern assisted IDEQ, IDPR, the U.S. EPA and other related agencies at both Parks by developing a risk management strategy that is protective of human health and the

environment, while allowing public access and preserving the historic and recreational value of the resource. The Park opened to the public in June 2009.

Example TIFO Humanitarian / Non-Profit Projects Directed by Dr. von Lindern

In 2005, the US National Academy of Sciences' exhaustive review of the BHSS cleanup effort determined the health response methodologies were sound and effective. Subsequently, Dr. von Lindern co-led the joint Research & Development initiative between TerraGraphics and the University of Idaho to apply environmental cleanup methodologies developed in Idaho mining districts to hazardous waste sites in low and middle-income countries. Humanitarian cleanups were undertaken in conjunction with local governments, universities, and NGOs in a variety of cultural, socio-economic and governmental venues in Russia, China, Dominican Republic, Senegal, and Nigeria. In 2012, he and Dr. Margrit von Braun sold the for-profit firm and founded TIFO as an independent non-profit organization to assist international communities in remediating hazardous waste sites. TIFO has conducted workshops and human health risk assessments in Kyrgyz Republic, Armenia, Slovenia, Bangladesh, and Mongolia in collaboration with local governments, universities, hospitals, and NGOs, including the international humanitarian organization Médecins Sans Frontières (MSF, Doctors Without Borders).

Lead Poisoning – Emergency Health Response, Haina, Dominican Republic 2007-2011.

The community of Paraiso del Dios bordered a former used lead acid battery recovery operation in the port city of Haina near Santo Domingo. In 1997, several hundred children were surveyed and found to have a mean blood lead level of 71 µg/dL (range: 9-234 µg/dL); twenty-eight percent (28%) of children required immediate medical treatment. Residents reported that several children suffered seizures during the factory's operational years and continue to exhibit learning disabilities. The factory closed in 2000 and a repository for waste materials was developed on-site. The site was then abandoned and was subject to extensive uncontrolled salvage activities. The concrete retaining wall was scavenged, releasing large amounts of buried waste into the community during rain events. The exposed wastes, exceeding 30% lead, were sold as scrap. Highly contaminated materials were recycled and used as building material and fill in the adjacent community. Children from the surrounding community accessed the industrial site on a daily basis, tracking soils from the site and exposing the rest of their families.

Dr. von Lindern designed and directed a sampling and risk assessment program in 2006-07, when the area was named one of the world's top ten most polluted sites. Extremely high lead concentrations were found on site and in adjacent residential lots. Contaminated wastes in the failed repository showed concentrations from 30% to 45% lead. Surface soil lead concentrations ranged from 4,000 to >300,000 mg/kg, orders of magnitude above the USEPA limit of 400 mg/kg. The project team then collaborated with the Ministries of Health and Environment to develop an intervention strategy recommending a blood lead monitoring and follow-up program, relocation of all high-level wastes to an off-site repository, an on-site repository for the low-level and mid-level soils, and dedication of the property as a public park with appropriate institutional controls to ensure sustainability. A blood lead monitoring program began in 2007 and found 80% of children >10 µg/dL, 24% >40 µg/dL, and 7% >70 µg/dL. In 2008, the Dominican Republic government commissioned a cleanup in which Dr. von Lindern provided technical assistance. More than 3000 cubic meters of hazardous wastes and 4000 cubic meters of contaminated soils were removed. The site was turned in to an "ecological park" with a dedication ceremony in 2010. The Ministry of Environment introduced the park as the first step in initiating a cleanup program for the entire country and dedicated an "ecological mural" to the Dominican environment and "heroes" of the cleanup effort.

Lead Poisoning – Emergency Health Response, Dakar, Senegal 2009-2011.

Thiaroye Sur Mer (TSM) was the site of Used Lead Acid Battery recovery since the 1970s. Multiple groups recovered lead from batteries to manufacture weights for local fishermen. Several thousand tons of discarded

battery sludge accumulated in the area over three decades. In 2007, dramatic increases in lead prices stimulated East Indian traders to purchase the lead oxide sludge. To minimize shipping costs, 200 local women were employed to sift out beach sand that had accumulated with the sludge. The process involved transporting, drying, sifting, and bagging the lead dust. Bags of lead product were stored in homes prior to sale. Many mothers brought their infants and toddlers with them to work. In 2007-08, 18 children died as a direct result of lead exposures. Mean blood lead levels in children were >100 μg/dL and individual levels were >350 μg/dL

Limited emergency remediation activities were undertaken in April and May of 2008. Three-hundred (300) tons of lead were removed from local homes. The World Health Organization (WHO) tested siblings of the deceased children and forty-one children were subsequently hospitalized and placed in temporary foster care. Massive flooding of the area during the rainy season delayed further action. After the flood subsided, TIFO collaborated with other partners to conduct extensive sampling and interviews of the TSM population. In collaboration with the Ministries of Health and Environment, Dr. von Lindern developed a health response and remediation strategy that was implemented in April 2009. The strategy included establishment of sentinel homes in the community where intensive interviews and sampling were conducted to determine the extent and severity of continuing exposures and to identify active lead exposure pathways. These homes and resident children were monitored to assess the effectiveness of the cleanup.

Lead Poisoning – Emergency Health Response, Zamfara and Niger State, Northern Nigeria, May 2010–Present

Beginning in 2010, Dr. von Lindern spent several months in northern Nigeria directing the characterization and remediation of the world's worst lead poisoning epidemic. The 2010-2013 epidemic in Zamfara, Nigeria was unprecedented in morbidity, mortality, and in the environmental health response. More than 400 young children died from acute lead poisoning associated with artisanal gold mining. Soil removal protocols developed at the U.S. Bunker Hill Superfund Site were adapted to local resources, labor practices, and cultural traditions. Dr. von Lindern and other TerraGraphics personnel worked cooperatively with local authorities, MSF, the Centers for Disease Control (CDC), the World Health Organization, the Blacksmith Institute, and government officials and villagers in remote areas to develop an emergency response and remove contaminated soils.

In 2011, TerraGraphics was recognized by the United Nations Environment Programme (UNEP) and Green Cross International with the Green Star Award, given to every two years in association with UN reviews of its environmental programs to recognize those who have made remarkable efforts to prevent, prepare for, and respond to environmental emergencies around the world. In 2012-13, remediation progressed from emergency response by international personnel to comprehensive cleanup implemented by the Nigerian government. TerraGraphics humanitarian successor, TIFO, partnered with MSF to provide guidance and assistance the Nigerian Federal, Zamfara State and local governments in the completion of the largest and most comprehensive cleanup implemented and funded by an African government. More than 27,000 m^3 of contaminated soils were removed from 820 residential areas and ore processing areas in eight villages, largely by hand labor, and disposed of in constructed landfills. Soil lead exposures decreased 97% for more than 17,000 villagers, allowing chelation treatment of 2349 children. Mean blood lead levels for children ≤5 years age declined from 173 μg/dL to <20 μg/dL over the four-year US $5M remedial program.

Subsequently, TIFO, MSF and other NGOs assisted local, state, and federal leadership in implementing long-term prevention and management programs in Zamfara State. In 2016, a second ASGM poisoning event killed 28 children in neighboring Niger State. The federal government requested TIFO assistance and mobilized trained technicians from Zamfara to lead the assessment and cleanup. Remediation was fully implemented with Nigerian funds, and Niger State assumed takeover of both medical and environmental operations and maintenance in 2018. This successful application was the impetus for the Nigerian Ministry of Mines and Steel/World Bank/MSF/TIFO sponsored Conference in Abuja in 2018, examining the legalization and support of ASGM as a mechanism to address poverty and population displacement in the Sahel, employing safer-mining initiatives.

Continued TIFO-Médecins Sans Frontières Collaborations: Bangladesh and Kyrgyzstan 2011-Present.

In 2014, following successful collaborations in west Africa, MSF and TIFO's partnered to assess and address pollutant-related hazards at formal and informal leather tanneries; small-scale plastic, aluminum, foundry, and textiles recycling operations; and artisanal family-scale scavenging and waste recovery and reuse operations in urban slums in Dhaka, Bangladesh. MSF has since been operating occupational health clinics employing environmental health/occupational remedies for several thousand workers and families.

Since 2016, TIFO and MSF have partnered with the Kyrgyz Ministry of Health (MOH) assessing the potential, and emergency response considerations, for seismic and climate-related catastrophic release of legacy mining and smelting hazardous wastes accumulated over 70 years of operations at the former Soviet Union's largest mercury and antimony factories. TIFO provided assistance with Staff Health and Safety planning and performing a Human Health Risk Assessment for women and children's health issues in the mercury/antimony/gold mining communities. In 2019, the joint TIFO/MSF/MOH team collected >500 soil, air, water and food samples to support health assessment and target blood, urine and hair surveys scheduled for summer 2020. These results will support establishing environmental/occupational health monitoring/intervention capacity in the local government, as Kyrgyz officials revitalize the Soviet-era mining operation to support the local economy and meet the growing demand for mercury in ASGM.

Gold and Strategic Minerals Development Impact Evaluations on Historic Tribal Lands, Intermountain West, USA, 2020 – Present.

TIFO's mission is to assist mining and mineral processing communities to operate as safely as practicable while maintaining essential economic activities. The unprecedented demand for gold and strategic metals has prompted several major exploration and mineral development proposals in western states. TIFO's international mission includes assessing and responding to health and environmental impacts of polluting activities on sovereign native and tribal lands within the US. In that regard TIFO supports scientifically-sound and transparent analyses of the environmental and human health issues faced by mining communities, and the development of solutions implemented within local socio-economic and cultural capabilities. Proposed gold, antimony, and cobalt mining in Idaho, Nevada and Washington States have the potential to adversely affect several reservations and aboriginal tribal lands. The Idaho Stibnite Gold Mine proposal, that claims it will meet 33% of the US antimony demand, is of interest because both the industry and the US regulatory arena have the capacity to implement best practices that are not available to poor communities throughout the world. Mining advocates allege these developments will be safe and secure, and are projecting unprecedented control levels for toxic contaminants. Conversely, the mining company consultants are arguing for relief from environmental regulatory requirements in these mining-friendly states. However, citizen-based interest groups and tribal authorities have limited capacity and resources to evaluate the complex environmental assessments and permit applications. Ironically, the Stibnite Gold Project is exploiting the same ores and metallurgical processes as the gold/antimony mining TIFO is assessing in Kyrgyzstan. As there are currently no smelters in the US that can process the antimony concentrates, the Idaho ores are currently projected to be exported to the same Chinese smelters processing the Kyrgyz ores. Through TIFO, Dr. von Lindern is providing independent review of these documents and submitting comments to the review agencies.

Regulatory Knowledge

Ian von Lindern has worked on projects regulated under Federal, State, local, and foreign regulations, including CERCLA, TSCA, CWA, CAA, NESHAPs, DOT, EPRCRA, SARA, NEPA, and RCRA in the U.S. He has provided litigation support and expert witness testimony in administrative and court proceedings. He has served on several U.S. government advisory panels, including the appointments pertinent to lead health and remediation as shown in the list below.

Special Appointments/Memberships/Affiliations

U.S. EPA Science Advisory Board. Peer Review. All Ages Lead Model (AALM). Washington, DC. October 16-20, 2019.

U.S. EPA External Peer Review. Draft Report, Proposed Modeling Approaches for a Health Based Benchmark for Lead in Drinking Water. Prepared for: U.S. Environmental Protection Agency, Office of Water, Washington, DC. June 27-28, 2017.

U.S. EPA External Peer Review. EPA's Approach for Estimating Exposures and Incremental Health Effects from Lead due to Renovation, Repair, and Painting Activities in Public and Commercial Buildings. Prepared for: U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC. January 2015.

U.S. EPA Science Advisory Board (CASAC). Review of the Integrated Science Assessment (ISA) for Lead in the Ambient Air. US EPA, Washington, D.C. 2012-2013

American University of Armenia, School of Public Health, Yerevan. Invited Professor, Graduate course Risk Assessment for Environmental Health Professionals for Master of Public Health (MPH) Students. 2012-present.

U.S. Centers for Disease Control and the Harvard University School of Public Health Initiative to address health effects of mining and smelting in the developing world. 2009-2013.

Affiliate Professor of Chemical Engineering, University of Idaho, Moscow, Idaho, 1981–2011

U.S. EPA Science Advisory Board. Review of the Lead National Ambient Air Quality Standard for Lead. U.S. EPA, Washington, DC. 2006-2008.

U.S. Clean Air Scientific Advisory Committee (CASAC). Review of the Air Quality Criteria Document for Lead. U.S. EPA, Washington, DC. 2010-2013, 2006-2007.

U.S. EPA Science Advisory Board. Review of EPA's Lead Renovation, Repair and Painting (LRRP) Activities. U.S. EPA, Washington, DC. 2007.

U.S. EPA Science Advisory Board. Review of EPA's Ad Hoc All-Ages Lead Model (AALM) Review Panel. U.S. EPA, Washington, DC. 2007.

U.S. EPA Science Advisory Board. Review Subcommittee for Urban Soil Lead Abatement Demonstration Project. U.S. EPA, Washington, DC, 1993-1995.

NIEHS Select Reviewer Grants Review Committee, Superfund/Hazardous Workers Training Program, NIEHS, RTP, NC. 1992.

Advisory Committee for Development of Lead Paint Abatement Guidelines for Public Housing in the United States, U.S. Dept of HUD, Washington, D.C., 1992.

U.S. EPA Science Advisory Board, Subcommittee Assessing the Consistency of Lead Health Regulations in U.S. EPA Programs, Special Report to the Administrator, Washington, D.C., 1992.

U.S. EPA Science Advisory Board, Review Subcommittee Assessing the Use of the Biokinetic Model for Lead Absorption in Children at RCRA/CERCLA sites. U.S. EPA, Washington DC, 1991.

Technical advisor and consultant to Latah County and North Central Health District Regional Solid Waste Advisory Committees, Moscow and Lewiston, ID. 1991.

Technical advisor to the National Alliance to End Lead Poisoning in Children, Washington, D.C. 1991-2001

NIEHS Select Reviewer Grants Review Committee, Superfund/Hazardous Workers Training Program, NIEHS, Research Triangle Park, NC, 1989-1993.

U.S. EPA Clean Air Scientific Advisory Committee (CASAC) Member, Subcommittee on Exposure Assessment Methodology, U.S. EPA, Washington D.C. 1988.

U.S. EPA Criteria Assessment Committee for Lead in the Ambient Air, RTP, NC. 1975-1986.

Additional Certifications/Training

PSMJ Conference for CEOs-2005

Ian H. von Lindern, Ph.D., P.E.

Publications

Tirima S, Bartrem C, von Lindern I, von Braun M, Lind D, Anka S, Abdullahi A. Food Contamination as a Pathway for Lead Exposure in Children During the 2010-2013 Lead Poisoning Epidemic in Zamfara, Nigeria. Journal of Environmental Sciences, 67:260-272, 2017.

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Exhibit B

United States
Environmental Protection
Agency

Office of Health and
Environmental Assessment
Washington DC 20460

EPA/600/8-87/045
August 1987

Research and Development

EPA

The Risk Assessment Guidelines of 1986

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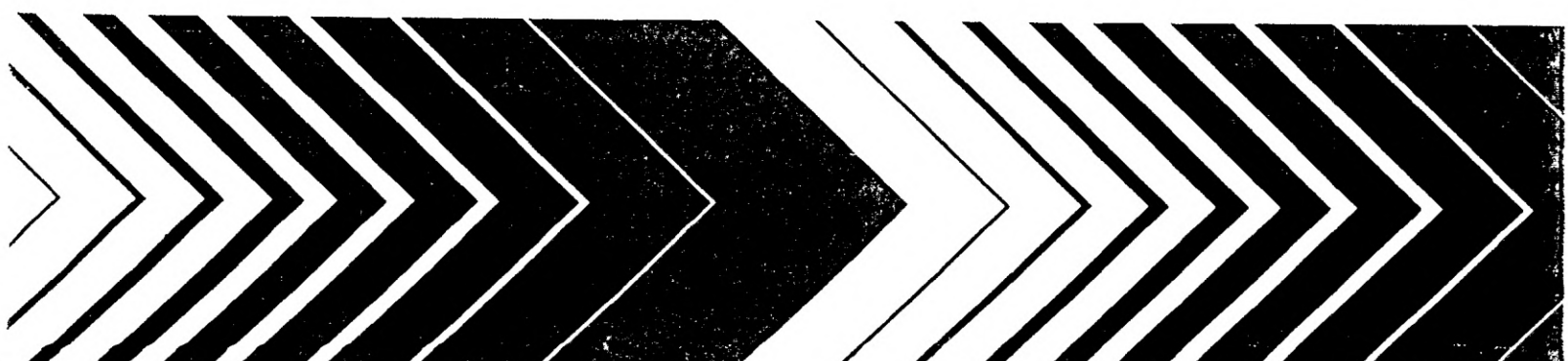

REC 6153

EPA/600/8-87/045
August 1987

THE RISK ASSESSMENT GUIDELINES OF 1986

U.S. Environmental Protection Agency
Washington, D.C.

TR 4489

DISCLAIMER

This document has been reviewed in accordance with U.S. Environmental Protection Agency policy and approved for publication. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

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PREFACE

On September 24, 1986, the U.S. Environmental Protection Agency (EPA) issued risk assessment guidelines relating to five areas: carcinogenicity, mutagenicity, chemical mixtures, suspect developmental toxicants, and estimating exposures (51 FR 33992-34054). The guidelines were developed to promote high technical quality and Agencywide consistency in the risk assessment process.

The guidelines were developed partly in response to a 1983 National Academy of Sciences publication entitled "Risk Assessment in the Federal Government: Managing the Process," which recommended that Federal regulatory agencies establish risk assessment guidelines. An EPA task force, convened by then Administrator William D. Ruckelshaus to study ways to improve the scientific foundation for Agency regulatory decisions, accepted the recommendation, and work on the guidelines began early in 1984.

The guidelines are products of a two-year Agency development and review process which included many scientists from the larger scientific community. They were developed as part of an interoffice guidelines development program under the auspices of the Office of Health and Environmental Assessment in the Agency's Office of Research and Development. The scientists involved were skilled in each topic, and early drafts were peer-reviewed by experts from academia, industry, public interest groups, and other governmental agencies. Subsequently, proposed guidelines were published in the *Federal Register*, reviewed by special panels of EPA's Science Advisory Board (SAB), and revised to take into account public and SAB comments. After final EPA review and Office of Management and Budget review, the guidelines were signed by EPA Administrator Lee M. Thomas on August 22, 1986, and published in the *Federal Register* on September 24, 1986.

Each of the five guidelines provides both technical information and science policy guidance relating to the conduct of EPA risk assessments and presentation of risk assessment information. The guidelines are sufficiently flexible to allow skilled scientists to make appropriate technical judgments on a case-by-case basis, giving full consideration to all relevant scientific information. The guidelines also stress that risk assessments should include a discussion of the strengths and weaknesses of each assessment by describing uncertainties, assumptions, and limitations, as well as the scientific basis and rationale for each assessment. They require risk assessors to inform Agency decisionmakers and the public about the assumptions used in and the implications of individual risk assessment conclusions, so that appropriate risk management decisions can be made and explained.

While these guidelines are published Agency documents, they should not be interpreted as static, but as the first step in the continuing process of identifying the best methods for assessing risk to environmental pollutants. Consequently, the risk assessment guidelines are constantly undergoing Agency scrutiny and will be revised in line with new methods and information, as appropriate.

This document presents the five guidelines as they originally appeared in the *Federal Register* but in a format that is easier to read.

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ABSTRACT

On September 24, 1986, the U.S. Environmental Protection Agency issued risk assessment guidelines relating to five areas: carcinogenicity, mutagenicity, chemical mixtures, suspect developmental toxicants, and estimating exposures (51 FR 33992-34054). The guidelines were developed to promote high technical quality and Agencywide consistency in the risk assessment process. This document presents the five guidelines as they originally appeared in the *Federal Register* but in a format that is easier to read.

TR 4493

51 FR 33992

GUIDELINES FOR CARCINOGEN RISK ASSESSMENT

SUMMARY: On September 24, 1986, the U.S. Environmental Protection Agency issued the following five guidelines for assessing the health risks of environmental pollutants.

Guidelines for Carcinogen Risk Assessment

Guidelines for Estimating Exposures

Guidelines for Mutagenicity Risk Assessment

Guidelines for the Health Assessment of Suspect Developmental Toxicants

Guidelines for the Health Risk Assessment of Chemical Mixtures

This section contains the Guidelines for Carcinogen Risk Assessment.

The Guidelines for Carcinogen Risk Assessment (hereafter "Guidelines") are intended to guide Agency evaluation of suspect carcinogens in line with the policies and procedures established in the statutes administered by the EPA. These Guidelines were developed as part of an interoffice guidelines development program under the auspices of the Office of Health and Environmental Assessment (OHEA) in the Agency's Office of Research and Development. They reflect Agency consideration of public and Science Advisory Board (SAB) comments on the Proposed Guidelines for Carcinogen Risk Assessment published November 23, 1984 (49 FR 46294).

This publication completes the first round of risk assessment guidelines development. These Guidelines will be revised, and new guidelines will be developed, as appropriate.

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SUPPLEMENTARY INFORMATION: In 1983, the National Academy of Sciences (NAS) published its book entitled *Risk Assessment in the Federal Government: Managing the Process*. In that book, the NAS recommended that Federal regulatory agencies establish "inference guidelines" to ensure consistency and technical quality in risk assessments and to ensure that the risk assessment process was maintained as a scientific effort separate from risk management. A task force within EPA accepted that recommendation and requested that Agency scientists begin to develop such guidelines.

General

The guidelines are products of a two-year Agencywide effort, which has included many scientists from the larger scientific community. These guidelines set forth principles and procedures to guide EPA scientists in the conduct of Agency risk assessments, and to inform Agency decision makers and the public about these procedures. In particular, the guidelines emphasize that risk assessments will be conducted on a case-by-case basis, giving full consideration to all relevant scientific information. This case-by-case approach means that Agency experts review the scientific information on each agent and use the most scientifically appropriate interpretation to assess risk. The guidelines also stress that this information will be fully presented in Agency risk assessment documents, and that Agency scientists will identify the strengths and weaknesses of each assessment by describing uncertainties, assumptions, and limitations, as well as the scientific basis and rationale for each assessment.

Finally, the guidelines are formulated in part to bridge gaps in risk assessment methodology and data. By identifying these gaps and the importance of the missing information to the risk assessment process, EPA wishes to encourage research and analysis that will lead to new risk assessment methods and data.

Guidelines for Carcinogen Risk Assessment

Work on the Guidelines for Carcinogen Risk Assessment began in January 1984. Draft guidelines were developed by Agency work groups composed of expert scientists from throughout the Agency. The drafts were peer-reviewed by expert scientists in the field of carcinogenesis from universities, environmental groups, industry, labor, and other governmental agencies. They were then proposed for public comment in the *FEDERAL REGISTER* (49 FR 46294). On November 9, 1984, the Administrator directed that Agency offices use the proposed guidelines in performing risk assessments until final guidelines become available.

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After the close of the public comment period, Agency staff prepared summaries of the comments, analyses of the major issues presented by the commentors, and proposed changes in the language of the guidelines to deal with the issues raised. These analyses were presented to review panels of the SAB on March 4 and April 22-23, 1985, and to the Executive Committee of the SAB on April 25-26, 1985. The SAB meetings were announced in the *FEDERAL REGISTER* as follows: February 12, 1985 (50 FR 5811) and April 4, 1985 (50 FR 13420 and 13421).

In a letter to the Administrator dated June 19, 1985, the Executive Committee generally concurred on all five of the guidelines, but recommended certain revisions, and requested that any revised guidelines be submitted to the appropriate SAB review panel chairman for review and concurrence on behalf of the Executive Committee. As described in the responses to comments (see Part B: Response to the Public and Science Advisory Board Comments), each guidelines document was revised, where appropriate, consistent with the SAB recommendations, and revised draft guidelines were submitted to the panel chairmen. Revised draft Guidelines for Carcinogen Risk Assessment were concurred on in a letter dated February 7, 1986. Copies of the letters are available at the Public Information Reference Unit, EPA Headquarters Library, as indicated elsewhere in this section.

Following this Preamble are two parts: Part A contains the Guidelines and Part B, the Response to the Public and Science Advisory Board Comments (a summary of the major public comments, SAB comments, and Agency responses to those comments).

The Agency is continuing to study the risk assessment issues raised in the guidelines and will revise these Guidelines in line with new information as appropriate.

References, supporting documents, and comments received on the proposed guidelines, as well as copies of the final guidelines, are available for inspection and copying at the Public Information Reference Unit (202-382-5926), EPA Headquarters Library, 401 M Street, S.W., Washington, DC, between the hours of 8:00 a.m. and 4:30 p.m.

I certify that these Guidelines are not major rules as defined by Executive Order 12291, because they are nonbinding policy statements and have no direct effect on the regulated community. Therefore, they will have no effect on costs or prices, and they will

[51 FR 33993]

have no other significant adverse effects on the economy. These Guidelines were reviewed by the Office of Management and Budget under Executive Order 12291.

August 22, 1986

Lee M. Thomas,

Administrator

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TR 4495

REC 6160

Part A: Guidelines for Carcinogen Risk Assessment

I. Introduction

This is the first revision of the 1976 Interim Procedures and Guidelines for Health Risk Assessments of Suspected Carcinogens (U.S. EPA, 1976; Albert et al., 1977). The impetus for this revision is the need to incorporate into these Guidelines the concepts and approaches to carcinogen risk assessment that have been developed during the last ten years. The purpose of these Guidelines is to promote quality and consistency of carcinogen risk assessments within the EPA and to inform those outside the EPA about its approach to carcinogen risk assessment. These Guidelines emphasize the broad but essential aspects of risk assessment that are needed by experts in the various disciplines required (e.g., toxicology, pathology, pharmacology, and statistics) for carcinogen risk assessment. Guidance is given in general terms since the science of carcinogenesis is in a state of rapid advancement, and overly specific approaches may rapidly become obsolete.

These Guidelines describe the general framework to be followed in developing an analysis of carcinogenic risk and some salient principles to be used in evaluating the quality of data and in formulating judgments concerning the nature and magnitude of the cancer hazard from suspect carcinogens. It is the intent of these Guidelines to permit sufficient flexibility to accommodate new knowledge and new assessment methods as they emerge. It is also recognized that there is a need for new methodology that has not been addressed in this document in a number of areas, e.g., the characterization of uncertainty. As this knowledge and assessment methodology are developed, these Guidelines will be revised whenever appropriate.

A summary of the current state of knowledge in the field of carcinogenesis and a statement of broad scientific principles of carcinogen risk assessment, which was developed by the Office of Science and Technology Policy (OSTP, 1985), forms an important basis for these Guidelines; the format of these Guidelines is similar to that proposed by the National Research Council (NRC) of the National Academy of Sciences in a book entitled *Risk Assessment in the Federal Government: Managing the Process* (NRC, 1983).

These Guidelines are to be used within the policy framework already provided by applicable EPA statutes and do not alter such policies. These Guidelines provide general directions for analyzing and organizing available data. They do not imply that one kind of data or another is prerequisite for regulatory action to control, prohibit, or allow the use of a carcinogen.

Regulatory decision making involves two components: risk assessment and risk management. Risk assessment defines the adverse health consequences of exposure to toxic agents. The risk assessments will be carried out independently from considerations of the consequences of regulatory action. Risk management combines the risk assessment with the directives of regulatory legislation, together with socioeconomic, technical, political, and other considerations, to reach a decision as to whether or how much to control future exposure to the suspected toxic agents.

Risk assessment includes one or more of the following components: hazard identification, dose-response assessment, exposure assessment, and risk characterization (NRC, 1983).

Hazard identification is a qualitative risk assessment, dealing with the process of determining whether exposure to an agent has the potential to increase the incidence of cancer. For purposes of these Guidelines, both malignant and benign tumors are used in the evaluation of the carcinogenic hazard. The hazard identification component qualitatively answers the question of how likely an agent is to be a human carcinogen.

Traditionally, quantitative risk assessment has been used as an inclusive term to describe all or parts of dose-response assessment, exposure assessment, and risk characterization. Quantitative risk assessment can be a useful general term in some circumstances, but the more explicit terminology developed by the NRC (1983) is usually preferred. The dose-response assessment defines the relationship between the dose of an agent and the probability of induction of a carcinogenic effect. This component usually entails an extrapolation from the generally high doses administered to experimental animals or exposures noted in epidemiologic studies to the exposure levels expected from human contact with the agent in the environment; it also includes considerations of the validity of these extrapolations.

The exposure assessment identifies populations exposed to the agent, describes their composition and size, and presents the types, magnitudes, frequencies, and durations of exposure to the agent.

[51 FR 33994]

In risk characterization, the results of the exposure assessment and the dose-response assessment are combined to estimate quantitatively the carcinogenic risk. As part of risk characterization, a summary of the strengths and weaknesses in the hazard identification, dose-response assessment, exposure assessment, and the public health risk estimates are presented. Major assumptions, scientific judgments, and, to the extent possible, estimates of the uncertainties embodied in the assessment are also presented, distinguishing clearly between fact, assumption, and science policy.

TR 4496

The National Research Council (NRC, 1983) pointed out that there are many questions encountered in the risk assessment process that are unanswerable given current scientific knowledge. To bridge the uncertainty that exists in these areas where there is no scientific consensus, inferences must be made to ensure that progress continues in the assessment process. The OSTP (1985) reaffirmed this position, and generally left to the regulatory agencies the job of articulating these inferences. Accordingly, the Guidelines incorporate judgmental positions (science policies) based on evaluation of the presently available information and on the regulatory mission of the Agency. The Guidelines are consistent with the principles developed by the OSTP (1985), although in many instances are necessarily more specific.

II. Hazard Identification

A. Overview

The qualitative assessment or hazard identification part of risk assessment contains a review of the relevant biological and chemical information bearing on whether or not an agent may pose a carcinogenic hazard. Since chemical agents seldom occur in a pure state and are often transformed in the body, the review should include available information on contaminants, degradation products, and metabolites.

Studies are evaluated according to sound biological and statistical considerations and procedures. These have been described in several publications (Interagency Regulatory Liaison Group, 1979; OSTP, 1985; Peto et al., 1980; Mantel, 1980; Mantel and Haenszel, 1959; Interdisciplinary Panel on Carcinogenicity, 1984; National Center for Toxicological Research, 1981; National Toxicology Program, 1984; U.S. EPA, 1983a, 1983b, 1983c; Haseman, 1984). Results and conclusions concerning the agent, derived from different types of information, whether indicating positive or negative responses, are melded together into a weight-of-evidence determination. The strength of the evidence supporting a potential human carcinogenicity judgment is developed in a weight-of-evidence stratification scheme.

B. Elements of Hazard Identification

Hazard identification should include a review of the following information to the extent that it is available.

1. *Physical-Chemical Properties and Routes and Patterns of Exposure.* Parameters relevant to carcinogenesis, including physical state, physical-chemical properties, and exposure pathways in the environment should be described where possible.

2. *Structure-Activity Relationships.* This section should summarize relevant structure-activity correlations that support or argue against the prediction of potential carcinogenicity.

3. Meta*bolic and Pharmacokinetic Properties.* This section should summarize relevant metabolic information. Information such as whether the agent is direct-acting or requires conversion to a reactive carcinogenic (e.g., an electrophilic) species, metabolic pathways for such conversions, macromolecular interactions, and fate (e.g., transport, storage, and excretion), as well as species differences, should be discussed and critically evaluated. Pharmacokinetic properties determine the biologically effective dose and may be relevant to hazard identification and other components of risk assessment.

4. To*xicologic Effects.* Toxicologic effects other than carcinogenicity (e.g., suppression of the immune system, endocrine disturbances, organ damage) that are relevant to the evaluation of carcinogenicity should be summarized. Interactions with other chemicals or agents and with lifestyle factors should be discussed. Prechronic and chronic toxicity evaluations, as well as other test results, may yield information on target organ effects, pathophysiological reactions, and preneoplastic lesions that bear on the evaluation of carcinogenicity. Dose-response and time-to-response analyses of these reactions may also be helpful.

5. *Short-Term Tests.* Tests for point mutations, numerical and structural chromosome aberrations, DNA damage/repair, and *in vitro* transformation provide supportive evidence of carcinogenicity and may give information on potential carcinogenic mechanisms. A range of tests from each of the above end points helps to characterize an agent's response spectrum.

Short-term *in vivo* and *in vitro* tests that can give indication of initiation and promotion activity may also provide supportive evidence for carcinogenicity. Lack of positive results in short-term tests for genetic toxicity does not provide a basis for discounting positive results in long-term animal studies.

6. *Long-Term Animal Studies.* Criteria for the technical adequacy of animal carcinogenicity studies have been published (e.g., U.S. Food and Drug Administration, 1982; Interagency Regulatory Liaison Group, 1979; National Toxicology Program, 1984; OSTP, 1985; U.S. EPA, 1983a, 1983b, 1983c; Feron et al., 1980; Mantel, 1980) and should be used to judge the acceptability of individual studies. Transplacental and multigenerational carcinogenesis studies, in addition to more conventional long-term animal studies, can yield useful information about the carcinogenicity of agents.

It is recognized that chemicals that induce benign tumors frequently also induce malignant

tumors, and that benign tumors often progress to malignant tumors (Interdisciplinary Panel on Carcinogenicity, 1984). The incidence of benign and malignant tumors will be combined when scientifically defensible (OSTP, 1985; Principle 8). For example, the Agency will, in general, consider the combination of benign and malignant tumors to be scientifically defensible unless the benign tumors are not considered to have the potential to progress to the associated malignancies of the same histogenic origin. If an increased incidence of benign tumors is observed in the absence of malignant tumors, in most cases the evidence will be considered as limited evidence of carcinogenicity.

The weight of evidence that an agent is potentially carcinogenic for humans increases (1) with the increase in number of tissue sites affected by the agent; (2) with the increase in number of animal species, strains, sexes, and number of experiments and doses showing a carcinogenic response; (3) with the occurrence of clear-cut dose-response relationships as well as a high level of statistical significance of the increased tumor incidence in treated compared to control groups; (4) when there is a dose-related shortening of the time-to-tumor occurrence or time to death with tumor; and (5) when there is a dose-related increase in the proportion of tumors that are malignant.

Long-term animal studies at or near the maximum tolerated dose level (MTD) are used to ensure an adequate power for the detection of carcinogenic

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activity (NTP, 1984; IARC, 1982). Negative long-term animal studies at exposure levels above the MTD may not be acceptable if animal survival is so impaired that the sensitivity of the study is significantly reduced below that of a conventional chronic animal study at the MTD. The OSTP (1985; Principle 4) has stated that,

> The carcinogenic effects of agents may be influenced by non-physiological responses (such as extensive organ damage, radical disruption of hormonal function, saturation of metabolic pathways, formation of stones in the urinary tract, saturation of DNA repair with a functional loss of the system) induced in the model systems. Testing regimes inducing these responses should be evaluated for their relevance to the human response to an agent and evidence from such a study, whether positive or negative, must be carefully reviewed.

Positive studies at levels above the MTD should be carefully reviewed to ensure that the responses are not due to factors which do not operate at exposure levels below the MTD. Evidence indicating that high exposures alter tumor responses by indirect mechanisms that may be unrelated to effects at lower exposures should be dealt with on an individual basis. As noted by the OSTP (1985), "Normal metabolic activation of carcinogens may possibly also be altered and carcinogenic potential reduced as a consequence [of high-dose testing]."

Carcinogenic responses under conditions of the experiment should be reviewed carefully as they relate to the relevance of the evidence to human carcinogenic risks (e.g., the occurrence of bladder tumors in the presence of bladder stones and implantation site sarcomas). Interpretation of animal studies is aided by the review of target organ toxicity and other effects (e.g., changes in the immune and endocrine systems) that may be noted in prechronic or other toxicological studies. Time and dose-related changes in the incidence of preneoplastic lesions may also be helpful in interpreting animal studies.

Agents that are positive in long-term animal experiments and also show evidence of promoting or cocarcinogenic activity in specialized tests should be considered as complete carcinogens unless there is evidence to the contrary because it is, at present, difficult to determine whether an agent is only a promoting or cocarcinogenic agent. Agents that show positive results in special tests for initiation, promotion, or cocarcinogenicity and no indication of tumor response in well-conducted and well-designed long-term animal studies should be dealt with on an individual basis.

To evaluate carcinogenicity, the primary comparison is tumor response in dosed animals as compared with that in contemporary matched control animals. Historical control data are often valuable, however, and could be used along with concurrent control data in the evaluation of carcinogenic responses (Haseman et al., 1984). For the evaluation of rare tumors, even small tumor responses may be significant compared to historical data. The review of tumor data at sites with high spontaneous background requires special consideration (OSTP, 1985; Principle 9). For instance, a response that is significant with respect to the experimental control group may become questionable if the historical control data indicate that the experimental control group had an unusually low background incidence (NTP, 1984).

For a number of reasons, there are widely diverging scientific views (OSTP, 1985; Ward et al., 1979a, b; Tomatis, 1977; Nutrition Foundation, 1983) about the validity of mouse liver tumors as an indication of potential carcinogenicity in humans when such tumors occur in strains with high spontaneous background incidence and when they constitute the only tumor response to an agent. These Guidelines take the position that when the only tumor response is in the mouse liver and when other conditions for a classification of "sufficient" evidence in animal studies are met (e.g., replicate studies, malignancy; see section IV), the data should be considered as "sufficient" evidence of carcinogenicity. It is understood that this classification could be changed on a case-by-case basis to "limited," if warranted, when factors such as the following, are observed: an increased incidence

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of tumors only in the highest dose group and/or only at the end of the study; no substantial dose-related increase in the proportion of tumors that are malignant; the occurrence of tumors that are predominantly benign; no dose-related shortening of the time to the appearance of tumors; negative or inconclusive results from a spectrum of short-term tests for mutagenic activity; the occurrence of excess tumors only in a single sex.

Data from all long-term animal studies are to be considered in the evaluation of carcinogenicity. A positive carcinogenic response in one species/strain/sex is not generally negated by negative results in other species/strain/sex. Replicate negative studies that are essentially identical in all other respects to a positive study may indicate that the positive results are spurious.

Evidence for carcinogenic action should be based on the observation of statistically significant tumor responses in specific organs or tissues. Appropriate statistical analysis should be performed on data from long-term studies to help determine whether the effects are treatment-related or possibly due to chance. These should at least include a statistical test for trend, including appropriate correction for differences in survival. The weight to be given to the level of statistical significance (the p-value) and to other available pieces of information is a matter of overall scientific judgment. A statistically significant excess of tumors of all types in the aggregate, in the absence of a statistically significant increase of any individual tumor type, should be regarded as minimal evidence of carcinogenic action unless there are persuasive reasons to the contrary.

7. Human Studies. Epidemiologic studies provide unique information about the response of humans who have been exposed to suspect carcinogens. Descriptive epidemiologic studies are useful in generating hypotheses and providing supporting data, but can rarely be used to make a causal inference. Analytical epidemiologic studies of the case-control or cohort variety, on the other hand, are especially useful in assessing risks to exposed humans.

Criteria for the adequacy of epidemiologic studies are well recognized. They include factors such as the proper selection and characterization of exposed and control groups, the adequacy of duration and quality of follow-up, the proper identification and characterization of confounding factors and bias, the appropriate consideration of latency effects, the valid ascertainment of the causes of morbidity and death, and the ability to detect specific effects. Where it can be calculated, the statistical power to detect an appropriate outcome should be included in the assessment.

The strength of the epidemiologic evidence for carcinogenicity depends, among other things, on the type of analysis and on the magnitude and specificity of the response. The weight of evidence increases rapidly with the number of adequate studies that show comparable results on populations exposed to the same agent under different conditions.

It should be recognized that epidemiologic studies are inherently capable of detecting only comparatively large increases in the relative risk of

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cancer. Negative results from such studies cannot prove the absence of carcinogenic action; however, negative results from a well-designed and well-conducted epidemiologic study that contains usable exposure data can serve to define upper limits of risk; these are useful if animal evidence indicates that the agent is potentially carcinogenic in humans.

C. Weight of Evidence

Evidence of possible carcinogenicity in humans comes primarily from two sources: long-term animal tests and epidemiologic investigations. Results from these studies are supplemented with available information from short-term tests, pharmacokinetic studies, comparative metabolism studies, structure-activity relationships, and other relevant toxicologic studies. The question of how likely an agent is to be a human carcinogen should be answered in the framework of a weight-of-evidence judgment. Judgments about the weight of evidence involve considerations of the quality and adequacy of the data and the kinds and consistency of responses induced by a suspect carcinogen. There are three major steps to characterizing the weight of evidence for carcinogenicity in humans: (1) characterization of the evidence from human studies and from animal studies individually, (2) combination of the characterizations of these two types of data into an indication of the overall weight of evidence for human carcinogenicity, and (3) evaluation of all supporting information to determine if the overall weight of evidence should be modified.

EPA has developed a system for stratifying the weight of evidence (see section IV). This classification is not meant to be applied rigidly or mechanically. At various points in the above discussion, EPA has emphasized the need for an overall, balanced judgment of the totality of the available evidence. Particularly for well-studied substances, the scientific data base will have a complexity that cannot be captured by any classification scheme. Therefore, the hazard identification section should include a narrative summary of the strengths and weaknesses of the evidence as well as its categorization in the EPA scheme.

The EPA classification system is, in general, an adaptation of the International Agency for Research on Cancer (IARC, 1982) approach for classifying the

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weight of evidence for human data and animal data. The EPA classification system for the characterization of the overall weight of evidence for carcinogenicity (animal, human, and other supportive data) includes: Group A -- Carcinogenic to Humans; Group B -- Probably Carcinogenic to Humans; Group C -- Possibly Carcinogenic to Humans; Group D -- Not Classifiable as to Human Carcinogenicity; and Group E -- Evidence of Non-Carcinogenicity for Humans.

The following modifications of the IARC approach have been made for classifying human and animal studies.

For human studies:

(1) The observation of a statistically significant association between an agent and life-threatening benign tumors in humans is included in the evaluation of risks to humans.

(2) A "no data available" classification is added.

(3) A "no evidence of carcinogenicity" classification is added. This classificaton indicates that no association was found between exposure and increased risk of cancer in well-conducted, well-designed, independent analytical epidemiologic studies.

For animal studies:

(1) An increased incidence of combined benign and malignant tumors will be considered to provide sufficient evidence of carcinogenicity if the other criteria defining the "sufficient" classification of evidence are met (e.g., replicate studies, malignancy; see section IV). Benign and malignant tumors will be combined when scientifically defensible.

(2) An increased incidence of benign tumors alone generally constitutes "limited" evidence of carcinogenicity.

(3) An increased incidence of neoplasms that occur with high spontaneous background incidence (e.g., mouse liver tumors and rat pituitary tumors in certain strains) generally constitutes "sufficient" evidence of carcinogenicity, but may be changed to "limited" when warranted by the specific information available on the agent.

(4) A "no data available" classification has been added.

(5) A "no evidence of carcinogenicity" classification is also added. This operational classification would include substances for which there is no increased incidence of neoplasms in at least two well-designed and well-conducted animal studies of adequate power and dose in different species.

D. Guidance for Dose-Response Assessment

The qualitative evidence for carcinogenesis should be discussed for purposes of guiding the dose-response assessment. The guidance should be given in terms of the appropriateness and limitations of specific studies as well as pharmacokinetic considerations that should be factored into the dose-response assessment. The appropriate method of extrapolation should be factored in when the experimental route of exposure differs from that occurring in humans.

Agents that are judged to be in the EPA weight-of-evidence stratification Groups A and B would be regarded as suitable for quantitative risk assessments. Agents that are judged to be in Group C will generally be regarded as suitable for quantitative risk assessment, but judgments in this regard may be made on a case-by-case basis. Agents that are judged to be in Groups D and E would not have quantitative risk assessments.

E. Summary and Conclusion

The summary should present all of the key findings in all of the sections of the qualitative assessment and the interpretive rationale that forms the basis for the conclusion. Assumptions, uncertainties in the evidence, and other factors that may affect the relevance of the evidence to humans should be discussed. The conclusion should present both the weight-of-evidence ranking and a description that brings out the more subtle aspects of the evidence that may not be evident from the ranking alone.

III. Dose-Response Assessment, Exposure Assessment, and Risk Characterization

After data concerning the carcinogenic properties of a substance have been collected, evaluated, and categorized, it is frequently desirable to estimate the likely range of excess cancer risk associated with given levels and conditions of human exposure. The first step of the analysis needed to make such estimations is the development of the likely relationship between dose and response (cancer incidence) in the region of human exposure. This information on dose-response relationships is coupled with information on the nature and magnitude of human exposure to yield an estimate of human risk. The risk-characterization step also includes an interpretation of these estimates in light of the biological, statistical, and exposure assumptions and uncertainties that have arisen throughout the process of assessing risk.

The elements of dose-response assessment are described in section III.A. Guidance on human exposure assessment is provided in another EPA

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document (U.S. EPA, 1986); however, section III.B. of these Guidelines includes a brief description of the specific type of exposure information that is useful for carcinogen risk assessment. Finally, in section III.C. on risk characterization, there is a description of the manner in which risk estimates should be presented so as to be most informative.

It should be emphasized that calculation of quantitative estimates of cancer risk does not

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require that an agent be carcinogenic in humans. The likelihood that an agent is a human carcinogen is a function of the weight of evidence, as this has been described in the hazard identification section of these Guidelines. It is nevertheless important to present quantitative estimates, appropriately qualified and interpreted, in those circumstances in which there is a reasonable possibility, based on human and animal data, that the agent is carcinogenic in humans.

It should be emphasized in every quantitative risk estimation that the results are uncertain. Uncertainties due to experimental and epidemiologic variability as well as uncertainty in the exposure assessment can be important. There are major uncertainties in extrapolating both from animals to humans and from high to low doses. There are important species differences in uptake, metabolism, and organ distribution of carcinogens, as well as species and strain differences in target-site susceptibility. Human populations are variable with respect to genetic constitution, diet, occupational and home environment, activity patterns, and other cultural factors. Risk estimates should be presented together with the associated hazard assessment (section III.C.3.) to ensure that there is an appreciation of the weight of evidence for carcinogenicity that underlies the quantitative risk estimates.

A. Dose-Response Assessment

1. *Selection of Data.* As indicated in section II.D., guidance needs to be given by the individuals doing the qualitative assessment (toxicologists, pathologists, pharmacologists, etc.) to those doing the quantitative assessment as to the appropriate data to be used in the dose-response assessment. This is determined by the quality of the data, its relevance to human modes of exposure, and other technical details.

If available, estimates based on adequate human epidemiologic data are preferred over estimates based on animal data. If adequate exposure data exist in a well-designed and well-conducted negative epidemiologic study, it may be possible to obtain an upper-bound estimate of risk from that study. Animal-based estimates, if available, also should be presented.

In the absence of appropriate human studies, data from a species that responds most like humans should be used, if information to this effect exists. Where, for a given agent, several studies are available, which may involve different animal species, strains, and sexes at several doses and by different routes of exposure, the following approach to selecting the data sets is used: (1) The tumor incidence data are separated according to organ site and tumor type. (2) All biologically and statistically acceptable data sets are presented. (3) The range of the risk estimates is presented with due regard to biological relevance (particularly in the case of animal studies) and appropriateness of route of exposure. (4) Because it is possible that human sensitivity is as high as the most sensitive responding animal species, in the absence of evidence to the contrary, the biologically acceptable data set from long-term animal studies showing the greatest sensitivity should generally be given the greatest emphasis, again with due regard to biological and statistical considerations.

When the exposure route in the species from which the dose-response information is obtained differs from the route occurring in environmental exposures, the considerations used in making the route-to-route extrapolation must be carefully described. All assumptions should be presented along with a discussion of the uncertainties in the extrapolation. Whatever procedure is adopted in a given case, it must be consistent with the existing metabolic and pharmacokinetic information on the chemical (e.g., absorption efficiency via the gut and lung, target organ doses, and changes in placental transport throughout gestation for transplacental carcinogens).

Where two or more significantly elevated tumor sites or types are observed in the same study, extrapolations may be conducted on selected sites or types. These selections will be made on biological grounds. To obtain a total estimate of carcinogenic risk, animals with one or more tumor sites or types showing significantly elevated tumor incidence should be pooled and used for extrapolation. The pooled estimates will generally be used in preference to risk estimates based on single sites or types. Quantitative risk extrapolations will generally not be done on the basis of totals that include tumor sites without statistically significant elevations.

Benign tumors should generally be combined with malignant tumors for risk estimates unless the benign tumors are not considered to have the potential to progress to the associated malignancies of the same histogenic origin. The contribution of the benign tumors, however, to the total risk should be indicated.

2. *Choice of Mathematical Extrapolation Model.* Since risks at low exposure levels cannot be measured directly either by animal experiments or by epidemiologic studies, a number of mathematical models have been developed to extrapolate from high to low dose. Different extrapolation models, however, may fit the observed data reasonably well but may lead to large differences in the projected risk at low doses.

As was pointed out by OSTP (1985; Principle 26),

> No single mathematical procedure is recognized as the most appropriate for low-dose extrapolation in carcinogenesis. When relevant biological evidence on mechanism of action exists (e.g., pharmacokinetics, target organ dose), the models or procedures

employed should be consistent with the evidence. When data and information are limited, however, and when much uncertainty exists regarding the mechanism of carcinogenic action, models or procedures which incorporate low-dose linearity are preferred when compatible with the limited information.

At present, mechanisms of the carcinogenesis process are largely unknown and data are generally limited. If a carcinogenic agent acts by accelerating the same carcinogenic process that leads to the background occurrence of cancer, the added effect of the carcinogen at low doses is expected to be virtually linear (Crump et al., 1976).

The Agency will review each assessment as to the evidence on carcinogenesis mechanisms and other biological or statistical evidence that indicates the suitability of a particular extrapolation model. Goodness-of-fit to the experimental observations is not an effective means of discriminating among models (OSTP, 1985). A rationale will be included to justify the use of the chosen model. In the absence of adequate information to the contrary, the linearized multistage procedure will be employed. Where appropriate, the results of using various extrapolation models may be useful for comparison with the linearized multistage procedure. When longitudinal data on tumor development are available, time-to-tumor models may be used.

It should be emphasized that the linearized multistage procedure leads to

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a plausible upper limit to the risk that is consistent with some proposed mechanisms of carcinogenesis. Such an estimate, however, does not necessarily give a realistic prediction of the risk. The true value of the risk is unknown, and may be as low as zero. The range of risks, defined by the upper limit given by the chosen model and the lower limit which may be as low as zero, should be explicitly stated. An established procedure does not yet exist for making "most likely" or "best" estimates of risk within the range of uncertainty defined by the upper and lower limit estimates. If data and procedures become available, the Agency will also provide "most likely" or "best" estimates of risk. This will be most feasible when human data are available and when exposures are in the dose range of the data.

In certain cases, the linearized multistage procedure cannot be used with the observed data as, for example, when the data are nonmonotonic or flatten out at high doses. In these cases, it may be necessary to make adjustments to achieve low-dose linearity.

When pharmacokinetic or metabolism data are available, or when other substantial evidence on the mechanistic aspects of the carcinogenesis process exists, a low-dose extrapolation model other than the linearized multistage procedure might be considered more appropriate on biological grounds. When a different model is chosen, the risk assessment should clearly discuss the nature and weight of evidence that led to the choice. Considerable uncertainty will remain concerning response at low doses; therefore, in most cases an upper-limit risk estimate using the linearized multistage procedure should also be presented.

3. *Equivalent Exposure Units Among Species.* Low-dose risk estimates derived from laboratory animal data extrapolated to humans are complicated by a variety of factors that differ among species and potentially affect the response to carcinogens. Included among these factors are differences between humans and experimental test animals with respect to life span, body size, genetic variability, population homogeneity, existence of concurrent disease, pharmacokinetic effects such as metabolism and excretion patterns, and the exposure regimen.

The usual approach for making interspecies comparisons has been to use standardized scaling factors. Commonly employed standardized dosage scales include mg per kg body weight per day, ppm in the diet or water, mg per m^2 body surface area per day, and mg per kg body weight per lifetime. In the absence of comparative toxicological, physiological, metabolic, and pharmacokinetic data for a given suspect carcinogen, the Agency takes the position that the extrapolation on the basis of surface area is considered to be appropriate because certain pharmacological effects commonly scale according to surface area (Dedrick, 1973; Freireich et al., 1966; Pinkel, 1958).

B. Exposure Assessment

In order to obtain a quantitative estimate of the risk, the results of the dose-response assessment must be combined with an estimate of the exposures to which the populations of interest are likely to be subject. While the reader is referred to the Guidelines for Estimating Exposures (U.S. EPA, 1986) for specific details, it is important to convey an appreciation of the impact of the strengths and weaknesses of exposure assessment on the overall cancer risk assessment process.

At present there is no single approach to exposure assessment that is appropriate for all cases. On a case-by-case basis, appropriate methods are selected to match the data on hand and the level of sophistication required. The assumptions, approximations, and uncertainties need to be clearly stated because, in some instances, these will have a major effect on the risk assessment.

In general, the magnitude, duration, and frequency of exposure provide fundamental information for estimating the concentration of the carcinogen to which the organism is exposed. These data are generated from monitoring information, modeling results, and/or reasoned estimates. An appropriate treatment of exposure should consider

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the potential for exposure via ingestion, inhalation, and dermal penetration from relevant sources of exposures including multiple avenues of intake from the same source.

Special problems arise when the human exposure situation of concern suggests exposure regimens, e.g., route and dosing schedule that are substantially different from those used in the relevant animal studies. Unless there is evidence to the contrary in a particular case, the cumulative dose received over a lifetime, expressed as average daily exposure prorated over a lifetime, is recommended as an appropriate measure of exposure to a carcinogen. That is, the assumption is made that a high dose of a carcinogen received over a short period of time is equivalent to a corresponding low dose spread over a lifetime. This approach becomes more problematical as the exposures in question become more intense but less frequent, especially when there is evidence that the agent has shown dose-rate effects.

An attempt should be made to assess the level of uncertainty associated with the exposure assessment which is to be used in a cancer risk assessment. This measure of uncertainty should be included in the risk characterization (section III.C.) in order to provide the decision-maker with a clear understanding of the impact of this uncertainty on any final quantitative risk estimate. Subpopulations with heightened susceptibility (either because of exposure or predisposition) should, when possible, be identified.

C. Risk Characterization

Risk characterization is composed of two parts. One is a presentation of the numerical estimates of risk; the other is a framework to help judge the significance of the risk. Risk characterization includes the exposure assessment and dose-response assessment; these are used in the estimation of carcinogenic risk. It may also consist of a unit-risk estimate which can be combined elsewhere with the exposure assessment for the purposes of estimating cancer risk.

Hazard identification and dose-response assessment are covered in sections II. and III.A., and a detailed discussion of exposure assessment is contained in EPA's Guidelines for Estimating Exposures (U.S. EPA, 1986). This section deals with the numerical risk estimates and the approach to summarizing risk characterization.

1. *Options for Numerical Risk Estimates.* Depending on the needs of the individual program offices, numerical estimates can be presented in one or more of the following three ways.

a. Unit Risk -- Under an assumption of low-dose linearity, the unit cancer risk is the excess lifetime risk due to a continuous constant lifetime exposure of one unit of carcinogen concentration. Typical exposure units include ppm or ppb in food or water, mg/kg/day by ingestion, or ppm or $\mu g/m^3$ in air.

b. Dose Corresponding to a Given Level of Risk -- This approach can be useful, particularly when using nonlinear extrapolation models where the unit risk would differ at different dose levels.

c. Individual and Population Risks -- Risks may be characterized either in terms of the excess individual lifetime risks, the excess number of cancers

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produced per year in the exposed population, or both.

Irrespective of the options chosen, the degree of precision and accuracy in the numerical risk estimates currently do not permit more than one significant figure to be presented.

2. *Concurrent Exposure.* In characterizing the risk due to concurrent exposure to several carcinogens, the risks are combined on the basis of additivity unless there is specific information to the contrary. Interactions of cocarcinogens, promoters, and inititators with known carcinogens should be considered on a case-by-case basis.

3. *Summary of Risk Characterization.* Whichever method of presentation is chosen, it is critical that the numerical estimates not be allowed to stand alone, separated from the various assumptions and uncertainties upon which they are based. The risk characterization should contain a discussion and interpretation of the numerical estimates that affords the risk manager some insight into the degree to which the quantitative estimates are likely to reflect the true magnitude of human risk, which generally cannot be known with the degree of quantitative accuracy reflected in the numerical estimates. The final risk estimate will be generally rounded to one significant figure and will be coupled with the EPA classification of the qualitative weight of evidence. For example, a lifetime individual risk of 2×10^{-4} resulting from exposure to a "probable human carcinogen" (Group B2) should be designated as 2×10^{-4} [B2] . This bracketed designation of the qualitative weight of evidence should be included with all numerical risk estimates (i.e., unit risks, which are risks at a specified concentration or concentrations corresponding to a given risk). Agency statements, such as *FEDERAL REGISTER* notices, briefings, and action memoranda, frequently include numerical estimates of carcinogenic risk. It is recommended that whenever these numerical estimates are used, the qualitative weight-of-evidence classification should also be included.

The section on risk characterization should summarize the hazard identification, dose-response assessment, exposure assessment, and the public health risk estimates. Major assumptions, scientific judgments, and, to the extent possible, estimates of

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the uncertainties embodied in the assessment are presented.

IV. EPA Classification System for Categorizing Weight of Evidence for Carcinogenicity from Human and Animal Studies (Adapted from IARC)

A. Assessment of Weight of Evidence for Carcinogenicity from Studies in Humans

Evidence of carcinogenicity from human studies comes from three main sources:

1. Case reports of individual cancer patients who were exposed to the agent(s).
2. Descriptive epidemiologic studies in which the incidence of cancer in human populations was found to vary in space or time with exposure to the agent(s).
3. Analytical epidemiologic (case-control and cohort) studies in which individual exposure to the agent(s) was found to be associated with an increased risk of cancer.

Three criteria must be met before a causal association can be inferred between exposure and cancer in humans:

1. There is no identified bias that could explain the association.
2. The possibility of confounding has been considered and ruled out as explaining the association.
3. The association is unlikely to be due to chance.

In general, although a single study may be indicative of a cause-effect relationship, confidence in inferring a causal association is increased when several independent studies are concordant in showing the association, when the association is strong, when there is a dose-response relationship, or when a reduction in exposure is followed by a reduction in the incidence of cancer.

The weight of evidence for carcinogenicity[1] from studies in humans is classified as:

1. Sufficient evidence of carcinogenicity, which indicates that there is a causal relationship between the agent and human cancer.
2. Limited evidence of carcinogenicity, which indicates that a causal interpretation is credible, but that alternative explanations, such as chance, bias, or confounding, could not adequately be excluded.
3. Inadequate evidence, which indicates that one of two conditions prevailed: (a) there were few pertinent data, or (b) the available studies, while showing evidence of association, did not exclude chance, bias, or confounding, and therefore a causal interpretation is not credible.
4. No data, which indicates that data are not available.
5. No evidence, which indicates that no association was found between exposure and an increased risk of cancer in well-designed and well-conducted independent analytical epidemiologic studies.

B. Assessment of Weight of Evidence for Carcinogenicity from Studies in Experimental Animals

These assessments are classified into five groups:

1. Sufficient evidence[2] of carcinogenicity, which indicates that there is an increased incidence of malignant tumors or combined malignant and benign tumors:[3] (a) in multiple species or strains; or (b) in multiple experiments (e.g., with different routes of administration or using different dose levels); or (c) to an unusual degree in a single experiment with regard to high incidence, unusual site or type of tumor, or early age at onset.

Additional evidence may be provided by data on dose-response effects, as well as information from short-term tests or on chemical structure.

2. Limited evidence of carcinogenicity, which means that the data suggest a carcinogenic effect but are limited because: (a) the studies involve a single species, strain, or experiment and do not meet criteria for sufficient evidence (see section IV. B.1.c); (b) the experiments are restricted by inadequate dosage levels, inadequate duration of exposure to the agent, inadequate period of follow-up, poor survival, too few animals, or inadequate reporting; or (c) an increase in the incidence of benign tumors only.
3. Inadequate evidence, which indicates that because of major qualitative or quantitative limitations, the studies cannot be interpreted as showing either the presence or absence of a carcinogenic effect.
4. No data, which indicates that data are not available.
5. No evidence, which indicates that there is no increased incidence of neoplasms in at least two well-designed

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and well-conducted animal studies in different species.

The classifications "sufficient evidence" and "limited evidence" refer only to the weight of the experimental evidence that these agents are carcinogenic and not to the potency of their carcinogenic action.

[1] For purposes of public health protection, agents associated with life-threatening benign tumors in humans are included in the evaluation.

[2] An increased incidence of neoplasms that occur with high spontaneous background incidence (e.g., mouse liver tumors and rat pituitary tumors in certain strains) generally constitutes "sufficient" evidence of carcinogenicity, but may be changed to "limited" when warranted by the specific information available on the agent.

[3] Benign and malignant tumors will be combined unless the benign tumors are not considered to have the potential to progress to the associated malignancies of the same histogenic origin.

C. Categorization of Overall Weight of Evidence for Human Carcinogenicity

The overall scheme for categorization of the weight of evidence of carcinogenicity of a chemical for humans uses a three-step process. (1) The weight of evidence in human studies or animal studies is summarized; (2) these lines of information are combined to yield a tentative assignment to a category (see Table 1); and (3) all relevant supportive information is evaluated to see if the designation of the overall weight of evidence needs to be modified. Relevant factors to be included along with the tumor information from human and animal studies include structure-activity relationships; short-term test findings; results of appropriate physiological, biochemical, and toxicological observations; and comparative metabolism and pharmacokinetic studies. The nature of these findings may cause one to adjust the overall categorization of the weight of evidence.

The agents are categorized into five groups as follows:

Group A -- Human Carcinogen

This group is used only when there is sufficient evidence from epidemiologic studies to support a causal association between exposure to the agents and cancer.

Group B -- Probable Human Carcinogen

This group includes agents for which the weight of evidence of human carcinogenicity based on epidemiologic studies is "limited" and also includes agents for which the weight of evidence of carcinogenicity based on animal studies is "sufficient." The group is divided into two subgroups. Usually, Group B1 is reserved for agents for which there is limited evidence of carcinogenicity from epidemiologic studies. It is reasonable, for practical purposes, to regard an agent for which there is "sufficient" evidence of carcinogenicity in animals as if it presented a carcinogenic risk to humans. Therefore, agents for which there is "sufficient" evidence from animal studies and for which there is "inadequate evidence" or "no data" from epidemiologic studies would usually be categorized under Group B2.

Group C -- Possible Human Carcinogen

This group is used for agents with limited evidence of carcinogenicity in animals in the absence of human data. It includes a wide variety of evidence, e.g., (a) a malignant tumor response in a single well-conducted experiment that does not meet conditions for sufficient evidence, (b) tumor responses of marginal statistical significance in studies having inadequate design or reporting, (c) benign but not malignant tumors with an agent showing no response in a variety of short-term tests for mutagenicity, and (d) responses of marginal statistical significance in a tissue known to have a high or variable background rate.

Group D -- Not Classifiable as to Human Carcinogenicity

This group is generally used for agents with inadequate human and animal evidence of carcinogenicity or for which no data are available.

Group E -- Evidence of Non-Carcinogenicity for Humans

This group is used for agents that show no evidence for carcinogenicity in at least two adequate animal tests in different species or in both adequate epidemiologic and animal studies.

The designation of an agent as being in Group E is based on the available evidence and should not be interpreted as a definitive conclusion that the agent will not be a carcinogen under any circumstances.

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TABLE 1.--ILLUSTRATIVE CATEGORIZATION OF EVIDENCE BASED ON ANIMAL AND HUMAN DATA[1]

Human evidence	Animal evidence				
	Sufficient	Limited	Inadequate	No data	No evidence
Sufficient	A	A	A	A	A
Limited	B1	B1	B1	B1	B1
Inadequate	B2	C	D	D	D
No data	B2	C	D	D	E
No evidence	B2	C	D	D	E

1 The above assignments are presented for illustrative purposes. There may be nuances in the classification of both animal and human data indicating that different categorizations than those given in the table should be assigned. Furthermore, these assignments are tentative and may be modified by ancillary evidence. In this regard all relevant information should be evaluated to determine if the designation of the overall weight of evidence needs to be modified. Relevant factors to be included along with the tumor data from human and animal studies include structure-activity relationships, short-term test findings, results of appropriate physiological, biochemical, and toxicological observations, and comparative metabolism and pharmacokinetic studies. The nature of these findings may cause an adjustment of the overall categorization of the weight of evidence.

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Part B: Response to Public and Science Advisory Board Comments

I. Introduction

This section summarizes the major issues raised during both the public comment period on the Proposed Guidelines for Carcinogen Risk Assessment published on November 23, 1984 (49 FR 46294), and also during the April 22-23, 1985, meeting of the Carcinogen Risk Assessment Guidelines Panel of the Science Advisory Board (SAB).

In order to respond to these issues the Agency modified the proposed guidelines in two stages. First, changes resulting from consideration of the public comments were made in a draft sent to the SAB review panel prior to their April meeting. Secondly, the guidelines were further modified in response to the panel's recommendations.

The Agency received 62 sets of comments during the public comment period, including 28 from corporations, 9 from professional or trade associations, and 4 from academic institutions. In general, the comments were favorable. The commentors welcomed the update of the 1976 guidelines and felt that the proposed guidelines of

1985 reflected some of the progress that has occurred in understanding the mechanisms of carcinogenesis. Many commentors, however, felt that additional changes were warranted.

The SAB concluded that the guidelines are "reasonably complete in their conceptual framework and are sound in their overall interpretation of the scientific issues" (Report by the SAB Carcinogenicity Guidelines Review Group, June 19, 1985). The SAB suggested various editorial changes and raised some issues regarding the content of the proposed guidelines, which are discussed below. Based on these recommendations, the Agency has modified the draft guidelines.

II. Office of Science and Technology Policy Report on Chemical Carcinogens

Many commentors requested that the final guidelines not be issued until after publication of the report of the Office of Technology and Science Policy (OSTP) on chemical carcinogens. They further requested that this report be incorporated into the final Guidelines for Carcinogen Risk Assessment.

The final OSTP report was published in 1985 (50 FR 10372). In its deliberations, the Agency reviewed the final OSTP report and feels that the Agency's guidelines are consistent with the principles established by the OSTP. In its review, the SAB agreed that the Agency guidelines are generally consistent with the OSTP report. To emphasize this consistency, the OSTP principles have been incorporated into the guidelines when controversial issues are discussed.

III. Inference Guidelines

Many commentors felt that the proposed guidelines did not provide a sufficient distinction between scientific fact and policy decisions. Others felt that EPA should not attempt to propose firm guidelines in the absence of scientific consensus. The SAB report also indicated the need to "distinguish recommendations based on scientific evidence from those based on science policy decisions."

The Agency agrees with the recommendation that policy, judgmental, or inferential decisions should be clearly identified. In its revision of the proposed guidelines, the Agency has included phrases (e.g., "the Agency takes the position that") to more clearly distinguish policy decisions.

The Agency also recognizes the need to establish procedures for action on important issues in the absence of complete scientific knowledge or consensus. This need was acknowledged in both the National Academy of Sciences book entitled *Risk Management in the Federal Government: Managing the Process* and the OSTP report on chemical carcinogens. As the NAS report states, "Risk assessment is an analytic process that is firmly based on scientific considerations, but it also requires judgments to be made when the available information is incomplete. These judgments inevitably draw on both scientific and policy considerations."

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The judgments of the Agency have been based on current available scientific information and on the combined experience of Agency experts. These judgments, and the resulting guidance, rely on inference; however, the positions taken in these inference guidelines are felt to be reasonable and scientifically defensible. While all of the guidance is, to some degree, based on inference, the guidelines have attempted to distinguish those issues that depended more on judgment. In these cases, the Agency has stated a position but has also retained flexibility to accommodate new data or specific circumstances that demonstrate that the proposed position is inaccurate. The Agency recognizes that scientific opinion will be divided on these issues.

Knowledge about carcinogens and carcinogenesis is progressing at a rapid rate. While these guidelines are considered a best effort at the present time, the Agency has attempted to incorporate flexibility into the current guidelines and also recommends that the guidelines be revised as often as warranted by advances in the field.

IV. Evaluation of Benign Tumors

Several commentors discussed the appropriate interpretation of an increased incidence of benign tumors alone or with an increased incidence of malignant tumors as part of the evaluation of the carcinogenicity of an agent. Some comments were supportive of the position in the proposed guidelines, i.e., under certain circumstances, the incidence of benign and malignant tumors would be combined, and an increased incidence of benign tumors alone would be considered an indication, albeit limited, of carcinogenic potential. Other commentors raised concerns about the criteria that would be used to decide which tumors should be combined. Only a few commentors felt that benign tumors should never be considered in evaluating carcinogenic potential.

The Agency believes that current information supports the use of benign tumors. The guidelines have been modified to incorporate the language of the OSTP report, i.e., benign tumors will be combined with malignant tumors when scientifically defensible. This position allows flexibility in evaluating the data base for each agent. The guidelines have also been modified to indicate that, whenever benign and malignant tumors have been combined, and the agent is considered a candidate for quantitative risk extrapolation, the contribution of benign tumors to the estimation of risk will be indicated.

V. *Transplacental and Multigenerational Animal Bioassays*

As one of its two proposals for additions to the guidelines, the SAB recommended a discussion of transplacental and multigenerational animal bioassays for carcinogenicity.

The Agency agrees that such data, when available, can provide useful information in the evaluation of a chemical's potential carcinogenicity and has stated this in the final guidelines. The Agency has also revised the guidelines to indicate that such studies may provide additional information on the metabolic and pharmacokinetic properties of the chemical. More guidance on the specific use of these studies will be considered in future revisions of these guidelines.

VI. Maximum Tolerated Dose

The proposed guidelines discussed the implications of using a maximum tolerated dose (MTD) in bioassays for carcinogenicity. Many commentors requested that EPA define MTD. The tone of the comments suggested that the commentors were concerned about the uses and interpretations of high-dose testing.

The Agency recognizes that controversy currently surrounds these issues. The appropriate text from the OSTP report has been incorporated into the final guidelines which suggests that the consequences of high-dose testing be evaluated on a case-by-case basis.

VII. Mouse Liver Tumors

A large number of commentors expressed opinions about the assessment of bioassays in which the only increase in tumor incidence was liver tumors in the mouse. Many felt that mouse liver tumors were afforded too much credence, especially given existing information that indicates that they might arise by a different mechanism, e.g., tissue damage followed by regeneration. Others felt that mouse liver tumors were but one case of a high background incidence of one particular type of tumor and that all such tumors should be treated in the same fashion.

The Agency has reviewed these comments and the OSTP principle regarding this issue. The OSTP report does not reach conclusions as to the treatment of tumors with a high spontaneous background rate, but states, as is now included in the text of the guidelines, that these data require special consideration. Although questions have been raised regarding the validity of mouse liver tumors in general, the Agency feels that mouse liver tumors cannot be ignored as an indicator of carcinogenicity. Thus, the position in the proposed guidelines has not been changed: an increased incidence of only mouse liver tumors will be regarded as "sufficient" evidence of carcinogenicity if all other criteria, e.g., replication and malignancy, are met with the understanding that this classification could be changed to "limited" if warranted. The factors that may cause this re-evaluation are indicated in the guidelines.

VIII. Weight-of Evidence Catagories

The Agency was praised by both the public and the SAB for incorporating a weight-of-evidence scheme into its evaluation of carcinogenic risk. Certain specific aspects of the scheme, however, were criticized.

1. Several commentors noted that while the text of the proposed guidelines clearly states that EPA will use all available data in its categorization of the weight of the evidence that a chemical is a carcinogen, the classification system in Part A, section IV did not indicate the manner in which EPA will use information other than data from humans and long-term animal studies in assigning a weight-of-evidence classification.

The Agency has added a discussion to Part A, section IV.C. dealing with the characterization of overall evidence for human carcinogenicity. This discussion clarifies EPA's use of supportive information to adjust, as warranted, the designation that would have been made solely on the basis of human and long-term animal studies.

2. The Agency agrees with the SAB and those commentors who felt that a simple classification of the weight of evidence, e.g., a single letter or even a descriptive title, is inadequate to describe fully the weight of evidence for each individual chemical. The final guidelines propose that a paragraph summarizing the data should accompany the numerical estimate and weight-of-evidence classification whenever possible.

3. Several commentors objected to the descriptive title E (No Evidence of Carcinogenicity for Humans) because they felt the title would be confusing to people inexperienced with the classification system. The title for Group E, No Evidence of Carcinogenicity for Humans, was thought by these commentors to suggest the absence of data. This group, however, is intended to be reserved for agents for which there exists credible data demonstrating that the agent is not carcinogenic.

Based on these comments and further discussion, the Agency has changed the

[51 FR 34003]

title of Group E to "Evidence of Non-Carcinogenicity for Humans."

4. Several commentors felt that the title for Group C, Possible Human Carcinogen, was not sufficiently distinctive from Group B, Probable Human Carcinogen. Other commentors felt that those agents that minimally qualified for Group C would lack sufficient data for such a label.

The Agency recognizes that Group C covers a range of chemicals and has considered whether to subdivide Group C. The consensus of the Agency's

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Carcinogen Risk Assessment Committee, however, is that the current groups, which are based on the IARC categories, are a reasonable stratification and should be retained at present. The structure of the groups will be reconsidered when the guidelines are reviewed in the future. The Agency also feels that the descriptive title it originally selected best conveys the meaning of the classification within the context of EPA's past and current activities.

5. Some commentors indicated a concern about the distinction between B1 and B2 on the basis of epidemiologic evidence only. This issue has been under discussion in the Agency and may be revised in future versions of the guidelines.

6. Comments were also received about the possibility of keeping the groups for animal and human data separate without reaching a combined classification. The Agency feels that a combined classification is useful; thus, the combined classification was retained in the final guidelines.

The SAB suggested that a table be added to Part A, section IV to indicate the manner in which human and animal data would be combined to obtain an overall weight-of-evidence category. The Agency realizes that a table that would present all permutations of potentially available data would be complex and possibly impossible to construct since numerous combinations of ancillary data (e.g., genetic toxicity, pharmacokinetics) could be used to raise or lower the weight-of-evidence classification. Nevertheless, the Agency decided to include a table to illustrate the most probable weight-of-evidence classification that would be assigned on the basis of standard animal and human data without consideration of the ancillary data. While it is hoped that this table will clarify the weight-of-evidence classifications, it is also important to recognize that an agent may be assigned to a final categorization different from the category which would appear appropriate from the table and still conform to the guidelines.

IX. Quantitative Estimates of Risk

The method for quantitative estimates of carcinogenic risk in the proposed guidelines received substantial comments from the public. Five issues were discussed by the Agency and have resulted in modifications of the guidelines.

1. The major criticism was the perception that EPA would use only one method for the extrapolation of carcinogenic risk and would, therefore, obtain one estimate of risk. Even commentors who concur with the procedure usually followed by EPA felt that some indication of the uncertainty of the risk estimate should be included with the risk estimate.

The Agency feels that the proposed guidelines were not intended to suggest that EPA would perform quantitative risk estimates in a rote or mechanical fashion. As indicated by the OSTP report and paraphrased in the proposed guidelines, no single mathematical procedure has been determined to be the most appropriate method for risk extrapolation. The final guidelines quote rather than paraphrase the OSTP principle. The guidelines have been revised to stress the importance of considering all available data in the risk assessment and now state, "The Agency will review each assessment as to the evidence on carcinogenic mechanisms and other biological or statistical evidence that indicates the suitability of a particular extrapolation model." Two issues are emphasized: First, the text now indicates the potential for pharmacokinetic information to contribute to the assessment of carcinogenic risk. Second, the final guidelines state that time-to-tumor risk extrapolation models may be used when longitudinal data on tumor development are available.

2. A number of commentors noted that the proposed guidelines did not indicate how the uncertainties of risk characterization would be presented. The Agency has revised the proposed guidelines to indicate that major assumptions, scientific judgments, and, to the extent possible, estimates of the uncertainties embodied in the risk assessment will be presented along with the estimation of risk.

3. The proposed guidelines stated that the appropriateness of quantifying risks for chemicals in Group C (Possible Human Carcinogen), specifically those agents that were on the boundary of Groups C and D (Not Classifiable as to Human Carcinogenicity), would be judged on a case-by-case basis. Some commentors felt that quantitative risk assessment should not be performed on any agent in Group C.

Group C includes a wide range of agents, including some for which there are positive results in one species in one good bioassay. Thus, the Agency feels that many agents in Group C will be suitable for quantitative risk assessment, but that judgments in this regard will be made on a case-by-case basis.

4. A few commentors felt that EPA intended to perform quantitative risk estimates on aggregate tumor incidence. While EPA will consider an increase in total aggregate tumors as suggestive of potential carcinogenicity, EPA does not generally intend to make quantitative estimates of carcinogenic risk based on total aggregate tumor incidence.

5. The proposed choice of body surface area as an interspecies scaling factor was criticized by several commentors who felt that body weight was also appropriate and that both methods should be used. The OSTP report recognizes that both scaling factors are in common use. The Agency feels that the choice of the body surface area scaling factor can be

justified from the data on effects of drugs in various species. Thus, EPA will continue to use this scaling factor unless data on a specific agent suggest that a different scaling factor is justified. The uncertainty engendered by choice of scaling factor will be included in the summary of uncertainties associated with the assessment of risk mentioned in point 1, above.

In the second of its two proposals for additions to the proposed guidelines, the SAB suggested that a sensitivity analysis be included in EPA's quantitative estimate of a chemical's carcinogenic potency. The Agency agrees that an analysis of the assumptions and uncertainties inherent in an assessment of carcinogenic risk must be accurately portrayed. Sections of the final guidelines that deal with this issue have been strengthened to reflect the concerns of the SAB and the Agency. In particular, the last paragraph of the guidelines states that "major assumptions, scientific judgments, and, to the extent possible, estimates of the uncertainties embodied in the assessment" should be presented in the summary characterizing the risk. Since the assumptions and uncertainties will vary for each assessment, the Agency feels that a formal requirement for a particular type of sensitivity analysis would be less useful than a case-by-case evaluation of the particular assumptions and uncertainties most significant for a particular risk assessment.

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GUIDELINES FOR MUTAGENICITY RISK ASSESSMENT

SUMMARY: On September 24, 1986, the U.S. Environmental Protection Agency issued the following five guidelines for assessing the health risks of environmental pollutants.

Guidelines for Carcinogen Risk Assessment

Guidelines for Estimating Exposures

Guidelines for Mutagenicity Risk Assessment

Guidelines for the Health Assessment of Suspect Developmental Toxicants

Guidelines for the Health Risk Assessment of Chemical Mixtures

This section contains the Guidelines for Mutagenicity Risk Assessment.

The Guidelines for Mutagenicity Risk Assessment (hereafter "Guidelines") are intended to guide Agency analysis of mutagenicity data in line with the policies and procedures established in the statutes administered by the EPA. These Guidelines were developed as part of an interoffice guidelines development program under the auspices of the Office of Health and Environmental Assessment (OHEA) in the Agency's Office of Research and Development. They reflect Agency consideration of public and Science Advisory Board (SAB) comments on the Proposed Guidelines for Mutagenicity Risk Assessment published November 23, 1984 (49 FR 46314).

This publication completes the first round of risk assessment guidelines development. These Guidelines will be revised, and new guidelines will be developed, as appropriate.

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SUPPLEMENTARY INFORMATION: In 1983, the National Academy of Sciences (NAS) published its book entitled *Risk Assessment in the Federal Government: Managing the Process*. In that book, the NAS recommended that Federal regulatory agencies establish "inference guidelines" to ensure consistency and technical quality in risk assessments and to ensure that the risk assessment process was maintained as a scientific effort separate from risk management. A task force within EPA accepted that recommendation and requested that Agency scientists begin to develop such guidelines.

General

The guidelines are products of a two-year Agencywide effort, which has included many scientists from the larger scientific community. These guidelines set forth principles and procedures to guide EPA scientists in the conduct of Agency risk assessments, and to inform Agency decision makers and the public about these procedures. In particular, the guidelines emphasize that risk assessments will be conducted on a case-by-case basis, giving full consideration to all relevant scientific information. This case-by-case approach means that Agency experts review the scientific information on each agent and use the most scientifically appropriate interpretation to assess risk. The guidelines also stress that this information will be fully presented in Agency risk assessment documents, and that Agency scientists will identify the strengths and weaknesses of each assessment by describing uncertainties, assumptions, and limitations, as well as the scientific basis and rationale for each assessment.

Finally, the guidelines are formulated in part to bridge gaps in risk assessment methodology and data. By identifying these gaps and the importance of the missing information to the risk assessment process, EPA wishes to encourage research and analysis that will lead to new risk assessment methods and data.

Guidelines for Mutagenicity Risk Assessment

Work on the Guidelines for Mutagenicity Risk Assessment began in January 1984. Draft guidelines were developed by Agency work groups composed of expert scientists from throughout the Agency. The drafts were peer-reviewed by expert scientists in the field of genetic toxicology from universities, environmental groups, industry, labor, and other governmental agencies. They were then proposed for public comment in the *FEDERAL REGISTER* (49 FR 46314). On November 9, 1984, the Administrator directed that Agency offices use the proposed guidelines in performing risk assessments until final guidelines become available.

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After the close of the public comment period, Agency staff prepared summaries of the comments, analyses of the major issues presented by the commentors, and preliminary Agency responses to those comments. These analyses were presented to review panels of the SAB on March 4 and April 22-23, 1985, and to the Executive Committee of the SAB on April 25-26, 1985. The SAB meetings were announced in the *FEDERAL REGISTER* as follows: February 12, 1985 (50 FR 5811) and April 4, 1985 (50 FR 13420 and 13421).

In a letter to the Administrator dated June 19, 1985, the Executive Committee generally concurred on all five of the guidelines, but recommended certain revisions, and requested that any revised guidelines be submitted to the appropriate SAB review panel chairman for review and concurrence on behalf of the Executive Committee. As described in the responses to comments (see Part B: Response to the Public and Science Advisory Board Comments), each guidelines document was revised, where appropriate, consistent with the SAB recommendations, and revised draft guidelines were submitted to the panel chairmen. Revised draft Guidelines for Mutagenicity Risk Assessment were concurred on in a letter dated September 24, 1985. Copies of the letters are available at the Public Information Reference Unit, EPA Headquarters Library, as indicated elsewhere in this section.

Following this Preamble are two parts: Part A contains the Guidelines and Part B, the Response to the Public and Science Advisory Board Comments (a summary of the major public comments, SAB comments, and Agency responses to those comments).

The Agency is continuing to study the risk assessment issues raised in the guidelines and will revise these Guidelines in line with new information as appropriate.

References, supporting documents, and comments received on the proposed guidelines, as well as copies of the final guidelines, are available for inspection and copying at the Public Information Reference Unit (202-382-5926), EPA Headquarters Library, 401 M Street, S.W., Washington, DC, between the hours of 8:00 a.m. and 4:30 p.m.

I certify that these Guidelines are not major rules as defined by Executive Order 12291, because they are nonbinding policy statements and have no direct effect on the regulated community. Therefore, they will have no effect on costs or prices, and they will have no other significant adverse effects on the economy. These Guidelines were reviewed by the Office of Management

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and Budget under Executive Order 12291.

August 22, 1986

Lee M. Thomas,

Administrator

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Part B: Response to Public and Science Advisory Board Comments

Part A: Guidelines for Mutagenicity Risk Assessment

I. Introduction

This section describes the procedures that the U.S. Environmental Protection Agency will follow in evaluating the potential genetic risk associated with human exposure to chemicals. The central purpose of the health risk assessment is to provide a judgment concerning the weight of evidence that an agent is a potential human mutagen, capable of inducing transmitted genetic changes, and, if so, to provide a judgment on how great an impact this agent is likely to have on public health. Regulatory decision making involves two components: risk assessment and risk management. Risk assessment estimates the potential adverse health consequences of exposure to toxic chemicals; risk management combines the risk assessment with the directives of the enabling regulatory legislation--together with socioeconomic, technical, political, and other considerations--to reach a decision as to whether or how much to control future exposure to the chemicals. The issue of risk management will not be dealt with in these Guidelines.

Risk assessment is comprised of the following components: hazard identification, dose-response assessment, exposure assessment, and risk characterization (1). Hazard identification is the qualitative risk assessment, dealing with the inherent toxicity of a chemical substance. The qualitative mutagenicity assessment answers the question of how likely an agent is to be a human mutagen. The three remaining components

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comprise quantitative risk assessment, which provides a numerical estimate of the public health consequences of exposure to an agent. The quantitative mutagenicity risk assessment deals with the question of how much mutational damage is likely to be produced by exposure to a given agent under particular exposure scenarios.

In a dose-response assessment, the relationship between the dose of a chemical and the probability of induction of an adverse effect is defined. The component generally entails an extrapolation from the high doses administered to experimental animals or noted in some epidemiologic studies to the low exposure levels expected from human contact with the chemical in the environment.

The exposure assessment identifies populations exposed to toxic chemicals, describes their composition and size, and presents the types, magnitudes, frequencies, and durations of exposure to the chemicals. This component is developed independently of the other components of the mutagenicity assessment and is addressed in separate Agency guidelines (2).

In risk characterization, the outputs of the exposure assessment and the dose-response assessment are combined to estimate quantitatively the mutation risk, which is expressed as either estimated increase of genetic disease per generation or per lifetime, or the fractional increase in the assumed background mutation rate of humans. In each step of the assessment, the strengths and weaknesses of the major assumptions need to be presented, and the nature and magnitude of uncertainties need to be characterized.

The procedures set forth in these Guidelines will ensure consistency in the Agency's scientific risk assessments for mutagenic effects. The necessity for a consistent approach to the evaluation of mutagenic risk from chemical substances arises from the authority conferred upon the Agency by a number of statutes to regulate potential mutagens. As appropriate, these Guidelines will apply to statutes administered by the Agency, including the Federal Insecticide, Fungicide, and Rodenticide Act; the Toxic Substances Control Act; the Clean Air Act; the Federal Water Pollution Control Act; the Safe Drinking Water Act; the Resource Conservation and Recovery Act; and the Comprehensive Environmental Response, Compensation, and Liability Act. Because each statute is administered by separate offices, a consistent Agency-wide approach for performing risk assessments is desirable.

The mutagenicity risk assessments prepared pursuant to these Guidelines will be utilized with the requirements and constraints of the applicable statutes to arrive at regulatory decisions concerning mutagenicity. The standards of the applicable statutes and regulations may dictate that additional considerations (e.g., the economic and social benefits associated with use of the chemical substance) will come into play in reaching appropriate regulatory decisions.

The Agency has not attempted to provide in the Guidelines a detailed discussion of the mechanisms of mutagenicity or of the various test systems that are currently in use to detect mutagenic potential. Background information on mutagenesis and mutagenicity test systems is available in "Identifying and Estimating the Genetic Impact of Chemical Mutagens", National Academy of Sciences (NAS) Committee on Chemical Environmental Mutagens (3), as well as in other recent publications (4, 5).

The Agency is concerned with the risk associated with both germ-cell mutations and somatic-cell mutations. Mutations carried in germ cells may be inherited by future generations and may contribute to genetic disease, whereas mutations occurring in somatic cells may be implicated in the etiology of several disease states, including cancer. These Guidelines, however, are only concerned with genetic damage as it relates to germ-cell mutations. The use of mutagenicity test results in the assessment of carcinogenic risk is described in the Guidelines for Carcinogen Risk Assessment (6).

As a result of the progress in the control of infectious diseases, increases in average human life span, and better procedures for identifying genetic disorders, a considerable heritable genetic disease burden has been recognized in the human population. It is estimated that at least 10% of all human disease is related to specific genetic abnormalities, such as abnormal composition, arrangement, or dosage of genes and chromosomes (3, 7, 8). Such genetic abnormalities can lead to structural or functional health impairments. These conditions may be expressed in *utero*; at the time of birth; or during infancy, childhood, adolescence, or adult life; they may be chronic or acute in nature. As a result, they often have a severe impact upon the affected individuals and their families in terms of physical and mental

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suffering and economic losses, and upon society in general, which often becomes responsible for institutional care of severely affected individuals. Some examples of genetic disorders are Down and Klinefelter syndromes, cystic fibrosis, hemophilia, sickle-cell anemia, and achondroplastic dwarfism. Other commonly recognized conditions that are likely to have a genetic component include hypercholesterolemia, hypertension, pyloric stenosis, glaucoma, allergies, several types of cancer, and mental retardation. These disorders are only a few of the thousands that are at least partially genetically determined (9).

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Estimation of the fraction of human genetic disorders that result from new mutations is difficult, although in certain specific cases insights are available (10). It is clear that recurring mutation is important in determining the incidence of certain genetic disorders, such as some chromosomal aberration syndromes (e.g., Down syndrome) and rare dominant and X-linked recessive diseases (e.g., achondroplasia and hemophilia A). For other single-factor disorders (e.g., sickle-cell anemia) and certain multifactorial disorders (e.g., pyloric stenosis), the contribution of new mutations to disease frequency is probably small. However, it is generally recognized that most newly-arising mutations that are phenotypically expressed are in some ways deleterious to the organism receiving them (3, 7, 8). Adverse effects may be manifested at the biochemical, cellular, or physiological levels of organization. Although mutations are the building blocks for further evolutionary change of species, it is believed that increases in the mutation rate could lead to an increased frequency of expressed genetic disorders in the first and subsequent generations.

Life in our technological society results in exposure to many natural and synthetic chemicals. Some have been shown to have mutagenic activity in mammalian and submammalian test systems, and thus may have the potential to increase genetic damage in the human population. Chemicals exhibiting mutagenic activity in various test systems have been found distributed among foods, tobacco, drugs, food additives, cosmetics, industrial compounds, pesticides, and consumer products. The extent to which exposure to natural and synthetic environmental agents may have increased the frequency of genetic disorders in the present human population and contributed to the mutational "load" that will be transmitted to future generations is unknown at this time. However, for the reasons cited above, it seems prudent to limit exposures to potential human mutagens.

A. Concepts Relating to Heritable Mutagenic Risk

These Guidelines are concerned with chemical substances or mixtures of substances that can induce alterations in the genome of either somatic or germinal cells. The mutagenicity of physical agents (e.g., radiation) is not addressed here. There are several mutagenic end points of concern to the Agency. These include point mutations (i.e., submicroscopic changes in the base sequence of DNA) and structural or numerical chromosome aberrations. Structural aberrations include deficiencies, duplications, insertions, inversions, and translocations, whereas numerical aberrations are gains or losses of whole chromosomes (e.g., trisomy, monosomy) or sets of chromosomes (haploidy, polyploidy).

Certain mutagens, such as alkylating agents, can directly induce alterations in the DNA. Mutagenic effects may also come about through mechanisms other than chemical alterations of DNA. Among these are interference with normal DNA synthesis (as caused by some metal mutagens), interference with DNA repair, abnormal DNA methylation, abnormal nuclear division processes, or lesions in non-DNA targets (e.g., protamine, tubulin).

Evidence that an agent induces heritable mutations in human beings could be derived from epidemiologic data indicating a strong association between chemical exposure and heritable effects. It is difficult to obtain such data because any specific mutation is a rare event, and only a small fraction of the estimated thousands of human genes and conditions are currently useful as markers in estimating mutation rates. Human genetic variability, small numbers of offspring per individual, and long generation times further complicate such studies. In addition, only disorders caused by dominant mutations, some sex-linked recessive mutations, and certain chromosome aberrations can be detected in the first generation after their occurrence. Conditions caused by autosomal recessive disorders (which appear to occur more frequently than dominant disorders) or by polygenic traits may go unrecognized for many generations. Therefore, in the absence of human epidemiological data, it is appropriate to rely on data from experimental animal systems as long as the limitations of using surrogate and model systems are clearly stated.

Despite species differences in metabolism, DNA repair, and other physiological processes affecting chemical mutagenesis, the virtual universality of DNA as the genetic material and of the genetic code provides a rationale for using various nonhuman test systems to predict the intrinsic mutagenicity of test chemicals. Additional support for the use of nonhuman systems is provided by the observation that chemicals causing genetic effects in one species or test system frequently cause similar effects in other species or systems. Evidence also exists that chemicals can induce genetic damage in somatic cells of exposed humans. For example, high doses of mutagenic chemotherapeutic agents have been shown to cause chromosomal abnormalities (11), sister chromatic exchange (11), and, quite probably, point mutations in human lymphocytes exposed *in vivo* (12). While these results are not in germ cells, they do indicate that it is possible to induce mutagenic events in human cells *in vivo*. Furthermore, a wide variety of different types of mutations have been observed in humans including numerical chromosome aberrations, translocations, base-pair substitutions, and frameshift mutations. Although the cause of these mutations is uncertain, it is clear from these observations that the human germ-cell DNA is subject to the same types of

mutational events that are observed in other species and test systems.

Certain test systems offer notable advantages: cost; anatomical, histological, and/or metabolic similarities to humans; suitability for handling large numbers of test organisms; a large data base; or a basis for characterizing genetic events.

B. Test Systems

Many test systems are currently available that can contribute information about the mutagenic potential of a test compound with respect to various genetic end points. These tests have recently been evaluated through the EPA Gene-Tox Programs and the results of Phase I have been published (5). The Agency's Office of Pesticides and Toxic Substances has published various testing guidelines for the detection of mutagenic effects (13, 14).

Test systems for detecting point mutations include those in bacteria, eukaryotic microorganisms, higher plants, insects, mammalian somatic cells in culture, and germinal cells of intact mammals. Data from heritable, mammalian germ-cell tests provide the best experimental evidence that a

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chemical is a potential human germ-cell mutagen since these tests require that mutations occur in germinal cells and that they are transmitted to the next generation. To date, the most extensively used test for the induction of heritable mutation is the mouse specific-locus test which measures the induction of recessive mutations at seven loci concerned with coat color and ear morphology. While this test has a large data base compared to other germ-cell assays, it is difficult to extrapolate results to humans since recessive mutations may occur more frequently than dominants, and the impact of recessive mutations is not seen for many generations. Information on frequencies of induced mutations resulting in health disorders in the first generation may be obtained from mouse systems designed to detect skeletal abnormalities, cataracts, or general morphological abnormalities. However, these assays have been used to a relatively limited extent, and there is a need for additional studies with known, chemical germ-cell mutagens to further characterize the test systems. Because large numbers of offspring must usually be generated in the systems described above, it is not expected that many chemicals will be tested using these systems. To obtain data on a large number of environmental chemicals, it will be necessary to rely on other tests to identify and characterize hazards from gene mutations.

Test systems for detecting structural chromosome aberrations have been developed in a variety of organisms including higher plants, insects, fish, birds, and several mammalian species. Many of these assays can be performed *in vitro* or *in vivo*, and in either germ or somatic cells. Procedures available for detecting structural chromosome aberrations in mammalian germ cells include measurement of heritable translocations or dominant lethality, as well as direct cytogenetic analyses of germ cells and early embryos in rodents.

Some chemicals may cause numerical chromosome changes (i.e., aneuploidy) as their sole mutagenic effect. These agents may not be detected as mutagens if evaluated only in tests for DNA damage, gene mutations, or chromosome breakage and rearrangement. Therefore, it is important to consider tests for changes in chromosome number in the total assessment of mutagenic hazards. Although tests for the detection of variation in the chromosome number are still at an early stage of development, systems exist in such diverse organisms as fungi, Drosophila, mammalian cells in culture, and intact mammals (e.g., mouse X-chromosome loss assay). Aneuploidy can arise from disturbances in a number of events affecting the meiotic process (15, 16). Although the mechanisms by which nondisjunction occurs are not well understood, mitotic structures other than DNA may be the target molecules for at least some mechanisms of induced nondisjunction.

Other end points that provide information bearing on the mutagenicity of a chemical can be detected by a variety of test systems. Such tests measure DNA damage in eukaryotic or prokaryotic cells, unscheduled DNA synthesis in mammalian somatic and germ cells, mitotic recombination and gene conversion in yeast, and sister-chromatid exchange in mammalian somatic and germ cells. Results in these assays are useful because the induction of these end points often correlates positively with the potential of a chemical to induce mutations.

In general, for all three end points (i.e., point mutations and numerical and structural aberrations), the Agency will place greater weight on tests conducted in germ cells than in somatic cells, on tests performed *in vivo* rather than *in vitro*, in eukaryotes rather than prokaryotes, and in mammalian species rather than in submammalian species. Formal numerical weighting systems have been developed (17); however, the Agency has concluded that these do not readily accommodate such variables as dose range, route of exposure, and magnitude of response.

The Agency anticipates that from time to time somatic cell data from chemically exposed human beings will be available (e.g., cytogenetic markers in peripheral lymphocytes). When possible, the Agency will use such data in conjunction with somatic and germ cell comparisons from *in vivo* mammalian experimental systems as a component in performing risk assessments.

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The test systems mentioned previously are not the only ones that will provide evidence of mutagenicity or related DNA effects. These systems are enumerated merely to demonstrate the breadth of the available techniques for characterizing mutagenic hazards, and to indicate the types of data that the Agency will consider in its evaluation of mutagenic potential of a chemical agent. Most systems possess certain limitations that must be taken into account. The selection and performance of appropriate tests for evaluating the risks associated with human exposure to any suspected mutagen will depend on sound scientific judgment and experience, and may necessitate consultation with geneticists familiar with the sensitivity and experimental design of the test system in question. In view of the rapid advances in test methodology, the Agency expects that both the number and quality of the tools for assessing genetic risk to human beings will increase with time. The Agency will closely monitor developments in mutagenicity evaluation and will refine its risk assessment scheme as better test systems become available.

II. Qualitative Assessment (Hazard Identification)

The assessment of potential human germ-cell mutagenic risk is a multistep process. The first step is an analysis of the evidence bearing on a chemical's ability to induce mutagenic events, while the second step involves an analysis of its ability to produce these events in the mammalian gonad. All relevant information is then integrated into a weight-of-evidence scheme which presents the strength of the information bearing on the chemical's potential ability to produce mutations in human germ cells. For chemicals demonstrating this potential, one may decide to proceed with an evaluation of the quantitative consequences of mutation following expected human exposure.

For hazard identification, it is clearly desirable to have data from mammalian germ-cell tests, such as the mouse specific-locus test for point mutations and the heritable translocation or germ-cell cytogenetic tests for structural chromosome aberrations. It is recognized, however, that in most instances such data will not be available, and alternative means of evaluation will be required. In such cases the Agency will evaluate the evidence bearing on the agent's mutagenic activity and the agent's ability to interact with or affect the mammalian gonadal target. When evidence exists that an agent possesses both these attributes, it is reasonable to deduce that the agent is a potential human germ-cell mutagen.

While mammalian germ-cell assays are presently primarily performed on male animals, a chemical cannot be considered to be a non-mutagen for mammalian germ cells unless it is shown to be negative in both sexes. Furthermore, because most mammalian germ-cell assays are performed in mice, it is noteworthy that the data from ionizing radiation suggest that the female mouse immature oocyte may not be an appropriate surrogate for the same stage in the human female in mutagenicity testing. However,

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mutagenicity data on the maturing and mature oocyte of the mouse may provide a useful model for human risk assessment.

A. Mutagenic Activity

In evaluating chemicals for mutagenic activity, a number of factors will be considered: 1) genetic end points (e.g., gene mutations, structural or numerical chromosomal aberrations) detected by the test systems, 2) sensitivity and predictive value of the test systems for various classes of chemical compounds, 3) number of different test systems used for detecting each genetic end point, 4) consistency of the results obtained in different test systems and different species, 5) aspects of the dose-response relationship, and 6) whether the tests are conducted in accordance with appropriate test protocols agreed upon by experts in the field.

B. Chemical Interactions in the Mammalian Gonad

Evidence for chemical interaction in the mammalian gonad spans a range of different types of findings. Each chemical under consideration needs to be extensively reviewed since this type of evidence may be part of testing exclusive of mutagenicity per se (e.g., reproduction, metabolism, and mechanistic investigations). Although it is not possible to classify clearly each type of information that may be available on a chemical, two possible groups are illustrated.

1. *Sufficient evidence* of chemical interaction is given by the demonstration that an agent interacts with germ-cell DNA or other chromatin constituents, or that it induces such end points as unscheduled DNA synthesis, sister-chromatid exchange, or chromosomal aberrations in germinal cells.

2. *Suggestive evidence* will include the finding of adverse gonadal effects such as sperm abnormalities following acute, subchronic, or chronic toxicity testing, or findings of adverse reproductive effects such as decreased fertility, which are consistent with the chemical's interaction with germ cells.

C. Weight-of-Evidence Determination

The evidence for a chemical's ability to produce mutations and to interact with the germinal target are integrated into a weight-of-evidence judgment that the agent may pose a hazard as a potential human germ-cell mutagen. All information bearing on the subject, whether indicative of potential concern or not, must be evaluated. Whatever

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evidence may exist from humans must also be factored into the assessment.

All germ-cell stages are important in evaluating chemicals because some chemicals have been shown to be positive in postgonial stages but not in gonia (18). When human exposures occur, effects on postgonial stages should be weighted by the relative sensitivity and the duration of the stages. Chemicals may show positive effects for some end points and in some test systems, but negative responses in others. Each review must take into account the limitations in the testing and in the types of responses that may exist.

To provide guidance as to the categorization of the weight of evidence, a classification scheme is presented to illustrate, in a simplified sense, the strength of the information bearing on the potential for human germ-cell mutagenicity. It is not possible to illustrate all potential combinations of evidence, and considerable judgment must be exercised in reaching conclusions. In addition, certain responses in tests that do not measure direct mutagenic end points (e.g., SCE induction in mammalian germ cells) may provide a basis for raising the weight of evidence from one category to another. The categories are presented in decreasing order of strength of evidence.

1. Positive data derived from human germ-cell mutagenicity studies, when available, will constitute the highest level of evidence for human mutagenicity.

2. Valid positive results from studies on heritable mutational events (of any kind) in mammalian germ cells.

3. Valid positive results from mammalian germ-cell chromosome aberration studies that do not include an intergeneration test.

4. Sufficient evidence for a chemical's interaction with mammalian germ cells, together with valid positive mutagenicity test results from two assay systems, at least one of which is mammalian (*in vitro* or *in vivo*). The positive results may both be for gene mutations or both for chromosome aberrations; if one is for gene mutations and the other for chromosome aberrations, both must be from mammalian systems.

5. Suggestive evidence for a chemical's interaction with mammalian germ cells, together with valid positive mutagenicity evidence from two assay systems as described under 4, above. Alternatively, positive mutagenicity evidence of less strength than defined under 4, above, when combined with sufficient evidence for a chemical's interaction with mammalian germ cells.

6. Positive mutagenicity test results of less strength than defined under 4, combined with suggestive evidence for a chemical's interaction with mammalian germ cells.

7. Although definitive proof of non-mutagenicity is not possible, a chemical could be classified operationally as a non-mutagen for human germ cells, if it gives valid negative test results for all end points of concern.

8. Inadequate evidence bearing on either mutagenicity or chemical interaction with mammalian germ cells.

III. Quantitative Assessment

The preceding section addressed primarily the processes of hazard identification, i.e., the determination of whether a substance is a potential germ-cell mutagen. Often, no further data will be available, and judgments will need to be based mainly on qualitative criteria. Quantitative risk assessment is a two-step process: determination of the heritable effect per unit of exposure (dose-response) and the relationship between mutation rate and disease incidence. The procedures that are presently accepted for the estimation of an increase in disease resulting from increased mutation have been described (3, 7, 8). Dose-response information is combined with anticipated levels and patterns of human exposure in order to derive a quantitative assessment (risk characterization).

A. Dose Response

Dose-response assessments can presently only be performed using data from *in vivo*, heritable mammalian germ-cell tests, until such time as other approaches can be demonstrated to have equivalent predictability. The morphological specific-locus and biochemical specific-locus assays can provide data on the frequencies of recessive mutations induced by different chemical exposure levels, and similar data can be obtained for heritable chromosomal damage using the heritable translocation test. Data on the frequencies of induced mutations resulting in health disorders in the first generation may be obtained from mouse systems designed to detect skeletal abnormalities, cataracts, or general morphological abnormalities. Assays that directly detect heritable health effects in the first generation may provide the best basis for predicting human health risks that result from mutagen exposure. The experimental data on induced mutation frequency are usually obtained at exposure levels much higher than those that will be experienced by human beings. An assessment of human risk is obtained by extrapolating the induced mutation frequency or the observed phenotypic

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effect downward to the approximate level of anticipated human exposure. In performing these extrapolations, the Agency will place greater weight on data derived from exposures and exposure rates that most closely simulate those experienced by the human population under study.

The Agency will strive to use the most appropriate extrapolation models for risk analysis

and will be guided by the available data and mechanistic considerations in this selection. However, it is anticipated that for tests involving germ cells of whole mammals, few dose points will be available to define dose-response functions. The Agency is aware that for at least one chemical that has been tested for mutations in mammalian germ cells, there exist departures from linearity at low exposure and exposure rates in a fashion similar to that seen for ionizing radiation that has a low linear energy transfer (19). The Agency will consider all relevant models for gene and chromosomal mutations in performing low-dose extrapolations and will choose the most appropriate model. This choice will be consistent both with the experimental data available and with current knowledge of relevant mutational mechanisms.

An experimental approach for quantitative assessment of genetic risk, which may have utility in the future, uses molecular dosimetry data from intact mammals in conjunction with mutagenicity and dosimetry data from other validated test systems (20). The intact mammal is used primarily for relating the exposure level for a given route of administration of a chemical to germ-cell dose, i.e., the level of mutagen-DNA interactions. This information is then used in conjunction with results obtained from mutagenicity test systems in which the relationship between the induction of mutations and chemical interactions with DNA can be derived. With mutagen-DNA interactions as the common denominator, a relationship can be constructed between mammalian exposure and the induced mutation frequency. The amount of DNA binding induced by a particular chemical agent may often be determined at levels of anticipated human exposure.

For some mutagenic events, DNA may not necessarily be the critical target. Interaction of chemicals with other macromolecules, such as tubulin, which is involved in the separation of chromosomes during nuclear division, can lead to chromosomal nondisjunction. At present, general approaches are not available for dose-response assessments for these types of mutations. Ongoing research should provide the means to make future assessments on chemicals causing aneuploidy.

B. Exposure Asssessment

The exposure assessment identifies populations exposed to toxic chemicals; describes their composition and size; and presents the types, magnitudes, frequencies, and durations of exposure to the chemicals. This component is developed independently of the other components of the mutagenicity assessment (2).

C. Risk Characterization

In performing mutagenicity risk assessments, it is important to consider each genetic end point individually. For example, although certain chemical substances that interact with DNA may cause both point and chromosomal mutations, it is expected that the ratio of these events may differ among chemicals and between doses for a given chemical. Furthermore, transmissible chromosomal aberrations are recoverable with higher frequencies from meiotic and postmeiotic germ-cell stages, which have a brief life span, than in spermatogonial stem cells, which can accumulate genetic damage throughout the reproductive life of an individual. For these reasons, when data are available, the Agency, to the best extent possible, will assess risks associated with all genetic end points.

Any risk assessment should clearly delineate the strengths and weaknesses of the data, the assumptions made, the uncertainties in the methodology, and the rationale used in reaching the conclusions, e.g., similar or different routes of exposure and metabolic differences between humans and test animals. When possible, quantitative risk assessments should be expressed in terms of the estimated increase of genetic disease per generation, or the fractional increase in the assumed background spontaneous mutation rate of humans (7). Examples of quantitative risk estimates have been published (7, 8, 21); these examples may be of use in performing quantitative risk assessments for mutagens.

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Part B: Response to Public and Science Advisory Board Comments

This section summarizes some of the issues raised in public and Science Advisory Board (SAB) comments on the Proposed Guidelines for Mutagenicity Risk Assessment published on November 23, 1984 (49 FR 46314). Unlike the other guidelines published on the same date, the Proposed Guidelines for Mutagenicity Risk Assessment contained a detailed section dealing with public comments received in response to the original proposal of 1980 (45 FR 74984). Several of the comments received in response to the proposed guidelines of 1984 were similar to those received in response to the proposed guidelines of 1980. Those comments are not addressed here because the position of the Agency on those issues has been presented in the responses included with the 1984 proposed guidelines (49 FR 46315- 46316).

A total of 44 comments were received in response to the proposed guidelines of 1984: 21 from manufacturers of regulated products, 10 from associations, 9 from government agencies, 2 from educational institutions, 1 from an individual, and 1 from a private consulting firm. The proposed guidelines and the public comments received were transmitted to the Agency's SAB prior to its public review of the proposed guidelines held April 22-23, 1985. The majority of the comments were favorable and expressed the opinion that the proposed guidelines accurately represent the existing state of knowledge in the field of mutagenesis. Several commentors offered suggestions for further clarification of particular issues, and many of the suggestions have been incorporated.

The two areas that received the most substantive comments were the sections concerning Weight-of-Evidence Determination and Dose Response. The comments on the proposed weight-of-evidence scheme ranged from suggestions for the elimination of a formal scheme to the expansion of the scheme to cover more potential data configurations. The SAB recommended an eight-level rank ordering scheme to define levels of evidence relating to human germ-cell mutagenicity. The Agency has incorporated this scheme into the Guidelines. Some commentors and the SAB suggested that the molecular dosimetry approach to dose-response data be presented as a concept that may be useful in the future rather than being available for use now. The Agency agrees that the data base at the present time is too sparse to recommend a general application of this approach to a wide range of chemical classes, and the Guidelines have been changed to reflect this. It should be noted, however, that the Agency strongly supports the development of molecular dosimetry methodologies as they relate to both an understanding of dose-response relationships and to methods for studying human exposure. A number of comments suggesting clarifications and editorial changes have been incorporated and the references have been expanded.

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GUIDELINES FOR THE HEALTH RISK ASSESSMENT OF CHEMICAL MIXTURES

SUMMARY: On September 24, 1986, the U.S. Environmental Protection Agency issued the following five guidelines for assessing the health risks of environmental pollutants.

Guidelines for Carcinogen Risk Assessment

Guidelines for Estimating Exposures

Guidelines for Mutagenicity Risk Assessment

Guidelines for the Health Assessment of Suspect Developmental Toxicants

Guidelines for the Health Risk Assessment of Chemical Mixtures

This section contains the Guidelines for the Health Risk Assessment of Chemical Mixtures.

The Guidelines for the Health Risk Assessment of Chemical Mixtures (hereafter "Guidelines") are intended to guide Agency analysis of information relating to health effects data on chemical mixtures in line with the policies and procedures established in the statutes administered by the EPA. These Guidelines were developed as part of an interoffice guidelines development program under the auspices of the Office of Health and Environmental Assessment (OHEA) in the Agency's Office of Research and Development. They reflect Agency consideration of public and Science Advisory Board (SAB) comments on the Proposed Guidelines for the Health Risk Assessment of Chemical Mixtures published January 9, 1985 (50 FR 1170).

This publication completes the first round of risk assessment guidelines development. These Guidelines will be revised, and new guidelines will be developed, as appropriate.

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SUPPLEMENTARY INFORMATION: In 1983, the National Academy of Sciences (NAS) published its book entitled *Risk Assessment in the Federal Government: Managing the Process*. In that book, the NAS recommended that Federal regulatory agencies establish "inference guidelines" to ensure consistency and technical quality in risk assessments and to ensure that the risk assessment process was maintained as a scientific effort separate from risk management. A task force within EPA accepted that recommendation and requested that Agency scientists begin to develop such guidelines.

General

The guidelines are products of a two-year Agencywide effort, which has included many scientists from the larger scientific community. These guidelines set forth principles and procedures to guide EPA scientists in the conduct of Agency risk assessments, and to inform Agency decision makers and the public about these procedures. In particular, the guidelines emphasize that risk assessments will be conducted on a case-by-case basis, giving full consideration to all relevant scientific information. This case-by-case approach means that Agency experts review the scientific information on each agent and use the most scientifically appropriate interpretation to assess risk. The guidelines also stress that this information will be fully presented in Agency risk assessment documents, and that Agency scientists will identify the strengths and weaknesses of each assessment by describing uncertainties, assumptions, and limitations, as well as the scientific basis and rationale for each assessment.

Finally, the guidelines are formulated in part to bridge gaps in risk assessment methodology and data. By identifying these gaps and the importance of the missing information to the risk assessment process, EPA wishes to encourage research and analysis that will lead to new risk assessment methods and data.

Guidelines for the Health Risk Assessment of Chemical Mixtures

Work on the Guidelines for the Health Risk Assessment of Chemical Mixtures began in January 1984. Draft guidelines were developed by Agency work groups composed of expert scientists from throughout the Agency. The drafts were peer-reviewed by expert scientists in the fields of toxicology, pharmacokinetics, and statistics from universities, environmental groups, industry, labor, and other governmental agencies. They were then proposed for public comment in the *FEDERAL REGISTER* (50 FR 1170). On November 9, 1984, the Administrator directed that Agency offices use the

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proposed guidelines in performing risk assessments until final guidelines become available. After the close of the public comment period, Agency staff prepared summaries of the comments, analyses of the major issues presented by the commentors, and preliminary Agency responses to those comments. These analyses were presented to review panels of the SAB on March 4 and April 22-23, 1985, and to the Executive Committee of the SAB on April 25-26, 1985. The SAB meetings were announced in the *FEDERAL REGISTER* as follows: February 12, 1985 (50 FR 5811) and April 4, 1985 (50 FR 13420 and 13421).

In a letter to the Administrator dated June 19, 1985, the Executive Committee generally concurred on all five of the guidelines, but recommended certain revisions, and requested that any revised guidelines be submitted to the appropriate SAB review panel chairman for review and concurrence on behalf of the Executive Committee. As described in the responses to comments (see Part B: Response to the Public and Science Advisory Board Comments), each guidelines document was revised, where appropriate, consistent with the SAB recommendations, and revised draft guidelines were submitted to the panel chairmen. Revised draft Guidelines for the Health Risk Assessment of Chemical Mixtures were concurred on in a letter dated August 16, 1985. Copies of the letters are available at the Public Information Reference Unit, EPA Headquarters Library, as indicated elsewhere in this section.

Following this Preamble are two parts: Part A contains the Guidelines and Part B, the Response to the Public and Science Advisory Board Comments (a summary of the major public comments, SAB comments, and Agency responses to those comments).

The SAB requested that the Agency develop a technical support document for these Guidelines. The SAB identified the need for this type of document due to the limited knowledge on interactions of chemicals in biological systems. Because of this, the SAB commented that progress in improving risk assessment will be particularly dependent upon progress in the science of interactions.

Agency staff have begun preliminary work on the technical support document and expect it to be completed by early 1987. The Agency is continuing to study the risk assessment issues raised in the guidelines and will revise these Guidelines in line with new information as appropriate.

[51 FR 34015]

References, supporting documents, and comments received on the proposed guidelines, as well as copies of the final guidelines, are available for inspection and copying at the Public Information Reference Unit (202-382-5926), EPA Headquarters Library, 401 M Street, S.W., Washington, DC, between the hours of 8:00 a.m. and 4:30 p.m.

I certify that these Guidelines are not major rules as defined by Executive Order 12291, because they are nonbinding policy statements and have no direct effect on the regulated community. Therefore, they will have no effect on costs or prices, and they will have no other significant adverse effects on the economy. These Guidelines were reviewed by the Office of Management and Budget under Executive Order 12291.

August 22, 1986

Lee M. Thomas,

Administrator

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Part A: Guidelines for the Health Risk Assessment of Chemical Mixtures

I. Introduction

The primary purpose of this document is to generate a consistent Agency approach for evaluating data on the chronic and subchronic effects of chemical mixtures. It is a procedural guide that emphasizes broad underlying principles of the various science disciplines (toxicology, pharmacology, statistics) necessary for assessing health risk from chemical mixture exposure. Approaches to be used with respect to the analysis and evaluation of the various data are also discussed.

It is not the intent of these Guidelines to regulate any social or economic aspects concerning risk of injury to human health or the environment caused by exposure to a chemical agent(s). All such action is addressed in specific statutes and federal legislation and is independent of these Guidelines.

While some potential environmental hazards involve significant exposure to only a single compound, most instances of environmental contamination involve concurrent or sequential exposures to a mixture of compounds that may induce similar or dissimilar effects over exposure periods ranging from short-term to lifetime. For the purposes of these Guidelines, mixtures will be defined as any combination of two or more chemical substances regardless of source or of spatial or temporal proximity. In some instances, the mixtures are highly complex consisting of scores of compounds that are generated simultaneously as by-products from a single source or process (e.g., coke oven emissions and diesel exhaust). In other cases, complex mixtures of related compounds are produced as commercial products (e.g., PCBs, gasoline and pesticide formulations) and eventually released to the environment. Another class of mixtures consists of compounds, often unrelated chemically or commercially, which are placed in the same area for disposal or storage, eventually come into contact with each other, and are released as a mixture to the environment. The quality and quantity of pertinent information available for risk assessment varies considerably for different mixtures. Occasionally, the chemical composition of a mixture is well characterized, levels of exposure to the population are known, and detailed toxicologic data on the mixture are available. Most frequently, not all components of the mixture are known, exposure data are uncertain, and toxicologic data on the known components of the mixture are limited. Nonetheless, the Agency may be required to take action because of the number of individuals at potential risk or because of the known toxicologic effects of these compounds that have been identified in the mixture.

The prediction of how specific mixtures of toxicants will interact must be based on an understanding of the mechanisms of such interactions. Most reviews and texts that discuss toxicant interactions attempt to discuss the biological or chemical bases of the interactions (e.g., Klaassen and Doull, 1980; Levine, 1973; Goldstein et al., 1974; NRC, 1980a; Veldstra, 1956; Withey, 1981). Although different authors use somewhat different classification schemes when discussing the ways in which toxicants interact, it generally is recognized that toxicant interactions may occur during any of the toxicologic processes that take place with a single compound: absorption, distribution, metabolism, excretion, and activity at the receptor site(s). Compounds may interact chemically, yielding a new toxic component or causing a change in the biological availability of the existing component. They may also interact by causing different effects at different receptor sites.

Because of the uncertainties inherent in predicting the magnitude and nature of toxicant interactions, the assessment of health risk from chemical mixtures must include a thorough discussion of all assumptions. No single approach is recommended in these Guidelines. Instead, guidance is given for the use of several approaches depending on the nature and quality of the data. Additional mathematical details are presented in section IV.

In addition to these Guidelines, a supplemental technical support document is being developed which will contain a thorough review of all available information on the toxicity of chemical mixtures and a discussion of research needs.

II. Proposed Approach

No single approach can be recommended to risk assessments for multiple chemical exposures. Nonetheless, general guidelines can be recommended depending on the type of mixture, the known toxic effects of its components, the availability of toxicity data on the mixture or similar mixtures,

[51 FR 34016]

the known or anticipated interactions among components of the mixture, and the quality of the exposure data. Given the complexity of this issue and the relative paucity of empirical data from which sound generalizations can be constructed, emphasis must be placed on flexibility, judgment, and a clear articulation of the assumptions and limitations in any risk assessment that is developed. The proposed approach is summarized in Table 1 and Figure 1 and is detailed below. An alphanumeric scheme for ranking the quality of the data used in the risk assessment is given in Table 2.

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A. Data Available on the Mixture of Concern

For predicting the effects of subchronic or chronic exposure to mixtures, the preferred approach usually will be to use subchronic or chronic health effects data on the mixture of concern and adopt procedures similar to those used for single compounds, either systemic toxicants or carcinogens (see U.S. EPA, 1986a-1986c). The risk assessor must recognize, however, that dose-response models used for single compounds are often based on biological mechanisms of the toxicity of single compounds, and may not be as well justified when applied to the mixture as a whole. Such data are most likely to be available on highly complex mixtures, such as coke oven emissions or diesel exhaust, which are generated in large quantities and associated with or suspected of causing adverse health effects. Attention should also be given to the persistence of the mixture in the environment as well as to the variability of the mixture composition over time or from different sources of emissions. If the components of the mixture are known to partition into different environmental compartments or to degrade or transform at different rates in the environment, then those factors must also be taken into account, or the confidence in and applicability of the risk assessment is diminished.

TABLE 1.-- RISK ASSESSMENT APPROACH FOR CHEMICAL MIXTURES

1. Assess the quality of the data on interactions, health effects, and exposure (see Table 2).
   a. If adequate, proceed to Step 2.
   b. If inadequate, proceed to Step 14.

2. Health effects information is available on the chemical mixture of concern .
   a. If yes, proceed to Step 3.
   b. If no, proceed to Step 4.

3. Conduct risk assessment on the mixture of concern based on health effects data on the mixture. Use the same procedures as those for single compounds. Proceed to Step 7 (optional) and Step 12.

4. Health effects information is available on a mixture that is similar to the mixture of concern.
   a. If yes, proceed to Step 5.
   b. If no, proceed to Step 7.

5. Assess the similarity of the mixture on which health effects data are available to the mixture of concern, with emphasis on any differences in components or proportions of components, as well as the effects that such differences would have on biological activity.
   a. If sufficiently similar, proceed to Step 6.
   b. If not sufficiently similar, proceed to Step 7.

6. Conduct risk assessment on the mixture of concern based on health effects data on the similar mixture. Use the same procedures as those for single compounds. Proceed to Step 7 (optional) and Step 12.

7. Compile health effects and exposure information on the components of the mixture.

8. Derive appropriate indices of acceptable exposure and/or risk on the individual components in the mixture. Proceed to Step 9.

9. Assess data on interactions of components in the mixtures.
   a. If sufficient quantitative data are available on the interactions of two or more components in the mixture, proceed to Step 10.
   b. If sufficient quantitative data are not available, use whatever information is available to qualitatively indicate the nature of potential interactions. Proceed to Step 11.

10. Use an appropriate interaction model to combine risk assessments on compounds for which data are adequate, and use an additivity assumption for the remaining compounds. Proceed to Step 11 (optional) and Step 12.

11. Develop a risk assessment based on an additivity approach for all compounds in the mixture. Proceed to Step 12.

12. Compare risk assessments conducted in Steps 5, 8, and 9. Identify and justify the preferred assessment, and quantify uncertainty, if possible. Proceed to Step 13.

13. Develop an integrated summary of the qualitative and quantitative assessments with special emphasis on uncertainties and assumptions. Classify the overall quality of the risk assessment, as indicated in Table 2. Stop.

14. No risk assessment can be conducted because of inadequate data on interactions, health effects, or exposure. Qualitatively assess the nature of any potential hazard and detail the types of additional data necessary to support a risk assessment. Stop.

Note. -- Several decisions used here, especially those concerning adequacy of data and similarity between two mixtures, are not precisely characterized and will require considerable judgment. See text.

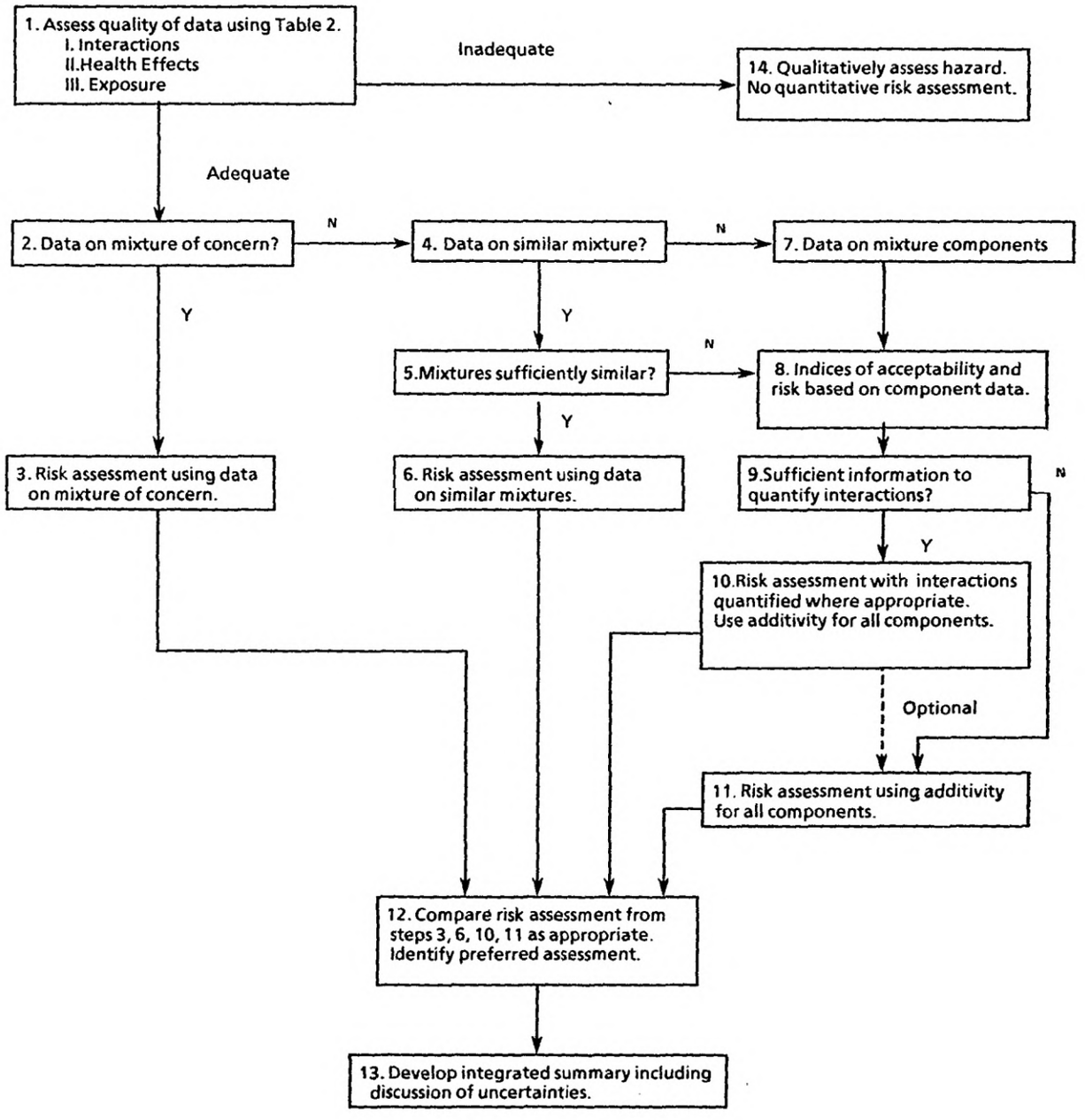

Figure 1. Flow chart of the risk assessment approach in Table 1. Note that it may be desirable to conduct all three assessments when possible (i.e., using data on the mixture, a similar mixture ,or the components) in order to make the fullest use of the available data. See text for further discussion.

TABLE 2. -- CLASSIFICATION SCHEME FOR THE QUALITY OF THE RISK ASSESSMENT OF THE MIXTURE[a]

Information on Interactions

I. Assessment is based on data on the mixture of concern.

II. Assessment is based on data on a sufficiently similar mixture.

III. Quantitative interactions of components are well characterized.

IV. The assumption of additivity is justified based on the nature of the health effects and on the number of component compounds.

V. An assumption of additivity cannot be justified, and no quantitative risk assessment can be conducted.

Health Effects Information

A. Full health effects data are available and relatively minor extrapolation is required.

B. Full health effects data are available but extensive extrapolation is required for route or duration of exposure or for species differences. These extrapolations are supported by pharmacokinetic considerations, empirical observations, or other relevant information.

C. Full health effects data are available, but extensive extrapolation is required for route or duration of exposure or for species differences. These extrapolations are not directly supported by the information available.

D. Certain important health effects data are lacking and extensive extrapolations are required for route or duration of exposure or for species differences.

E. A lack of health effects information on the mixture and its components in the mixture precludes a quantitative risk assessment.

Exposure Information[b]

1. Monitoring information either alone or in combination with modeling information is sufficient to accurately characterize human exposure to the mixture or its components.

2. Modeling information is sufficient to reasonably characterize human exposure to the mixture or its components.

3. Exposure estimates for some components are lacking, uncertain, or variable. Information on health effects or environmental chemistry suggest that this limitation is not likely to substantially affect the risk assessment.

4. Not all components in the mixture have been identified or levels of exposure are highly uncertain or variable. Information on health effects or environmental chemistry is not sufficient to assess the effect of this limitation on the risk assessment.

5. The available exposure information is insufficient for conducting a risk assessment.

B. Data Available on Similar Mixtures

If the risk assessment is based on data from a single mixture that is known to be generated with varying compositions depending on time or different emission sources, then the confidence in the applicability of the data to a risk assessment also is diminished. This can be offset to some degree if data are available on several mixtures of the same components that have different component ratios which encompass the temporal or spatial differences in composition of the mixture of concern. If such data are available, an attempt should be made to determine if significant and systematic differences exist among the chemical mixtures. If significant differences are noted, ranges of risk can be estimated based on the toxicologic data of the various mixtures. If no significant differences are noted, then a single risk assessment may be adequate, although the range of ratios of the components in the mixtures to which the risk assessment applies should also be given.

If no data are available on the mixtures of concern, but health effects data are available on a similar mixture (i.e., a mixture having the same components but in slightly different ratios, or having several common components but lacking one or more components, or having one or more additional components), a decision must be made whether the mixture on which health effects data are available is or is not "sufficiently similar" to the mixture of concern to permit a risk assessment. The determination of "sufficient similarity" must be made on a case-by-case basis, considering not only the uncertainties associated with using data on a dissimilar mixture but also the uncertainties of using other approaches such as additivity. In determining reasonable similarity, consideration should be given to any information on the components that differ or are contained in markedly different proportions between the mixture on which health effects data are available and the mixture of concern. Particular emphasis should be placed on any toxicologic or pharmacokinetic data on the components or the mixtures which would be useful in assessing the significance of any chemical difference between the similar mixture and the mixtures of concern.

Even if a risk assessment can be made using data on the mixtures of concern or a reasonably similar mixture, it may be desirable to conduct a risk assessment based on toxicity data on the

[a] See text for discussion of sufficient similarity, adequacy of data, and justification for additivity assumptions.

[b] See the Agency's Guidelines for Estimating Exposures (U.S. EPA, 1986d) for more complete information on performing exposure assessments and evaluating the quality of exposure data.

components in the mixture using the procedure outlined in section II.B. In the case of a mixture containing carcinogens and toxicants, an approach based on the mixture data alone may not be sufficiently protective in all cases. For example, this approach for a two-component mixture of one carcinogen and one toxicant would use toxicity data on the mixture of the two compounds. However, in a chronic study of such a mixture, the presence of the toxicant could mask the activity of the carcinogen. That is to say, at doses of the mixture sufficient to induce a carcinogenic effect, the toxicant could induce mortality so that at the maximum tolerated dose of the mixture, no carcinogenic effect could be observed. Since carcinogenicity is considered by the Agency to be a nonthreshold effect, it may not be prudent to construe the negative results of such a bioassay as indicating the absence of risk at lower doses. Consequently, the mixture approach should be modified to allow the risk assessor to evaluate the potential for masking, of one effect by another, on a case-by-case basis.

C. Data Available Only on Mixture Components

If data are not available on an identical or reasonably similar mixture, the risk assessment may be based on the toxic or carcinogenic properties of the components in the mixture. When little or no quantitative information is available on the potential interaction among the components, additive models (defined in the next section) are recommended for systemic toxicants. Several studies have demonstrated that dose additive models often predict reasonably well the toxicities of mixtures composed of a substantial variety of both similar and dissimilar compounds (Pozzani et al., 1959; Smyth et al., 1969, 1970; Murphy, 1980). The problem of multiple toxicant exposure has been addressed by the American Conference of Governmental Industrial Hygienists (ACGIH, 1983), the Occupational Safety and Health Administration (OSHA, 1983), the World Health Organization (WHO, 1981), and the National Research Council (NRC, 1980a, b). Although the focus and purpose of each group was somewhat different, all groups that recommended an approach elected to adopt some type of dose additive model. Nonetheless, as discussed in section IV, dose additive models are not the most biologically plausible approach if the compounds do not have the same mode of toxicologic action. Consequently, depending on the nature of the risk assessment and the available information on modes of action and patterns of joint action, the

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most reasonable additive model should be used.

1. Systemic Toxicants. For systemic toxicants, the current risk assessment methodology used by the Agency for single compounds most often results in the derivation of an exposure level which is not anticipated to cause significant adverse effects. Depending on the route of exposure, media of concern, and the legislative mandate guiding the risk assessments, these exposure levels may be expressed in a variety of ways such as acceptable daily intakes (ADIs) or reference doses (RfDs), levels associated with various margins of safety (MOS), or acceptable concentrations in various media. For the purpose of this discussion, the term "acceptable level" (AL) will be used to indicate any such criteria or advisories derived by the Agency. Levels of exposure (E) will be estimates obtained following the most current Agency Guidelines for Estimating Exposures (U.S. EPA, 1986d). For such estimates, the "hazard index" (HI) of a mixture based on the assumption of dose addition may be defined as:

$$HI = E_1/AL_1 + E_2/AL_2 + \ldots + E_i/AL_i \qquad \text{(II-1)}$$

where:

E_i = exposure level to the ith toxicant* and
AL_i = maximum acceptable level for the ith toxicant.

Since the assumption of dose addition is most properly applied to compounds that induce the same effect by similar modes of action, a separate hazard index should be generated for each end point of concern. Dose addition for dissimilar effects does not have strong scientific support, and, if done, should be justified on a case-by-case basis in terms of biological plausibility.

The assumption of dose addition is most clearly justified when the mechanisms of action of the compounds under consideration are known to be the same. Since the mechanisms of action for most compounds are not well understood, the justification of the assumption of dose addition will often be limited to similarities in pharmacokinetic and toxicologic characteristics. In any event, if a hazard index is generated, the quality of the experimental evidence supporting the assumption of dose addition must be clearly articulated.

The hazard index provides a rough measure of likely toxicity and requires cautious interpretation. The hazard index is only a numerical indication of the nearness to acceptable limits of exposure or the degree to which acceptable exposure levels are exceeded. As this index approaches unity, concern for the potential hazard of the mixture increases. If the index exceeds unity, the concern is the same as if an individual chemical exposure exceeded its acceptable level by the same proportion. The hazard index does not define dose-response relationships, and its numerical value should not be construed to be a direct estimate of risk. Nonetheless, if sufficient data are available to derive individual acceptable levels for a spectrum of effects (e.g., MFO induction,

*See the Agency's guidelines (U.S. EPA, 1986d) for information on how to estimate this value.

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variabilities of the acceptable levels are known, or if the acceptable levels are given as ranges (e.g., associated with different margins of safety), then the hazard index should be presented with corresponding estimates of variation or range. Most studies on systemic toxicity report only descriptions of the effects in each dose group. If dose-response curves are estimated for systemic toxicants, however, dose-additive or response-additive assumptions can be used, with preference given to the most biologically plausible assumption (see section IV for the mathematical details).

2. Carcinogens. For carcinogens, whenever linearity of the individual dose-response curves has been assumed (usually restricted to low doses), the increase in risk P (also called excess or incremental risk), caused by exposure d, is related to carcinogenic potency B, as:

$$P = d\,B \qquad \text{(II-2)}$$

For multiple compounds, this equation may be generalized to:

$$P = \Sigma d_i\,B_i \qquad \text{(II-3)}$$

This equation assumes independence of action by the several carcinogens and is equivalent to the assumption of dose addition as well as to response addition with completely negative correlation of tolerance, as long as $P < 1$ (see section IV). Analogous to the procedure used in equation II-1 for systemic toxicants, an index for n carcinogens can be developed by dividing exposure levels (E) by doses (DR) associated with a set level of risk:

$$HI = E_1/DR_1 + E_2/DR_2 + \ldots + E_n/DR_n \qquad \text{(II-4)}$$

Note that the less linear the dose-response curve is, the less appropriate equations II-3 and II-4 will be, perhaps even at low doses. It should be emphasized that because of the uncertainties in estimating dose-response relationships for single compounds, and the additional uncertainties in combining the individual estimate to assess response from exposure to mixtures, response rates and hazard indices may have merit in comparing risks but should not be regarded as measures of absolute risk.

3.Interactions. None of the above equations incorporates any form of synergistic or antagonistic interaction. Some types of information, however, may be available that suggest that two or more components in the mixture may interact. Such information must be assessed in terms of both its relevance to subchronic or chronic hazard and its suitability for quantitatively altering the risk assessment.

For example, if chronic or subchronic toxicity or carcinogenicity studies have been conducted that permit a quantitative estimation of interaction for two chemicals, then it may be desirable to consider using equations detailed in section IV, or modifications of these equations, to treat the two compounds as a single toxicant with greater or lesser potency than would be predicted from additivity. Other components of the mixture, on which no such interaction data are available, could then be separately treated in an additive manner. Before such a procedure is adopted, however, a discussion should be presented of the likelihood that other compounds in the mixture may interfere with the interaction of the two toxicants on which quantitative interaction data are available. If the weight of evidence suggests that interference is likely, then a quantitative alteration of the risk assessment may not be justified. In such cases, the risk assessment may only indicate the likely nature of interactions, either synergistic or antagonistic, and not quantify their magnitudes.

Other types of information, such as those relating to mechanisms of toxicant interaction, or quantitative estimates of interaction between two chemicals derived from acute studies, are even less likely to be of use in the quantitative assessment of long-term health risks. Usually it will be appropriate only to discuss these types of information, indicate the relevance of the information to subchronic or chronic exposure, and indicate, if possible, the nature of potential interactions, without attempting to quantify their magnitudes.

When the interactions are expected to have a minor influence on the mixture's toxicity, the assessment should indicate, when possible, the compounds most responsible for the predicted toxicity. This judgment should be based on predicted toxicity of each component,

[51 FR 34020]

based on exposure and toxic or carcinogenic potential. This potential alone should not be used as an indicator of the chemicals posing the most hazard.

4.Uncertainties. For each risk assessment, the uncertainties should be clearly discussed and the overall quality of the risk assessment should be characterized. The scheme outlined in Table 2 should be used to express the degree of confidence in the quality of the data on interaction, health effects, and exposure.

a. Health Effects--In some cases, when health effects data are incomplete, it may be possible to argue by analogy or quantitative structure-activity relationships that the compounds on which no health effects data are available are not likely to significantly affect the toxicity of the mixture. If a risk assessment includes such an argument, the limitations of the approach must be clearly articulated. Since a methodology has not been adopted for estimating an acceptable level (e.g., ADI) or carcinogenic potential for single compounds based either on quantitative structure-activity relationships or on the results of short-term screening tests, such methods are not at present

recommended as the sole basis of a risk assessment on chemical mixtures.

b. Exposure Uncertainties--The general uncertainties in exposure assessment have been addressed in the Agency's Guidelines for Estimating Exposures (U.S. EPA, 1986d). The risk assessor should discuss these exposure uncertainties in terms of the strength of the evidence used to quantify the exposure. When appropriate, the assessor should also compare monitoring and modeling data and discuss any inconsistencies as a source of uncertainty. For mixtures, these uncertainties may be increased as the number of compounds of concern increases.

If levels of exposure to certain compounds known to be in the mixture are not available, but information on health effects and environmental persistence and transport suggest that these compounds are not likely to be significant in affecting the toxicity of the mixture, then a risk assessment can be conducted based on the remaining compounds in the mixture, with appropriate caveats. If such an argument cannot be supported, no final risk assessment can be performed until adequate monitoring data are available. As an interim procedure, a risk assessment may be conducted for those components in the mixture for which adequate exposure and health effects data are available. If the interim risk assessment does not suggest a hazard, there is still concern about the risk from such a mixture because not all components in the mixture have been considered.

c. Uncertainties Regarding Composition of the Mixture--In perhaps a worst case scenario, information may be lacking not only on health effects and levels of exposure, but also on the identity of some components of the mixture. Analogous to the procedure described in the previous paragraph, an interim risk assessment can be conducted on those components of the mixture for which adequate health effects and exposure information are available. If the risk is considered unacceptable, a conservative approach is to present the quantitative estimates of risk, along with appropriate qualifications regarding the incompleteness of the data. If no hazard is indicated by this partial assessment, the risk assessment should not be quantified until better health effects and monitoring data are available to adequately characterize the mixture exposure and potential hazards.

III. Assumptions and Limitations

A. Information on Interactions

Most of the data available on toxicant interactions are derived from acute toxicity studies using experimental animals in which mixtures of two compounds were tested, often in only a single combination. Major areas of uncertainty with the use of such data involve the appropriateness of interaction data from an acute toxicity study for quantitatively altering a risk assessment for subchronic or chronic exposure, the appropriateness of interaction data on two component mixtures for quantitatively altering a risk assessment on a mixture of several compounds, and the accuracy of interaction data on experimental animals for quantitatively predicting interactions in humans.

The use of interaction data from acute toxicity studies to assess the potential interactions on chronic exposure is highly questionable unless the mechanism(s) of the interaction on acute exposure were known to apply to low-dose chronic exposure. Most known biological mechanisms for toxicant interactions, however, involve some form of competition between the chemicals or phenomena involving saturation of a receptor site or metabolic pathway. As the doses of the toxicants are decreased, it is likely that these mechanisms either no longer will exert a significant effect or will be decreased to an extent that cannot be measured or approximated.

The use of information from two-component mixtures to assess the interactions in a mixture containing more than two compounds also is questionable from a mechanistic perspective. For example, if two compounds are known to interact, either synergistically or antagonistically, because of the effects of one compound on the metabolism or excretion of the other, the addition of a third compound which either chemically alters or affects the absorption of one of the first two compounds could substantially alter the degree of the toxicologic interaction. Usually, detailed studies quantifying toxicant interactions are not available on multicomponent mixtures, and the few studies that are available on such mixtures (e.g., Gullino et al., 1956) do not provide sufficient information to assess the effects of interactive interference.

Concerns with the use of interaction data on experimental mammals to assess interactions in humans is based on the increasing appreciation for systematic differences among species in their response to individual chemicals. If systematic differences in toxic sensitivity to single chemicals exist among species, then it seems reasonable to suggest that the magnitude of toxicant interactions among species also may vary in a systematic manner. Consequently, even if excellent chronic data are available on the magnitude of toxicant interactions in a species of experimental mammal, there is uncertainty that the magnitude of the interaction will be the same in humans. Again, data are not available to properly assess the significance of this uncertainty.

Last, it should be emphasized that none of the models for toxicant interaction can predict the magnitude of toxicant interactions in the absence of extensive data. If sufficient data are available to

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estimate interaction coefficients as described in section IV, then the magnitude of the toxicant interactions for various proportions of the same components can be predicted. The availability of an interaction ratio (observed response divided by predicted response) is useful only in assessing the magnitude of the toxicant interaction for the specific proportions of the mixture which was used to generate the interaction ratio.

The basic assumption in the recommended approach is that risk assessments on chemical mixtures are best conducted using toxicologic data on the mixture of concern or a reasonably similar mixture. While such risk

[51 FR 34021]

assessments do not formally consider toxicologic interactions as part of a mathematical model, it is assumed that responses in experimental mammals or human populations noted after exposure to the chemical mixture can be used to conduct risk assessments on human populations. In bioassays of chemical mixtures using experimental mammals, the same limitations inherent in species-to-species extrapolation for single compounds apply to mixtures. When using health effects data on chemical mixtures from studies on exposed human populations, the limitations of epidemiologic studies in the risk assessment of single compounds also apply to mixtures. Additional limitations may be involved when using health effects data on chemical mixtures if the components in the mixture are not constant or if the components partition in the environment.

B. Additivity Models

If sufficient data are not available on the effects of the chemical mixture of concern or a reasonably similar mixture, the proposed approach is to assume additivity. Dose additivity is based on the assumption that the components in the mixture have the same mode of action and elicit the same effects. This assumption will not hold true in most cases, at least for mixtures of systemic toxicants. For systemic toxicants, however, most single compound risk assessments will result in the derivation of acceptable levels, which, as currently defined, cannot be adapted to the different forms of response additivity as described in section IV.

Additivity models can be modified to incorporate quantitative data on toxicant interactions from subchronic or chronic studies using the models given in section IV or modifications of these models. If this approach is taken, however, it will be under the assumption that other components in the mixture do not interfere with the measured interaction. In practice, such subchronic or chronic interactions data seldom will be available. Consequently, most risk assessments (on mixtures) will be based on an assumption of additivity, as long as the components elicit similar effects.

Dose-additive and response-additive assumptions can lead to substantial errors in risk estimates if synergistic or antagonistic interactions occur. Although dose additivity has been shown to predict the acute toxicities of many mixtures of similar and dissimilar compounds (e.g., Pozzani et al., 1959; Smyth et al., 1969, 1970; Murphy, 1980), some marked exceptions have been noted. For example, Smyth et al. (1970) tested the interaction of 53 pairs of industrial chemicals based on acute lethality in rats. For most pairs of compounds, the ratio of the predicted LD_{50} to observed LD_{50} did not vary by more than a factor of 2. The greatest variation was seen with an equivolume mixture of morpholine and toluene, in which the observed LD_{50} was about five times less than the LD_{50} predicted by dose addition. In a study by Hammond et al. (1979), the relative risk of lung cancer attributable to smoking was 11, while the relative risk associated with asbestos exposure was 5. The relative risk of lung cancer from both smoking and asbestos exposure was 53, indicating a substantial synergistic effect. Consequently, in some cases, additivity assumptions may substantially underestimate risk. In other cases, risk may be overestimated. While this is certainly an unsatisfactory situation, the available data on mixtures are insufficient for estimating the magnitude of these errors. Based on current information, additivity assumptions are expected to yield generally neutral risk estimates (i.e., neither conservative nor lenient) and are plausible for component compounds that induce similar types of effects at the same sites of action.

IV. Mathematical Models and the Measurement of Joint Action

The simplest mathematical models for joint action assume no interaction in any mathematical sense. They describe either dose addition or response addition and are motivated by data on acute lethal effects of mixtures of two compounds.

A. Dose Addition

Dose addition assumes that the toxicants in a mixture behave as if they were dilutions or concentrations of each other, thus the true slopes of the dose-response curves for the individual compounds are identical, and the response elicited by the mixture can be predicted by summing the individual doses after adjusting for differences in potency; this is defined as the ratio of equitoxic doses. Probit transformation typically makes this ratio constant at all doses when parallel straight lines are obtained. Although this assumption can be applied to any model (e.g., the one-hit model in NRC, 1980b), it has been most often used in toxicology with the log-dose probit response model, which will be used to illustrate the assumption of dose addition.

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Suppose that two toxicants show the following log-dose probit response equations:

$$Y_1 = 0.3 + 3 \log Z_1 \quad \text{(IV-1)}$$
$$Y_2 = 1.2 + 3 \log Z_2 \quad \text{(IV-2)}$$

where Y_i is the probit response associated with a dose of Z_i ($i=1,2$). The potency, p, of toxicant #2 with respect to toxicant #1 is defined by the quantity Z_1/Z_2 when $Y_1 = Y_2$ (that is what is meant by equitoxic doses). In this example, the potency, p, is approximately 2. Dose addition assumes that the response, Y, to any mixture of these two toxicants can be predicted by:

$$Y = 0.3 + 3 \log (Z_1 + pZ2) \quad \text{(IV-3)}$$

Thus, since p is defined as Z_1/Z_2, equation IV-3 essentially converts Z_2 into an equivalent dose of Z by adjusting for the difference in potency. A more generalized form of this equation for any number of toxicants is:

$$Y = a_1 + b \log (f_1 + \Sigma f_i p_i) + b \log Z \quad \text{(IV-4)}$$

where:

a_1 = the y-intercept of the dose-response equation for toxicant #1
b = the slope of the dose-response lines for the toxicants
f_i = the proportion of the ith toxicant in the mixture
p_i = the potency of the ith toxicant with respect to toxicant #1 (i.e., Z_1/Z_i), and
Z = the sum of the individual doses in the mixture.

A more detailed discussion of the derivation of the equations for dose addition is presented by Finney (1971).

B. Response Addition

The other form of additivity is referred to as response addition. As detailed by Bliss (1939), this type of joint action assumes that the two toxicants act on different receptor systems and that the correlation of individual tolerances may range from completely negative ($r=-1$) to completely positive ($r=+1$). Response addition assumes that the response to a given concentration of a mixture of toxicants is completely determined by the responses to the components and the pairwise correlation coefficient. Taking P as the proportion of organisms responding to a mixture of two toxicants which evoke individual responses of P_1 and P_2, then

$P = P_1$ if $r = 1$ and $P_1 \geq P_2$ (IV-5)
$P = P_2$ if $r = 1$ and $P_1 < P_2$ (IV-6)
$P = P_1 + P_2 (1-P_1)$ if $r = 0$ (IV-7)
$P = P_1 + P_2$ if $r = -1$ and $P \leq 1$. (IV-8)

More generalized mathematical models for this form of joint action have been given by Plackett and Hewlett (1948).

C. Interactions

All of the above models assume no interactions and therefore do not incorporate measurements of synergistic or antagonistic effects. For measuring toxicant interactions for mixtures of two compounds, Finney (1942) proposed the

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following modification of equation IV-4 for dose addition:

$$Y = a_1 + b \log (f_1 + pf_2 + K[pf_1f_2]^{0.5}) + b \log Z \quad \text{(IV-9)}$$

where a_1, b, f_1, f_2, p, and Z are defined as before, and K is the coefficient of interaction. A positive value of K indicates synergism, a negative value indicates antagonism, and a value of zero corresponds to dose addition as in equation IV-4. Like other proposed modifications of dose addition (Hewlett, 1969), the equation assumes a consistent interaction throughout the entire range of proportions of individual components. To account for such asymmetric patterns of interaction as those observed by Alstott et al. (1973), Durkin (1981) proposed the following modification to equation IV-9:

$$Y = a_1 + b \log (f_1 + pf_2 + K_1f_1[pf_1f_2]^{0.5} + K_2f_2[pf_1f_2]^{0.5}) + b \log Z \quad \text{(IV-10)}$$

in which $K(pf_1f_2)^{0.5}$ is divided into two components, $K_1f_1(pf_1f_2)^{0.5}$ and $K_2f_2(pf_1f_2)^{0.5}$. Since K_1 and K_2 need not have the same sign, apparent instances of antagonism at one receptor site and synergism at another receptor site can be estimated. When K_1 and K_2 are equal, equation IV-10 reduces to equation IV-9. It should be noted that to obtain a reasonable number of degrees of freedom in the estimation of K in equation IV-9 or K_1 and K_2 in equation IV-10, the toxicity of several different combinations of the two components must be assayed along with assays of the toxicity of the individual components. Since this requires experiments with large numbers of animals, such analyses have been restricted for the most part to data from acute bioassays using insects (e.g., Finney, 1971) or aquatic organisms (Durkin, 1979). Also, because of the complexity of experimental design and the need for large numbers of animals, neither equation IV-9 nor equation IV-10 has been generalized or applied to mixtures of more than two toxicants. Modifications of response-additive models to include interactive terms have also been proposed, along with appropriate statistical tests for the assumption of additivity (Korn and Liu, 1983; Wahrendorf et al., 1981).

In the epidemiologic literature, measurements of the extent of toxicant interactions, S, can be expressed as the ratio of observed relative risk to relative risk predicted by some form of additivity assumption. Analogous to the ratio of interaction in classical toxicology studies, $S = 1$ indicates no interaction, $S > 1$ indicates synergism, and $S < 1$ indicates antagonism. Several models for both

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additive and multiplicative risks have been proposed (e.g., Hogan et al., 1978; NRC, 1980b; Walter, 1976). For instance, Rothman (1976) has discussed the use of the following measurement of toxicant interaction based on the assumption of risk additivity:

$$S = (R_{11} - 1)/(R_{10} + R_{01} - 2) \qquad \text{(IV-11)}$$

where R_{10} is the relative risk from compound #1 in the absence of compound #2, R_{01} is the relative risk from compound #2 in the absence of compound #1, and R_{11} is the relative risk from exposure to both compounds. A multiplicative risk model adapted from Walter and Holford (1978, equation 4) can be stated as:

$$S = R_{11}/(R_{10}R_{01}) \qquad \text{(IV-12)}$$

As discussed by both Walter and Holford (1978) and Rothman (1976), the risk-additive model is generally applied to agents causing diseases while the multiplicative model is more appropriate to agents that prevent disease. The relative merits of these and other indices have been the subject of considerable discussion in the epidemiologic literature (Hogan et al., 1978; Kupper and Hogan, 1978; Rothman, 1978; Rothman et al., 1980; Walter and Holford, 1978). There seems to be a consensus that for public health concerns regarding causative (toxic) agents, the additive model is more appropriate.

Both the additive and multiplicative models assume statistical independence in that the risk associated with exposure to both compounds in combination can be predicted by the risks associated with separate exposure to the individual compounds. As illustrated by Siemiatycki and Thomas (1981) for multistage carcinogenesis, the better fitting statistical model will depend not only upon actual biological interactions, but also upon the stages of the disease process which the compounds affect. Consequently, there is no *a priori* basis for selecting either type of model in a risk assessment. As discussed by Stara et al. (1983), the concepts of multistage carcinogenesis and the effects of promoters and cocarcinogens on risk are extremely complex issues. Although risk models for promoters have been proposed (e.g., Burns et al., 1983), no single approach can be recommended at this time.

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Part B: Response to Public and Science Advisory Board Comments

I. Introduction

This section summarizes some of the major issues raised in public comments on the Proposed Guidelines for the Health Risk Assessment of Chemical Mixtures published on January 9, 1985 (50 FR 1170). Comments were received from 14 individuals or organizations. An issue paper reflecting public and external review comments was presented to the Chemical Mixtures Guidelines Panel of the Science Advisory Board (SAB) on March 4, 1985. At its April 22-23, 1985, meeting, the SAB Panel provided the Agency with additional suggestions and recommendations concerning the Guidelines. This section also summarizes the issues raised by the SAB.

The SAB and public commentors expressed diverse opinions and addressed issues from a variety of perspectives. In response to comments, the Agency has modified or clarified many sections of the Guidelines, and is planning to develop a technical support document in line with the SAB recommendations. The discussion that follows highlights significant issues raised in the comments, and the Agency's response to them. Also, many minor recommendations, which do not warrant discussion here, were adopted by the Agency.

II. Recommended Procedures

A. Definitions

Several comments were received concerning the lack of definitions for certain key items and the general understandability of certain sections. Definitions have been rewritten for several terms and the text has been significantly rewritten to clarify the Agency's intent and meaning.

Several commentors noted the lack of a precise definition of "mixture," even though several classes of mixtures are discussed. In the field of chemistry, the term "mixture" is usually differentiated from true solutions, with the former defined as nonhomogeneous multicomponent systems. For these Guidelines, the term "mixture" is defined as "...any combination of two or more chemicals regardless of spatial or temporal homogeneity of source" (section 1). These Guidelines are intended to cover risk assessments for any situation where the population is exposed or potentially exposed to two or more compounds of concern. Consequently, the introduction has been revised to clarify the intended breadth of application.

Several commentors expressed concern that "sufficient similarity" was difficult to define and that the Guidelines should give more details concerning similar mixtures. The Agency agrees and is planning research projects to improve on the definition. Characteristics such as composition and toxic end-effects are certainly important, but the best indicators of similarity in terms of risk assessment have yet to be determined. The discussion in the Guidelines emphasizes case-by-case judgment until the necessary research can be performed. The Agency considered but rejected adding an example, because it is not likely that any single example would be adequate to illustrate the variety in the data and types of judgments that will be required in applying this concept. Inclusion of examples is being considered for the technical support document.

B. Mixtures of Carcinogens and Systemic Toxicants

The applicability of the preferred approach for a mixture of carcinogens and systemic (noncarcinogenic) toxicants was a concern of several public commentors as well as the SAB. The Agency realizes that the preferred approach of using test data on the mixture itself may not be sufficiently protective in all cases. For example, take a simple two-component mixture of one carcinogen and one toxicant. The preferred approach would lead to using toxicity data on the mixture of the two compounds. However, it is possible to set the proportions of each component so that in a chronic bioassay of such a mixture, the presence of the toxicant could mask the activity of the carcinogen. That is to say, at doses of

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the mixture sufficient for the carcinogen to induce tumors in the small

[51 FR 34024]

experimental group, the toxicant could induce mortality. At a lower dose in the same study, no adverse effects would be observed, including no carcinogenic effects. The data would then suggest use of a threshold approach. Since carcinogenicity is considered by the Agency to be a nonthreshold effect, it may not be prudent to construe the negative results of such a bioassay as indicating the absence of risk at lower doses. Consequently, the Agency has revised the discussion of the preferred approach to allow the risk assessor to evaluate the potential for masking of carcinogenicity or other effects on a case-by-case basis. Another difficulty occurs with such a mixture when the risk assessment needs to be based on data for the mixture components. Carcinogens and systemic toxicants are evaluated by the Agency using different approaches and generally are described by different types of data: response rates for carcinogens vs. effect descriptions for toxicants. The Agency recognizes this difficulty and recommends research to develop a new assessment model for combining these dissimilar data sets into one risk estimate. One suggestion in the interim is to present separate risk estimates for the dissimilar end points, including carcinogenic, teratogenic, mutagenic, and systemic toxicant components.

III. Additivity Assumption

Numerous comments were received concerning the assumption of additivity, including:

a. the applicability of additivity to "complex" mixtures;
b. the use of dose additivity for compounds that induce different effects;
c. the interpretation of the Hazard Index; and
d. the use of interaction data.

Parts of the discussion in the proposed guidelines concerning the use of additivity assumptions were vague and have been revised in the final Guidelines to clarify the Agency's intent and position.

A. Complex Mixtures

The issue of the applicability of an assumption of additivity to complex mixtures containing tens or hundreds of components was raised in several of the public comments. The Agency and its reviewers agree that as the number of compounds in the mixture increases, an assumption of additivity will become less reliable in estimating risk. This is based on the fact that each component estimate of risk or an acceptable level is associated with some error and uncertainty. With current knowledge, the uncertainty will increase as the number of components increases. In any event, little experimental data are available to determine the general change in the error as the mixture contains more components. The Agency has decided that a limit to the number of components should not be set in these Guidelines. However, the Guidelines do explicitly state that as the number of compounds in the mixture increases, the uncertainty associated with the risk assessment is also likely to increase.

B. Dose Additivity

Commentors were concerned about what appeared to be a recommendation of the use of dose additivity for compounds that induce different effects. The discussion following the dose additivity equation was clarified to indicate that the act of combining all compounds, even if they induce dissimilar effects, is a screening procedure and not the preferred procedure in developing a hazard index. The Guidelines were further clarified to state that dose (or response) additivity is theoretically sound, and therefore best applied for assessing mixtures of similar acting components that do not interact.

C. Interpretation of the Hazard Index

Several comments addressed the potential for misinterpretation of the hazard index, and some questioned its validity, suggesting that it mixes science and value judgments by using "acceptable" levels in the calculation. The Agency agrees with the possible confusion regarding its use and has revised the Guidelines for clarification. The hazard index is an easily derived restatement of dose additivity, and is, therefore, most accurate when used with mixture components that have similar toxic action. When used with components of unknown or dissimilar action, the hazard index is less accurate and should be interpreted only as a rough indication of concern. As with dose addition, the uncertainty associated with the hazard index increases as the number of components increases, so that it is less appropriate for evaluating the toxicity of complex mixtures.

D. Use of Interaction Data

A few commentors suggested that any interaction data should be used to quantitatively alter the risk assessment. The Agency disagrees. The current information on interactions is meager, with only a few studies comparing response to the mixture with that predicted by studies on components. Additional uncertainties include exposure variations due to changes in composition, mixture dose, and species differences in the extent of the interaction. The Agency is constructing an interaction data base in an attempt to answer some of these issues. Other comments concerned the use of different types of interaction data. The Guidelines restrict the use of interaction data to that obtained from whole animal bioassays of a duration appropriate to the risk assessment. Since such data are frequently lacking, at least for chronic or subchronic effects, the issue is whether to allow for the use of other information such as acute data, *in*

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vitro data, or structure-activity relationships to quantitatively alter the risk assessment, perhaps by use of a safety factor. The Agency believes that sufficient scientific support does not exist for the use of such data in any but a qualitative discussion of possible synergistic or antagonistic effects.

IV. Uncertainties and the Sufficiency of the Data Base

In the last two paragraphs of section II of the Guidelines, situations are discussed in which the risk assessor is presented with incomplete toxicity, monitoring, or exposure data. The SAB, as well as several public commentors, recommended that the "risk management" tone of this section be modified and that the option of the risk assessor to decline to conduct a risk assessment be made more explicit.

This is a difficult issue that must consider not only the quality of the available data for risk assessment, but also the needs of the Agency in risk management. Given the types of poor data often available, the risk assessor may indicate that the risk assessment is based on limited information and thus contains no quantification of risk. Nonetheless, in any risk assessment, substantial uncertainties exist. It is the obligation of the risk assessor to provide an assessment, but also to ensure that all the assumptions and uncertainties are articulated clearly and quantified whenever possible.

The SAB articulated several other recommendations related to uncertainties, all of which have been followed in the revision of the Guidelines. One recommendation was that the summary procedure table also be presented as a flow chart so that all options are clearly displayed. The SAB further recommended the development of a system to express the level of confidence in the various steps of the risk assessment.

The Agency has revised the summary table to present four major options: risk assessment using data on the mixture

[51 FR 34025]

itself, data on a similar mixture, data on the mixture's components, or declining to quantify the risk when the data are inadequate. A flow chart of this table has also been added to more clearly depict the various options and to suggest the combining of the several options to indicate the variability and uncertainties in the risk assessment.

To determine the adequacy of the data, the SAB also recommended the development of a system to express the level of confidence associated with various steps in the risk assessment process. The Agency has developed a rating scheme to describe data quality in three areas: interaction, health effects, and exposure. This classification provides a range of five levels of data quality for each of the three areas. Choosing the last level in any area results in declining to perform a quantitative risk assessment due to inadequate data. These last levels are described as follows:

Interactions:

An assumption of additivity cannot be justified, and no quantitative risk assessment can be conducted.

Health effects:

A lack of health effects information on the mixture and its components precludes a quantitative risk assessment.

Exposure:

The available exposure information is insufficient for conducting a risk assessment.

Several commentors, including the SAB, emphasized the importance of not losing these classifications and uncertainties farther along in the risk management process. The discussion of uncertainties has been expanded in the final Guidelines and includes the recommendation that a discussion of uncertainties and assumptions be included at every step of the regulatory process that uses risk assessment.

Another SAB comment was that the Guidelines should include additional procedures for mixtures with more than one end point or effect. The Agency agrees that these are concerns and revised the Guidelines to emphasize these as additional uncertainties worthy of further research.

V. Need for a Technical Support Document

The third major SAB comment concerned the necessity for a separate technical support document for these Guidelines. The SAB pointed out that the scientific and technical background from which these Guidelines must draw their validity is so broad and varied that it cannot reasonably be synthesized within the framework of a brief set of guidelines. The Agency is developing a technical support document that will summarize the available information on health effects from chemical mixtures, and on interaction mechanisms, as well as identify and develop mathematical models and statistical techniques to support these Guidelines. This document will also identify critical gaps and research needs.

Several comments addressed the need for examples on the use of the Guidelines. The Agency has decided to include examples in the technical support document.

Another issue raised by the SAB concerned the identification of research needs. Because little emphasis has been placed on the toxicology of mixtures until recently, the information on mixtures is limited. The SAB pointed out that identifying research needs is critical to the risk assessment process, and the EPA should ensure that these needs are considered in the research planning process. The Agency will include a section in the

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technical support document that identifies research needs regarding both methodology and data.

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GUIDELINES FOR THE HEALTH ASSESSMENT OF SUSPECT DEVELOPMENTAL TOXICANTS

SUMMARY: On September 24, 1986, the U.S. Environmental Protection Agency issued the following five guidelines for assessing the health risks of environmental pollutants.

Guidelines for Carcinogen Risk Assessment

Guidelines for Estimating Exposures

Guidelines for Mutagenicity Risk Assessment

Guidelines for the Health Assessment of Suspect Developmental Toxicants

Guidelines for the Health Risk Assessment of Chemical Mixtures

This section contains the Guidelines for the Health Assessment of Suspect Developmental Toxicants.

The Guidelines for the Health Assessment of Suspect Developmental Toxicants (hereafter "Guidelines") are intended to guide Agency analysis of developmental toxicity data in line with the policies and procedures established in the statutes administered by the EPA. These Guidelines were developed as part of an interoffice guidelines development program under the auspices of the Office of Health and Environmental Assessment (OHEA) in the Agency's Office of Research and Development. They reflect Agency consideration of public and Science Advisory Board (SAB) comments on the Proposed Guidelines for the Health Assessment of Suspect Developmental Toxicants published November 23, 1984 (49 FR 46324).

This publication completes the first round of risk assessment guidelines development. These Guidelines will be revised, and new guidelines will be developed, as appropriate.

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SUPPLEMENTARY INFORMATION: In 1983, the National Academy of Sciences (NAS) published its book entitled *Risk Assessment in the Federal Government: Managing the Process*. In that book, the NAS recommended that Federal regulatory agencies establish "inference guidelines" to ensure consistency and technical quality in risk assessments and to ensure that the risk assessment process was maintained as a scientific effort separate from risk management. A task force within EPA accepted that recommendation and requested that Agency scientists begin to develop such guidelines.

General

The guidelines are products of a two-year Agencywide effort, which has included many scientists from the larger scientific community. These guidelines set forth principles and procedures to guide EPA scientists in the conduct of Agency risk assessments, and to inform Agency decision makers and the public about these procedures. In particular, the guidelines emphasize that risk assessments will be conducted on a case-by-case basis, giving full consideration to all relevant scientific information. This case-by-case approach means that Agency experts review the scientific information on each agent and use the most scientifically appropriate interpretation to assess risk. The guidelines also stress that this information will be fully presented in Agency risk assessment documents, and that Agency scientists will identify the strengths and weaknesses of each assessment by describing uncertainties, assumptions, and limitations, as well as the scientific basis and rationale for each assessment.

Finally, the guidelines are formulated in part to bridge gaps in risk assessment methodology and data. By identifying these gaps and the importance of the missing information to the risk assessment process, EPA wishes to encourage research and analysis that will lead to new risk assessment methods and data.

Guidelines for the Health Assessment of Suspect Developmental Toxicants

Work on the Guidelines for the Health Assessment of Suspect Developmental Toxicants began in January 1984. Draft guidelines were developed by Agency work groups composed of expert scientists from throughout the Agency. The drafts were peer-reviewed by expert scientists in the field of developmental toxicology from universities, environmental groups, industry, labor, and other governmental agencies. They were then proposed for public comment in the *FEDERAL REGISTER* (49 FR 46324). On November 9, 1984, the Administrator directed that Agency offices use the proposed guidelines in performing risk assessments until final guidelines become available.

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After the close of the public comment period, Agency staff prepared summaries of the comments, analyses of the major issues presented by the commentors, and preliminary Agency responses to those comments. These analyses were presented to review panels of the SAB on March 4 and April 22-23, 1985, and to the Executive Committee of the SAB on April 25-26, 1985. The SAB meetings were announced in the *FEDERAL REGISTER* as follows: February 12, 1985 (50 FR 5811) and April 4, 1985 (50 FR 13420 and 13421).

In a letter to the Administrator dated June 19, 1985, the Executive Committee generally concurred on all five of the guidelines, but recommended certain revisions, and requested that any revised guidelines be submitted to the appropriate SAB review panel chairman for review and concurrence on behalf of the Executive Committee. As described in the responses to comments (see Part B: Response to the Public and Science Advisory Board Comments), each guidelines document was revised, where appropriate, consistent with the SAB recommendations, and revised draft guidelines were submitted to the panel chairmen. Revised draft Guidelines for the Health Assessment of Suspect Developmental Toxicants were concurred on in a letter dated July 26, 1985. Copies of the letters are available at the Public Information Reference Unit, EPA Headquarters Library, as indicated elsewhere in this section.

Following this Preamble are two parts: Part A contains the Guidelines and Part B, the Response to the Public and Science Advisory Board Comments (a summary of the major public comments, SAB comments, and Agency responses to those comments).

The SAB suggested that the Agency pursue additional follow-up work on quantitative risk assessment. Several efforts are currently underway within the Agency on quantitative risk assessment models and procedures, the relationship of maternal and developmental toxicity, and the evaluation and interpretation of postnatal studies. In addition, a document addressing research needs is being prepared to highlight those areas that are in need of further study.

The Agency is continuing to study the risk assessment issues raised in the guidelines and will revise these Guidelines in line with new information as appropriate.

References, supporting documents, and comments received on the proposed

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guidelines, as well as copies of the final guidelines, are available for inspection and copying at the Public Information Reference Unit (202-382-5926), EPA Headquarters Library, 401 M Street, S.W., Washington, DC, between the hours of 8:00 a.m. and 4:30 p.m.

I certify that these Guidelines are not major rules as defined by Executive Order 12291, because they are nonbinding policy statements and have no direct effect on the regulated community. Therefore, they will have no effect on costs or prices, and they will have no other significant adverse effects on the economy. These Guidelines were reviewed by the Office of Management and Budget under Executive Order 12291.

August 22, 1986

Lee M. Thomas,

Administrator

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Part A: Guidelines for the Health Assessment of Suspect Developmental Toxicants

I. Introduction

These Guidelines describe the procedures that the U.S. Environmental Protection Agency will follow in evaluating potential developmental toxicity associated with human exposure to environmental toxicants. In 1980, the Agency sponsored a conference that addressed issues related to such evaluations (1) and provided some of the scientific basis for these risk assessment Guidelines. The Agency's authority to regulate substances that have the potential to interfere adversely with human development is derived from a number of statutes which are implemented through multiple offices within the Agency. Because many different offices evaluate developmental toxicity, there is a need for intra-Agency consistency in the approach to assess these types of effects. The procedures described here will promote consistency in the Agency's assessment of developmental toxic effects.

The developmental toxicity assessments prepared pursuant to these Guidelines will be utilized within the requirements and constraints of the applicable statutes to arrive at regulatory decisions concerning developmental toxicity. These Guidelines provide a general format for analyzing and organizing the available data for conducting risk assessments. The Agency previously has issued testing guidelines (2, 3) that provide protocols designed to determine the potential of a test substance to induce structural and/or other abnormalities in the developing conceptus. These risk assessment Guidelines do not change any statutory or regulatory prescribed standards for the type of data necessary for regulatory action, but rather provide guidance for the interpretation of studies that follow the testing guidelines, and in addition, provide limited information for interpretation of other studies (e.g., epidemiologic data, functional developmental toxicity studies, and short-term tests) which are not routinely required, but which may be encountered when reviewing data on particular agents. Moreover, risk assessment is just one component of the regulatory process and defines the adverse health consequences of exposure to a toxic agent. The other component, risk management, combines risk assessment with the directives of the enabling regulatory legislation, together with socioeconomic, technical, political, and other considerations, to reach a decision as to whether or how much to control future exposure to the suspected toxic agent. The issue of risk management will not be addressed in these Guidelines.

The background incidence of developmental defects in the human population is quite large. For example, approximately 50% of human conceptuses fail to reach term (4); approximately 3% of newborn children are found to have one or more significant congenital malformations at birth, and by the end of the first postnatal year, about 3% more are found to have serious developmental defects (5, 6). Of these, it is estimated that 20% of human developmental defects are of known genetic transmission, 10% are attributable to known environmental factors, and the remainder result from unknown causes (7). Approximately 7.4% of children are reduced in weight at birth (i.e., below 2500 g) (8). Exposure to agents affecting development can result in multiple manifestations (malformation, functional impairment, altered growth, and/or lethality). Therefore, assessment efforts should encompass a wide array of adverse developmental end points, such as spontaneous abortions, stillbirths, malformations, early postnatal mortality, and other adverse functional or physical changes that are manifested postnatally.

Numerous agents have been shown to be developmental toxicants in animal test systems (9). Several of them have also been shown to be the cause of adverse developmental effects in humans, including alcohol, aminopterin, busulfan, chlorobiphenyls, diethylstilbestrol, isotretinoin, organic mercury, thalidomide, and valproic acid (10, 11, 12, 13). Although a number of agents found to be positive in animal studies have not shown clear evidence of hazard in humans, usually the human data available are inadequate to determine a cause and effect relationship. Comparisons of human and animal data have been made for a limited number of agents that are positive in humans (13, 14). In these comparisons, there was almost always concordance of effects between humans and at least one species tested; also, the minimally effective dose (MED) for the most sensitive animal species was approximately 0.5 to 50 times the human

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MED, not accounting for differences in the incidence of effect at the MED. Thus, there is some limited basis for estimating the risk of exposure to human development based on data from animal studies.

The National Research Council (15) has defined risk assessment as being comprised of some or all of the following components: hazard identification, dose-response assessment, exposure assessment, and risk characterization. In general, the process of assessing the risk of human developmental toxicity may be adapted to this format. However, due to special considerations in assessing developmental toxicity, which will be discussed later in these Guidelines, it is not always possible to follow the exact standards as defined for each component.

Hazard identification is the qualitative risk assessment in which all available experimental animal and human data are used to determine if an agent is likely to cause developmental toxicity. In considering developmental toxicity, these Guidelines will address not only malformations, but

also fetal wastage, growth alteration, and functional abnormalities that may result from developmental exposure to environmental agents.

The dose-response assessment defines the relationship of the dose of an agent and the occurrence of developmental toxic effects. According to the National Research Council (15), this component would usually include the results of an extrapolation from high doses administered to experimental animals or noted in epidemiologic studies to the low exposure levels expected for human contact with the agent in the environment. Since at present there are no mathematical extrapolation models that are generally accepted for developmental toxicity, the Agency, for the most part, uses uncertainty (safety) factors and margins of safety, which will be discussed in these Guidelines. Appropriate models are being sought by the Agency for application to data in this area.

The exposure assessment identifies populations exposed to the agent, describes their composition and size, and presents the types, magnitudes, frequencies, and durations of exposure to the agent.

In risk characterization, the exposure assessment and the dose-response assessment are combined to estimate some measure of the risk of developmental toxicity. As part of risk characterization, a summary of the strengths and weaknesses in each component of the assessment are presented along with major assumptions, scientific judgments, and, to the extent possible, estimates of the uncertainties.

II. Definitions and Terminology

The Agency recognizes that there are differences in the use of terms in the field of developmental toxicology. For the purposes of these Guidelines the following definitions and terminology will be used.

Developmental Toxicology--The study of adverse effects on the developing organism that may result from exposure prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the life span of the organism. The major manifestations of developmental toxicity include: 1) death of the developing organism, 2) structural abnormality, 3) altered growth, and 4) functional deficiency.

Embryotoxicity and Fetotoxicity--Any toxic effect on the conceptus as a result of prenatal exposure; the distinguishing feature between the two terms is the stage of development during which the injury occurred. The terms, as used here, include malformations and variations, altered growth, and *in utero* death.

Altered Growth--An alteration in offspring organ or body weight or size. Changes in body weight may or may not be accompanied by a change in crown-rump length and/or in skeletal ossification. Altered growth can be induced at any stage of development, may be reversible, or may result in a permanent change.

Functional Developmental Toxicology--The study of the causes, mechanisms, and manifestations of alterations or delays in functional competence of the organism or organ system following exposure to an agent during critical periods of development pre- and/or postnatally.

Malformations and Variations--A malformation is usually defined as a permanent structural change that may adversely affect survival, development, or function. The term teratogenicity, which is used to describe these types of structural abnormalities, will be used in these Guidelines to refer only to structural defects. A variation is used to indicate a divergence beyond the usual range of structural constitution that may not adversely affect survival or health. Distinguishing between variations and malformations is difficult since there exists a continuum of responses from the normal to the extreme deviant. There is no generally accepted classification of malformations and variations. Other terminology that is often used, but no better defined, includes anomalies, deformations, and aberrations.

III. Qualitative Assessment (Hazard Identification of Developmental Toxicants)

Developmental toxicity is expressed as one or more of a number of possible end points that may be used for evaluating the potential of an agent to cause abnormal development. The four types of effects on the conceptus that may be produced by developmental exposure to toxicants include death, structural abnormality, altered growth, and functional deficits. Of these, the first three types of effects are traditionally measured in laboratory animals using the conventional developmental toxicity (also called teratogenicity or Segment II) testing protocol as well as in other study protocols, such as the multigeneration study. Functional deficits are seldom evaluated in routine studies of environmental agents. This section will discuss the end points examined in routinely used protocols as well as the evaluation of data from other types of studies, including functional studies and short-term tests. Transplacental carcinogenesis, another type of developmental effect, will not be discussed in detail here since, at present, it is considered more appropriate to use the Guidelines for Carcinogen Risk Assessment (16) for assessing the human risk for these types of effects. Also, mutational events may occur as part of developmental toxicity, and in practice, are difficult to discriminate from other possible mechanisms of developmental toxicity. The Guidelines for Mutagenicity Risk Assessment (17) should be consulted in cases where genetic damage is suspected.

A. Laboratory Animal Studies of Developmental Toxicity: End Points and Their Interpretation

The most commonly used protocol for assessing developmental toxicity in laboratory animals involves the administration of a test substance to pregnant animals (usually mice, rats, or rabbits) during the period of major organogenesis, evaluation of maternal responses throughout pregnancy, and examination of the dam and the uterine contents just prior to term (2, 3, 18, 19, 20). Other protocols may use exposure periods of one to a few days to investigate periods of particular sensitivity for induction of anomalies in specific organs or organ systems (21).In

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addition, developmental toxicity may be evaluated in studies involving exposure of one or both parents prior to conception, of the conceptus during pregnancy and over several generations, or of offspring during the late prenatal and early postnatal periods. These Guidelines are intended to provide information for interpreting developmental effects related to any of these types of exposure. Since many of the end points evaluated also are related to effects on the parental reproductive systems, these Guidelines will be used in conjunction with those to be published in the future by EPA on male and female reproductive toxicity.

Study designs should include a high dose, which produces some maternal or adult toxicity (i.e., a level which at the least produces marginal but significantly reduced body weight, weight gain, or specific organ toxicity, and at the most produces no more than 10% mortality); a low dose, which demonstrates a no observed effect level (NOEL) for adult and offspring effects; and at least one intermediate dose level. A concurrent control group treated with the vehicle used for agent administration should be included. The route of exposure should be based on expected human exposure considerations, although data from other routes may sometimes be useful, especially if supported by pharmacokinetic information. Test animals should be selected based on considerations of species, strain, age, weight, and health status, and should be randomized to dose groups in order to reduce bias and provide a basis for performing valid statistical tests.

The next three sections discuss individual end points of maternal and developmental toxicity as measured in the conventional developmental toxicity study, the multigeneration study, and, on occasion, in postnatal studies. Other end points specifically related to reproductive toxicity will be covered in the relevant reproductive toxicity guidelines. The fourth section deals with the integrated evaluation of all data, including the relative effects of exposure on maternal animals and their offspring, which is important in assessing the level of concern about a particular agent.

1. End Points of Maternal Toxicity. A number of end points that may be observed as possible indicators of maternal toxicity are listed in Table 1. Maternal mortality is an obvious end point of toxicity; however, a number of other end points can be observed which may give an indication of the subtle effects of an agent. For example, in well-conducted studies, the fertility and gestation indices provide information on the general fertility rate of the animal stock used and are important indicators of toxic effects if treatment begins prior to mating or implantation. Changes in gestation length may indicate effects on the process of parturition.

Table 1.--End Points of Maternal Toxicity

Mortality
Fertility Index (no. with seminal plugs or sperm/no. mated)
Gestation Index (no. with implants/no. with seminal plugs or sperm)
Gestation Length (when allowed to deliver pups)
Body Weight
- Treatment days (at least first, middle, and last treatment days)
- Sacrifice day

Body Weight Change
- Throughout gestation
- During treatment (including increments of time within treatment period)
- Post-treatment to sacrifice
- Corrected maternal (body weight change throughout gestation minus gravid uterine weight or litter weight at sacrifice)

Organ Weights (in cases of suspected specific organ toxicity)
- Absolute
- Relative to body weight

Food and Water Consumption (where relevant)
Clinical Evaluations (on days of treatment and at sacrifice)
- Types and incidence of clinical signs
- Enzyme markers
- Clinical chemistries

Gross Necropsy and Histopathology

Body weight and the change in body weight are viewed collectively as indicators of maternal toxicity for most species, although these end points may not be as useful in rabbits, because body weight changes in rabbits are not good indicators of pregnancy status. Body weight changes may provide more information than a daily body weight measured during treatment or during gestation. Changes in weight during treatment could occur that would not be reflected in the total weight change throughout gestation, because of compensatory weight gain that may occur following treatment but before sacrifice. For this reason, changes in weight during treatment

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can be examined as another indicator of maternal toxicity.

Changes in maternal body weight corrected for gravid uterine weight at sacrifice may indicate whether the effect is primarily maternal or fetal. For example, there may be a significant reduction in weight gain throughout gestation and in gravid uterine weight, but no change in corrected maternal weight gain which would indicate primarily an intrauterine effect. Conversely, a change in corrected weight gain and no change in gravid uterine weight suggests primarily maternal toxicity and little or no intrauterine effect. An alternate estimate of maternal weight change during gestation can be obtained by subtracting the sum of the weights of the fetuses. However, this weight does not include the uterine tissue, placental tissue, or the amniotic fluid.

Changes in other end points should also be determined. For example, changes in relative and absolute organ weights may be signs of a maternal effect when an agent is suspected of causing specific organ toxicity. Food and water consumption data are useful, especially if the agent is administered in the diet or drinking water. The amount ingested (total and relative to body weight) and the dose of the agent (relative to body weight) can then be calculated, and changes in food and water consumption related to treatment can be evaluated along with changes in body weight and body weight gain. Data on food and water consumption are also useful when an agent is suspected of affecting appetite, water intake, or excretory function. Clinical evaluations of toxicity may also be used as indicators of maternal toxicity. Daily clinical observations may be useful in describing the profile of maternal toxicity. Enzyme markers and clinical chemistries may be useful indicators of exposure but must be interpreted carefully as to whether or not a change constitutes toxicity. Gross necropsy and histopathology data (when specified in the protocol) may aid in determining toxic dose levels.

2. End Points of Developmental Toxicity. Because the maternal animal, and not the conceptus, is the individual treated during gestation, data generally should be calculated as incidence per litter or as number and percent of litters with particular end points.Table 2 indicates the way in which offspring and litter end points may be expressed.

Table 2.--End Points of Developmental Toxicity.

Litters with implants

- No. implantation sites/dam
- No. corpora lutea (CL)/dam[a]
- Percent preimplantation loss

$$\frac{(\text{CL} - \text{implantations}) \times 100}{\text{CL}}$$ [a]

- No. and percent live offspring/litter
- No. and percent resorptions/litter
- No. and percent litters with resorptions

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- No. and percent late fetal deaths/litter
- No. and percent nonlive (late fetal deaths + resorptions) implants/litter
- No. and percent litters with nonlive implants
- No. and percent affected (nonlive + malformed) implants/litter
- No. and percent litters with affected implants
- No. and percent litters with total resorptions
- No. and percent stillbirths/litter

Litters with live offspring[b]

- No. and percent litters with live offspring
- No. and percent live offspring/litter
- Viability of offspring[c]
- Sex ratio/litter
- Mean offspring body weight/litter[c]
- Mean male body weight/litter[c]
- Mean female body weight/litter[c]
- No. and percent externally malformed offspring/litter
- No. and percent viscerally malformed offspring/litter
- No. and percent skeletally malformed offspring/litter
- No. and percent malformed offspring/litter
- No. and percent litters with malformed offspring
- No. and percent malformed males/litter
- No. and percent malformed females/litter
- No. and percent offspring with variations/litter
- No. and percent litters having offspring with variations
- Types and incidence of individual malformations
- Types and incidence of individual variations
- Individual offspring and their malformations and variations (grouped according to litter and dose)
- Clinical signs[c]
- Gross necropsy and histopathology

[a] Important when treatment begins prior to implantation. May be difficult in mice.

[b] Offspring refers both to fetuses observed prior to term or to pups following birth. The end points examined depend on the protocol used for each study.

[c] Measured at selected intervals until termination of the study.

When treatment begins prior to implantation, an increase in preimplantation loss could indicate an adverse effect either on the developing blastocyst or on the process of implantation itself. If treatment begins around the time of implantation (i.e., day 6 of gestation in the mouse, rat, or rabbit), an increase in preimplantation loss probably reflects normal variability in the animals being used, but the data should be examined carefully to determine whether or not the effect is dose related. If preimplantation

loss is related to dose in either case, further studies would be necessary to determine the mechanism and extent of such effects.

The number and percent of live offspring per litter, based on all litters, may include litters that have no live implants. The number and percent resorptions or late fetal deaths per litter gives some indication of when the conceptus died, and the number and percent nonlive implants per litter (postimplantation loss) is a combination of resorptions and late fetal deaths. The number and percent of litters showing an increased incidence for these end points is generally useful but may be less useful than incidence per litter because, in the former case, a litter is counted whether it has one or all resorbed, dead, or nonlive implants.

If a significant increase in postimplantation loss is found after exposure to an agent, the data may be compared not only with concurrent controls, but also with recent historical control data, since there is considerable interlitter variability in the incidence of postimplantation loss (22). If a given study control group exhibits an unusually high or low incidence of postimplantation loss compared to historical controls, then scientific judgment must be used to determine the adequacy of the studies for risk assessment purposes.

The end point for affected implants (i.e., the combination of nonlive and malformed conceptuses) gives an indication of the total intrauterine response to an agent and sometimes reflects a better dose-response relationship than does the incidence of nonlive or malformed offspring taken individually. This is especially true at the high end of the dose-response curve in cases when the incidence of nonlive implants per litter is greatly increased. In such cases, the malformation rate may appear to decrease because only unaffected offspring have survived. If the incidence of prenatal death or malformation is unchanged, then the incidence of affected implants will not provide any additional dose-response information. In studies where maternal animals are allowed to deliver pups normally, the number of stillbirths per litter should also be noted.

The number of live offspring per litter, based on those litters that have one or more live offspring, may be unchanged even though the incidence of nonlive in all litters is increased. This could occur either because of an increase in the number of litters with no live offspring, or an increase in the number of implants per litter. A decrease in the number of live offspring per litter should be accompanied by an increase in the incidence of nonlive implants per litter, unless the implant numbers differ among dose groups. In postnatal studies, the viability of live born offspring should be determined at selected intervals until termination of the study.

The sex ratio per litter, as well as the body weights of males and females, can be examined to determine whether or not one sex is preferentially affected by the agent. However, this is an unusual occurrence.

A change in offspring body weight is a sensitive indicator of developmental toxicity, in part because it is a continuous variable. In some cases, offspring weight reduction may be the only indicator of developmental toxicity; if so, there is always a question remaining as to whether weight reduction is a permanent or transitory effect. A permanent weight change may be considered more severe than a transitory change, although little is known about the long-term consequences of short-term fetal or neonatal weight changes. When fetal or neonatal weight reduction is the only indicator of developmental toxicity, data from the two-generation reproduction study (2), if available, may be useful for evaluating these parameters. Ideally, follow-up studies to evaluate postnatal viability, growth, and survival through weaning should be conducted. There are other factors that should be considered in the evaluation of fetal or neonatal weight changes. For example, in polytocous animals, fetal and neonatal weights are usually inversely correlated with litter size, and the upper end of the dose-response curve may be confounded by smaller litters and increased fetal or neonatal weight. Additionally, the average body weight of males is greater than that of females in the more commonly used laboratory animals.

Live offspring should be examined for external, visceral, and skeletal malformations. If only a portion of the litter is examined, then it is preferable that those examined be randomly selected from each litter. An increase in the incidence of malformed offspring may be indicated by a change in one or more of the following end points: the incidence of malformed offspring per litter, the number and percent of litters with malformed offspring, or the number of offspring or litters with a particular malformation that appears to increase with dose as indicated by the incidence of individual types of malformations.

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Other ways of examining the data include the incidence of external, visceral, and skeletal malformations which may indicate which general systems are affected. A listing of individual offspring with their malformations and variations may give an indication of the pattern of developmental deviations. All of these methods of expressing and examining the data are valid for determining the effects of an agent on structural development. However, care must be taken to avoid counting offspring more than once in evaluating any single end point based on number or percent of offspring or litters. The incidence of individual types of malformations and variations should be examined

for significant changes which may be masked if the data on all malformations and variations are pooled. Appropriate historical control data are helpful in the interpretation of malformations and variations, especially those that normally occur at a low incidence apparently unrelated to dose in an individual study. Although a dose-related increase in malformations is interpreted as an adverse developmental effect of exposure to an agent, the significance of anatomical variations is more difficult to determine, and must take into account what is known about developmental stage (e.g., with skeletal ossification), background incidence of certain variations (e.g., 12 or 13 pairs of ribs in rabbits), or other strain - or species-specific factors. However, if variations are significantly increased in a dose-related manner, these should also be evaluated as a possible indication of developmental toxicity. The Interagency Regulatory Liaison Group noted that dose-related increases in defects, which may occur spontaneously, are as relevant as dose-related increases in any other developmental toxicity end points (23).

3. *Functional Developmental Toxicology.* Developmental effects, which are inducible by exogenous agents, are not limited to death, structural abnormalities, and altered growth. Rather, it has been demonstrated in a number of instances that subtle alterations in the functional competence of an organ or a variety of organ systems may result from exposure during critical developmental periods that may occur between conception and sexual maturation. Often, these functional defects are observed at dose levels below those at which gross malformations are evident (24). At present, such testing is not routinely required in the United States. However, data from postnatal studies, when available, are considered very useful for the assessment of the relative importance and severity of findings in the fetus and neonate. Often, the long-term consequences of adverse developmental outcomes at birth are unknown, and further data on postnatal development and function may contribute valuable information. When regulatory statutes permit, studies designed to evaluate adverse fetal or neonatal outcomes have been requested (e.g., the Office of Pesticide Programs has sometimes requested postnatal studies where the reversibility of study findings were at issue). In some cases, useful data can be derived from well-executed multigeneration studies.

Much of the early work in functional developmental toxicology was related to behavioral evaluations, and the term "behavioral teratology" became prominent in the mid 1970s. Less work has been done on other functional systems, but sufficient data have accumulated to indicate that the cardiopulmonary, immune, endocrine, digestive, urinary, nervous, and reproductive systems are subject to alterations in functional competence (25, 26). Currently, there are no standard testing procedures, although some attempts are being made to standardize and evaluate tests and protocols (27). The functional evaluation of specific systems often involves highly specialized training and equipment. The routine use of such test procedures may not always be practical, but may be extremely important in determining the nature of a suspected alteration in terms of its biological significance and dose-response relationship.

The interpretation of data from functional developmental toxicology studies is limited due to the lack of knowledge about the underlying toxicological mechanisms and their significance. However, since such data are sometimes encountered in the risk assessment of particular agents, some guidance is provided here concerning general concepts of study design and evaluation.

a. Several aspects of study design are similar to those important in standard developmental toxicity studies (e.g., a dose-response approach with the highest dose producing minimal overt maternal or perinatal toxicity, number of litters large enough for adequate statistical power, randomization of animals to dose groups, litter generally considered the statistical unit, etc.).

b. A replicate study design provides added confidence in the interpretation of data.

c. Use of a pharmacological challenge may be valuable in evaluating function and "unmasking" effects not otherwise detectable, particularly in the case of organ systems that are endowed with a reasonable degree of functional reserve capacity.

d. Use of functional tests with a moderate degree of background variability may be more sensitive to the effects of an agent than are tests with low variability that may be impossible to disrupt without being life-threatening. Butcher et al. (28) have discussed this with relation to behavioral end points.

e. A battery of functional tests usually provides a more thorough evaluation of the functional competence of an animal; tests conducted at several ages may provide more information about maturational changes.

f. Critical periods for the disruption of functional competence include both the prenatal and the postnatal periods to the time of sexual maturation, and the effect is likely to vary depending on the time and degree of exposure.

Although interpretation of functional data may be difficult at present, there are at least three ways in which the data from these studies may be useful for risk assessment purposes: 1) to help elucidate the long-term consequences of fetal and neonatal findings; 2) to indicate the potential for an agent to cause functional alterations, and the effective doses relative to those that produce other forms of toxicity;

and 3) for existing environmental agents, to focus on organ systems to be evaluated in exposed human populations.

4. *Overall Evaluation of Maternal and Developmental Toxicity.* As discussed previously, individual end points are evaluated in developmental toxicity studies, but an integrated evaluation must be done considering all maternal and developmental end points in order to interpret the data fully. Developmental toxicity is considered to be an increase in the incidence of malformed offspring, decreased viability (prenatal or postnatal), altered growth, and/or functional deficits.

The level of concern for a developmental toxic effect is related to several issues, including the relative toxicity of an agent to the offspring versus the adult animal, and the long-term consequences of findings in the fetus or neonate. Those agents which produce developmental toxicity at a dose that is not toxic to the maternal animal are of greatest concern because the developing organism appears to be selectively affected or more sensitive than the adult. However, when developmental effects are produced only

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at maternally toxic doses, the types of developmental effects should be examined carefully, and not discounted as being secondary to maternal toxicity. Current information is inadequate to assume that developmental effects at maternally toxic doses result only from the maternal toxicity; rather, when the lowest observed effect level is the same for the adult and developing organisms, it may simply indicate that both are sensitive to that dose level. Moreover, the maternal effects may be reversible while effects on the offspring may be permanent. These are important considerations for agents to which humans may be exposed at minimally toxic levels either voluntarily or in the workplace, since several agents are known to produce adverse developmental effects at minimally toxic doses in adult humans (e.g., smoking, alcohol).

Approaches for ranking agents for their selective developmental toxicity are being developed; Schardein (10) has reviewed several of these. Of current interest are approaches that develop ratios relating an adult toxic dose to a developmental toxic dose (29, 30, 31, 32). Ratios near unity indicate that developmental toxicity occurs only at doses producing maternal toxicity; as the ratio increases, there is a greater likelihood of developmental effects occurring without maternal manifestations. Although further exploration and validation are necessary, such approaches may ultimately help in identifying those agents that pose the greatest threat and should be given higher priority for further testing (33).

5. *Short-term Testing in Developmental Toxicity.* The need for short-term tests for developmental toxicity has arisen from the large number of agents in or entering the environment, the interest in reducing the number of animals used for routine testing, and the expense of testing. Two approaches are considered here in terms of their contribution to the overall testing process: 1) an *in vivo* mammalian screen, and 2) a variety of *in vitro* systems. Currently, neither approach is considered as a replacement for routine *in vivo* developmental toxicity testing in experimental animals, and should not be used to make the final decision as to whether an agent is a positive or negative developmental toxicant; rather, such tests may be useful as tools for assigning priorities for further, more extensive testing. Although such short-term tests are not routinely required, data are sometimes encountered in the review of chemicals; the comments are provided here for guidance in the evaluation of such data.

a. *In Vivo* Mammalian Developmental Toxicity Screen. The most widely studied *in vivo* approach is that developed by Chernoff and Kavlock (34) which uses the pregnant mouse. This approach is based on the hypothesis that a prenatal injury, which results in altered development, will be manifested postnatally as reduced viability and/or impaired growth. In general, the test substance is administered over the period of major organogenesis at a single dose level that will elicit some degree of maternal toxicity. A second lower dose level may be used which potentially will reduce the chances of false positive results. The pups are counted and weighed shortly after birth, and again after 3-4 days. End points that are considered in the evaluation include: general maternal toxicity (including survival and weight gain), litter size, and viability, weight, and gross malformations in the offspring. Basic priority-setting categories for more extensive testing have been suggested: 1) agents that induce perinatal death should receive highest priority, 2) agents inducing perinatal weight changes should be ranked lower in priority, and 3) agents inducing no effect should receive the lowest priority (34). Another scheme that has been proposed applies a numerical ranking to the results as a means of prioritizing agents for further testing (35, 36).

The mouse was chosen originally for this test because of its low cost, but the procedure should be easily applicable to other species. However, the test will only predict the potential for developmental toxicity of an agent in the species utilized and does not improve the ability to extrapolate risk to other species, including humans. The Office of Toxic Substances has developed testing guidelines for this procedure (37). Although the testing guidelines are available, such procedures are not routinely

required, and further validation is currently being carried out (38).

b. *In Vitro* Developmental Toxicity Screens. Test systems that fall under the general heading of "*in vitro*" developmental toxicity screens include any system that employs a test subject other than the intact pregnant mammal. These systems have long been used to assess events associated with normal and abnormal development, but only recently have they been considered for their potential as screens in testing (39, 40, 41). Many of these systems are now being evaluated for their ability to predict the developmental toxicity of various agents in intact mammalian systems. This validation process requires certain considerations in study design, including defined end points for toxicity and an understanding of the system's ability to handle various test agents (40, 42). A list of agents for use in such validation studies has been developed (43).

6. *Statistical Considerations.* In the assessment of developmental toxicity data, statistical considerations require special attention. Since the litter is generally considered the experimental unit in most developmental toxicity studies, the statistical analyses should be designed to analyze the relevant data based on incidence per litter or on the number of litters with a particular end point. The analytical procedures used and the results, as well as an indication of the variance in each end point, should be clearly indicated in the presentation of data. Analysis of variance (ANOVA) techniques, with litter nested within dose in the model, take the litter variable into account but allow use of individual offspring data and an evaluation of both within and between litter variance as well as dose effects. Nonparametric and categorical procedures have also been widely used for binomial or incidence data. In addition, tests for dose-response trends can be applied. Although a single statistical approach has not been agreed upon, a number of factors important in the analysis of developmental toxicity data have been discussed (23, 44).

Studies that employ a replicate experimental design (e.g., two or three replicates with 10 litters per dose per replicate rather than a single experiment with 20-30 litters per dose group) allow for broader interpretation of study results since the variability between replicates can be accounted for using ANOVA techniques. Replication of effects due to a given agent within a study, as well as between studies or laboratories, provides added strength in the use of data for the estimation of risk.

An important factor to determine in evaluating data is the power of a study (i.e., the probability that a study will demonstrate a true effect), which is limited by the sample size used in the study, the background incidence of the end point observed, the variability in the incidence of the end point, and the analysis method. As an example, Nelson and Holson (45) have shown that the number of litters needed to detect a 5 or 10% change was dramatically lower for fetal weight (a continuous variable with low variability) than for resorptions (a binomial response with high variability). With the current recommendation in

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testing protocols being 20 rodents per dose group (2, 3), it is possible to detect an increased incidence of malformations in the range of 5 to 12 times above control levels, an increase of 3 to 6 times the *in utero* death rate, and a decrease of 0.15 to 0.25 times the fetal weight. Thus, even within the same study, the ability to detect a change in fetal weight is much greater than for the other end points measured. Consequently, for statistical reasons only, changes in fetal weight are often observable at doses below those producing other signs of developmental toxicity. Any risk assessment should present the detection sensitivity for the study design used and for the end point(s) evaluated.

Although statistical analyses are important in determining the effects of a particular agent, the biological significance of data should not be overlooked. For example, with the number of end points that can be observed in developmental toxicity studies, a few statistically significant differences may occur by chance. On the other hand, apparent trends with dose may be biologically relevant even though statistical analyses do not indicate a significant effect. This may be true especially for the incidence of malformations or *in utero* death where a relatively large difference is required to be statistically significant. It should be apparent from this discussion that a great deal of scientific judgment based on experience with developmental toxicity data and with principles of experimental design and statistical analysis may be required to adequately evaluate such data.

B. Human Studies

Because of the ethical considerations involved, studies with deliberate dosing of humans are not done. Therefore, dose-effect developmental toxicity data from humans are limited to those available from occupational, environmental, or therapeutic exposures. While animal studies provide dose-response data that can be used in the extrapolation of risk to humans, good epidemiologic data provide the best information for assessing human risk.

The category of "human studies" includes both epidemiologic studies and other reports of cases or clusters of events. While case reports have been important in identifying several human teratogens, they are potentially of greater value in identifying topics for further investigation (46). The data from case reports are often of an anecdotal or highly selected nature, and thus are of limited usefulness for risk assessment except when a unique defect is produced, as with thalidomide, or when the agent is

so potent as to greatly increase the incidence of a particular defect(s).

As there are many different designs for epidemiologic studies, simple rules for their evaluation do not exist. The assessment of epidemiologic studies requires a sophisticated level of understanding of the appropriate epidemiologic and statistical methods and interpretation of the findings. Factors that increase a study's usefulness for risk assessment include such things as the examination of multiple end points and exposure levels, the validity of the data, and proper control of other risk factors, effect modifiers, and confounders in the study design and/or analysis. A more in-depth discussion can be found elsewhere (47).

As described earlier, a single developmental toxicant can result in multiple end points (malformations, functional impairment, altered growth, and/or lethality). These end points can be thought of as sequential competing risks. For example, a malformed fetus spontaneously aborted would not be observed in a study of births with malformations (48). Very early conceptus losses may not be identified in human populations, whereas in most laboratory animal studies, all resorption sites can be identified. Many epidemiologic studies, especially of the case-control design, have focused on one end point, possibly missing a true effect of exposure. Furthermore, some studies have selected one type or class of malformations to study. Since an agent can result in different spectra of malformations following exposure at different times in the pregnancy (49), limiting a study to one class of malformation may give misleading results. Malformations can be meaningfully grouped only if there is a logical underlying teratogenic mechanism or pathogenetic pathway. As a minimum, malformations, deformations, and disruptions should be separated.

The power, or probability of a study to detect a true effect, is dependent upon the size of the study group, the frequency of the outcome in the general population, and the level of excess risk to be identified. Rarer outcomes, such as malformations, require thousands of pregnancies to have a high probability of detecting an increase in risk. More common outcomes, such as fetal loss, require hundreds of pregnancies to have the same probability (8, 23, 50, 51, 52, 53). The confidence one has in the results of a study with negative findings is directly related to the power of the study to detect clinically meaningful differences in incidence for the end points studied.

As in animal studies, pregnancies within the same family (or litter) are not independent events. In animal studies, the litter is generally used as the unit of measure. This approach is difficult in humans since the pregnancies are sequential, with the risk factors changing for the different pregnancies (23, 51, 54). If more than one pregnancy per family is included, and this is often necessary due to small study groups, the use of non-independent observations overestimates the true size of the population at risk and artificially increases the significance level (54).

Other criteria for evaluating epidemiologic studies include the following (23, 50, 52, 55, 56, 57, 58):

1. The potential for complete or relatively complete ascertainment of events for study. This can vary by outcome and by data source; for example, if hospital records are used, early fetal losses will be underascertained, but a more complete list of pregnancies could be obtained by interviewing the women. Congenital malformations can be more completely ascertained using hospital records than birth certificates. Studies with relatively complete ascertainment of events, or at least low probability of unbiased ascertainment, should carry more weight.

2. Validity (accuracy) of the data. Recall of past events in interviews may be faulty, while hospital files contain data recorded at the time of the event (but may be incomplete). Validation of interview data with an independent source, where possible, increases confidence in the results of the study.

3. Collection of data on other risk factors, effect modifiers, and confounders. Data on smoking, alcohol consumption, drug use, and environmental and occupational exposure, etc., during pregnancy should be examined and controlled for in the study design and/or analysis where appropriate. The analytic techniques used to control for these factors require careful consideration in their application and interpretation.

C. Other Considerations

1. *Pharmacokinetics.* Extrapolation of data between species can be aided considerably by the availability of data on the pharmacokinetics of a particular agent in the species tested and, if possible, in humans. Information on half-lives, placental metabolism and transfer, and concentrations of the parent compound and metabolites in the

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maternal animal and conceptus may be useful in predicting risk for developmental toxicity. Such data may also be helpful in defining the dose-response curve, developing a more accurate comparison of species sensitivity including that of humans (59, 60), determining dosimetry at target sites, and comparing pharmacokinetic profiles for various dosing regimens or routes of exposure. Pharmacokinetic studies in developmental toxicology are most useful if conducted in pregnant animals at the stage when developmental insults occur. The correlation of pharmacokinetic parameters and developmental toxicity data may be

useful in determining the contribution of specific pharmacokinetic parameters to the effects observed (61).

2. *Comparisons of Molecular Structure.* Comparisons of the chemical or physical properties of an agent with those of known developmental toxicants may provide some indication of a potential for developmental toxicity. Such information may be helpful in setting priorities for testing of agents or for evaluation of potential toxicity when only minimal data are available. Structure/activity relationships have not been well studied in developmental toxicology, although data are available that suggest structure-activity relationships for certain classes of chemicals (e.g., glycol ethers, steroids, retinoids). Under certain circumstances (e.g., in the case of new chemicals), this is one of several procedures used to evaluate the potential for toxicity when little or no data are available.

D. Weight-of-Evidence Determination

Information available from studies discussed previously, whether indicative of potential concern or not, must be evaluated and factored into the risk assessment. The types of data may vary from chemical to chemical, and certain types of data may be more relevant than other types in performing developmental toxicity assessments. The primary considerations are the human data (which are seldom available) and the experimental animal data. The qualitative assessment for developmental toxicity should include statements concerning the quality of the data, the resolving power of the studies, the number and types of end points examined, the relevance of route and timing of exposure, the appropriateness of the dose selection, the replication of the effects, the number of species examined, and the availability of human case reports, case series, and/or epidemiologic study data. In addition, pharmacokinetic data and structure-activity considerations, as well as other factors that may affect the quality, should be taken into account. Therefore, all data pertinent to developmental toxicity should be examined in the evaluation of a chemical's potential to cause developmental toxicity in humans, and sound scientific judgment should be exercised in interpreting the data in terms of the risk for adverse human developmental health effects.

IV. Quantitative Assessment

Risk assessment involves the description of the nature and often the magnitude of potential human risk, including a description of any attendant uncertainty. In the final phase of the risk assessment (risk characterization), the results of the qualitative evaluation (hazard identification), the dose-response, and the exposure assessments are combined to give qualitative and/or quantitative estimates of the developmental toxicity risk. A summary of the strengths and weaknesses of the hazard identification, dose-response assessment, and exposure assessment should be discussed. Major assumptions, scientific judgments, and, to the extent possible, estimates of the uncertainties in the assessment also should be presented.

A. Dose-Response Assessment

When quantitative human dose-effect data are available and with sufficient range of exposure, dose-response relationships may be examined. However, such data have rarely been available; thus, other methods have been used in developmental toxicology for estimating exposure levels that are unlikely to produce adverse effects in humans. The dose-response assessment is usually based on the evaluation of tests performed in laboratory animals. Evidence for a dose-response relationship is an important criterion in the assessment of developmental toxicity, although this may be based on limited data from standard three-dose studies. As mentioned earlier (section III. A. 2.), however, traditional dose-response relationships may not always be observed for some end points. For example, as the exposure level rises, embryo/fetolethal levels may be reached, resulting in an observed decrease in malformations with increasing dose (49, 51). The potential for this relationship indicates that dose-response relationships for individual end points as well as combinations of end points (e.g., dead and malformed combined) must be carefully examined and interpreted.

Although dose-response data are important in this area, the approaches frequently employed in attempts to extrapolate to humans has involved simply the use of uncertainty (safety) factors and margins of safety, which in some respects are conceptually similar. However, uncertainty factors and margins of safety are computed differently and are often used in different regulatory situations. The choice of approach is dependent upon many factors, including the statute involved, the situation being addressed, the data base used, and the needs of the decision-maker. The final uncertainty factor used and the acceptability of the margin of safety are risk management decisions, but the scientific issues that must be taken into account are addressed here.

The uncertainty factor approach results in a calculated exposure level believed to be unlikely to cause any toxic developmental response in humans. The size of the uncertainty factor will vary from agent to agent and will require the exercise of scientific judgment (10, 62), taking into account interspecies differences, the nature and extent of human exposure, the slope of the dose-response curve, the types of developmental effects observed, and the relative dose levels for maternal and developmental toxicity in the test species. The uncertainty factor selected is then divided into the NOEL for the most sensitive end point obtained from

the most appropriate and/or sensitive mammalian species examined to obtain an acceptable exposure level. Currently, there is no one laboratory animal species that can be considered most appropriate for predicting risk to humans (10). Each agent should be considered on a case-by-case basis.

The margin of safety approach derives a ratio of the NOEL from the most sensitive species to the estimated human exposure level from all potential sources (63). The adequacy of the margin of safety is then considered, based on the weight of evidence, including the nature and quality of the hazard and exposure data, the number of species affected, dose-response relationships, and other factors such as benefits of the agent.

Although the standard study design for a developmental toxicity study calls for a low dose that demonstrates a NOEL, there may be circumstances where a risk assessment is based on the results of a study in which a NOEL for developmental toxicity could not be identified. Rather, the lowest dose administered caused significant effect(s) and was identified as the lowest observed effect level (LOEL). In circumstances where only a LOEL is available, it may be appropriate to apply

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an additional uncertainty factor. The magnitude of this additional factor is dependent upon scientific judgment. In some instances, additional studies may be needed to strengthen the confidence in this additional uncertainty factor.

B. Exposure Assessment

The results of the dose-response assessment are combined with an estimate of human exposure in order to obtain a quantitative estimate of risk. The Guidelines for Estimating Exposures are published separately (64) and will not be discussed in detail here. In general, the exposure assessment describes the magnitude, duration, schedule, and route of exposure. This information is developed from monitoring data and from estimates based on modeling of environmental exposures. Unique considerations relevant to developmental toxicity are duration and period of exposure as related to stage of development (i.e., critical periods), and the possibility that a single exposure may be sufficient to produce adverse developmental effects (i.e., chronic exposure is not a necessary prerequisite for developmental toxicity to be manifested). Also, it should be recognized that exposure of almost any segment of the human population (i.e., fertile men and women, the conceptus, and the child up to the age of sexual maturation) may lead to risk to the developing organism.

Data on exposure to humans may be qualitative or quantitative. The qualitative data could be surrogate data, such as employment or residence histories; quantitative or dose data are frequently not available. Exposures at different stages of the reproductive process can result in different outcomes (49). In laboratory studies, these time periods can be carefully controlled. In human studies, especially retrospective ones, linking of specific time periods and specific exposures, even on a qualitative level, may be difficult due to errors of recall or record keeping (where records are available). The increased probability of misclassification of exposure status may affect the ability of a study to recognize a true effect (8, 23, 52, 65, 66).

Exposure may be defined at a specific point in time, or the cumulative lifetime exposure up to a specific point in time. Each of these definitions carries an implicit assumption about the underlying relationship between exposure and outcome. For example, a cumulative exposure measure assumes that total lifetime exposure is important, with a greater probability of effect with greater total exposure; a dichotomous exposure measure (ever exposed versus never exposed) assumes an irreversible effect of exposure; and exposure at a specific time in the reproductive process assumes that only concurrent exposure is important. The appropriate exposure depends on the outcome(s) studied, the biologic mechanism affected by exposure, and the half-life of the exposure. Unbiased misclassification of exposure, due either to poor data or to an inappropriate exposure variable, may result in missing an effect of the agent under study.

C. Risk Characterization

Many uncertainties have been pointed out in these Guidelines which are associated with the toxicological and exposure components of risk assessments in developmental toxicology. In the past, these uncertainties have often not been readily apparent or consistently presented. The presentation of any risk assessment for developmental toxicity should be accompanied by statements concerning the strength of the hazard evaluation (see section III. D. for more detail) as well as dose-response relationships, estimates of human exposure, and any other factors that affect the quality and precision of the assessment. The dose-response and exposure data are combined to estimate risk based on a NOEL for any adverse developmental effect. The uncertainty factor selected or margin of safety calculated should be sufficiently qualified as to the assumptions used and the accuracy of the estimates.

At present, there are no mathematical models that are generally accepted for estimating developmental toxicity responses below the applied dose range. This is due primarily to a lack of understanding of the biological mechanisms underlying developmental toxicity, intra/interspecies differences in the types of developmental events, the influence of maternal effects on the dose-response curve, and whether or not a threshold exists below which no effect will be

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produced by an agent. Many developmental toxicologists assume a threshold for most developmental effects; this assumption is based largely on the biological rationale that the embryo is known to have some capacity for repair of the damage or insult (49), and that most developmental deviations are probably multifactorial in nature (67). The existence of a NOEL in an animal study does not prove or disprove the existence or level of a true threshold; it only defines the highest level of exposure under the conditions of the test that are not associated with a significant increase in effect. The use of NOELs and uncertainty factors or margins of safety are attempts to ensure that the allowable levels are below those that will produce a significant increase in developmental effects.

Discussions of risk extrapolation procedures have noted that further work is needed to improve mathematical tools for developing estimates of potential human developmental risk (62, 68). Gaylor (69) has suggested an approach for controlling risk that combines the use of mathematical models for low-dose estimation of risk with the application of an uncertainty factor based on a preselected level of allowable risk. This approach is similar to approaches proposed for carcinogenesis, but does not preclude the possibility of a threshold, and may provide a more quantitative approach to controlling risk. Several such approaches are being examined. For the most part, the Agency will continue to use uncertainty factors and margins of safety as described above. Other appropriate methods for expressing risk are being sought and will be applied if considered acceptable.

These Guidelines summarize the procedures that the U.S. Environmental Protection Agency will follow in evaluating the potential for agents to cause developmental toxicity. These Guidelines will be reviewed and updated as advances are made in the field, since it is evident that our ability to evaluate and predict human developmental toxicity is imprecise. Further studies that 1) delineate the mechanisms of developmental toxicity and pathogenesis, 2) provide comparative pharmacokinetic data, and 3) elucidate the functional modalities that may be altered by exposure to toxic agents will aid in the interpretation of data and interspecies extrapolation. These types of studies, along with further evaluation of the relationship between maternal and fetal toxicity and the concept of a threshold in developmental toxicity, will provide for the development of improved mathematical models to more precisely assess risk.

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Part B: Response to Public and Science Advisory Board Comments

I. Introduction

This section summarizes some of the issues raised in public comments on the Proposed Guidelines for the Health Assessment of Suspect Developmental Toxicants published November 23, 1984 (49 FR 46324). Comments were received from 44 individuals or organizations. The Agency's initial summary of comments was presented to the Developmental Toxicity Guidelines Panel of the Science Advisory Board (SAB) at its organizational meeting on March 4, 1985. At its April 22-23, 1985, meeting, the Panel provided the Agency with its suggestions and recommendations concerning the Guidelines.

The SAB and public comments were diverse and addressed issues from a variety of perspectives. In general, the comments were favorable and in support of the Guidelines. The SAB Panel noted that the field of developmental toxicology is particularly weak with respect to quantitative assessment and recommended that further efforts be given to developing alternative methods for quantitative estimates of risk for developmental toxicity. They also indicated that further discussion of the relationship of maternal toxicity to fetal toxicity could be added. Concern was expressed that these Guidelines be coordinated with the reproductive toxicity guidelines which are currently being developed.

In response to the comments, the Agency has modified or clarified many sections of the Guidelines. For purposes of this discussion, only the most significant issues reflected by the public and SAB comments are discussed. Several minor recommendations, which do not warrant discussion here, were considered by the Agency in the revision of these Guidelines.

II. Coordination With Other Guidelines

A. Other Risk Assessment Guidelines

Several commentors raised concerns about aspects of developmental toxicity (e.g., paternally-mediated effects, effects of subchronic exposures, transplacental carcinogenesis, etc.) that were not covered in these Guidelines, and how these Guidelines will integrate with those on male and female reproductive toxicity which are still under development.

The Guidelines have been revised to indicate that developmental toxicity may result from several different types of exposure, including parental exposure prior to conception, acute or subacute exposure during organogenesis, perinatal and postnatal development to the time of sexual maturation, or subchronic exposure as would be the case in multigeneration studies. These Guidelines provide information for interpreting developmental effects related to any of the types of exposure mentioned above. End points of developmental toxicity, which are measured in multigeneration studies, have been added to Table 2 and discussed in the text. Transplacental carcinogenesis, although considered a developmental effect, will be evaluated and assessed in terms of human risk according to the Guidelines for Carcinogen Risk Assessment. Careful attention will be paid to integrating these developmental toxicity risk assessment Guidelines and the male and female reproductive toxicity risk assessment guidelines, which are currently being written, so that overlapping material is not in conflict, and no pertinent information is overlooked. Since the developmental and reproductive toxicity guidelines are being developed by Agency committees that have overlapping membership within the Agency, such integration will be ensured.

B. Coordination With Testing Guidelines

Several commentors indicated that these Guidelines did not make clear enough the fact that testing guidelines are already in place and that these guidelines were intended only for the purposes of risk assessment.

The Guidelines have been revised to indicate that they do not constitute any changes in current testing guidelines, but rather they are intended to provide guidance for the interpretation of studies that follow the testing guidelines. In addition, limited information is provided for interpretation of other studies (e.g., functional developmental toxicity studies and short-term tests) which are not routinely required or for which there are no current testing guidelines, but which may be encountered when reviewing data on particular agents.

III. Definitions

Several questions were raised about definitions of terminology, due to lack of clarity or inconsistency with other parts of these Guidelines or the testing guidelines.

As indicated in the Guidelines, there are differences in the use of terms in the field of developmental toxicology, and the terms have been defined so that the reader may understand how the terms are being used. Several minor changes in the definitions have been made

[51 FR 34040]

to make them more consistent. For example, the definition for developmental toxicology has been expanded to include the wide range of exposure situations that may result in developmental effects. The term functional teratology has been changed to functional developmental toxicology, and the term

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teratogenicity has been discussed in the section on malformations and variations.

IV. Qualitative Assessment

A. Maternal and Developmental Toxicity

Several commentors noted the need for a better discussion of how maternal toxicity affects the evaluation of developmental toxic effects.

The Agency has taken the approach in these Guidelines of discussing in detail the individual end points of maternal and offspring toxicity, then giving guidance relating to an overall evaluation of the data in Part A, section III.A.4. This approach is consistent with the philosophy reflected in the Guidelines as follows: Those agents that cause developmental effects at doses lower than those causing maternal toxicity are of greatest concern, but developmental effects at doses that also produce maternal toxicity shoud not be discounted as secondary to maternal effects. Rather, when the lowest observed effect level (LOEL) is the same for maternal and developmental toxicity, it may indicate similar sensitivities to the agent, and maternal effects may be reversible while developmental effects may be permanent.

B. Functional Developmental Toxicity

Several commentors raised concern about the premature use of functional data in the risk assessment process. On the other hand, the SAB Panel felt that these tests were very valuable in assessing developmental toxicity.

The Agency does not routinely require such testing, and these Guidelines do not suggest requirements. However, in the review of data on existing chemicals, such data are sometimes encountered and must be evaluated by the Agency. The discussion in the Guidelines is intended to delineate the current state of the art, and to indicate to what extent the data currently may be used for risk assessment purposes.

C. Short-Term Testing

Several commentors stressed the need for further refinement, validation, and comparative testing to determine the credibility of short-term tests for developmental toxicity. The appropriateness of single dose level screens for the purpose of prioritization was endorsed by the SAB Panel with the reservation that too many false positives might occur, and that positive agents in these screens would be permanently labelled as positive developmental toxicants.

Since data from these types of test procedures may be encountered in the assessment of chemicals, the Agency felt it appropriate to give guidance as to how these should be evaluated. The Guidelines have been revised to clearly indicate that these tests are not routinely required, shoud not be considered as a replacement for routine *in vivo* developmental toxicity testing in mammals, and should not be used to make the final decision as to whether an agent is a positive or negative developmental toxicant.

D. Comparisons of Molecular Structure

Comments suggested that not much is known about structure-activity relationships for developmental toxicants, and that this procedure should not be used except in the case of hormone analogs.

A statement has been added to indicate that structure-activity relationships have not been well-studied in developmental toxicology, but under certain circumstances, e.g., in the case of the premanufacturing notice process (TSCA, section 5), the evaluation of molecular structure is one of several procedures used by the Agency to evaluate potential toxicity and to support requests for testing of new chemicals.

V. Quantitative Assessment

Most comments related to the appropriateness of using uncertainty (safety) factors, margins of safety, and no observed effect levels (NOELs). Some commentors felt that the concept of threshold was not adequately discussed in the Guidelines.

These Guidelines are intended to reflect current Agency policy and practice. Although more quantitative assessment of developmental toxicity data are desirable, and efforts are currently ongoing within the Agency to evaluate other approaches, the current practice is to use the NOEL (or the LOEL if a NOEL is not available), and to apply an uncertainty factor or to calculate the margin of safety. This practice is based in large part on the lack of understanding of the biological mechanisms involved. The uncertainty factor used or acceptability of the margin of safety are considered risk management decisions, but the scientific issues that must be taken into account are discussed in these Guidelines. An experimentally determined NOEL does not prove or disprove the existence of a threshold, although many developmental toxicologists assume a threshold for most developmental effects because of known repair capabilities in developing systems and the fact that many developmental alterations are multifactorial in nature.

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GUIDELINES FOR ESTIMATING EXPOSURES

SUMMARY: On September 24, 1986, the U.S. Environmental Protection Agency issued the following five guidelines for assessing the health risks of environmental pollutants.

Guidelines for Carcinogen Risk Assessment

Guidelines for Estimating Exposures

Guidelines for Mutagenicity Risk Assessment

Guidelines for the Health Assessment of Suspect Developmental Toxicants

Guidelines for the Health Risk Assessment of Chemical Mixtures

This section contains the Guidelines for Estimating Exposures.

The Guidelines for Estimating Exposures (hereafter "Guidelines") are intended to guide Agency analysis of exposure assessment data in line with the policies and procedures established in the statutes administered by the EPA. These Guidelines were developed as part of an interoffice guidelines development program under the auspices of the Office of Health and Environmental Assessment (OHEA) in the Agency's Office of Research and Development. They reflect Agency consideration of public and Science Advisory Board (SAB) comments on the Proposed Guidelines for Exposure Assessment published November 23, 1984 (49 FR 46304).

This publication completes the first round of risk assessment guidelines development. These Guidelines will be revised, and new guidelines will be developed, as appropriate.

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SUPPLEMENTARY INFORMATION: In 1983, the National Academy of Sciences (NAS) published its book entitled *Risk Assessment in the Federal Government: Managing the Process.* In that book, the NAS recommended that Federal regulatory agencies establish "inference guidelines" to ensure consistency and technical quality in risk assessments and to ensure that the risk assessment process was maintained as a scientific effort separate from risk management. A task force within EPA accepted that recommendation and requested that Agency scientists begin to develop such guidelines.

General

The guidelines are products of a two-year Agencywide effort, which has included many scientists from the larger scientific community. These guidelines set forth principles and procedures to guide EPA scientists in the conduct of Agency risk assessments, and to inform Agency decision makers and the public about these procedures. In particular, the guidelines emphasize that risk assessments will be conducted on a case-by-case basis, giving full consideration to all relevant scientific information. This case-by-case approach means that Agency experts review the scientific information on each agent and use the most scientifically appropriate interpretation to assess risk. The guidelines also stress that this information will be fully presented in Agency risk assessment documents, and that Agency scientists will identify the strengths and weaknesses of each assessment by describing uncertainties, assumptions, and limitations, as well as the scientific basis and rationale for each assessment.

Finally, the guidelines are formulated in part to bridge gaps in risk assessment methodology and data. By identifying these gaps and the importance of the missing information to the risk assessment process, EPA wishes to encourage research and analysis that will lead to new risk assessment methods and data.

Guidelines for Estimating Exposures

Work on the Guidelines for Estimating Exposures began in January 1984. Draft guidelines were developed by Agency work groups composed of expert scientists from throughout the Agency. The drafts were peer-reviewed by expert scientists in the field of exposure assessment from universities, environmental groups, industry, labor, and other governmental agencies. They were then proposed for public comment in the *FEDERAL REGISTER* (49 FR 46304). On November 9, 1984, the Administrator directed that Agency offices use the proposed guidelines in performing risk assessments until final guidelines become available.

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After the close of the public comment period, Agency staff prepared summaries of the comments, analyses of the major issues presented by the commentors, and preliminary Agency responses to those comments. These analyses were presented to review panels of the SAB on March 4 and April 22-23, 1985, and to the Executive Committee of the SAB on April 25-26, 1985. The SAB meetings were announced in the *FEDERAL REGISTER* as follows: February 12, 1985 (50 FR 5811) and April 4, 1985 (50 FR 13420 and 13421).

In a letter to the Administrator dated June 19, 1985, the Executive Committee generally concurred on all five of the guidelines, but recommended certain revisions, and requested that any revised guidelines be submitted to the appropriate SAB review panel chairman for review and concurrence on behalf of the Executive Committee. As described in the responses to comments (see Part B: Response to the Public and Science Advisory Board Comments), each guidelines document was revised, where appropriate, consistent with the SAB recommendations, and revised draft guidelines were submitted to the panel chairmen. Revised draft Guidelines for Estimating Exposures were concurred on in a letter dated January 13, 1986. Copies of the letters are available at the Public Information Reference Unit, EPA Headquarters Library, as indicated elsewhere in this section.

Following this Preamble are two parts: Part A contains the Guidelines and Part B, the Response to the Public and Science Advisory Board Comments (a summary of the major public comments, SAB comments, and Agency responses to those comments).

The SAB requested that the Agency develop guidelines on the principles for the measurement of pollutant concentrations in the various environmental media and for the uses of environmental measurements for exposure assessment. This effort is currently underway.

The Agency also will provide technical support documents that contain detailed technical information needed to implement the Guidelines. Two of these technical reports entitled "Development of Statistical Distributions or Ranges of Standard Factors Used in Exposure Assessments" (available from the National Technical Information Service, PB85-242667) and "Methodology for Characterization of Uncertainty in Exposure Assessments" (available from the National Technical Information Service, PB85-240455) are currently available. Technical support documents will be revised periodically to reflect improvements in exposure assessment methods and new information or experience.

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The Agency is continuing to study the risk assessment issues raised in the Guidelines and will revise these Guidelines in line with new information, as appropriate.

References, supporting documents, and comments received on the proposed guidelines, as well as copies of the final guidelines, are available for inspection and copying at the Public Information Reference Unit (202-382-5926), EPA Headquarters Library, 401 M Street, S.W., Washington, DC, between the hours of 8:00 a.m. and 4:30 p.m.

I certify that these Guidelines are not major rules as defined by Executive Order 12291, because they are nonbinding policy statements and have no direct effect on the regulated community. Therefore, they will have no effect on costs or prices, and they will have no other significant adverse effects on the economy. These Guidelines were reviewed by the Office of Management and Budget under Executive Order 12291.

August 22, 1986

Lee M. Thomas,

Administrator

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Part A: Guidelines for Estimating Exposures

I. Introduction

These Guidelines provide the Agency with a general approach and framework for carrying out human or nonhuman exposure assessments for specified pollutants. The Guidelines have been developed to assist future assessment activities and encourage improvement in those EPA programs that require, or could benefit from, the use of exposure assessments. The Guidelines are procedural. They should be followed to the extent possible in instances where exposure assessment is a required element in the regulatory process or where exposure assessments are carried out on a discretionary basis by EPA management to support regulatory or programmatic decisions.

This document, by laying out a set of questions to be considered in carrying out an exposure assessment, should help avoid inadvertent mistakes of omission. Ideally, exposure assessments are based on measured data. EPA recognizes that gaps in data will be common, but the Guidelines will nevertheless serve to assist in organizing the data that are available, including new data developed as part of the exposure assessment. In the absence of sufficient reliable data and the time to obtain appropriate measurements, exposure assessments may be based on validated mathematical models. Whenever possible, exposure assessments based on modeling should be complemented by reliable measurements. Furthermore, it is understood that the level of detail found in the exposure assessments depends on the scope of the assessment.

These Guidelines should also promote consistency among various exposure assessment activities that are carried out by the Agency. Consistency with respect to common physical, chemical, and biological parameters, with respect to assumptions about typical exposure situations, and with respect to the characterization of uncertainty of estimates, will enhance the comparability of results and enable the Agency to improve the state-of-the-art of exposure assessment over time through the sharing of common data and experiences.

It is recognized that the main objective of an exposure assessment is to provide reliable data and/or estimates for a risk assessment. Since a risk assessment requires the coupling of exposure information and toxicity or effects information, the exposure assessment process should be coordinated with the toxicity/effects assessment. This document provides a common approach to format, which should simplify the process of reading and evaluating exposure assessments and thereby increase their utility in assessing risk.

As the Agency performs more exposure assessments, the Guidelines will be revised to reflect the benefit of experience.

II. General Guidelines and Principles

A. Exposure and Dose

Exposure has been defined by Committee E-47, Biological Effects and Environmental Fate, of the American Society for Testing and Materials, as the contact with a chemical or physical agent. The magnitude of the exposure is determined by measuring or estimating the amount of an agent available at the exchange boundaries, i.e., lungs, gut, skin, during some specified time. Exposure assessment is the determination or estimation (qualitative or quantitative) of the magnitude, frequency, duration, and route of exposure. Exposure assessments may consider past, present, and future exposures with varying techniques for each phase, e.g., modeling of future exposures, measurements of existing exposure, and biological accumulation for past exposures. Exposure assessments are generally combined with environmental and health effects data in performing risk assessments.

In considering the exposure of a subject to a chemical agent, there are several related processes. The contact between the subject of concern and the agent may lead to the intake of some of the agent. If absorption occurs, this constitutes an uptake (or an absorbed dose). When biological tissue or fluid measurements indicate the presence of a chemical, exposures may be estimated from these data. Presence of a chemical in such biological samples is the most direct indication that an exposure has occurred. The route of exposure generally impacts the extent of absorption and should be considered in performing risk assessments.

[51 FR 34044]

B. Decision Path to Determine Scope of the Assessment

The first step in preparing an exposure assessment should be the circumscription of the problem at hand to minimize effort by use of a narrowing process. A decision path that describes this process is shown in Figure 1. As illustrated in Figure 1, the preliminary assessment and the in-depth assessment are two major phases in this logic path.

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The preliminary assessment phase should commence by considering what risk is under study. Within this framework, a data base should be compiled from readily available scientific data and exposure information based on manufacturer, processor, and user practices. Next, the most likely areas of exposure (manufacturing, processing, consumer, distribution, disposal, water and food, etc.) should be identified. The preliminary exposure assessments should be based on data derived from environmental measurements. When a limited amount of measurement data is available, estimates may be based on modeling. Since a complete data search may not be possible, well identified

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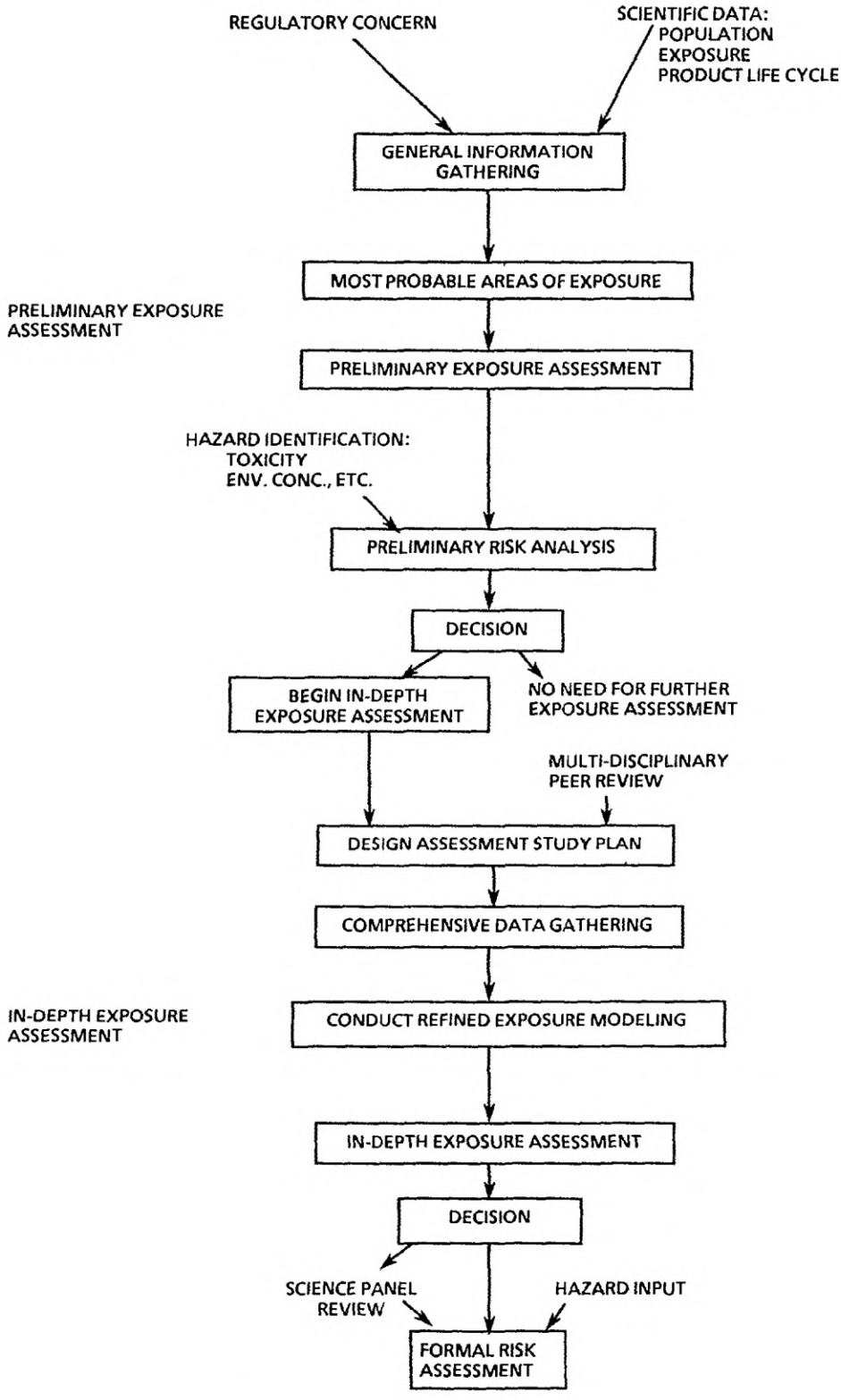

Figure 1. Decision path for exposure assessment.

assumptions and order of magnitude estimates may be used to further narrow the exposure areas of concern.

Data from this preliminary exposure assessment can then be coupled with toxicity information to perform a preliminary risk analysis. As a result of this analysis, a decision will be made that either an in-depth exposure assessment is necessary or that there is no need for further exposure information. The organization and contents of an in-depth exposure assessment are given in the following section.

In assembling the information base for either a preliminary assessment or a more detailed assessment, its adequacy should be ascertained by addressing the following considerations:

- Availability of information in every area needed for an adequate assessment;
- Quantitative and qualitative nature of the data;
- Reliability of information;
- Limitations on the ability to assess exposure.

C. Uncertainty

Exposure assessments are based on measurements, simulation model estimates, and assumptions about parameters used in approximating actual exposure conditions. Actual measurements should be used whenever possible. Both data and assumptions contain varying degrees of uncertainty which influence the accuracy of exposure assessments. Consequently, evaluation of uncertainty is an important part of all exposure assessments.

The uncertainty analyses performed will vary depending on the scope of the assessment, the quantity and quality of measurements, and the type and complexity of mathematical models used. A discussion of the types of analyses used for quantifying uncertainties in exposures is presented in the next section.

III. Organization and Contents of an Exposure Assessment

A. Overview

A suggested outline for an exposure assessment document is given in Exhibit 1. The five major topics to be addressed within most exposure assessments are as follows: Source(s), Exposure Pathways, Measured or Estimated Concentrations and Duration, Exposed Population(s), and Integrated Exposure Analysis. These five topics are appropriate for exposure assessments in general, whether the assessments are of global, national, regional, local, site specific, workplace related, or other scope. The topics are appropriate for exposure assessments on new or existing chemicals and radionuclides. They are also applicable to both single media and multimedia assessments. Since exposure assessments are performed at different levels of detail, the extent to which any assessment contains items listed in Exhibit 1 depends upon its scope. The outline is a guide to organize the data whenever they are available.

Exhibit 1.--Suggested Outline for an Exposure Assessment

1. Executive Summary
2. Introduction
   a. Purpose
   b. Scope
3. General Information for Each Chemical or Mixture
   a. Identity
      (1) Molecular formula and structure, synonyms, and Chemical Abstracts Service (CAS) number
      (2) Description of grades, contaminants, and additives
      (3) Other identifying characteristics
   b. Chemical and Physical Properties
4. Sources
   a. Characterization of Production and Distribution
   b. Uses
   c. Disposal
   d. Summary of Environmental Releases
5. Exposure Pathways and Environmental Fate
   a. Transport and Transformation
   b. Identification of Principal Pathways of Exposure
   c. Predicting Environmental Distribution
6. Measured or Estimated Concentrations
   a. Uses of Measurements
   b. Estimation of Environmental Concentrations
7. Exposed Populations
   a. Human Populations
      (1) Population size and characteristics
      (2) Population location
      (3) Population habits
   b. Nonhuman Populations (where appropriate)
      (1) Population size and characteristics
      (2) Population location
      (3) Population habits
8. Integrated Exposure Analysis
   a. Calculation of Exposure
      (1) Identification of the exposed population and critical elements of the ecosystem
      (2) Identification of pathways of exposure
   b. Human Dosimetry and Biological Measurements
   c. Development of Exposure Scenarios and Profiles
   d. Evaluation of Uncertainty
      (1) Introduction
      (2) Assessments based on limited initial data
      (3) Assessments based on subjective estimates of input variable distributions
      (4) Assessments based on data for model input variables
      (5) Assessments based on data for exposure
      (6) Summary
9. References
10. Appendices

B. Detailed Explanation of Outline

1. Executive Summary. The "Executive Summary" should be written so that it can stand on its own as a miniature report. Its main focus should be on a succinct description of the procedures used, assumptions employed, and summary tables or charts of the results. A brief discussion of the uncertainties associated with the results should be included.

2. Introduction (Purpose and Scope). This section should state the intended purpose of the exposure assessment and identify the agent being

investigated, the types of sources and exposure routes included, and the populations of concern.

3. General Information for Each Chemical or Mixture.

a. Identity.

(1) Molecular formula and structure, synonyms, and Chemical Abstracts Service number.

(2) Description of grades, contaminants, and additives.

(3) Other identifying characteristics.

b. Chemical and Physical Properties. This subsection should provide a summary description of the chemical and physical properties of the agent. Particular attention should be paid to the features that would affect its behavior in the environment.

4. Sources. The points at which a substance is believed to enter the environment should be described, along with any known rates of entry. (Points of entry may be indoors as well as outdoors; environments include indoor settings such as offices as well as outdoor environments.) A detailed exposure assessment should include a study of sources, production, uses, destruction/disposal, and environmental release of a substance. The studies

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should include a description of human activities with respect to the substance and the environmental releases resulting from those activities. It should account for the controlled mass flow of the substance from creation to destruction and provide estimates of environmental releases at each step in this flow. Seasonal variations in environmental releases should also be examined. All sources of the substance should be accounted for with the sum of the uses, destruction, and the environmental releases. The environmental releases can be described in terms of geographic and temporal distribution and the receiving environmental media, with the form identified at the various release points.

a.Characterization of Production and Distribution. All sources of the substance's release to the environment, consistent with the scope of the assessment, should be included, such as production, extraction, processing, imports, stockpiles, transportation, accidental/ incidental production as a side reaction, and natural sources. The sources should be located, and activities involving exposure to the substance should be identified.

b. Uses. The substance should be traced from its sources through various uses (with further follow-up on the products made to determine the presence of the original material as an impurity), e.g., exports, stockpile increases, etc.

c. Disposal. This subsection should contain an evaluation of disposal sites and destruction processes, such as incineration of industrial chemical waste, incineration of the substance as part of an end-use item in municipal waste, landfilling of wastes, biological destruction, or destruction in the process of using the end product. Hazardous contaminants of the substance may be included, and products containing the substance as a contaminant may be followed from production through destruction/disposal.

d. Summary of Environmental Releases. Estimates should be made of the quantities of the substance released to the various environmental media. Sources of release to the environment include production, use, distribution/transport, natural sources, disposal, and contamination of other products. Environmental releases should be presented at a reasonable level of detail. Extremely detailed exposure estimates would attempt to specify the following information for each significant emission source: location, amount of the substance being released as a function of time to each environmental medium, physical characteristics of the emission source, and the physical and chemical form of the substance being released. Evaluation of the uncertainties associated with the emission estimates should be given. A detailed discussion of the procedures for estimating uncertainty is presented in section 8.d.

5. Exposure Pathways and Environmental Fate. The exposure pathways section should address how an agent moves from the source to the exposed population or subject. For a less detailed assessment, broad generalizations on environmental pathways and fate may be made. In the absence of data, e.g., for new substances, fate estimates may have to be predicted by analogy with data from other substances. Fate estimates may also be made by using measurements and/or models and laboratory-derived process rate coefficients. At any level of detail, certain pathways may be judged insignificant and not pursued further.

For more detailed assessments involving environmental fate, the analysis of sources described previously should provide the amount and rate of emissions to the environment, and possibly the locations and form of the emissions. The environmental pathways and fate analysis follows the substance from its point of initial environmental release, through the environment, to its ultimate fate. It may result in an estimation of the geographic and temporal distribution of concentrations of the substance in the various contaminated environmental media.

a. Transport and Transformation. The substance, once released to the environment, may be transported (e.g., convected downstream in water or on suspended sediment, through the atmosphere, etc.) or physically transformed (e.g., volatilized, melted, absorbed/desorbed, etc.); may undergo chemical transformation, such as photolysis, hydrolysis, oxidation, and reduction; may undergo biotransformation, such as biodegradation; or may accumulate in one or more media. Thus, the environmental behavior of a substance should be

evaluated before exposures are assessed. Factors that should be addressed include:

- How does the agent behave in air, water, soil, and biological media? Does it bioaccumulate or biodegrade? Is it absorbed or taken up by plants?
- What are the principal mechanisms for change or removal in each of the environmental media?
- Does the agent react with other compounds in the environment?
- Is there intermedia transfer? What are the mechanisms for intermedia transfer? What are the rates of the intermedia transfer or reaction mechanisms?
- How long might the agent remain in each environmental medium? How does its concentration change with time in each medium?
- What are the products into which the agent might degrade or change in the environment? Are any of these degradation products ecologically or biologically harmful? What is the environmental behavior of the harmful products?
- Is a steady-state concentration distribution in the environment, or in specific segments of the environment, achieved? If not, can the nonsteady-state distribution be described?
- What is the resultant distribution in the environment--for different media, different types or forms of the agent, for different geographical areas, at different times or seasons?

b. Identification of Principal Pathways of Exposure. The principal pathway analysis should evaluate the sources, locations, and types of environmental releases, together with environmental behavioral factors, to determine the significant routes of human and environmental exposure to the substance. Thus, by listing the important characteristics of the environmental release (entering media, emission rates, etc.) and the agent's behavior (intermedia transfer, persistence, etc.) after release to each of the entering media, it should be possible to follow the movement of the agent from its initial release to its subsequent fate in the environment. At any point in the environment, human or environmental exposure may occur. Pathways that result in major concentrations of the agent and high potential for human or environmental contact are the principal exposure pathways.

c. Predicting Environmental Distribution. Models may be used to predict environmental distributions of chemicals. Model estimates of environmental distribution of chemicals are based on measurements whenever feasible. In predicting environmental distributions of chemicals, available measurements must be considered.

In this section an estimation is made, using appropriate models, of representative concentrations of the agent in different environmental media, and its time-dependence in specific geographical locations (e.g., river basins, streams, etc.).

6. Measured or Estimated Concentrations.

a. Uses of Measurements. Measurements are used to identify releases (source terms) and, in the

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exposure pathways and fate assessments, to quantitatively estimate both release rates and environmental concentrations. Some examples of uses of measurements are: sampling of stacks or discharge pipes for emissions to the environment, testing of products for chemical or radionuclide content, testing of products for chemical or radioactive releases, sampling of appropriate points within a manufacturing plant to determine releases from industrial processes or practices, sampling of potentially exposed populations using personal dosimeters, and sampling of solid waste for chemical or radionuclide content. These data should be characterized as to accuracy, precision, and representativeness. If actual environmental measurements are unavailable, concentrations can be estimated by various means, including the use of fate models (see previous section) or, in the case of new chemicals, by analogy with existing chemicals.

Measurements are a direct source of information for exposure analysis. Furthermore, reliable measurements can be used to calibrate or extrapolate models or calculations to assess environmental distributions. However, environmental pathway and fate analysis may be needed in addition to the measured data for the following reasons: for most pollutants, particularly organic and new chemicals, measurements are limited; analysis of measured data does not often yield relationships between environmental releases and environmental concentration distribution in media or geographic locations that have not been measured; analysis of measurements does not provide information on how and where biota influence the environmental distribution of a pollutant; and measured concentrations may not be traceable to individual sources.

b. Estimation of Environmental Concentrations. Concentrations of agents should be estimated for all environmental media that might contribute to significant exposures. Generally, the environmental concentrations are estimated from measurements, mathematical models, or a combination of the two. If environmental measurements are not limited by sample size or inaccuracies, then exposure assessments based on measurements have precedence over estimates based on models.

The concentrations must be estimated and presented in a format consistent with available dose-response information. In some cases an estimate of annual average concentration will be sufficient, while in other cases the temporal distribution of concentrations may be required. Future environmental concentrations resulting from current or past releases may also be projected. In some cases, both the temporal and geographic distributions of the concentration may be assessed.

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Moreover, if the agent has natural sources, the contribution of these to environmental concentrations may be relevant. These "background" concentrations may be particularly important when the results of tests of toxic effects show a threshold or distinctly nonlinear dose-response.

The uncertainties associated with the estimated concentrations should be evaluated by an analysis of the uncertainties of the model parameters and input variables. When the estimates of the environmental concentrations are based on mathematical models, the model results must be compared to available measurements, and any significant discrepancies should be discussed. Reliable, analytically-determined values must be given precedence over estimated values whenever significant discrepancies are found.

7. Exposed Populations. Populations selected for study may be done *a priori*, but frequently the populations will be identified as a result of the sources and fate studies. From an analysis of the distribution of the agent, populations and subpopulations (i.e., collections of subjects) at potentially high exposure can be identified, which will then form the basis for the populations studied. Subpopulations of high sensitivity, such as pregnant women, infants, chronically ill, etc., may be studied separately.

Census and other survey data may be used to identify and describe the population exposed to various contaminated environmental media. Depending on the characteristics of available toxicological data, it may be appropriate to describe the exposed population by other characteristics such as species, subspecies-age-sex distribution, and health status.

In many cases, exposed populations can be described only generally. In some cases, however, more specific information may be available on matters such as the following:

a. Human Populations

(1) Population size and characteristics (e.g., trends, sex/age distribution)

(2) Population location

(3) Population habits-- transportation habits, eating habits, recreational habits, workplace habits, product use habits, etc.

b. Nonhuman Populations (where appropriate)

(1) Population size and characteristics (e.g., species, trends)

(2) Population location

(3) Population habits

8. Integrated Exposure Analysis. The integrated exposure analysis combines the estimation of environmental concentrations (sources and fate information) with the description of the exposed population to yield exposure profiles. Data should be provided on the size of the exposed populations; duration, frequency, and intensity of exposure; and routes of exposure. Exposures should be related to sources.

For more detailed assessments, the estimated environmental concentrations should be considered in conjunction with the geographic distribution of the human and environmental populations. The behavioral and biological characteristics of the exposed populations should be considered, and the exposures of populations to various concentration profiles should be estimated. The results can be presented in tabular or graphic form, and an estimate of the uncertainty associated with them should be provided.

a. Calculation of Exposure. The calculation of exposure involves two major aspects:

(1) Identification of the exposed population and critical elements of the ecosystem.

The estimate of environmental concentrations also should give the geographical areas and environmental media contaminated. The stated purpose of the assessment should have described the human and environmental subjects for which exposures are to be calculated. If the subjects are not listed, the contaminated geographical areas and environmental media can be evaluated to determine subject populations. The degree of detail to be used in defining the exposed population distribution depends on the concentration gradient over geographic areas.

(2) Identification of pathways of exposure.

(a) Identification and description of the routes by which the substances travel from production site, through uses, through environmental releases/sources, through transport and fate processes, to the target population.

(b) Quantitative estimates of the amounts of the chemical following each exposure pathway. Such estimates allow the various pathways to be put in the perspective of relative importance.

From the geographic and temporal distribution of environmental

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concentrations, the exposed population, the behavioral characteristics, and the critical elements of the ecosystem, exposure distributions can be estimated. The results of exposure calculation should be presented in a format that is consistent with the requirements of the dose-response functions which may later be used in a risk assessment. For example, when health risks caused by exposure over extended durations are considered, average daily exposure over the duration of exposure usually is calculated. When lifetime risks are considered, average daily exposure over a lifetime usually is calculated. In contrast, when health risks caused by exposures over short durations are considered, exposure rates are calculated over short time intervals to ensure that peak risks are defined. Many exposure assessments are based on the average exposure occurring over the exposure period. The range of possible exposures is usually divided into intervals,

and the exposures within each interval are counted. The results can be presented in tabular form or as a histogram.

The population residing in a specific geographic area may be exposed to a substance from several exposure routes. For each exposure route, exposure of individuals in these populations may be determined by summing the contribution of all sources to the exposure route. When exposures involve more than one exposure route, the relative amounts of a substance absorbed is usually route dependent. Consequently, total absorbed dose estimates must account for these differences. Because EPA regulates sources of releases, the contribution to exposures from each type of source being considered should be displayed. Exposure estimates should be presented for each significant exposure route, and the results should be tabulated in such a way that total externally applied and absorbed dose can be determined.

b. Human Dosimetry and Biological Measurements. Biological measurements of human body fluids and tissues for substances or their metabolites can be used to estimate current or past exposure to chemicals. When analytical methods are available, chemicals that have been absorbed into the body can be measured in body tissue and fluid. Such measurements may be used to estimate human exposure if the chemical substances leave in the body reliable indicators of exposure. Furthermore, although a compound may be relatively easy to detect in body tissue, for some compounds, attributing body burdens to specific environmental releases may be difficult because of limited ability to obtain environmental measurements or appropriate metabolic data.

c. Development of Exposure Scenarios and Profiles. Depending on the scope of the exposure assessment, the total exposure may be fractionated into one or more "exposure scenarios" to facilitate quantification. As an example, Table 1 lists seven very broad scenarios: Occupational, Consumer, Transportation, Disposal, Food, Drinking Water, and Ambient. For each of the scenarios, the major topics necessary to quantify exposure include sources, pathways, measurements, and population characteristics. Investigation of only one scenario may be necessary for the scope of some assessments. For example, a pesticide application exposure assessment may consider the occupational scenario which would address the exposure to applicators and populations in the vicinity of the site. An exposure assessment around a hazardous waste site may focus on the disposal scenario. The exposure assessment

TABLE 1.--EXPOSURE ASSESSMENT INFORMATION NEEDS FOR VARIOUS EXPOSURE SCENARIOS

Exposure scenario	Sources	Fate	Population Characteristics	Measurement
Occupational (chemical production).	Site/plant locations, in-plant/on-site materials balance.	Physical and chemical properties models.	Workers, families, population around sites/plants.	In-plant/on-site releases, ambient levels surrounding site/plants; human dosimetry.
Consumer (direct use of chemical or inadvertent use).	Consumption rates, distribution pattern amounts in products.	Physical and chemical properties, shelf life release rates, models.	Consumers	Levels in products releases.
Transportation / storage/spills.	Patterns of distribution and transportation; models for spills.	Physical and chemical properties, environmental fate models.	Storage, transportation workers, general population in area.	Releases, ambient levels.
Disposal (include incineration, landfill).	Materials balance around disposal method, efficiency,releases to environment.	Fate within disposal process; environmental fate of releases; models.	Workers at site of disposal, general population around site.	Releases, levels at various points within process, ambient levels.
Food	Food chain, packaging, additives.	Food chain models, fate during preparation or processing of food.	General population, nonhuman population.	Levels in food, feedstuff; food chain sampling.
Drinking water	Groundwater, surface water, distribution system.	Leach rates from pipes, chlorination processes, fate in water; models.	General population.	Levels in drinking water, groundwater, surface water, treatment plants.
Ambient	Releases to environment; air, land, water.	Environmental fate models.	General population, nonhuman population.	Ambient air, water, soil, etc.; human dosimetry.

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also may consider other scenarios. The more extensive and comprehensive the scope, the more scenarios are usually involved.

It will usually be advantageous in performing an exposure assessment to identify exposure scenarios, quantify the exposure in each scenario, and then integrate the scenarios to estimate total exposure. In this "integrated exposure analysis," the summation of independent exposures from different scenarios (keeping exposure routes separate) often will result in a breakout of exposure by subpopulations, since the individual scenarios usually treat exposure by subpopulation. Therefore, the integration of the scenarios, or integrated exposure analysis, will often result in an exposure profile.

For each exposed subpopulation, exposure profiles should include the size of the group, the make-up of the group (age, sex, etc.), the source of the agent, the exposure pathways, the frequency and the intensity of exposure by each route (dermal, inhalation, etc.), the duration of exposure, and the form of the agent when exposure occurs. Assumptions and uncertainties associated with each scenario and profile should be clearly discussed.

d. Evaluation of Uncertainty.

(1) Introduction. Often an exposure assessment progresses through several stages of refinement. The purpose of these Guidelines is to present methods appropriate for characterization of uncertainty for assessments at various stages of refinement, from assessments based on limited initial data to those based on extensive data.

The appropriate method for characterizing uncertainty for an exposure assessment depends upon the underlying parameters being estimated, the type and extent of data available, and the estimation procedures utilized.

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The uncertainty of interest is always with regard to the population characteristic being estimated. For example, when the population distribution of exposures is being estimated, characterization of uncertainty addresses the possible differences between the estimated distribution of exposure and the true population distribution of exposure.

An exposure assessment quantifies contact of a substance with affected population members (human or nonhuman subjects). The measure of contact (e.g., environmental level or absorbed dose) depends upon what is needed to predict risk. An integrated exposure assessment quantifies this contact via all routes of exposure (inhalation, ingestion, and dermal) and all exposure pathways (e.g., occupational exposure, exposure from consumption of manufactured goods, etc.). The exposed population generally is partitioned into subpopulations such that the likely exposure of all members of a subpopulation is attributable to the same sources. The exposure for each member of a subpopulation is then the sum of exposures over a fixed set of sources and pathways. The measured or estimated exposures for members of a subpopulation are ideally used to estimate the subpopulation distribution of exposure or characteristics thereof. However, a lack of sufficient information sometimes precludes estimation of the subpopulation distributions of exposure and only summary measures of this distribution, such as the mean, minimum, maximum, etc., are estimated. In each case, characterization of uncertainty for the exposure assessment primarily addresses limitations of the data and the estimation procedures. The proportions of the population members in the individual subpopulations are usually estimated and can be used (by combining estimated distributions for the subpopulations) to estimate the distribution of exposure for the total population. Uncertainty concerning the sizes of the subpopulations should be addressed by discussing limitations of the data and estimation methods as well as by tabulating confidence interval estimates for the population sizes whenever possible.

(2) Assessments based on limited initial data. The initial exposure assessment for a substance may be based on limited data for exposure and/or input variables for an exposure prediction model (i.e., an equation that expresses exposure as a function of one or more input variables). These data might be either extant data or data produced by an initial small-scale study. The limited initial data frequently are insufficient to permit estimation of the entire distribution of exposure. Instead, summary measures of this distribution, such as the mean, minimum, and maximum, are usually estimated.

If the assessment is based on measured exposures, the methods used to characterize uncertainty depend mainly upon whether or not the data result from a probability sample for which the probability of inclusion is known for each sample member. Characterization of uncertainty for an assessment based on a probability sample of exposures is discussed later in section 8.d.(5). If the measured exposures are not based on a probability sample, acknowledgement that no strictly valid statistical inferences can be made beyond the units actually in the sample is one aspect of the characterization of uncertainty. If inference procedures are implemented, the assumptions upon which these inferences are based (e.g., treatment of the sample as if it were a simple random sample, or assumption of an underlying model) should be explicitly stated and justified. The data collection methods and inherent limitations of the data should also be discussed.

An initial exposure assessment also may be based on limited data, such as estimated ranges, for input variables for an exposure prediction model. The exposure prediction model would be derived from a postulated exposure scenario that describes the pathways from sources to contact with population members. If the data were only sufficient to support estimates of the ranges of the input variables, the exposure assessment might be limited

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to a sensitivity analysis. The purpose of the sensitivity analysis would be to identify influential model input variables and develop bounds on the distribution of exposure. A sensitivity analysis would estimate the range of exposures that would result as individual model input variables were varied from their minumum to their maximum possible values with the other input variables held at fixed values, e.g., their midranges. The overall minimum and maximum possible exposures usually would be estimated also. For an exposure assessment of this type, the uncertainty would be characterized by describing the limitations of the data used to estimate possible ranges of model input variables and by discussing justification for the model. Justification of the model should include a description of the exposure scenario, choice of model input variables, and the functional form of the model. Sensitivity to the model formulation also can be investigated by replicating the sensitivity analysis for plausible alternative models.

The sensitivity analysis can be enhanced by computing the predicted exposures that result from all possible input variable combinations. If each input variable has only a finite set of possible values, the set of all possible combinations of the input variables can be formed, and the predicted exposure can be computed for each combination. These exposure predictions can be used to form a distribution of exposures by counting the number of occurrences at each exposure level or interval of exposures. This is equivalent to estimating the distribution of exposures that results from treating all input variable combinations as equally likely. This procedure can also be applied by transforming continuous input variables into discrete ones and representing them by equally spaced points. In the limit, as the equal spaces become small and the number of points becomes large, the distribution of exposure that results from counting occurrences of exposure levels is equivalent to estimating the distribution of exposures that results from statistically independent, continuous input variables with uniform distributions on the estimated ranges. This estimated distribution of exposure values can be produced by Monte Carlo simulation, one of the methods of mathematical statistics. The Monte Carlo method consists of randomly generating input variate values and using these to compute corresponding exposure levels, generating an exposure distribution via many iterations. Interpretation of statistics based on this exposure distribution would be in terms of the equally likely input variable combinations. For example, the 95th percentile of this distribution would be the exposure level exceeded by only 5% of the exposures resulting from treating all combinations of input variable values as equally likely. Although this distribution of exposures cannot be interpreted as an estimate of the population distribution (unless the input variables actually are statistically independent and uniformly distributed), it provides additional information for making regulatory decisions. Characterization of uncertainty would include a discussion of limitations of the data and justification for the model as discussed above. Sensitivity to model formulation could also be investigated by estimating the distribution of exposure that results from using the

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same uniform input variable distributions with plausible alternative models and comparing the estimated percentiles.

(3) Assessments based on subjective estimates of input variable distributions. If a model has been formulated that expresses exposure as a function of one or more input variables, the methods of mathematical statistics, such as Monte Carlo simulation, can be used to estimate the population distribution of exposure from an estimate of the joint distribution of the model input variables. Ideally, model input variables should be represented by empirically-validated probability distributions. In some cases, it may be possible to formulate an estimate of the joint distribution of model input variables from discussions with subject matter experts (e.g., via histograms for statistically-independent input variables). The estimated population distribution of exposure will be equivalent to the distribution discussed in section 8.d.(2) for equally likely combinations of input variable values only when the input variable distributions supported are independent uniform distributions. When qualitative knowledge of input variable distributions is used to estimate the population distribution of exposure, uncertainty is characterized by discussing justification for the presumed model and input variable distributions. Alternative models and/or alternative input variable distributions also should be discussed. Sensitivity to these alternatives can be investigated by estimating the distributions of exposure that result from plausible alternatives and comparing the percentiles of the estimated exposure distributions. All available data, even if data are limited, should be used to validate the presumed input variable distributions and the predicted distribution of exposure.

(4) Assessments based on data for model input variables. The exposure assessment based on an estimate of the joint probability distribution for model input variables can be refined by collecting sample survey data for model input variables for a sample of population members. The population distribution of exposure can then be estimated by computing the expected exposure for each sample member based on the model. These expected exposures can be used to directly compute confidence interval estimates for percentiles of the exposure distribution. Alternatively, the sample survey data can be used to compute joint confidence interval estimates for percentiles of the input variable

distribution, which can then be used to generate confidence interval estimates for percentiles of the exposure distribution. In either case, the interval estimates for percentiles of the exposure distribution are a useful quantitative characterization of uncertainty.

Characterization of uncertainty for the exposure assessment would contain a thorough discussion of limitations of the data and justification for the model used to compute expected exposures. The design of the sample survey used to produce the data base should also be discussed. If a probability sample were not used, the lack of a probability sample would be an additional source of uncertainty. Any assumptions used in computing the confidence interval estimates, such as independence of model input variables, should be explicitly stated and justified. Sensitivity to model formulation can be investigated by estimating the distribution of exposure for plausible alternative models and comparing the estimated percentiles, if sample survey data have been collected for the input variables of the alternative models. Appropriate available data for exposure should be used to validate the predicted distribution of exposure. If specific probability distributions have been presumed for any model input variables, the data for these variables should be used to test for goodness of fit for these distributions.

(5) Assessments based on data for exposure. A major reduction in the uncertainty associated with an exposure assessment can be achieved by directly measuring the exposure for a sufficiently large sample of members of the affected population. This reduction in uncertainty is achieved by eliminating the use of a model to predict exposure. The measured exposure levels can be used to directly estimate the population distribution of exposure and confidence interval estimates for percentiles of the exposure distribution. Direct confidence interval estimates also can be computed for other characteristics of the exposure distribution, such as the mean exposure.

These confidence interval estimates are then the primary characterization of uncertainty for the exposure assessment. Limitations of the data and design of the sample survey used to collect the data also should be discussed. If the sample was not a probability sample, this would again be an additional source of uncertainty.

(6) Summary. A summary of the primary methods recommended for characterizing uncertainty in exposure assessments is presented in Table 2. Virtually all exposure assessments, except those based on measured exposure levels for a probability sample of population members, rely upon a model to predict exposure. The model may be any mathematical function, simple or complex, that expresses an individual's exposure as a function of one or more input variables. Whenever a model that has not been validated is used as the basis for an exposure assessment, the uncertainty associated with the exposure assessment may be substantial. The primary characterization of uncertainty is at least partly qualitative in this case, i.e., it includes a description of the assumptions inherent in the model and their justification. Plausible alternative models should be discussed. Sensitivity of the exposure assessment to model formulation can be investigated by replicating the assessment for plausible alternative models.

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When an exposure assessment is based on directly measured exposure levels for a probability sample of population members, uncertainty can be greatly reduced and described quantitatively. In this case, the primary sources of uncertainty are measurement errors and sampling errors. The effects of these sources of error are measured quantitatively by confidence interval estimates of percentiles of the exposure distribution. Moreover, the sampling errors can be limited by taking a large sample.

Whenever it is not feasible to take a large sample, it is sometimes possible to obtain at least some data for exposure and model input variables. These data should be used to assess goodness of fit of the model and/or presumed distributions of input variables. This substantially reduces the amount of quantitative uncertainty for estimation of the distribution of exposure and is strongly recommended. It is recognized, however, that it may not be feasible to collect such data.

9.References. The references should contain a listing of all reports, documents, articles, memoranda, contacts, etc. that have been cited in the report.

10.Appendices. The appendices may contain such items as memoranda and letters that are not readily accessible, other tables of measurements, detailed lists of emission sources, detailed tables of exposures, process flow diagrams, mathematical model formulations, or any other item that may be needed to describe or document the exposure assessment.

Part B: Response to Public and Science Advisory Board Comments

I. Introduction

This section summarizes some of the issues raised in public comments on the Proposed Guidelines for Exposure Assessment published November 23, 1984 (49 FR 46304). Comments were received from 29 individuals or organizations. The Agency's initial summary of comments was presented to the Exposure Assessment Guidelines Review Group of the Science Advisory Board (SAB) on March 4, 1985. At its April 22-23, 1985, meeting, the panel provided the Agency with suggestions and recommendations concerning the Guidelines.

The SAB and public commentors expressed diverse opinions and addressed issues from a variety of perspectives. While most commentors supported the Guidelines, two urged withdrawal of the

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TABLE 2.--SUMMARY OF PRIMARY METHODS FOR CHARACTERIZING UNCERTAINTY FOR ESTIMATING EXPOSURES

Type and extent of data	Population characteristic being estimated	Primary methods for characterizing uncertainty	
		Qualitative methods	Quantitative methods
Measured exposures for a large sample of population members.	Distribution of exposure.	1. Limitations of the survey design and measurement techniques.	1. Confidence interval estimates for percentiles of the exposure distribution. 2. Goodness of fit for exposure models, if any have been postulated.
Measured exposures for a small sample of population members.	Summary parameter(s) of the exposure distribution, e.g., mean or a percentile.	1. Limitations of the survey design and. measurement techniques.	1. Confidence interval estimate for the summary parameter(s). 2. Goodness of fit for exposure models,. if any have been postulated.
Measured model input variables for a large sample of population members.	Distribution of exposure.	1. Limitations of the survey.design and measurement techniques. 2. Validity of the exposure model.	1. Confidence interval estimates for percentiles of the exposure distribution. 2. Goodness of fit for input variable distribution functions, if any have been postulated. 3. Estimated distribution of exposure based on alternative models.
Estimated distributions of model input variables.	Distribution of exposure.	1. Validity of the exposure model. 2. Limitations of the data. or other basis for the input variable distributions.	1. Confidence interval estimates for percentiles of the exposure distribution. 2. Goodness of fit for input variable distributions, if input variable data are available. 3. Estimated distribution of exposure based on alternative models.
Limited data for model input variables.	Minimum, maximum, and range of the exposure distribution.	1. Limitations of the data. 2. Validity of the exposure model.	If input variable data are very limited, e.g., some extant data collected for other purposes, quantitative characterization of uncertainty may not be possible.

document. The SAB Panel recommended that supplementary guidelines be written on the use of measurements in preparing exposure assessments. In addition, the Panel wished to see a greater emphasis in the current Guidelines on the use of measured data rather than models in generating exposure assessments. The Panel recommended that the technical support document entitled "Methodology for Characterization of Uncertainty in Exposure Assessments" be expanded with additional examples.

In response to the comments, the Agency has modified or clarified many sections of the Guidelines, and is planning to develop supplementary guidance in line with the SAB recommendations. The discussion that follows highlights significant issues raised in the comments, and the Agency's response to them. Also, many minor recommendations, which do not warrant discussion here, were adopted by the Agency.

II. General Information

A. Acceptable Latitude of Approach

Some commentors believe the Guidelines are too general and allow too much latitude in choice of approach and do not assure that "all" data, sources, limitations, etc. are considered before an exposure assessment is conducted. Others suggested that the Agency specify models to be used while others thought that only measured data should be allowed.

The Guidelines were developed to provide assistance in carrying out exposure assessments. The approach suggested is deliberately general in order to accommodate the development of exposure assessments with different levels of detail depending on the scope of the assessment. The Agency does not agree with the inclusion of such restrictive terminology as "in all cases." We cannot foresee all possible cases. We believe reasonable flexibility is a necessary ingredient for the proper implementation of the Guidelines while relying on uncertainty and sensitivity analyses to put the quality of the approach in perspective.

B. Technical Nature of Guidelines

Some commentors believe the language of the document is too technical for the lay person to understand; one commentor expressed misgivings concerning the "state-of-the-art" methods available for conducting exposure assessments.

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While the Agency recognizes that the public has an interest in the Guidelines and invites comments from the public, the Guidelines are intended for use by technical/professional people. Providing guidelines written in lay terms would result in insufficient technical specifications to the professionals in the development of scientifically acceptable exposure assessments.

The Agency believes that the suggested procedures and methods in the Guidelines are commonly accepted. The Guidelines do not suggest the use of ad hoc, untested, and unvalidated procedures, but stress the use of the best scientific methods available with maximum analysis of existing data. This is both a scientific and practical approach that reflects the level of consensus within the Agency.

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C. Measurements vs. Modeling

Some commentors support the use of measurements alone to develop an exposure assessment. Some believed there should be no data restraints; others thought all data should be validated. Other commentors argued for the use of simulation model estimates without measurements. One commentor objected to the use of unvalidated models to perform exposure assessments. In its review, the SAB strongly encouraged the Agency to develop a supplement to the current Guidelines on the development and use of measurements for exposure assessments.

The Agency encourages the use of validated measurements when available. The Guidelines specifically state that "Reliable, analytically determined values should be given precedence over estimated values. . ." and analytically determined values ". . .can be used to calibrate. . . models. . .to assess environmental distribution." Furthermore, in practice, exposure assessments performed by the Agency use published models with varying degrees of testing and validation. It is our belief that transport process models have been adequately validated over many years in most cases.

Furthermore, the Agency has revised the Guidelines to reflect the SAB suggestions that exposure assessments based on reliable measured data are preferred over model estimates whenever feasible.

III. Data Availability and Uncertainty Analysis

A. Information Uses

Some commentors asked for guidance in the use of information that may be false and how to deal with the potential situation when different models give different results. Others asked for model selection criteria.

The Guidelines clearly state the considerations that need to be addressed when assembling information bases for exposure assessments. Two considerations are: qualitative and quantitative nature of the data and the reliability of the information. Whether the exposure assessment is based on measurements or simulation model estimates, an evaluation of uncertainties associated with the data including source data and assumptions is necessary and important.

When there is uncertainty in the scientific facts, it is Agency policy to err on the side of public safety. The Agency intends to be realistic, but will not arbitrarily select midranges of environmental distributions that may compromise human health. In addition, quality assurance is an important matter that requires detailed attention. The collection of measured data and the development of methods to collect measurements are done by another office within the EPA. These issues will be handled by the Office of Acid Deposition, Environmental Monitoring, and Quality Assurance as they develop the supplemental guidelines for measurement of exposure.

Substantial work is currently being done on the development of mathematical model selection criteria. Results of these efforts will be published as a technical support document containing detailed information to further implement the Guidelines.

B. Worst-Case Estimates

A few commentors were concerned that worst-case estimates would be used when data are nonexistent or limited. The Guidelines do not encourage the use of worst-case assessments, but rather the development of realistic assessments based on the best data available.

A technical support document and a substantial section of the Guidelines currently discuss evaluation of uncertainty in order to produce objective assessments using the best (not worst-case) estimates available either for preliminary or in-depth exposure assessments. However, the Agency will err on the side of public health when evaluating uncertainties when data are limited or nonexistent.

IV. Evaluation of Uncertainties

A. Uncertainty Analysis

Many commentors felt that the sections of the Guidelines that dealt with uncertainty needed amplification while some sections as written were confusing. Some urged that uncertainty evaluation be presented and documented for each section within a specific exposure scenario in order to judge the overall plausibility of the assessment in reaching regulatory decisions.

Since the accuracy of an exposure assessment is influenced by the degrees of uncertainty contained in both data and assumptions, the Guidelines call for the evaluation of these uncertainties. The technical support document, Methodology for

Characterization of Uncertainty in Exposure Assessments (available from the National Technical Information Service, PB85-240455), describes in detail how such analyses can be performed. The Guidelines suggest that the uncertainty characterization include a discussion of the limitations of the data and estimation procedures as the justification for the model chosen. A sensitivity analysis of the exposure assessment is appropriate if the data were only able to support the estimates of ranges of the input variables. By identifying model input variables that determine the bounds on the distribution of exposure, the range of exposure, which results as individual model input variables are varied from minimum to maximum possible values as other variables remain constant, constitutes the sensitivity analysis. Further sensitivity of model formulation can be examined by repeating the sensitivity analysis for plausible alternative models.

Nothing in the Guidelines precludes estimation of uncertainty for each specific exposure scenario. The Agency has encouraged the evaluation of uncertainty in each aspect of the exposure assessment, which could impact the total risk estimate. It is important to estimate the level of uncertainty in risk assessments so that decisions based on risk assessment will reflect total uncertainty. The information presented in the Guidelines or the technical support documents properly and adequately describes the extent and quality of appropriate uncertainty analysis. Recognizing that the basis for the decision to refine a preliminary exposure assessment involves risk management, the Agency, at the suggestion of many commentors, decided to strike from the Guidelines the paragraph beginning "If the maximum possible exposure. . . ." in section III.B.8.d.(2).

B. Population Characterization

The Guidelines state that identification of populations and subpopulations at potentially high exposure forms the basis of the populations to be studied. Separate studies of sensitive subpopulation can also be included. Population characteristics, such as age and/or sex distributions, can be derived from the use of geographic and activity-specific data. Uncertainty related to estimation of a population characteristic include a discussion of the data limitations and the estimation procedures. In addition, uncertainty in estimating sizes of sensitive subpopulations should include estimates of confidence intervals.

Some commentors suggested the inclusion of additional characteristics, such as occupational and life style factors, and the inclusion of additional guidance concerning potential pitfalls when conducting population exposure

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assessments. Others expressed concern that the exposure of a particular subpopulation would be combined with other exposures to produce an average exposure level for the general population.

The section describing population characterization encompasses, in general terms, the many characteristics that may be available, including life style factors, to describe exposed populations. The Agency agrees that there are difficulties associated with epidemiologic studies. The relationship between exposure assessments and epidemiologic studies is currently being investigated and will be the subject of a future technical support document and the further refinement of the Guidelines.

V. Clarification of Terminology

A. Exposure vs. Dose

Commentors expressed concern with the American Society for Testing and Materials (ASTM) definition of exposure. Concern was also raised about the assertion that exposures can be estimated when biological tissues for fluid measurements indicate the presence of a chemical. Some commentors found difficulty in the wording of the last sentence in section II.A., specifically "The route of exposure. . .impacts. . .the overall exposure. . . ."

It is the Agency's opinion that the members who served on the ASTM Committee E-47 had expertise in exposure assessment. The scientists and engineers cumulatively possessed many years of experience in exposure assessment. In addition, no technical society has presented an alternate definition of exposure. The Agency will consider changing the definition if a reasonable alternate definition is written and agreed upon by the scientific community.

The Agency agrees with the commentors who were concerned that the wording provided in the Guidelines that the presence of a chemical in biological tissue can be used to estimate exposure is not correct in all cases. Consequently, the word "can" was changed to "may" to reflect the current level of understanding between tissue residue and exposure (II.A., 2nd paragraph, 4th sentence). The Agency agrees with several commentors' concerns that the route of exposure impacts the overall absorbed dose, not the overall exposure, and the Guidelines reflect this change (II.A., last sentence).

B. Mixtures and Synergism

Some commentors thought more discussion was necessary on the effect of chemical mixtures and potential synergistic effect on exposure. The Guidelines for the Health Risk Assessment of Chemical Mixtures includes a discussion of chemical synergism. The Agency recognizes the need to do further work in the area of exposure to mixtures. It is recommended that this be identified as an area requiring further research.

REC 6232

These Guidelines stress the need to determine the products into which the chemical might degrade or react in the environment and to determine if any of these products are ecologically or biologically harmful.

C. Removal and Creation Steps

Some commentors urged that more emphasis be placed on changes that occur once the materials have entered the ambient environment. Other commentors argued that our current understanding will not allow a comprehensive treatment, particularly for metabolic processes.

These Guidelines state the need to address how a chemical agent moves from the source to the exposed population, which may result in the estimation of geographic and temporal distributions in various environmental media. The Guidelines also state the need to know such factors as, for example, whether the chemical agent bioaccumulates or by what mechanism the agent is removed from each medium and the role of any degradation products on ecological safety. We have already stated that guidance for analysis of metabolism data is an area of ongoing research which includes consideration of metabolism data in the calculation of whole organism dose from one species to another.

VI. Purpose, Philosophy, and Results

Several commentors raised questions related to the basic style of the Guidelines. Among the issues raised were:

- the role of exposure assessment in risk assessment/risk management (many comments directed to appropriateness of Figure 1);
- statutory/regulatory authority and uses of results; and
- the need for peer review of assessments and periodic updating of Guidelines.

A deliberate effort to separate risk assessment from risk management has been made. The management of complex issues such as procedural issues, which include coordination or linkage among divisions in the Agency, are best dealt with by management and not in Guidelines.

The decision pathway (Figure 1) was included in the Guidelines at the recommendation of the SAB. It has drawn many comments. The changes suggested would include additional detail and steps that would diminish the value of the graphic. However, the figure has been truncated to remove risk management steps.

In order to remain consistent with the separation of risk assessment and risk management, any directions to consider applicable laws or regulatory decisions have been stricken from the Guidelines.

The Agency agrees that peer review is an important aspect of the assessment process. However, emergency cases may not allow peer review in preliminary assessments. All nonemergency exposure assessments have been peer reviewed and will continue to be peer reviewed. Finally, it is clearly stated in the Guidelines that periodic revision of the document will be done to reflect the benefit of experience and knowledge.

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Exhibit C



Guidance Document

First, Second, and Third Tier Review of Toxic Air Pollution Sources (Chapter 173-460 WAC)

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Publication and Contact Information

This document is available on the Department of Ecology's website at www.ecy.wa.gov/biblio/0802025.html.

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Introduction

Ecology and local air quality agencies use first, second and third tier review to regulate emissions of toxic air pollutants. Hundreds of potentially toxic chemicals are released into the air each year in Washington. Excess exposures to these chemicals can cause serious illnesses and premature deaths. Widespread exposure probably accounts for some of the occurrences of various types of cancers within our population.

This publication is to help toxic air pollution sources understand and use the first, second, and third tier review sections of the notice of construction application. Requirements for first, second, and third tier review are found in Chapter 173-460 Washington Administrative Code (WAC).

First Tier Review

What is first tier review?

First tier review is part of a notice of construction application for a new or modified toxic air pollutant source. It compares your project emissions to the toxic air pollutant values listed in WAC 173-460-150.

How do I know if I need to do a first tier review?

You will need to do a first tier review if potential emissions from your project exceed the de minimis emission levels specified in WAC 173-460-150. Your potential emissions are the expected worst-case emissions from your facility, considering its physical and operational design.

How do I get first tier review?

You do not need to submit a separate petition for first tier review. The notice of construction application you file with the permitting agency serves as your petition for first tier review. Typically, the permitting agency will conduct a first tier review on every notice of construction application it receives.

What issues must I address before the order can be issued?

You must show that the emission increases from all new or modified emission units are below the acceptable source impact level (ASIL):

- after application of best available control technology for air toxics (tBACT); and
- at any location outside of your property boundary.

You can find the ASILs in WAC 173-460-150.

How can I show that emissions are below the ASIL?

You can show emissions are below the ASIL by:

- demonstrating that the emissions are at or below the small quantity emission rates (SQER);
- using a screening model (such as AERSCREEN); or
- using a refined air dispersion model (such as AERMOD).

What can I do if emissions exceed the ASIL?

You have several options, including:

- revise the project and application;
- negotiate an enforceable limit;
- off-set the emissions by reducing emissions from another on-site emission unit;
- submit a second tier petition;
- submit a third tier petition; or
- withdraw the application.

How do I off-set the new emissions by reducing them at another emission unit?

You must meet several criteria in order to get this option approved:

- the emission reductions must be actual reductions;
- the reductions must be modeled against all affected receptors; and
- when the emission increases and reductions are modeled together at the receptor, the modeling must demonstrate that the off-set proposal results in emission values lower than the ASIL.

Who approves a first tier analysis?

Your permitting agency will review the first tier analysis and either approve or deny it.

What happens if my first tier analysis is approved?

If your permitting agency approves the first tier analysis, it will include the approval decision in an "Order of Approval." For permits issued by Ecology, guidelines for issuing this order and requirements for notifying the public are in WAC 173-400-110. Other permitting agencies may have their own guidelines. The order may contain the following:

- emission limits for each toxic air pollutant (TAP) subject to review;
- a method of assuring compliance with TAP limits (usually monitoring, reporting, and operation restrictions);
- a statement of the Best Available Control Technology for Air Toxics (tBACT) for each TAP; and
- enforcement criteria for voluntary emission reductions, including monitoring, record-keeping, and reporting requirements.

What happens if my first tier analysis is not approved?

If emission increases still exceed the ASIL and other options do not work, you can submit a petition for second tier review.

Are there any exemptions from the first tier review process?

Yes. A list of exemptions from new source review is in WAC 173-400-110. Also, your permitting agency might have its own list of exemptions. Exemptions for toxic air pollutants and criteria pollutants are related because the permit process procedures, definitions, and exemptions are the same for both.

Exemptions are divided into two broad categories:

- emission unit and activity exemptions; and
- exemptions based on emissions.

To see if your project is exempt, read the emission unit and activity listing in WAC 173-400-110(4 and 5), and contact your permitting agency. De minimis emission values for toxic air pollutants are in WAC 173-460-150. You must consider all of the new or modified emission units together. For the project to be exempt, emissions from all of the individual emission units added together must be below the de minimis values.

Second Tier Review

What is second tier review?

Like first tier review, second tier review is part of a notice of construction application for a new or modified toxic air pollutant source. You need to do a second tier review if any of your project's toxic air pollutant emissions exceed the ASIL after you have completed a first tier review. In this step of the notice of construction application process, the applicant submits a health impacts assessment to Ecology. Ecology will review the health risks associated with your project.

How do I get second tier review?

Submit a petition for second tier review to Ecology, with a copy to the permitting agency that has jurisdiction. The application form includes the Health Impact Assessment Checklist and is available at: http://www.ecy.wa.gov/biblio/ecy070415.html

What is the review process for a second tier petition?

Ecology's air toxics engineer, toxicologist, and air quality modeler work together on second tier petitions. The review process includes:

- pre-application conference;
- a second tier petition and payment of applicable fees;
- HIA protocol; and
- HIA document.

Pre-application conference

After Ecology is notified that a proposed project requires second tier review, Ecology recommends you have a pre-application conference with Ecology staff before you submit a second tier petition. The pre-application conference:

- helps you identify regulatory issues before you commit a significant amount of time and resources toward a specific course of action;
- lets you know early in the process what you need to address in the Health Impact Assessment, which can avoid unnecessary delays later on; and
- helps you identify the review criteria for your project, so that you can present your proposal accurately.

You and your consulting team need to attend the conference. The team typically includes an engineer, plant operations manager, and other specialists involved in your proposal. You and your team will meet with an Air Quality Program engineer, toxicologist, and air quality modeler.

The permit writer who reviewed your first tier analysis will also attend, whether they work for Ecology or a local air quality agency.

At the conference, you, your team, and Ecology staff will review the following information:

- required permits, approvals, and fees;
- protocol for the health impact analysis;
- the refined air dispersion modeling methods used to estimate TAP levels;
- typical project review timelines;
- application regulations;
- the public hearing process; and
- any other questions you might have.

The amount of information Ecology can give you at the conference depends on the level of detail you provide about the project. Because the conference takes place early in the process, Ecology will not be able to anticipate all the relevant project details. Ecology will give you a protocol to follow that tells you what to do next.

The conference **will not** provide:

- a detailed toxicology analysis or modeling review; or
- a final recommendation on a proposal.

To schedule a pre-application conference, call Matt Kadlec at (360) 407-6817 or Gary Palcisko at (360) 407-7338. They will work with you to find a time that works for everyone. The conference is typically held at Ecology's Headquarters building at:

300 Desmond Drive SE
Lacey, WA 98503

Second tier review petition and fees

After the pre-application conference, the applicant submits to Ecology a petition and applicable fees for second tier review, with a copy to the permitting agency that has jurisdiction. The application form includes the Health Impact Assessment Checklist and is available at: http://www.ecy.wa.gov/biblio/ecy070415.html. You can find more information on applicable fees starting on page 31.

HIA protocol

The applicant must also submit an HIA protocol. Ecology will review the HIA protocol after the applicant submits the $10,000 initial fee with the HIA protocol and completed second tier application. Basic information required for HIA protocol is included later in this document.

HIA document

After Ecology approves the HIA Protocol, the applicant prepares and submits an HIA document. Ecology toxicologists will review the HIA to determine if health impacts are adequately characterized. Ecology will provide substantive and non-substantive comments on the HIA document and will request the applicant revise the HIA document if necessary. This process can be repeated until the applicant prepares an acceptable final HIA document. Ecology's project engineer or delegate will review portions of the HIA that involve the project's engineering specifications. Likewise, Ecology's dispersion modeler will review portions of the HIA that involve toxic air pollutant (TAP) concentration modeling. Following confirmations by the engineer and modeler, Ecology's project toxicologist will review risk assessment portions of the HIA. The toxicologist will then communicate to all parties the results of the HIA review.

Once an acceptable HIA document has been prepared, Ecology will prepare a brief staff report which summarizes Ecology's review of the HIA and includes recommendation(s) to the local permitting authority about the petition. Ecology will:

- post the applicant's final HIA document, Ecology's staff report, and Ecology's cover letter on Ecology's air toxics review web page (http://www.ecy.wa.gov/programs/air/Tier2/Tier2_infosite.html);
- make a final recommendation for approval or denial of the project; and
- send the recommendation to you and the permitting agency, which issues the actual approval order.

Ecology's decision on the second tier petition must be included in the final decision on the notice of construction application.

Who approves a petition for second tier review?

Only Ecology staff can review, approve, or deny a second tier petition.

What materials should I provide, and when?

In the pre-application conference, you will be given a protocol for preparing the required documentation for the second tier petition. After the pre-application conference, the permitting agency (either a local air quality agency or one of Ecology's regional offices) will provide a preliminary order of approval directly to Ecology. Then, follow this protocol to provide information:

Provide to Ecology:

- the results of the refined air dispersion modeling for all pollutants that exceed the SQERs; and
- a full copy of the second tier petition (containing a Health Impacts Assessment).

Provide to the permitting agency that reviewed your first tier analysis:

- a full copy of the second tier petition.

Is public involvement required?

Yes. Public involvement is required for any project that needs a second tier review. It may be limited to a public notice and public comment period, or Ecology may determine that a public hearing is needed. If a public hearing is held, Ecology and the permitting agency will hold a joint public hearing to streamline the public review process. Ecology staff will explain the second tier recommendation at the public hearing. You and your consultants should be prepared to explain your project and answer questions at the public hearing.

What can I do if Ecology does not approve the second tier petition?

If Ecology denies the second tier petition, the permitting agency may not approve the project. At that point, you have the following options:

- revise the project and application;
- propose emission reductions from an off-site emission unit;
- submit a third tier petition; or
- withdraw the application.

My project triggers second tier review. Are there any exemptions from the second tier review process?

No. If your project triggers second tier review, you must submit a second tier petition to Ecology before your project can be approved. If you think that your project will not meet the approval criteria of a second tier review, you may opt to submit a third tier petition instead of a second tier petition.

Third Tier Review

What is third tier review?

You can submit a petition for third tier review if the health risks from your project exceed the second tier review thresholds. In third tier review, your petition requests that the director of Ecology approve the project based on a risk management analysis.

How do I submit a petition for third tier review?

Submit your petition for third tier review to Ecology, with a copy to the permitting agency that has jurisdiction.

What materials should I provide, and when?

The materials required for a third tier review are the same as for a second tier review. You may submit the third tier petition at the same time you submit the second tier petition. Prior denial of a second tier petition submitted under WAC 173-460-090 is not required. The permitting agency (either a local air quality agency or one of Ecology's regional offices) will provide a preliminary order of approval directly to Ecology. Then follow this protocol to provide information:

Provide to Ecology:

- the results of the refined air dispersion modeling for all pollutants that exceed the SQERs;
- a full copy of the third tier petition (containing a health impacts assessment); and
- a description of environmental benefits of the proposal.

Provide to the permitting authority that reviewed your first tier analysis:

- a full copy of the third tier petition.

In addition to the above documentation, you may propose voluntary measures to reduce community exposure to pollutants emitted by your project. Voluntary measures might include voluntary reduction of emissions from existing unmodified emissions units at your facility or at another facility.

What is the review process for a third tier petition?

Ecology's air toxics engineer, toxicologist, and air quality modeler work together to prepare a recommendation to the director of Ecology to either approve or deny a third tier petition. Within 30 days after you've submitted the petition, Ecology will:

- review it for completeness; and
- provide you a letter stating the petition is complete or listing needed information if it is not complete.

Within 60 days after determining that your petition is complete, Ecology will:

- write a draft technical support document and send it to you and the permitting agency for review and comment;
- address any questions or concerns brought up during review;
- together with you, initiate a minimum 30-day public notice and public comment period;
- together with you, schedule a public hearing.

After the public hearing, Ecology will review and address all comments. Ecology will then prepare the final recommendation and technical support document, and send them to you and the permitting authority, which issues the actual approval order.

Ecology's final recommendation on the third tier petition must be included in the final decision on the notice of construction application.

What criteria will Ecology follow to approve or deny a petition for third tier review?

Before approving your third petition, Ecology's director must find that the following conditions are met:

- proposed emission controls represent at least tBACT;
- a health impact assessment addressing all of Ecology's requirements has been completed; and
- approval of the project will result in a greater environmental benefit to the state of Washington.

Is public involvement required?

Yes. Public involvement is required for any project that needs a third tier review. The public involvement process must include a public notice and public comment period, as well as a public hearing. The purpose of the public hearing is to present the results of the third tier review and to

answer any questions from the public. You and your consultants should be prepared to explain your project and answer questions at the public hearing.

What can I do if Ecology does not approve the third tier petition?

If Ecology denies the third tier petition, the permitting agency may not approve the project. At that point, you have the following options:

- revise the project and application;
- propose emission reductions from an off-site emission unit; or
- withdraw the application.

My project triggers third tier review. Are there any exemptions from the third tier review process?

No. If your project triggers third tier review, you must submit a third tier petition before your project can be approved.

Health Impact Assessment

This section helps toxic air pollution sources prepare a health impact assessment (HIA) as part of second tier or third tier review, as required in Chapter 173-460 WAC. Ecology's Air Quality Program recommends that permit applicants preparing an HIA refer to the Air Toxics Hot Spots Program Guidance Manual for Preparation of Health Risk Assessments, published in March 2015 by the Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. (See the citation list at the end of this document.)

The guidance manual addresses the techniques used to assess health risks of airborne contaminants released by new or modified stationary sources like those permitted in Washington. Most of the techniques described in the Hot Spots Program Guidance Manual are common to other regulatory risk assessment applications. However, applicants may need additional analyses depending on their unique circumstances. Applicants should contact Ecology before beginning work on their HIA in order to assure that all WAC 173-460-090 requirements will be satisfied. In general, using the Hot Spots Program Guidance Manual risk assessment procedures and report presentation will speed up Ecology's review. It will also minimize the chance that applicants will need to revise and resubmit their HIA.

What is an HIA?

An HIA looks at how emissions of toxic air pollutants from a specific project will affect public health. It involves several steps, including hazard identification, exposure analysis, toxic response, and risk characterization.

Who needs to submit an HIA?

Second and third tier petitions always need an HIA.

How do I submit an HIA?

When you submit a petition for a second or third tier review, the HIA will be included in your pre-application conference.

Why do I need a pre-application conference?

Pre-application conferences help you learn about regulatory issues before you commit a significant amount of time and resources to a specific course of action. At the pre-application conference, Ecology will tell you what issues need to be addressed in the HIA. This will help you avoid unnecessary costs and delays.

What documentation do I submit with an HIA?

Because each HIA is tailored to fit a specific project, each one may require different documentation. Generally, you will need to include:

- A map of the site and neighborhood showing:
    - location of new or modified emission points;
    - local zoning of the affected area;
    - locations of and distances (in meters) between the sources; and
    - residences, businesses, roadways, public properties, and public or private facilities serving population subgroups such as schools, nursing homes, hospitals, and for certain TAPs, private and public drinking water wells (note the well depth).

- Hazard identification, including:
    - a list of all TAPs (as defined in Chapter 173-460 WAC) that will be emitted by the facility, and
    - a physical description of those TAPs.

For details, refer to the sections below titled "Dispersion Modeling Protocol and Report Contents," "Contents of the Health Impact Assessment," and "Outline of the Health Impact Assessment Report."

What do I need to submit about the TAP concentrations?

You must show how you derived the TAP concentration levels. Include the following:

- emission rates, in grams per unit of time, at the maximum possible rate;
- modeled concentration estimates in $\mu g/m^3$ or ppb (disclose the emissions factors used in modeling);
- any available monitoring measurement results; and
- any uncertainties and assumptions in deriving concentration levels.

You must also disclose the cross-media transport of the emissions in the environment, the environmental persistence, the degradation pathways, and the final fate of the toxic air pollutants. This means describe the movement of proposed toxic air emissions from air into water and/or soil which people may be exposed to. Generally, the inhalation pathway of exposure is the largest contributor to the total dose. However, there are situations where a non-inhalation pathway contributes substantially to total dose. You can get detailed guidance on this subject from a variety of authorities, for example EPA's Guidelines for Exposure Assessment (1992) and Exposure Factors Handbook (2011) and OEHHA's Air Toxics Hot Spots Program Guidance Manual for Preparation of Health Risk Assessments (2015, chapter five). (See the citation list at the end of this document.)

What materials must I include to assess exposure?

You must identify the TAP exposure pathways, including the following:

- Disclose the total daily intake of TAPs attributable to the project source as well as the background sources. EPA has some ambient air concentration estimates in their NATA database.
- Estimate the durations of exposure, including long-term averages, short-term peaks and worst-case scenarios. Detail the exposure parameters associated with sensitive population subgroups. You can get detailed guidance on this subject from a variety of authorities, including EPA's Guidelines for Exposure Assessment (1992) and Exposure Factors Handbook (2011) and OEHHA's Air Toxics Hot Spots Program Guidance Manual for Preparation of Health Risk Assessments, (2015, chapter five). (See the citation list at the end of this document.) Identify the potentially exposed populations. Give special emphasis to any subpopulations that might be unusually susceptible to any TAPs emitted by your project.
- Using the information on the location of potentially exposed populations, show the TAP concentrations at the points where people might be exposed to the pollutants in question.

What issues do I need to address in the toxicity discussion?

The toxicity discussion should focus on the effects relevant to the proposed toxic air pollutant concentrations. The following issues should be thoroughly discussed:

- toxic effects of the toxic air pollutants;
- exposure levels associated with specific effects;
- exposure patterns and duration of exposure as established by studies of the toxic effects;
- any quantitative, chronic toxicity values including:
    - inhalation reference concentration or similar hazard-based concentrations;
    - cancer unit risk factor estimates;
    - slope factor or carcinogenic potency estimates; and
- any quantitative intermediate and short-term acute toxicity values.

What issues do I need to address in the risk/hazard assessment section?

Provide a discussion of offsetting reductions in risk that might accrue to society as a result of completing the proposed facility modification. This typically includes a:

- qualitative discussion of the risks;
- quantitative discussion of the risks with appropriate toxicity measures, calculated cancer risks, and the hazard index;
- discussion of uncertainties in the risk assessment;

- discussion of acceptability of risk with regard to guidelines in Chapter 173-460 WAC; and
- discussion of the extent to which the proposed facility might affect human health.

What issues do I need to address in the uncertainty section?

There is always some level of uncertainty associated with risk assessment. While uncertainty encompasses those factors that are not known, and could be eliminated or reduced with scientific studies, we are not asking you to conduct original research. We want you to disclose your level of confidence in the data used to substantiate your conclusions.

Risk can be over or underestimated because of many factors, including:

- extrapolation of toxicity data in animals to humans;
- uncertainty in the estimation of emissions;
- uncertainty in the air dispersion models;
- interactive effects of exposure to more than one carcinogen or toxicant;
- uncertainty in the exposure estimates; and
- uncertainty about the extent of toxicant susceptibility variation within human populations.

The HIA mentions subpopulations. What is an example of a sensitive or understudied subpopulation?

Children are a subpopulation whose hematological nervous, endocrine, and immune systems are still developing. They may be more sensitive to the effects of carcinogens on their developing systems. These sensitivities are not included in the worker population and risk estimates based on occupational epidemiological data, which are based on adult populations.

Who reviews the HIA?

Ecology's Air Quality Program toxicologists review HIAs. While the toxicologists are reviewing the HIA, the engineer and dispersion modeling staff review other portions of the second or third tier petition. They determine if tBACT and refined modeling are sufficient.

Note that though Ecology's toxicologists review HIA documentation; they are not authorized to prepare the applicant's assessment.

What can I do if Ecology does not approve the HIA?

You have the following options:

- revise the project and application;
- propose emission reductions from an off-site or on-site emission unit;
- submit a third tier petition (See WAC 173-460-100); or
- withdraw the application.

Where can I get more information on the HIA?

Contact either of the Air Quality Program toxicologists:

Matt Kadlec
(360) 407-6817
matt.kadlec@ecy.wa.gov

Gary Palcisko
(360) 407-7338
gary.palcisko@ecy.wa.gov

Contents of the Health Impact Assessment Protocol

Applicants must submit a Health Impacts Assessment Protocol before submitting a draft HIA. The protocol ensures that the applicant will submit sufficient information and is intended to prevent delays caused by incomplete analyses. The protocol should contain a description of how the applicant intends to estimate the health impacts posed by TAPs subject to second tier review. Generally, an applicant will need to provide an air quality analysis that demonstrates compliance with both national ambient air quality standards and toxics review. The following items need to be included in the Health Impact Assessment Protocol:

Emissions Estimate

- Quantify short- and long-term emission rates,
  - mass per hour, day, year;
- Report emission factors and their source and justification;
- Report applicable emission standards and ASILs;
- Provide background concentrations, if known.

Source Characteristics

- Site plan showing fence line, emission units, and other structures;
- Modeling parameters.

Model and Model Assumptions

- AERMOD is to be used in most situations.

Meteorology

- Identify representative surface meteorological data.
  - 5 years of continuous quality-assured/quality-controlled meteorological data/QC'd upper air data

Receptor Grid

- Recommended receptor grid spacing to ensure that sampling error does not reduce the maximum computed concentration by more than 10%:

Distance from Source [m]	Grid Spacing [m]
0 – 150	12.5
150 – 400	25
400 – 900	50
900 - 2000	100
2000 - 4500	300
> 4500	600

Deposition

- For some TAPs, applicants may need to estimate deposition so that multi-pathway exposures can be assessed. These TAPs include:
    - 4,4'-Methylene dianiline
    - Creosotes
    - Diethylhexylphthalate
    - Hexachlorocyclohexanes
    - PAHs
    - PCBs
    - Cadmium & compounds
    - Chromium VI and compounds
    - Inorganic arsenic and compounds
    - Beryllium and compounds
    - Lead and compounds
    - Mercury and compounds
    - Nickel
    - Fluorides (including hydrogen fluoride)
    - Dioxins and furans

Model Output/Results

- Files provided to Ecology
- Modeling results to be used to demonstrate compliance or assess risk

Receptors

- Identify receptors where the ASIL is exceeded.
  - Identify maximally-exposed residential, workplace receptors and point(s) of maximum impact. (**Note**: Maximally-impacted receptors around a site can vary depending on concentration averaging time.)

Short-term and long-term risk-based exposure concentrations

Depending on which chemicals are being evaluated and the type of receptor that is impacted, short-term and/or long-term ambient concentrations are needed.

- Short-term = typically 1-hr., 8-hr., 24-hr. concentrations
- Long-term = typically annual average concentration

Acute and chronic non-cancer hazard (1-hr., 8-hr., 24-hr., annual exposure concentrations)

For all non-carcinogenic toxic air pollutants exceeding their SQERs:

- Identify relevant short-term and long-term non-cancer toxicity values for chemicals exceeding SQERs
  - For example: EPA RfCs, OEHHA RELs, ATSDR MRL

- Calculate Hazard Quotients (HQ)
  - Exposure concentration ($\mu g/m^3$) divided by risk-based concentration ($\mu g/m^3$)

- For multiple chemicals with similar toxic effects (i.e., same tissue or organ system), calculate Hazard Index
  - Sum hazard quotients with same averaging time and similar toxic effects for all toxic air pollutants that exceed the SQER

- Determine the frequency and geographic extent that short- and long-term concentrations exceed relevant toxicity values (i.e., HQs > 1)

Cancer risk (annual exposure concentrations)

For all carcinogenic toxic air pollutants exceeding their ASILs and SQERs:

- Identify existing inhalation unit risk factors or cancer potency factors
- Calculate lifetime increased cancer risk from exposure to each TAP
- Calculate the sum of cancer risks for all chemicals emitted in excess of SQER to produce the total increased cancer risk from project
- Identify population exposed in excess of one per million and estimate total population risk from project

Outline of the Health Impact Assessment Report

In general, the HIA should provide information about:

- Project description
- Emissions
- Air dispersion modeling
- ASIL screening
- Risk assessment
  - Hazard identification, exposure, dose-response (which criteria are used to estimate risk), risk characterization, uncertainty
  - Discussion of acceptability of risk

Recommended Outline of an HIA

Note: Not every item below will be required in every HIA report. Ecology staff will discuss the specific requirements of your HIA report during the pre-application meeting.

Project description

- Project overview
- Physical location
  - Address, city, county
  - Land use (zoning) in areas adjacent to project
  - Site map showing emission points, property boundary, off-site receptors (outside any limited public access boundary maintained around the facility, and the locations of any buildings and their usage (i.e., housing, business, school, etc.))

SQER and ASIL comparison

- Comparison of facility emission rates of TAPs to their respective SQER
  - Model concentrations of those that exceed their SQER
  - Compare results to their ASIL(s)
- Refined dispersion modeling to estimate off-site concentration of those TAPs to their respective ASILs
- If a chemical exceeds its ASIL at an off-site location, then a health impact assessment is performed.

Hazard identification

- Identification of the TAPs that may pose a threat to human health (those that exceed ASILs and those that exceed SQERs with similar effects).
- Physical description of the TAP (s) emitted in amounts greater than their SQER and overview of each chemical's toxicity (i.e., affected tissue/organ and the critical effect. For example, acrolein: Eyes and respiratory tract; eye irritation and respiratory epithelium lesions).
- Potential for cross-media transport in the environment, environmental persistence, degradation pathways, and final fate of the TAP(s). Provide public water solubility data, and degradation half-lives in air, water, and soil.

Identification of places with potentially-exposed people (off-site)

- For example, residences, businesses, parks, schools, hospitals within the geographic extent where estimated concentrations are greater than the ASIL.

Discussion of TAP concentrations

- Using the information on location of potentially-exposed populations, TAP concentrations that exceed ASIL(s) should be given at points where humans might come into contact with the TAP(s).
- Derivation of the concentration levels should be discussed.
- Concentration estimates, in $\mu g/m^3$ by modeling and emissions factors used in modeling.
  - Averaging times may vary depending on the project and potentially-exposed receptors, but examples are:
    - Maximum 1-hr., 8-hr., and 24-hr. exposure – for chemicals that have the potential to cause acute effects over a short time
    - Annual average exposure – for chemicals that have the potential to cause cancer or other chronic effects
    - Display results on maps

Exposure assessment

- Identification of TAP exposure pathways
- Development of total daily intake attributable to source and background sources (existing ambient air concentration estimates for some pollutants are available in EPA's NATA)
  - Durations of exposure, including long-term averages, short-term peaks, and worst-case scenarios
  - Exposures at maximally-effected residence(s), business(es), and fence line (limited public access boundary) places
  - Exposure parameters associated with sensitive population subgroups. For example, situations where children may be frequently exposed may warrant child-specific exposure parameters.

Toxicity (should focus on effects relevant to proposed TAP concentrations)

- Description of toxic effect(s)
- Exposure levels associated with effect(s)
- Exposure pattern and duration of exposure in studies of toxic effects
- Any quantitative, chronic toxicity values
  - Inhalation reference concentration or similar hazard-based concentrations
  - Cancer unit risk factor estimates
  - Oral risk based concentrations for substances evaluated through multi-pathways of exposure
- Quantitative intermediate/short-term toxicity values
- Discussion of how the site-specific toxicity value considers exposure duration and frequency at the site

Risk/hazard characterization

- Qualitative discussion of the risk(s)
- Quantitative discussion of the risk(s)
  - With appropriate measure(s) of toxicity
  - Calculated cancer risk(s)
- Hazard quotients and hazard indexes, if there are any co-acting combinations of TAPs. (Critical effect –specific hazard indexes for TAPs emitted at rates above their SQERs for any co-acting combination of such TAPs.)

Discussion of uncertainty and variability of numeric values used in the HIA

A HIA is composed of many numeric values – each with its own uncertainty and/or variability. Uncertainty is that which is not known about a factor that influences its value. Variability occurs when a quantity that is repeatedly measured exhibits values that differ. It can be quantified using descriptive statistics such as the range.

Discussion of acceptability of risk with regard to guidelines in Chapter 173-460 WAC

- Increased cancer risk is no more than 10 per million
- Non-cancer hazard quotients or indexes are less than one, or Ecology determined that non-cancer hazards are acceptable

Second and Third Tier Review Timeline

Step 1: Applicant submits to Ecology:

- full copy of the second or third tier petition (including all of the elements discussed in the HIA protocol);
- results of the refined air dispersion modeling for all pollutants that exceed the ASILs;
- preliminary order of approval issued by the permitting agency (The permitting agency will generally provide the preliminary order of approval directly to Ecology. The permitting agency is either a local air quality agency or one of Ecology's regional offices.); and
- description of environmental benefits of the proposal (for a **third tier petition**).

Step 2: Within 30 days after receiving the petition, Ecology will:

- review it for completeness; and
- issue a letter stating the petition is complete or list all information needed to complete the petition.

Step 3: Within 60 days after determining a petition is complete, Ecology will:

- write a draft technical support document and send it to the applicant and permitting agency for review and comment;
- address any questions or concerns brought up during that review;
- for a **second tier petition**, make a final decision to recommend approval or denial of the project, and send the **final second tier** recommendation to the applicant and the permitting agency;
- for a **third tier petition**, prepare a third tier review recommendation and technical support document for public comment, and send them to the applicant and the permitting agency.

Step 4: Permitting agency initiates a public comment period on the draft notice of construction approval

After receiving Ecology's recommendation on the second or third tier petition, the permitting agency and the applicant must:

- provide a minimum 30-day public notice and a public comment period before approving or denying a notice of construction application involving second or third tier review;
- include the draft notice of construction approval order and Ecology's recommendation on the second or third tier petition as part of the public review documents;

- hold a public hearing to discuss the third tier petition and to answer questions from the public; and
- in consultation with Ecology, address any questions or concerns brought up during the public comment period.

Step 5: Final approval or denial of the project by the permitting agency

- If Ecology recommends approval of the project, the permitting agency may approve the notice of construction application.
- If Ecology recommends denial of the project, the permitting agency may not approve the project.

Second and Third Tier Review Fees

Purpose

This section explains second and third tier review fees and key process changes to applicants and consultants who submit health impact assessments under Chapter 173-460 WAC. These changes were prompted by a 2011 fee rule that changes the way Ecology collects fees and charges time for work spent reviewing health impact assessment documents.

Background

Beginning July 1, 2011, Ecology changed the fee schedule for permitting activities covered under our new source review program. These fee increases, which were authorized by the 2011 legislature, must support the cost of issuing a permit. Ecology accomplishes this by collecting an initial fee with the application that will cover a set number of review hours (base hours), depending on application type and a $95 per hour fee for the hours above base needed to complete the review and issue the permit. A notice summarizing all of the changes made by Ecology to the permitting fees regulation is available at http://www.ecy.wa.gov/biblio/1102028.html.

How the 2011 Fee Structure Affects Second and Third Tier Review

Under the 2011 fee structure, each member of Ecology's toxics review team will provide approximately 2 hours of pre-application assistance to the applicant. Time spent on pre-application assistance will not be counted toward the permit fee (not toward the initial fee or any additional fee) billed to the applicant, and will be provided in the form of one meeting between the applicant and Ecology, as well as any required advanced preparation for that meeting. Our goal in this pre-application assistance is to provide you with the majority of the information you need to prepare your health impact assessment protocol for submission to Ecology.

Once Ecology has provided information in the meeting, we will still be available to offer limited guidance to you as you prepare your protocol; however, the next step is for you to submit a health impact assessment (HIA) protocol along with the initial review fee of $10,000. The fee must be submitted with the protocol to Ecology's fiscal office before Ecology will review or approve the HIA protocol.

The HIA protocol must be accompanied by a completed application for second or third tier review. The application form includes the Health Impact Assessment Checklist and is available at http://www.ecy.wa.gov/biblio/ecy070415.html.

Alternate Method for Continuing Discussions with Ecology

It is our goal that you know how to proceed to develop the HIA by the end of the pre-application meeting. If you think your project needs more than a 2-hour meeting with Ecology, you have three choices:

- Submit the Application for Second Tier Review or Third Tier Review along with your $10,000 check. Ecology will meet with you to help you prepare your HIA and we will track our time against your initial fee.
- Enter into a contract with Ecology for additional upfront work. The rate is $95 per hour. We charge the same rate for working on your project under either option.
- Request Ecology stop working on the project once the 2 hours of "free" (included in the initial review fee) pre-application assistance are used up.

The Initial Fee You Submit May Not Cover the Cost of Processing Your Petition

The $10,000 initial fee you submit covers up to 106 hours of Ecology's review time. Ecology will track the number of hours spent on your project and will notify you when we approach the 106 hours covered by the initial fee. If the total number of review hours exceeds 106 hours, Ecology will bill you $95 per hour for each additional hour worked. We will bill you at the end of the process just before we issue a final decision. You must pay the bill before Ecology will issue a decision on your petition.

Public Hearing

The applicant is responsible for costs associated with a public hearing, if one is held. This includes staff time to prepare for the public hearing, travel time to and from the public hearing, time spent conducting the public hearing, time spent responding to public comments, and publications costs for a newspaper notice.

Changes to HIA Review Procedure

Ecology's goal is to complete our review of the HIA in a timely manner so that applicants are not charged additional hourly charges. To accomplish this goal, Ecology has changed the way we review the health impact assessment. The primary changes to our review procedure include:

- Ecology will provide the minimum amount of pre-application assistance necessary to advise the applicant of the demonstrations and submittals necessary to meet permitting requirements (one meeting lasting about 2 hours).

- Ecology will review the HIA protocol after the applicant submits the $10,000 initial fee with the HIA protocol and complete second or third tier application. The HIA protocol review process can be one of continuous improvement, until an acceptable HIA protocol has been prepared.

- Based on the approved HIA protocol, the applicant will prepare and submit an HIA document for review by Ecology.
- Ecology will provide substantive and non-substantive comments on the HIA document and will request the applicant revise the HIA document, as necessary. This process can be one of continuous improvement, until an acceptable final HIA document has been prepared by the applicant. Ecology's project engineer or delegate will review portions of the HIA that involve the project's engineering specifications. Likewise, Ecology's meteorological modeler will review portions of the HIA that involve toxic air pollutant (TAP) concentration modeling. Following confirmations by the engineer and modeler, Ecology's project toxicologist will review risk assessment portions of the HIA. The toxicologist will then communicate to all parties the results of their review of the HIA.
- Once an acceptable HIA document has been prepared, Ecology will prepare a brief staff report which summarizes Ecology's review of the HIA and includes a recommendation(s) to the local permitting authority regarding the petition.
- Ecology will post the applicant's final HIA document and Ecology's staff report and cover letter on Ecology's air toxics review web page.

Who to Contact for More Information

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Exhibit D

EPA/630/R-03/003F
March 2005

Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens

Risk Assessment Forum
U.S. Environmental Protection Agency
Washington, DC 20460

TR 4605

REC 6270

DISCLAIMER

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PREFACE

U.S. Environmental Protection Agency (EPA or the Agency) cancer risk assessments may be conducted differently than envisioned in this Supplemental Guidance for many reasons including, for example, new information, new scientific understanding, or different science policy judgment. The practice of risk assessment with respect to accounting for early-life exposures to toxicants continues to develop, and specific components of this Supplemental Guidance may become outdated or may otherwise require modification in individual settings. It is EPA's intent to use, to the extent practicable and consistent with Agency statutes and regulations, the best available science in its risk assessments and regulatory actions, and this Supplemental Guidance is not intended to provide any substantive or procedural obstacle in achieving that goal. Therefore, the Supplemental Guidance has no binding effect on EPA or on any regulated entity. Where EPA does use the approaches in the Supplemental Guidance in developing risk assessments, it will be because EPA has decided in the context of that risk assessment that the approaches from the Supplemental Guidance are suitable and appropriate. This judgment will be tested through peer review, and the risk assessment will be modified to use different approaches if appropriate.

This Supplemental Guidance is intended for guidance only. It does not establish any substantive "rules" under the Administrative Procedure Act or any other law and has no binding effect on EPA or any regulated entity, but instead represents a non-binding statement of policy.

The Supplemental Guidance addresses a number of issues pertaining to cancer risks associated with early-life exposures generally, but provides specific guidance on potency adjustment only for carcinogens acting through a mutagenic mode of action. This guidance recommends for such chemicals, a default approach using estimates from chronic studies (i.e., cancer slope factors) with appropriate modifications to address the potential for differential risk of early-lifestage exposure. Default adjustment factors are meant to be used only when no chemical-specific data are available to assess directly cancer susceptibility from early-life exposure to a carcinogen acting through a mutagenic mode of action.

The Agency considered both the advantages and disadvantages of extending the recommended, age dependent adjustment factors for carcinogenic potency to carcinogenic agents for which the mode of action remains unknown. EPA recommends these factors only for carcinogens acting through a mutagenic mode of action based on a combination of analysis of available data and long-standing science policy positions that set out the Agency's overall approach to carcinogen risk assessment, e.g., the use of a linear, no threshold extrapolation procedure in the absence of data in order to be health protective. In general, the Agency prefers

to rely on analyses of data rather than on general defaults. When data are available for a susceptible lifestage, they should be used directly to evaluate risks for that chemical and that lifestage on a case-by-case basis. In the case of nonmutagenic carcinogens, when the mode of action is unknown, the data were judged by EPA to be too limited and the modes of action too diverse to use this as a category for which a general default adjustment factor approach can be applied. In this situation per the Agency's *Guidelines for Carcinogen Risk Assessment*, a linear low-dose extrapolation methodology is recommended. It is the Agency's long-standing science policy position that use of the linear low-dose extrapolation approach (without further adjustment) provides adequate public health conservatism in the absence of chemical-specific data indicating differential early-life susceptibility or when the mode of action is not mutagenicity.

The Agency expects to produce additional supplemental guidance for other modes of action, as data from new research and toxicity testing indicate it is warranted. EPA intends to focus its research, and to work collaboratively with its federal partners, to improve understanding of the implications of early life exposure to carcinogens. Development of guidance for estrogenic agents and chemicals acting through other processes resulting in endocrine disruption and subsequent carcinogenesis, for example, might be a reasonable priority in light of the human experience with diethylstilbesterol and the existing early-life animal studies. It is worth noting that each mode of action for endocrine disruption will probably require separate analysis.

As the Agency examines additional carcinogenic agents, the age groupings may differ from those recommended for assessing cancer risks from early-life exposure to chemicals with a mutagenic mode of action. Puberty and its associated biological changes, for example, involve many biological processes that could lead to changes in susceptibility to the effects of some carcinogens, depending on their mode of action. The Agency is interested in identifying lifestages that may be particularly sensitive or refractory for carcinogenesis, and believes that the mode of action framework described in the Agency's *Guidelines for Carcinogen Risk Assessment* is an appropriate mechanism for elucidating these lifestages. For each additional mode of action evaluated, the various age groupings determined to be at differential risk may differ from those described in this Supplemental Guidance. For example, the age groupings selected for the age-dependent adjustments were initially selected based on the available data, i.e., for the laboratory animal age range representative of birth to < 2 years in humans. More limited data and information on human biology are being used to determine a science-informed policy regarding 2 to < 16 years. Data were not available to refine the latter age group. If more data become available regarding carcinogens with a mutagenic mode of action, consideration may be given to further refinement of these age groups.

Access to data and other information relating to the Cancer Guidelines (U.S. EPA, 2005) and this Supplemental Guidance will be through EPA's Risk Assessment Forum website, under Publications, Guidelines, Guidelines for Cancer Risk Assessment. The URL is http://www.epa.gov/cancerguidelines. The data and results of analyses are available in spreadsheets.

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1. INTRODUCTION

Cancer risk to children in the context of the U.S. Environmental Protection Agency's cancer guidelines (U.S. EPA, 2005) includes both early-life exposures that may result in the occurrence of cancer during childhood and early-life exposures that may contribute to cancers later in life. The National Research Council (NRC, 1994) recommended that "EPA should assess risks to infants and children whenever it appears that their risks might be greater than those of adults." This document focuses on cancer risks from early-life exposure compared with those from exposures occurring later in life. Evaluating childhood cancer and childhood exposures resulting in cancer later in life are related, but separable, issues.

Historically, the focus on cancer has been as a disease associated with aging, resulting from extended exposure duration with prolonged latency periods before the cancers appear. Because much of cancer epidemiology addresses occupational exposures and because rodent cancer studies are designed to last approximately a lifetime (two years) beginning after sexual maturity, the cancer database used by EPA and other agencies for risk assessment focuses on adults. However, extensive literature demonstrates that exposures early in life (i.e., transplacental or *in utero*, early postnatal, lactational) in animals can result in the development of cancer (reviewed in Toth, 1968; Della Porta and Terracini, 1969; Druckery, 1973; Rice, 1979; Vesselinovitch et al., 1979; Rice and Ward, 1982; Vesselovitch et al., 1983; Anderson et al., 2000). Thus, one element in extending analyses to children is to evaluate the extent to which exposures early in life would alter the incidence of cancers observed later in life, compared with the incidence observed with adult-only exposures (Anderson et al., 2000; NRC, 1993).

The causes of cancer encompass a variety of possible risk factors, including genetic predisposition (Tomlinson et al., 1997), diet, lifestyle, associations with congenital malformations (Bosland, 1996), and exposure to biological and physical agents and chemicals in the environment. In some cases, tumors in adults and children have been compared (Anderson et al., 2000; Ginsberg et al., 2002). Children and adults generally develop the same spectrum of tumors when they have inherited gene and chromosomal mutations, such as Li-Fraumeni syndrome (Birch et al., 1998). With ionizing radiation, which operates through a mutagenic mode of action, both the young and the old develop many of the same tumors, with the difference being that children are more susceptible for a number of tumor types (NRC, 1990; U.S. EPA, 1994; UNSCEAR, 2000). Studies with anticancer drugs (cytotoxic and immunosuppressive) demonstrate a similar spectrum of tumors (Hale et al., 1999; Kushner et al., 1998; Larson et al., 1996; Nyandoto et al., 1998). Various viral infections, such as Epstein Barr and hepatitis B, lead to lymphoma and liver cancer, respectively, in both age groups (Lindahl et

al., 1974; Mahoney, 1999). These observations in humans indicate that the mode of action for these agents would be the same or similar for adults and children.

Although there are similarities between childhood and adult tumors, significant differences are also known to exist (Grufferman, 1998; Israel, 1995). Tumors of childhood generally consist more of embryonic cell tumors, while adults have more carcinomas. Leukemias, brain and other nervous system tumors, lymphomas (lymph node cancers), bone cancers, soft tissue sarcomas, kidney cancers, eye cancers, and adrenal gland cancers are the most common cancers of children, while skin, prostate, breast, lung, and colorectal cancers are the most common in adults (Ries et al., 1999; U. S. Cancer Statistics Working Group, 2002). Some tumors are unique to the young, including several with well established genetic bases, such as tumors of the kidney (Wilms' tumor) or eye (retinoblastoma) (Anderson et al., 2000; Israel, 1995).

The relative rarity in the incidence of childhood cancers and a lack of animal testing guidelines with perinatal[1] exposure impede a full assessment of children's cancer risks from exposure to chemicals in the environment. Unequivocal evidence of childhood cancer in humans occurring from chemical exposures is limited (Anderson et al., 2000). Established risk factors for the development of childhood cancer include radiation and certain pharmaceutical agents used in chemotherapy (Reise, 1999). There is some evidence in humans for adult tumors resulting from perinatal exposure. Pharmacological use of diethylstilbesterol (DES) during pregnancy to prevent miscarriages induced clear cell adenocarcinoma of the vagina in a few daughters exposed *in utero* though this tumor was not observed in exposed mothers (Hatch et al., 1998; Robboy et al., 1984; Vessey, 1989). In addition to the limited human data, there are examples of transplacental carcinogens in animal studies, such as recent studies with nickel and arsenic (Diwan et al., 1992; Waalkes et al., 2003), as well as studies suggesting that altered development can affect later susceptibility[2] to cancer induced by exposure to other chemicals (Anderson et al., 2000; Birnbaum and Fenton, 2003).

Infrequently, perinatal exposure in animals has been shown to induce tumors of different types than those observed with adult exposures. Studies with saccharin (Cohen et al., 1995; Whysner and Williams, 1996; IARC, 1999) and ascorbate (Cohen et al., 1998; Cohen et al., 1995; NTP, 1983) found cancer when exposures were initiated in the perinatal period. In

[1] Perinatal is defined as the time around birth and may include both prenatal (prior to birth) and postnatal (after birth) periods.

[2] Susceptibility is defined here as an increased likelihood of an adverse effect, often discussed in terms of relationship to a factor that can be used to describe a human subpopulation (e.g., lifestage, demographic feature, or genetic characteristic). The terms "susceptibility" and "sensitivity" are used with a variety of definitions in published literature making it essential that readers are aware of these differences in terminology across documents.

contrast, studies submitted to the Food and Drug Administration of approximately a dozen other food additives and colorings that were not adult carcinogens did not indicate cancer, even when perinatal exposures occurred (U.S. EPA, 1996). When observed, the differences between childhood and adult cancers suggest the importance of evaluating the impacts of maternal exposures during pregnancy as well as exposures to children (Anderson et al., 2000). The effects of maternal exposures and transplacental carcinogens require separate evaluation and are not quantitatively evaluated in the analysis presented below.

The limited human information described briefly above is supported by a number of animal bioassays that include both perinatal and adult exposures to chemicals. Standard animal bioassays generally begin dosing after the animals are 6-8 weeks old, when many organs and systems are almost fully developed, though substantial growth in body size continues thereafter (as more fully discussed in Hattis et al., 2005). The literature can be divided roughly into three types of exposure scenarios: those that include *repeated* exposures for the early postnatal to juvenile period, as compared with chronic later-life dosing; *lifetime* (i.e., combined perinatal and adult) exposure as compared with chronic later-life dosing; and those that include more *acute* exposures, such as a single intraperitoneal (ip) or subcutaneous injection, for both early-life and later-life dosing. In the early-life exposure studies that are available, perinatal exposure usually induces higher incidence of tumors later in life than the incidence seen in standard bioassays where adult animals only were exposed; some examples include diethylnitrosamine (DEN) (Peto et al., 1984), benzidine (Vesselinovitch et al., 1979), DDT (Vesselinovitch et al., 1979), and polybrominated biphenyls (PCBs) (Chhabra et al., 1993a). Reviews comparing early-life carcinogenesis bioassays with standard bioassays for a limited number of chemicals (McConnell, 1992; Miller et al., 2002; U.S. EPA, 1996) have concluded:

- The same tumor sites usually are observed following either perinatal or adult exposure.
- Perinatal exposure in conjunction with adult exposure usually increases the incidence of tumor bearing animals or reduces the latent period before tumors are observed.

There is limited evidence to inform the mode(s) of action leading to differences in tumor type and tumor incidence following early-life exposure and exposure later in life. Differences in the capacity to metabolize and clear chemicals at different ages can result in larger or smaller internal doses of the active agent(s), either increasing or decreasing risk (Ginsberg et al., 2002; Renwick, 1998). There is reason to surmise that some chemicals with a mutagenic mode of action, which would be expected to cause irreversible changes to DNA, would exhibit a greater effect in early-life versus later-life exposure. Several studies have shown increased susceptibility

of weanling animals to the formation of DNA adducts following exposure to vinyl chloride (Laib et al., 1989; Morinello et al., 2002a; Morinello et al., 2002b). Additionally, even though not used quantitatively in the analyses in this document, a recent analysis of *in vivo* transplacental micronucleus assays indicated that fetal tissues generally are more sensitive than maternal tissues for induction of micronuclei from mutagenic chemicals (Hayashi et al., 2000), providing qualitative support for the early-life susceptibility. Similarly, the neonatal mouse model for carcinogenesis, which uses two doses prior to weaning followed by observation of tumors at one year, shows carcinogenic responses for mutagenic agents (Flammang et al., 1997; McClain et al., 2001). These results are consistent with the current understanding of biological processes involved in carcinogenesis, which leads to a reasonable expectation that children can be more susceptible to carcinogenic agents than adults (Anderson et al., 2000; Birnbaum and Fenton, 2003; Ginsberg, 2003; Miller et al., 2002; Scheuplein et al., 2002). Some aspects potentially leading to childhood susceptibility include the following issues.

- More frequent cell division during development can result in enhanced fixation of mutations due to the reduced time available for repair of DNA lesions and clonal expansion of mutant cells gives a larger population of mutants (Slikker et al, 2004).
- Some embryonic cells, such as brain cells, lack key DNA repair enzymes.
- Some components of the immune system are not fully functional during development (Holladay and Smialowicz, 2000; Holsapple et al., 2003).
- Hormonal systems operate at different levels during different lifestages (Anderson et al., 2000).
- Induction of developmental abnormalities can result in a predisposition to carcinogenic effects later in life (Anderson et al., 2000; Birnbaum and Fenton, 2003; Fenton and Davis, 2002).

The methodology that has been generally used by the U.S. EPA to estimate cancer risk associated with oral exposures relies on estimation of the lifetime average daily dose, which can account for differences between adults and children with respect to exposure factors such as eating habits and body weight. However, susceptibility differences with respect to early lifestages are not taken into consideration because cancer slope factors[3] are based upon effects

[3] Cancer slope factor – An upper bound estimate of the increased cancer risk from a lifetime exposure to an agent. This estimate, usually expressed in units of proportion (of a population) affected per unit exposure (e.g., mg/kg-day or ug/m^3), is generally reserved for use in the low-dose region of the dose-response relationship. It is often the statistical upper bound on the potency and therefore the risk. "Upper bound" in this context is a plausible

observed following exposures to adult humans or sexually mature animals. Since a much larger database exists for chemicals inducing cancer in adult humans or sexually mature animals, it is necessary to determine whether adjustment of such adult-based cancer slope factors would be appropriate when assessing cancer risks associated with exposures early in life. The analysis undertaken here addresses this issue, focusing upon studies that define the potential duration and degree of increased susceptibility that may arise from childhood, defined as early-life (typically postnatal and juvenile animal) exposures. Some of these analyses, along with a more complete description of the procedures used, have been published (Barton et al., 2005). The analysis presented in this Supplemental Guidance and in the published article form the basis for developing Supplemental Guidance for evaluating cancer susceptibility associated with early-life exposures.

upper limit to the true probability.

2. PROCEDURES

This section describes the steps taken to assess potential susceptibility to early-life exposure to carcinogenic compounds compared with adult and whole-life exposure. The readily available literature was reviewed to identify animal studies that compared tumor incidence between early-life and adult-only exposures or between early-life-and-adult and adult-only exposures. Studies were categorized by length of exposure; those studies with quantitative information to estimate tumor incidence over time for early-life and adult exposures were identified. These studies provided the basis for quantitatively estimating the difference in susceptibility between early-life and adult exposures, as described below. Finally, summaries of available human data for radiation exposure were reviewed in the context of tumor incidence from early-life versus later-in-life exposure.

2.1. DATA SOURCES FOR ANIMAL STUDIES

Studies in the literature included in this analysis are those that report tumor response from experiments that included both early-life and adult exposure as separate experimental groups. Initial studies for consideration were identified through review articles and a search of the National Toxicology Program (NTP) database. Reviews of the literature regarding cancer susceptibility from early-life exposure in animals include McConnell (1992), Ginsberg (2003), Anderson et al. (2000), Miller et al. (2002) and U.S. EPA (1996). A literature search was conducted utilizing key words and MeSH headings (Medline) from studies identified in the available reviews. The list of chemicals included in this analysis for quantitative evaluation is shown in Table 1a and 1b.

Abstracts or papers were reviewed to determine if a study provided information that could be used for quantitative analysis. The criteria used to decide if a study could be included in the quantitative analysis were:

- Exposure groups at different post-natal ages in the same study or same laboratory, if not concurrent (to control for a large number of potential cross-laboratory experimental variables including pathological examinations),

- Same strain/species (to eliminate strain-specific responses confounding age-dependent responses),

- Approximately the same dose within the limits of diets and drinking water intakes that obviously can vary with age (to eliminate dose-dependent responses confounding age-dependent responses),

- Similar latency period following exposures of different ages (to control for confounding latency period for tumor expression with age-dependent responses), arising from sacrifice at >1 year for all groups exposed at different ages, where early-life exposure can occur up to about 7 weeks. Variations of around 10 to 20% in latency period are acceptable,

- Postnatal exposure for juvenile rats and mice at ages younger than the standard 6 to 8 week start for bioassays; prenatal (*in utero*) exposures are not part of the current analysis. Studies that have postnatal exposure were included (without adjustment) even if they also involved prenatal exposure,

- "Adult" rats and mice exposure beginning at approximately 6 to 8 weeks old or older, i.e. comparable to the age at initiation of a standard cancer bioassay (McConnell, 1992). Studies with animals only at young ages do not provide appropriate comparisons to evaluate age-dependency of response (e.g., the many neonatal mouse cancer studies). Studies in other species were used a supporting evidence, because they are relatively rare and the determination of the appropriate comparison ages across species is not simple, and

- Number of affected animals and total number of animals examined are available or reasonably reconstructed for control, young, and adult groups (i.e., studies reporting only percent response or not including a control group would be excluded unless a reasonable estimate of historical background for the strain was obtainable).

Tables 2 and 3 include information on the methods and results from the animal studies identified in Table 1b. Pertinent information on species, sex, dosing regimen, and tumor incidence is given. Additionally, the "Notes" column includes general information about the relationship between tumor incidence, animal age at first dosing, and sex. The data in Tables 2 and 3 were used for the calculations, described below, for estimating potentially increased cancer risk from early-life exposure.

The available literature includes a wide range of exposure scenarios. This range is due in part to the lack of a defined protocol for early-life testing and the difficulty of standardizing and administering doses preweaning. As noted previously, the literature can be divided roughly into three types of exposure scenarios: those that include repeated exposures for the early postnatal to juvenile period, as compared with chronic later-life dosing; lifetime (i.e., combined perinatal and adult) exposure as compared with chronic later-life dosing; and those that include more acute exposures, such as a single intraperitoneal (ip) or subcutaneous injection, for both early-life and later-life dosing. Table 2 includes the studies that had early postnatal to juvenile exposures, adult chronic exposures, and lifetime exposures. Table 3 includes studies with acute exposures. A discussion of the implications of the different exposure scenarios is included in Section 3.

Studies were identified for more than 50 chemicals not included in Tables 2 and 3 that demonstrated carcinogenesis following perinatal exposure, but did not directly compare exposures at different ages. A large number of studies address *in utero* exposures only. More than 100 chemicals (with both negative and positive findings) have been studied in the neonatal mouse assay, but this assay does not have a comparable adult exposure (Flammang et al., 1997; McClain et al., 2001; Fujii, 1991). Studies across laboratories often varied in their use of animal strains (e.g., for AZT studies, Diwan et al., 1999 used CD-1 mice, while NTP, 1999 used $B6C3F_1$ mice). Studies of tamoxifen use two Wistar-derived strains and had very different periods for tumor expression, i.e., sacrifice at 20 months for adult-exposed rats and natural death up to 35 months for juvenile-exposed rats, with uterine tumors observed in animals dying after 22 months (Carthew et al., 2000; Carthew et al., 1996; Carthew et al., 1995). Due to these factors, the chemicals that belong to this group were not evaluated quantitatively. In addition, there were studies assessing radiation in animals (Covelli et al., 1984; Di et al., 1990; Sasaki et al., 1978). The radiation data were not analyzed in depth, in part because there are recognized differences in toxicokinetics and toxicodynamics between radiation and chemicals with a mutagenic mode of action for carcinogenesis. Even though the data on A-bomb survivors provide information for many different cancer sites in humans with a single exposure involving all ages, a number of national and international committees of experts have analyzed and modeled these data to develop risk estimates for various specific applications. Furthermore, lack of uniformity regarding radiation doses, gestational age at exposure, and the animal strains used make it difficult to make comparisons across studies (Preston et al., 2000).

2.2. EVALUATING THE MODE OF ACTION OF CARCINOGENS

Evaluation of the mode of action of a carcinogen was based upon a weight-of-evidence approach. Multiple modes of action are associated with the chemicals in this database, but a number are associated with mutagenicity (i.e., benzo(a)pyrene, benzidine, dibenzanthracene, diethylnitrosamine, dimethylbenz(a)anthracene, dimethylnitrosamine, ethylnitrosourea, 3-methylcholanthrene, methylnitrosourea, safrole, urethane, and vinyl chloride). Determination of carcinogens that are operating by a mutagenic mode of action entails evaluation of short-term testing results for genetic endpoints, metabolic profiles, physicochemical properties, and structure-activity relationship (SAR) analyses in a weight-of-evidence approach (Dearfield et al., 1991; U.S. EPA, 1986, 1991; Waters et al., 1999), as has been done for several chemicals (e.g., Dearfield et al., 1999; McCarroll et al., 2002; U.S. EPA, 2000a). Key data for a mutagenic mode of action may be evidence that the carcinogen or a metabolite is DNA reactive and/or has the ability to bind to DNA. Also, such carcinogens usually produce positive effects in multiple test

systems for different genetic endpoints, particularly gene mutations and structural chromosome aberrations, and in tests performed *in vivo* which generally are supported by positive tests *in vitro*. Additionally, carcinogens may be identified as operating via a mutagenic mode of action if they have similar properties and SAR to established mutagenic mode of action.

2.3. QUANTITATIVE METHODS

To estimate the potential difference in susceptibility between early-life and adult exposure, we calculated the estimated ratio of the cancer potency from early-life exposure compared to the estimated cancer potency from adult exposure. The cancer potency was estimated from a one-hit model, or a restricted form of the Weibull model, which is commonly used to estimate cumulative incidence for tumor onset. The general form of the equation is:

P(dose) = 1-[1-P(0)]exp(-cancer potency*dose)

The ratio of juvenile to adult cancer potencies were calculated by fitting this model to the data for each age group. The model fit depended upon the design of the experiment that generated the data. Two designs should be handled separately: experiments in which animals are exposed either as juveniles or as adults (with either a single or multiple dose in each period), and experiments in which exposure begins either in the juvenile or in the adult period, but once begun, continues through life.

For the first case, the model equations are:

$$P_A = P_0 + (1 - P_0)(1 - e^{-m_A \delta_A}) \qquad (1)$$
$$P_J = P_0 + (1 - P_0)\left(1 - e^{-m_A e^{\lambda} \delta_J}\right)$$

where:

subscripts A and J refer to the adult and juvenile period, respectively,
λ is the natural logarithm of the juvenile:adult cancer potency ratio,
P_0 is the fraction of control animals with the particular tumor type being modeled,
P_x is the fraction of animals exposed in age period x with the tumor,
m_A is the rate of accumulation of "hits" per unit of time for adults, i.e., the cancer potency, and
δ_x is the duration or number of exposures during age period x.

For a substantial number of data sets (acute exposures), $\delta_J = \delta_A = 1$. We are interested in

determining λ, which is the logarithm of the estimated ratio of juvenile to adult cancer potencies, a measure of potential susceptibility for early-life exposure.

For the second kind of design, the model equations should take into account that exposures that were initiated in the juvenile period continue through the adult period. The model equations for the fraction of animals exposed only as adults with tumors in this design are the same as in the first design, but the fraction of animals whose first exposure occurred in the juvenile period is:

$$P_J = P_0 + (1 + P_0)\left(1 - e^{-m_A e^{\lambda}(\delta_J - \delta_A) - m_A \delta_A}\right) \quad (2)$$

All symbols in (eq. 2) have the same interpretation as their counterparts in (eq. 1), but now δ_J includes the duration of exposure during the juvenile period as well as the subsequent adult period.

Parameters in these models were estimated using Bayesian methods (see, for example, Carlin and Louis, 2000), and all inferences about the ratios were based on the marginal posterior distribution of λ. Some of these analyses, including a more complete description of the procedures (including the potential effect of alternative Bayesian priors that have been examined) have been published (Barton et al., 2005). The data for estimating each ratio were in the form of numbers of animals tested and number affected for each of control, juvenile-exposed, and adult-exposed animals, and duration of exposure for each of the juvenile-exposed and adult-exposed groups. A few data sets had separate control groups for the juvenile-exposed and adult-exposed groups, and equations 1 and 2 were modified accordingly. The likelihood for the parameters in the model was the product of three (or four, if there were two control groups) binomial probabilities: for the number of animals with tumors in the control group(s), for the juvenile-exposed group, and for the adult-exposed group. The prior for P_0 (the fraction of control animals with a particular tumor) was right triangular (right angle at the origin), based on the assumption that control incidences should be relatively low. (The base of the distribution is one, as P_0 can not exceed one. As this is a probability distribution, the area of the triangle is one. Therefore, its height at the origin must be 2.) The effect of exposure in adults is quantified by the extra risk, Q, where the probability that an animal has a tumor is $P_0 + (1 - P_0)Q$. So, from equations 1, $Q = 1 - e^{-m_A \delta_A}$, Q was given a uniform prior on the interval (0,1), reflecting total ignorance about the extra risk of adult exposure. Finally, the prior for λ was Gaussian with mean 0 (corresponding to a median or geometric mean ratio of one) and standard deviation 3. The prior for the log ratio of juvenile to adult cancer potency has some influence over the posterior estimates for the ratio of juvenile to adult potency. The magnitude of that influence depends on

the amount of support in the data for different values of the log ratio. The prior also effectively downweights extremely large or small values for the juvenile to adult potency ratio. Three priors for the standard deviation were evaluated (Barton et al., 2005, see Appendix), with the intent of finding the largest prior, i.e., one that would contain the least informative assumption for the prior. A standard deviation of 9 was tried, but some of the intervals would not converge. A standard deviation of 3 worked well, allowed ratio estimates to be derived, with all of the data of interest. An intermediate value of 6 was also examined to ascertain if a less informative prior could be used. While the intervals converged, a sensitivity analysis showed that this value for the standard deviation resulted in sufficient down-weighting of the ratios with limited information that these data would not influence the result. This was considered an unreasonable bias, so a standard deviation of 3 was used for the further analyses. A further discussion of these analyses can be found in Barton et al. (2005).

The posterior distribution for the unknown parameters in these models is the product of the likelihood from the data and the priors (the "unnormalized" prior), divided by a normalization constant that is the integral of the unnormalized prior over the ranges of all the parameters. This normalization constant was computed using numerical integration, as were posterior means and variances and marginal posterior quantiles for the log-ratio λ. All numerical computations were carried out in the R statistical programming language (version 1.8.1; R Development Core Team, 2003).

This method produced a posterior mean ratio of the early-life to adult cancer potency, which is an estimate of the potential susceptibility of early-life exposure to carcinogens. If the ratio was greater than one, this indicated that the experiment found that there was greater susceptibility from early-life exposure. If the ratio was less than one, this indicated that the experiment found that there was less susceptibility from early-life exposure. Summaries of the individual ratios from each of the dose groups from the different experiments for different groupings were also calculated (for example for all acute exposures of chemicals that are carcinogenic by a mutagenic mode of action). The summary ratios were constructed from the individual ratios within a group, by variance-weighting the means of each ratio. The individual, posterior means were weighted by using reciprocals of their posterior variance. This weighting procedure is commonly used because it gives greater weight to those studies for which the variances, i.e., the uncertainties, are smaller. Because the ratios were calculated as log ratios (see eq. 1), exponentiating the resulting inverse-variance-weighted mean yielded inverse-variance-weighted geometric means of ratios.

2.4. IONIZING RADIATION

A supporting role was assigned to the available human radiation data, where cancer incidence in adults who were children at the time of the atomic bomb (A-bomb) exposure was compared with cancer incidence in adults who were older at the time of exposure. Although there are recognized differences in toxicokinetics and toxicodynamics between radiation and chemical carcinogens with a mutagenic mode of action, the data on A-bomb survivors provide information for many different cancer sites in humans with a single exposure involving all ages. In addition to the richness of the data, a number of national and international committees of experts have analyzed and modeled these data to develop risk estimates for various specific applications.

The report of the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR, 2000, with Scientific Annexes) lists more than 80 studies, in addition to the reports of the Japanese A-bomb survivors, in which at least one type of cancer was measured in humans who were exposed either intentionally or accidentally to some form of ionizing radiation. However only the A-bomb survivor reports have relevant information on incidence of early-life exposures. One of the more recent papers cited in the UNSCEAR report, by Thompson et al. (1994), contains detailed data on the incidence of 21 different cancers in 37,270 exposed A-bomb survivors (42,702 unexposed). Also, EPA has used data from the A-bomb survivors to develop age-specific relative risk coefficients using various methods for transporting the risk from the Japanese population to the U.S. population (U.S. EPA, 1994). It is beyond the scope of this effort to present all of the radiation data or a discussion of the various analyses and modeling efforts. Rather, information relevant to comparing cancer risks from juvenile versus adult exposure from UNSCEAR (2000) and U.S. EPA (1994; 1999) is presented as representative findings to determine whether the radiation data are similar qualitatively to the chemical findings. More detailed data on the A-bomb survivors can be found in Delongchamp et al. (1997) and Preston et al. (2000).

As previously noted, several studies have assessed radiation in animal studies (Covelli et al., 1984; Di et al., 1990; Sasaki et al., 1978). However, lack of uniformity regarding radiation doses, gestational age at exposure, and the animal strains used make it difficult to compare the experimental data on cancer induction after prenatal irradiation (Preston et al., 2000).

3. RESULTS

3.1. QUALITATIVE EVALUATION OF THE DATABASE

The question addressed in this analysis was whether, and how, available quantitative scientific data could inform risk assessment policy choices for adjusting cancer slope factors when they are used in the assessment of cancer risk from childhood exposure. Cancer slope factors are, with few exceptions, based on adult human epidemiology or standard chronic adult rodent bioassays, which do not address the impacts of early-life exposures. Thus, the critical data are either human epidemiological data on childhood exposures resulting in adult cancer or research studies with rodents involving early postnatal exposures. The major human data available are from radiation exposures (studies summarized in Tables 9-11), with very limited data available for humans exposed during childhood to chemicals (reviewed in Anderson et al., 2000; Miller et al., 2002).

A review of the literature identified several hundred references reporting more than 50 chemicals that have been shown to be able to cause cancer following perinatal exposure (Table 1a) (reviewed in Toth, 1968; Della Porta and Terracini, 1969; Druckery, 1973, Rice, 1979; Vesselinovitch et al., 1979; Rice and Ward, 1982; Vesselovitch et al.; 1983; Fujii, 1991; Anderson et al., 2000). Studies (or groups of studies from a single laboratory on a given chemical) that directly provided quantitative data on carcinogenesis following early postnatal exposures and adult exposures to chemicals in animals were identified for 18 chemicals, listed in Table 1b, 2, and 3. Of the identified studies, there were 11 chemicals involving repeated exposures during early postnatal and adult lifestages (Table 1b) and 8 chemicals using acute exposures (typically single doses) at different ages (Table 1b). Some of the studies evaluated single tissues or organs for tumors (e.g., only liver), while others evaluated multiple tissues and organs (Tables 2 and 3). Mice, rats, or both species and sometimes multiple strains were tested. These studies serve as the basis for the quantitative analyses presented later in the results.

In addition to the studies identified in Table 1b, studies were identified with early postnatal and early-life exposures that were evaluated qualitatively but not quantitatively. Some of these studies are notable and provide important supporting information. Two recent studies used transgenic mouse models for human tumors. Increased multiplicity of colon tumors was observed following earlier versus later azoxymethane exposures (Paulsen et al., 2003). Shortened mammary tumor latency following estradiol exposure occurred when exposures occurred between 8 and 18 weeks as opposed to earlier or later, which is generally consistent with the incidence results analyzed for DMBA (Yang et al., 2003). Several notable examples exist of developmental windows leading to cancer susceptibilities that were not observable in

adults. Several potent estrogenic chemicals including DES, tamoxifen, and genistein produce uterine tumors with early postnatal exposures of mice, though there also appear to be strain-dependent differences in the tumor sites in adult mice (Gass et al., 1964; Greenman et al., 1990; Newbold et al., 1990, 1997, 1998, 2001). Developmental susceptibilities are believed to play a key role in effects observed with saccharin (Cohen et al., 1995; Whysner and Williams, 1996) and ascorbate (Cohen et al., 1998; NTP, 1983), with bladder tumors arising when early-life exposures occurred. Studies with several species, including rat, mouse, and opossum, indicate that nervous systems tumors associated with exposures to ENU and several other chemicals appear to be highly dependent upon exposures occurring within certain windows, particularly prenatal ones (Rice, 1979; Rice and Ward, 1982; Jurgelski et al., 1979).

Analyses of the difference in cancer risk from exposures during different lifetime periods ideally should address both the period of potential susceptibility and the magnitude of the susceptibility. Available studies used a variety of study designs (see Tables 2 and 3), which can be valuable because they provide different information (Figure 1). However, variations in study design can result in a lack of comparability across chemicals, and can limit information on the consistency of effects with different chemicals acting through different modes of action. The acute dosing (largely single dose) studies (Table 3) are valuable because they involve identical exposures with explicitly defined doses and time periods demonstrating that differential tumor incidences arise exclusively from age-dependent susceptibility. These studies address both the period and magnitude of susceptibility. They were not as appropriate for quantitative adjustments for the cancer potency estimates because of their limitations, including that most used subcutaneous or ip injection that historically have not been considered quantitatively relevant routes of environmental exposure for human cancer risk assessment by EPA, and that these routes of exposure are expected to have only partial or a complete absence of first pass metabolism that is likely to affect potency estimates.

The repeated dosing studies with exposures during early postnatal or adult lifetime provide useful information on the relative impact of repeated exposures at different lifestages and may be more likely to have exposure occur during a window of susceptibility, if there is one. One notable difference in study designs was that studies with repeated early postnatal exposure were included in the analysis even if they also involved earlier maternal and/or prenatal exposure, while studies addressing only prenatal exposure were not otherwise a part of this analysis. Another notable difference among studies involved the tissues that were evaluated for tumors: some studies focused on a single tissue, particularly liver, while others evaluated multiple tissues.

Comparisons within a single repeated dosing study may have limitations for evaluating

differential susceptibility because exposures to the chemical can differ during the different lifestages, particularly when dietary or drinking water exposures are involved. A notable example is the PCB study (Chhabra et al., 1993a), in which mobilization of such lipid-soluble chemicals into mother's milk would be expected to result in infants receiving much larger exposures than other lifestages. While lactational transfer is just as relevant to human nursing offspring, this difference in exposure obscures the extent to which the early lifestage is quantitatively more susceptible (i.e., part of the increased early-life cancer risk arises from higher exposure than during the adult period). Maternal metabolism of compounds such as diphenylhydantoin (DPH) (Chhabra et al., 1993b) also may result in lower exposure during lactation, potentially underestimating the early-lifestage risk, if the parent compound is the active form of the chemical. Similar issues exist due to normal age-dependent changes in food and water consumption. Ascribing differential effects observed in animal studies solely to lifestage susceptibility must be done carefully as there may also be differences in the exposures. There are substantial and clear benefits, therefore, from experimental consistency when comparisons are made directly within a study (e.g., same species and strain, consistent pathological evaluation).

One issue to note is the rationale for the organization of the available data. It was observed that the results across a broad range of chemicals with a variety of modes of action were somewhat variable. Therefore, consistent with the approach of the EPA cancer guidelines (U.S. EPA, 2005), an approach based on mode of action appeared to be a common framework for analysis. Variability in lifestage-dependent susceptibility and susceptibility across a range of modes of action was further supported by theoretical analyses using multistage and two-stage models of carcinogenesis (Goddard and Krewski, 1995; Murdoch et al., 1992).

3.2. QUANTITATIVE EVALUATION OF THE DATABASE

As described in the Section 2.3, the potential difference in susceptibility between early-life and adult exposure was calculated as the estimated ratio of cancer potency from early-life exposure over the cancer potency from adult exposure. Tables 4-7 present the results of the quantitative analysis using the studies that were determined qualitatively to have appropriate study designs (Tables 2 and 3) containing sufficient information to analyze. Based on the studies available, the calculations were organized into four tables: (1) compounds acting through a primarily mutagenic mode of action, where the compound was administered by a chronic dosing regimen to adults and repeated dosing in the early postnatal period (Table 4); (2) compounds acting through a primarily nonmutagenic mode of action, where the compound was administered by a chronic dosing regimen to adults and repeated dosing in the early postnatal period (Table 5);

(3) compounds acting through a primarily mutagenic mode of action, where the compounds were administered by an acute dosing regimen (Table 6); and (4) compounds acting primarily through either a mutagenic or nonmutagenic mode of action with chronic adult dosing and repeated early postnatal dosing (Table 7). In these tables, the 2.5% and 97.5% are percentiles of the posterior distribution. For a Bayesian distribution, these percentiles function in a manner similar to the 95% confidence limits for other types of statistical analyses. The results are discussed below, followed by a description of results from analyses of studies of humans exposed to radiation.

3.2.1. Carcinogens with a Mutagenic Mode of Action

The most informative database on early-lifestage susceptibility exists for chemicals with a well-accepted mutagenic mode of action (e.g., diethylnitrosamine, vinyl chloride). This database includes both single-dose studies and repeated-dose studies involving periods of postnatal and/or chronic exposure. These studies help define the periods of increased vulnerability and the magnitude of the susceptibility. The acute dosing studies demonstrate that the age-dependent responses are not due to differences in exposure, because these studies explicitly control the exposure.

3.2.1.1. *Early Postnatal, Juvenile, and Adult Repeated Dosing Studies of Chemicals with a Mutagenic Mode of Action*

Studies comparing repeated dosing for early-life, adult, or lifetime exposures exist for six carcinogens with a mutagenic mode of action [benzidine, diethylnitrosamine (DEN), 3-methylcholanthrene, safrole, urethane, and vinyl chloride]; DEN also had acute dosing studies. Lifetime (i.e., combined juvenile and adult) compared to adult exposure studies were analyzed for DEN, safrole, and urethane, while studies comparing juvenile with adult exposures were analyzed for benzidine, 3-methylcholanthrene, safrole, and vinyl chloride. These chemicals all require metabolic activation to the active carcinogenic form. Analysis of the tumors arising per unit time of exposure found that juvenile exposures with each chemical could be more effective than adult exposures were at inducing tumors (Tables 4 and 7; Figure 2, a graphic representation of the posterior, unweighted geometric means and their 95% confidence intervals, for the ratios of juvenile to adult cancer potency for carcinogens acting through a mutagenic mode of action). The weighted geometric mean for repeat and lifetime exposures is 10.4; for acute exposures the weighted geometric mean value is 1.5. For benzidine and safrole, there was a notable sex difference, with high liver tumor incidence observed for early postnatal exposures of male, but not female, mice. For both the acute and the repeated/lifetime data, the 95th percentile of the individual, unweighted geometric means is above 10 (Figure 2).

This analysis focused upon the duration of exposure as a surrogate for dose, essentially assuming that the doses animals received during the different periods of these studies were similar. This assumption is a limitation of the analysis because these studies involved exposures via lactation (i.e., dosing the mother prior to weaning), drinking water, diet, or inhalation, which have the potential to deliver different doses at different lifestages. However, the range of the magnitudes of the tumor incidence ratios of juvenile to adult exposures is similar (Table 8) for the repeated dosing studies (0.12 – 111, weighted geometric mean 10.5, 42% of ratios greater than 1), lifetime dosing studies (0.18 – 79, weighted geometric mean 8.7, 67% of ratios greater than 1), and acute dosing studies (0.01 – 178, weighted geometric mean 1.5, 55% of ratios greater than 1), suggesting that these differences in dosing are not the sole determinant of the increased incidence of early tumors, i.e., uncertainty and variability remain. Because these comparisons include different chemicals with different tissue specificities, it may be informative to consider liver as a target organ affected by all of these chemicals. The range of the magnitudes of the liver tumor incidence ratios of juvenile to adult exposures is similar for the repeated dosing studies (0.12 – 111, weighted geometric mean 41.8, 86% of ratios greater than 1, Table 4), lifetime dosing studies (0.47 – 79, weighted geometric mean 14.9, 80% of ratios greater than 1, Table 7), and acute dosing studies (0.1 – 40, weighted geometric mean 8.1, 77% of ratios greater than 1, Table 8). Thus, the repeated dose studies support the concept that early-lifestage exposure to carcinogenic chemicals with a mutagenic mode of action would lead to an increased tumor incidence compared with adult exposures of a similar duration and dose.

3.2.1.2. *Acute Dosing Studies of Chemicals with a Mutagenic Mode of Action*

Acute dosing studies are available for eight carcinogens with a mutagenic mode of action that were administered to mice or rats [benzo[a]pyrene (BaP), dibenzanthracene (DBA), Diethylnitrosamine (DEN), dimethylbenzanthracene (DMBA), dimethylnitrosamine (DMN), ethylnitrosourea (ENU), methylnitrosourea (NMU), and urethane (also known as ethyl carbamate)] (Table 1b). Except for ENU and NMU, these compounds require metabolic activation to their active carcinogenic forms. These acute dosing studies generally compared a single exposure during the first few weeks of life with the identical or similar exposure in young adult animals (Tables 3 and 6). Many of these studies compared exposures during the preweaning period (i.e., approximately day 21 for rats and mice) with effects around week 6, which is approximately the age at which typical chronic bioassays begin dosing animals. These studies largely were by subcutaneous or ip injection, which historically have not been considered quantitatively relevant routes of environmental exposure for human cancer risk assessment by EPA. For purposes of comparing age-dependent susceptibilities to tumor development, these

data are highly relevant. The injection route typically alters the pharmacokinetic time courses of the parent compound and the metabolites compared with oral or other exposures due to altered kinetics of absorption and metabolism. However, for these compounds and the systemic organ effects observed, there are several pharmacokinetic reasons to believe that the age-dependent trends would be similar with other routes of exposure. These compounds are expected to be reasonably well absorbed orally, comparable with injection routes, and largely require metabolic activation, so partial or complete absence of first pass metabolism in the injection studies would be similar to or underestimate metabolic activation when compared with oral exposure.

The early exposures often resulted in higher incidence of tumors than later exposures, with increased early susceptibilities up to 178-fold (unweighted ratios in Table 6 range from 0.011 to 178, with a weighted geometric mean of 1.5, and 55% of ratios greater than 1, Figure 2, Table 8). Examples of the general age-dependent decline in susceptibility of tumor response include BaP (liver tumors), DEN (liver tumors), ENU (liver and nervous system tumors), and urethane (liver and lung tumors). While generally the Day 1 and Day 15 time points were higher than later time points, in several cases similar tumor incidence was observed at both these early times (e.g., ENU-induced kidney tumors, Tables 6 and 8).

While the degree of susceptibility generally declines during the early postnatal period through puberty into early adulthood, there are exceptions due perhaps to pubertal periods of tissue development (e.g., mammary tissues) or very early development of xenobiotic metabolizing enzymes. One such exception was the increased incidence of mammary tumors in 5-8 week old rats given DMBA, compared with older or younger rats (Meranze et al., 1969; Russo et al., 1979). Meranze et al. (1969) reported 8% mammary tumors following a single dose of DMBA at less than two weeks, 56% if given once to animals between 5 and 8 weeks old, and 15% when given once to 26 week old rats. Thus, a ratio of 7.1 is obtained when comparing susceptibilities of 5–8 week and 26-week-old rats (Table 6) compared to a ratio of 0.2 when comparing the exposure at 2 weeks versus 26 weeks. A similar effect was observed by Russo et al. (1979); see Table 3. This observation corresponds well with pubertal development of the mammary tissue, with ovarian function commencing between 3 and 4 weeks (after the < 2 week time point in the Meranze et al., 1969 study), and mammary ductal growth and branching occurring such that it is approximately two-thirds complete by week 5, consistent with the 5–8 week susceptible period of Meranze et al. (Silberstein, 2001). While this differs from the general trend previously discussed, it indicates susceptibility later in the juvenile period rather than earlier. Another example of deviation from the general trend toward an age-dependent decline is DEN-induced lung tumors that were somewhat lower in incidence following exposure on day 1 than observed for the day 15 or day 42 exposures (Vesselinovitch et al., 1975) (Tables 3 and 6).

There are substantial differences in the early-life susceptibility of different tissues observed in the acute studies (Table 8). It should be noted that the target tissues vary with chemical, so the number of chemicals for which data are available varies for each tissue. Several tissues have weighted geometric mean ratios of greater than 1 including kidney, leukemia, liver, lymph, mammary, nerve, reticular tissue, thymic lymphoma, and uterus/vagina. Some of these, such as the nerve and mammary tumors, appear to have a very specific window of susceptibility, as noted above, and the ratios were much higher if the exposure occurred during this window. Tissues with weighted mean ratios less than 1 include forestomach, harderian gland, ovaries, and thyroid. Lung has a weighted geometric mean of 1. Many of the studies produced very high lung tumor responses regardless of age, so the results are difficult to interpret, as illustrated by the dose-response data with urethane in Rogers (1951) in which the increased early susceptibility is only apparent when the dose is low. The large numbers of studies with high lung tumor responses at all ages contribute to the differences in the weighted geometric means for the acute and for the repeated dosing studies.

Overall, the acute dosing studies support the concept that early-lifestage exposure to carcinogenic chemicals with a mutagenic mode of action would lead to an increased incidence of tumors compared with adult exposures of a similar dose and duration. These studies generally use the same dose and duration at all ages, and thus do not have the type of issues discussed for the repeated dosing studies. On the other hand, the acute dosing studies have limitations that were sufficient to decide that they should not be included in the quantitative adjustment of cancer potency. First, as mentioned in the previous paragraph, the large number of studies of lung tumors with almost 100% response observed at all doses and all ages would significantly bias the median ratio toward unity for a reason based on study design rather than biology. Second, cancer potency estimates are usually derived from chronic exposures. Therefore, any adjustment to those potencies should be, if possible, from similar exposures. Third, most exposures of concern to the Agency are from repeated or chronic exposures rather than acute exposures. Finally, many of the acute studies used ip exposures, which is not the usual route of exposure for environmental chemicals. Thus, the repeated and lifetime studies are more appropriate for the purpose of this analysis.

3.2.2. Carcinogens With Modes of Action Other Than Mutagenicity

Studies comparing tumors observed at the same sites following early postnatal and chronic adult exposures in a single protocol were available for six chemicals that do not act through a mutagenic mode of action [amitrole, dichlorodiphenyltrichloroethane (DDT), dieldrin, ethylene thiourea (ETU), diphenylhydantoin (DPH), polybrominated biphenyls (PBB)] (Table 5).

These chemicals cause tumors through several different, not necessarily well defined, modes of action. For example, thyroid hormone disruption by ETU causes thyroid tumors; some PBBs act through aryl hydrocarbon (Ah) receptors, while others are phenobarbital-like pleiotrophic inducers of liver enzymes and liver tumors. Three of these studies evaluated only mouse liver tumors (amitrole, DDT, dieldrin), while the other three evaluated a large number of tissues in both mice and rats (ETU, DPH, PBB). These studies generally included a combined perinatal and adult exposure as well as the separate perinatal or adult-only groups. It should be noted that no acute perinatal dosing studies of carcinogenesis were identified for these agents; such protocols are generally considered largely non-responsive for modes of action other than mutagenicity and potent estrogenicity (e.g., DES).

For five chemicals (amitrole, DDT, dieldrin, PBB and DPH), the same tumors were observed from early and/or adult exposures, though the studies for amitrole, DDT, and dieldrin only evaluates the animals for liver tumors. With ETU, no tumors in mice or rats were observed following perinatal exposure alone (except a small, not-statistically-significant increase in male rat thyroid tumors), while thyroid tumors were observed in adult rats and thyroid, liver, and pituitary tumors in adult mice. Analysis of the incidence of tumors per time of exposure shows early-lifestage susceptibilities. The range of the magnitudes of the tumor incidence ratios of juvenile to adult exposures is similar for the repeated dosing studies (0.06–13.3, weighted geometric mean 2.2, 27% of ratios greater than 1, Tables 5 and 8) and lifetime dosing studies (0.15–36, weighted geometric mean 3.4, 21% of ratios greater than 1, Tables 7 and 8). These ranges and means are similar to those for chemicals with a mutagenic mode of action, though the means and maximums are somewhat lower. Again, liver tumors are common to these chemicals. The range of the magnitudes of liver tumor incidence ratios of juvenile to adult exposures also is similar for the repeated dosing studies (0.06–13.3, weighted geometric mean 2.6, 43% of ratios greater than 1, Tables 5 and 8) and lifetime dosing studies (0.15–36, weighted geometric mean 5.8, 33% of ratios greater than 1, Tables 7 and 8).

The major factor that complicates the interpretation of the results is that these studies, except with DDT and dieldrin, involved dietary feeding initially to the mother, which potentially could increase or decrease the dose received by the pups. Due to the maternal dosing during pregnancy and lactation, the extent to which offspring received similar doses during different early and adult lifestages is particularly uncertain for DPH, ETU, and PBBs. Oral gavage doses in young animals were selected to approximate the average daily dose in adult dietary studies based on standard estimates of feed consumption in the studies with DDT and dieldrin, while the amitrole study involved dietary feeding postnatally to the mother so the young were dosed via lactation. In addition, DDT, dieldrin, and some PBBs are more persistent in the body than are

most chemicals, leading to a prolonged exposure even following limited dosing. Thus, these studies provide evidence that early lifestages can be more susceptible to exposures to chemicals causing cancer through a variety of modes of action other than mutagenicity. However, the studies with ethylene thiourea, which acts via thyroid disruption, indicate that this is not necessarily the case for all modes of action.

3.2.3. Ionizing Radiation

As mentioned previously, the UNSCEAR, Annex I (2000) includes information derived from a wide range of both intentional (generally diagnostic or therapeutic medical) and accidental radiation exposures. Only information derived from the Japanese population (referred to as the Life Span Study in the UNSCEAR Annex I) is presented here. A statistically significant excess cancer mortality associated with radiation has been found among the bomb survivors for the following types of cancer: esophagus, stomach, colon, liver, lung, bone and connective tissue, skin, breast, urinary tract, and leukemia. Tables 9 and 10 are extracted from the tables in UNSCEAR, Annex I. The excess relative risk (ERR) is the increased cancer rate relative to an unexposed population; an ERR of 1 corresponds to a doubling of the cancer rate. Because of the low numbers of cancers in individual sites within narrow age groups, the ERRs for the various solid tumors and leukemia were presented only as less than or greater than 20 years of age at the time of exposure. The larger number of thyroid tumors enable a more detailed breakout shown in Table 10. Most sites show greater risks in the younger than in the older ages.

The U.S. EPA (1994) document presents a methodology for estimation of cancer risks in the U.S. population due to low-LET (linear energy transfer) radiation exposures using data from the Atomic Bomb Survivor Study (ABSS) as well as from selected medical exposures. The report developed mortality risk coefficients using several models that took into account age and gender dependence of dosimetry, radiogenic risk, and competing causes of death as well as transporting of risks across populations. The risk projections were updated using more recent vital statistics in a report that also included an uncertainty analysis (U.S. EPA, 1999). Details of the derivation of these coefficients are available at http://www.epa.gov/radiation/docs/rad_risk.pdf .

Table 11 contains the calculated age-specific risk coefficients derived from the application of the various models to the ABSS data. For most of the sites in the table, the risk coefficients are higher in the earlier age groups; liver, bone, skin, and kidney coefficients are age-independent and only esophageal cancer coefficients increase with increasing age. Also of note is that the coefficients generally are higher for females. Similar to the information from the UNSCEAR (2000) Annex, most sites show greater risks in the younger ages than the older ages.

However, a comparison of the two tables seems to show reversal of risks for some sites as a function of age at exposure. While the high sampling variability in the epidemiological data for some ages may contribute to this apparent reversal, the choice of risk models and associated parameters also is a factor.

4. DISCUSSION

The challenge for this analysis was how to use the existing, but limited, scientific database on early postnatal and juvenile exposures to carcinogens to inform a science policy decision on whether, and if so how, to assess the risk from childhood exposures to chemicals for which we have evidence of carcinogenicity only in adult humans or sexually mature laboratory animals. The database overall is of limited size (particularly compared with the number of chemicals that have been studied in adult occupational epidemiological studies or chronic bioassays). The majority of the human data involves exposures to ionizing radiation or DES (Anderson et al., 2000). More than 50 chemicals have been demonstrated to cause cancer following perinatal exposures in animals (without adult exposures), but only a subset of the chemicals have comparative studies across ages. The comparative experimental studies used 18 chemicals, 12 of which had mutagenic modes of action and 6 of which had data from repeated or lifetime exposures. Other analyses of similar data have found similar results (Hattis et al. 2005), but have focused on other aspects of the data, e.g., gender differences.

Previously published or internal U.S. EPA analyses have concluded that the standard animal bioassay protocols usually do not miss chemicals that would have been identified as carcinogens if perinatal exposures had been undertaken (McConnell, 1992; Miller et al., 2002; U.S. EPA, 1996). Given the increased complexity and costs of chronic bioassays with perinatal exposures, a limited number of such studies have been performed. However, these are the studies that largely constitute the available database for this analysis. In addition to the chronic bioassays with perinatal exposures, there are studies with acute dosing at different lifestages and a large number of studies with perinatal exposures without a directly comparative adult study.

Two other kinds of information can contribute toward developing a scientifically informed policy: theoretical analyses and analyses of stop studies.[4] Theoretical analyses suggest that the differential susceptibility would depend in part on the mode of action (i.e., at what step in the cancer process(s) the chemical was acting) and that the use of the average daily exposure prorated over a lifetime may underestimate or overestimate the cancer risk when exposures are time-dependent (Goddard and Krewski, 1995; Murdoch et al., 1992). Evidence for old-age-dependent promotion of basophilic foci in rats by peroxisome proliferators appears to provide a concrete example consistent with these theoretical analyses (Cattley et al., 1991; Kraupp-Grasl et al., 1991). The stop studies performed by the National Toxicology Program began exposure at the standard post-weaning age, but stopped exposure after varying periods of months. Other groups of animals were exposed for a full two years; all animals were evaluated

[4] Stop studies are studies in which exposure is halted after a predetermined period.

for tumors at the end of two years regardless of the duration of exposure (Halmes et al., 2000). Related data also are available from the stop studies with vinyl chloride (Drew et al., 1983). Analysis by Halmes et al. (2000) showed that, for six of the eleven chemicals and half the tumor sites, the assumption that the cancer risk would be equal when the product of concentration and time (i.e., C x T) was constant was incorrect, and usually underestimated risk, as more of the risk came from the beginning of the exposure rather than the end. This dependence of risk on both duration and intensity of exposure did not appear to be correlated with mutagenicity. It should be noted that these stop studies all involved exposures early in the life of the animal (as opposed to a limited number of cancer studies that looked at later periods of life; e.g., Drew et al., 1983), but the extent to which the differences in tumor outcome result from increased susceptibility in these early periods or the extended period for expression of the cancer cannot be evaluated. These stop studies also used doses as high as or higher than the highest dose used in the two-year exposure. This latter factor clearly had a significant effect for two chemicals, causing tumors at higher doses that were not observed at lower doses. These results suggest that pharmacokinetic or other dose-rate dependencies can make the effects of exposures at high doses different from those exposures at lower doses. While not directly informative about early childhood exposures, these studies provide a perspective on the common cancer risk assessment practice of averaging exposures over a lifetime, especially those that include earlier lifestages. Thus, alternative methods for estimating risks from short-term exposures during childhood should be considered.

Information on different lifestage susceptibilities to cancer risks for humans exists for ionizing radiation. The effects of chemical mutagens at different lifestages on cancer induction are derived from laboratory animal studies. While the induction of cancer by ionizing radiation and the induction of cancer by chemical mutagens are not identical processes, both involve direct damage to DNA as critical causal steps in the process. In both cases, the impacts of early exposure can be greater than the impacts of later exposures, probably due to some combination of early-lifestage susceptibility and the longer periods for observation of effects. As indicated in Tables 9 and 10, A-bomb survivors exhibited different lifestage dependencies at different tumor sites, though the total radiation-related incidence of tumors showed a general slow decline with age at exposure. However, as previously noted, there are apparent differences at some sites between the two tables. In addition to the sampling and modeling differences, the excess risk values in Table 9 are based on Japanese baselines while the coefficients in Table 10 reflect UNSCEAR's effort to transport the risks from the Japanese population to that of the United States. However, it is clear that the total radiation-related tumor incidence showed a general slow decline with age at exposure.

The studies in rodents of chemicals with mutagenic modes of action similarly support a

general decline in induced cancer risk with age at exposure and similarly show some differences for individual tumor sites. In general, the earliest two or three postnatal weeks in mice and rats appeared to be the most susceptible, though some degree of increased susceptibility through puberty in rats (beginning around 5–7 weeks) and mice (beginning around 4–6 weeks) for some types of tumors exists.

All the acute dosing studies that demonstrated carcinogenicity with animals of different ages used chemicals with a mutagenic mode of action (Tables 4 and 6). These studies provide the clearest demonstrations of periods of differential susceptibility because the exposure rate is constant at the different ages. The repeated dose studies also include several of the most informative studies for assessing perinatal carcinogenesis, notably those on vinyl chloride and DEN (Tables 2 and 4). The vinyl chloride studies by Maltoni and colleagues are part of a large series of studies on this compound that included exposures to different concentrations for varying durations, including some at early lifestages (Maltoni et al., 1984). The DEN study by Peto et al. (1984) used a unique chronic study design in which groups of rats were exposed to multiple drinking water concentrations starting at 3, 6, or 20 weeks of life. This design provides information on the susceptibility of early exposure periods within a nearly lifetime exposure.

Beyond the analysis described here, there are conceptual biological rationales that would suggest DNA-damaging agents would have greater impacts on early lifestages. Growth involves substantial levels of cell replication, even in organs that in adults are only very slowly replicating, thus increasing the likelihood that a cell will undergo division before the DNA damage caused by the mutagen has been repaired. Increased replication also can lead to a greater division of initiated cells, leading to a larger number of initiated cells per specified dose. These periods of cell replication can vary for different tissues. For example, DMBA appears to be more effective at initiating mammary tumors in 6-8 week old rats, which are undergoing development of that tissue, than during earlier or later periods (Meranze et al., 1969). While tumor promotion processes can be very dependent upon the duration of promotion, initiation processes can occur in relatively brief periods (e.g., the single-dose studies in animals or radiation exposure in humans). Most tumors take extended periods to develop, making damage that occurs earlier in life more likely to result in tumors prior to death than would exposures that occur later in life. While some of these observations may also pertain to other modes, all of them (with some differences among tumor sites) appear to be potentially relevant to a greater susceptibility to mutagenic modes of action during early-life stages (vs. later-life stages).

The information on lifestage susceptibility for chemicals inducing cancers through modes of action other than direct DNA interaction is more varied, showing an increase in tumor incidence during perinatal exposure versus exposures of mature animals (e.g., polybrominated

biphenyls induced liver tumors), no tumors from perinatal exposure (e.g., ethylene thiourea induced thyroid tumors), no effect of combined perinatal and adult exposure (e.g., DPH liver tumors in rats and female mice), and different tumors from perinatal exposure versus adult exposure (e.g., DES, ascorbate). These variations are likely a result of the modes of action of these chemicals and the pharmacokinetic differences in doses during different periods of life. No studies were evaluated that were directly comparable to the single-dose studies with mutagens, which clearly show significant differences in tumor responses after explicitly controlled doses at different lifestages.

Some evidence for an effect of early-lifestage exposures on tumor incidence was observed in studies with polybrominated biphenyls, amitrole, DDT, dieldrin, and diphenylhydantoin. These studies show increased incidence of tumors in mice from perinatal exposure, though only those for polybrominated biphenyls were statistically significant. (A nonstatistically significant increase also was observed in male rats with polybrominated biphenyls.) Combined perinatal and adult exposures generally gave statistically significant increases, though not necessarily for each sex and species (rat and mice) in the diphenylhydantoin and polybrominated biphenyl studies.

There are important demonstrations of chemicals acting through modes of action other than mutagenic to cause different tumor types with early-lifestage exposures compared with exposures for adults, e.g., tamoxifen and DES (Carthew et al., 2000; Carthew et al., 1996, Gass et al., 1964; Newbold et al., 1990, 1997, 1998). In addition, studies with *in utero* exposure to atrazine (Fenton and Davis, 2002), DES, and arsenic (Waalkes et al., 2003) indicate that early-life exposures to compounds can alter susceptibility of endocrine and reproductive organs. Three of these compounds (i.e., DES, genistein, and tamoxifen) bind to the estrogen receptor. Ongoing studies on ethinyl estradiol, nonylphenol, and genistein by the National Toxicology Program will add to this database for estrogens (Laurenzana et al., 2002; Newbold et al., 2001). These studies will evaluate cancer incidence in offspring exposed *in utero*, during lactation, and through adulthood via diet. A study with genistein found uterine tumor development to be dependent upon early-lifestage exposures (Newbold et al., 2001). Another recent study of estrogen found a shorter latency for mammary tumors in mice exposed at 8 and 12 weeks as compared to mice exposed at 4 or 18 weeks, indicating a susceptible period between 8 to 12 weeks of exposure (Yang, 2003). Thus, there is an actively growing database from which to consider issues of childhood exposure and cancer for compounds acting through the estrogen receptor or other mechanisms of endocrine disruption.

The ability to estimate with any accuracy the juvenile to adult cancer potency ratio depends very much on the experimental design used. The lifetime design has less ability to

distinguish increased susceptibility from early-life exposure than the other types of designs. Consider two different experimental designs. In the first, the "lifetime" design, a group of animals are exposed starting as juveniles, and exposure continues through adulthood. A second group are exposed only in adulthood, and the juvenile:adult ratio results from a comparison of tumor incidences in the two groups. In the second, the "repeated" design, one group of animals is exposed only during the juvenile period, and is then followed through adulthood to assess tumor incidence, and a second group of animals is exposed only through adulthood. The lifetime design turns out to be a particularly insensitive design for estimating the juvenile:adult ratio.

The following example demonstrates the magnitude of the problem: Suppose the risk per day of exposure of a chemical is ten fold greater in the juvenile period as in the adult period, and animals exposed through adulthood at a particular dose level have an extra risk of 60% for having at least one tumor, while 1% of control animals have tumors. The adult exposure period is 94 weeks, while the juvenile exposure period is 4 weeks. Thus, in the lifetime design, the group of animals exposed as juveniles will receive a total of 98 weeks of exposure, (4 in juvenile and 94 in adult), while those receiving the adult-only exposure receive 94 weeks of exposure. In the repeated design, animals exposed as juveniles receive only 4 weeks of exposure, while the adults receive 94 weeks, just as in the lifetime design. Each group starts with 50 animals. Under these assumptions, using equations (1) and (2) from Section 2.3, the expected number of animals with tumors in the three treatment groups (control, juvenile-exposed, adult-exposed groups) in the two designs is:

	Number of animals with tumors		
	Control	**Early-life exposure**	**Adult exposure**
Lifetime	1	36	30
Repeated	1	16	30

Notice that in the "lifetime" design, only six more juvenile-exposed animals have tumors than in the adult-exposed group, whereas in the "repeated" design, 16 juvenile-exposed animals have tumors. The data in the lifetime design are consistent with the hypothesis of no tumors being induced during the juvenile period: the ratios 36/50 and 30/50 are not statistically significantly different. In other words, the data from the lifetime design are statistically consistent with the hypothesis of *no risk at all* during the juvenile period, even though the real response is a 10 times greater risk from early-life exposure. The difference between the results from the two different study designs is due to the one-hit model: each additional week of a long exposure contributes less than the previous week to the total number of animals with tumors.

Note that, even if the one-hit model is not correct, chronic exposure probably results in a non-statistically significant increase for the lifetime exposure including juveniles as compared with only adult exposure.

The proper measure of relative potency of an exposure in the juvenile period relative to an exposure in the adult period is the ratio of doses in the two periods that give the same incidence of tumors. However, most of the data sets used in this report contained only one non-control dose, precluding the extensive dose-response modeling that would be required to estimate this ratio of doses. However, this document largely considered chemicals for which a mutagenic mode of action has been established and for which a linear, no-threshold dose-response function is assumed for the low-dose range being considered for risk assessment. In the case of the linear dose-response function, the analysis of the relative response from the same dose will produce the same value as ratio of doses that produces the same incidence of tumors.

For a one-hit dose-response equation, the probability of developing a tumor after the same dose and duration in the juvenile or adult period is

$$P_a = 1 - (1 - P_0)e^{-m_a x}$$
$$P_j = 1 - (1 - P_0)e^{-m_j x}$$

for dose x. Suppose we want to calculate the dose D_a or D_j that results in a given incidence of tumors after an adult or juvenile exposure. From equation 1, D_a and D_j equal:

$$D_a = \frac{-\ln\left(\frac{1-P_c}{1-P_0}\right)}{m_a}$$
$$D_j = \frac{-\ln\left(\frac{1-P_c}{1-P_0}\right)}{m_j}$$

Thus, the ratio $D_a/D_j = m_j/m_a$, the ratio calculated in this document.

In summary, this analysis supports the conclusion that there can be greater susceptibility for the development of tumors as a result of exposures to chemicals acting through a mutagenic mode of action, when the exposures occur in early lifestages as compared with later lifestages. Thus, this Supplemental Guidance recommends for chemicals with a mutagenic mode of action for carcinogenesis when chemical-specific data on early-life exposure are absent, a default

approach using estimates from chronic studies (i.e., cancer slope factors) with appropriate modifications to address the potential for differential risk of early-lifestage exposure. For chemicals acting through a non-mutagenic mode of action, e.g., hormonally mediated carcinogens, the available data suggest that other approaches may need to be developed for addressing cancer risk estimates from childhood exposures. This is a particular concern because the tumors arising from hormonally active chemicals appear to involve different sites when exposure is during early-life versus adulthood, an effect that has been observed relatively infrequently. Development of such approaches would require additional research to provide an expanded scientific basis for their support, including additional research and the possible development of new toxicity testing protocols that consider early lifestage dosing.

The current data do also not allow analysis of some issues of potential interest for risk assessment, e.g., potential increased risk of childhood cancer, from *in utero* or childhood exposures. Assessing the role of environmental exposures on childhood cancers is difficult, but additional research could include epidemiological studies or experimental studies with animals genetically designed to express cancers analogous to human childhood cancers. Rigorous quantification of exposure doses at different lifestages and in rodent pups in experimental studies would be useful for evaluating whether there is greater childhood susceptibility. Pharmacokinetic modeling could better define the internal doses to improve determination of the magnitude of increased susceptibility.

5. GUIDANCE FOR ASSESSING CANCER RISKS FROM EARLY-LIFE EXPOSURE

Consistent with the approach and recommendations of the U.S. EPA cancer risk assessment guidelines (U.S. EPA, 2004), any assessment of cancer susceptibility will begin with a critical analysis of the available information. Figure 3 shows the proposed steps in the process. The potential for increased susceptibility to cancer from early-life exposure, relative to comparable exposure later in life, generally warrants explicit consideration for each assessment.

When developing quantitative estimates of cancer risk, the Agency recommends integration of age-specific values for both exposure and toxicity/potency where such data are available and appropriate. Children, in general, are expected to have some exposures that differ from those of adults (either higher or lower), due to differences in size, physiology, and behavior. For example, children are generally assumed to eat more food and drink more water relative to their body weight than adults. Children's normal activities, such as putting their hands into their mouths or playing on the ground, can result in exposures to contaminants that adults do not encounter. Moreover, children and adults exposed to the same concentration of an agent in food, water, or air may receive different (higher or lower) internal doses due to differences, for example, in intake, metabolism, or absorption rates. Children are less likely than adults to be exposed to products typically used in industrial settings and often have more limited diets than adults. When assessing risks, if the data are available and relevant, it is important to include exposure that is measured or modeled for all lifestages, including exposures during childhood and during adulthood. EPA continues to develop better tools for assessing childhood exposure differences, such as the *Child-Specific Exposure Factors Handbook* (U.S. EPA, 2002a), and models, such as Stochastic Human Exposure and Dose Simulation (SHEDS) and Consolidated Human Activity Database (CHAD) (McCurdy et al., 2000; Zartarian et al., 2000)

Mode-of-action studies can be a source of data on quantitative differences between children and adults (Figure 3, Box 1). If the available information is sufficient to establish the agent's mode of action for early-life and adult exposures, then the implications for early-life exposure of that mode of action are used to develop separate risk estimates for childhood exposure. Pertinent information can be obtained both from agent-specific studies and from other

studies that investigate the general properties of the particular mode of action. All data indicating quantitative differences between children and adults are considered in developing those portion(s) of the risk estimates for exposure estimates that include childhood exposure. Some examples include the potential for children to have a different internal dose of the active agent or a change in a key precursor event (see Section 2.4.3.4 of the *Guidelines for Cancer Risk Assessment*).

When the mode of action cannot be established (Figure 3, Box 2), the policy choice would be to use linear extrapolation to lower doses such that risk estimates are based on a lifetime average daily exposure without further adjustment. No general adjustment is recommended at this time. This policy choice is consistent with past U.S. EPA practice that has been favorably evaluated over the years. The result would be expected to produce plausible upper bound risk estimates, based on the use of linear extrapolation as a default in the absence of information on the likely shape of the dose-response curve.

When a mode of action other than mutagenicity is established, if it is nonlinear (Figure 3, Box 3) or linear (Figure 3, Box 4), no general adjustment is recommended at this time. Although the available studies (discussed previously) indicates that higher or lower cancer risks may result from early-life exposure, there is insufficient information or analyses currently available to determine a general adjustment at this time. As other modes of action become better understood, this information may include data on quantitative differences between children and adults. If such data are available, an analysis of the differences could be used to adjust risk estimates for childhood exposure. EPA expects to expand this Supplemental Guidance to specifically address modes of action other than mutagenicity when sufficient data are available and analyzed.

When the data indicate a mutagenic mode of action,[5] the available studies (discussed

5 Determination of chemicals that are operating by a mutagenic mode of action entails evaluation of test results for genetic endpoints, metabolic profiles, physicochemical properties, and structure-activity analyses in a weight-of-evidence approach (Waters et al., 1999). Established protocols are used to generate the data (Cimino, 2001; OECD, 1998; U.S. EPA, 2002b); however, it is recognized that newer methods and technologies such as those arising from genomics can provide useful data and insights to a mutagenic mode of action. Carcinogens acting through a mutagenic mode of action generally interact with DNA and can produce such effects as DNA adducts and/or breakage. Carcinogens with a mutagenic mode of action often produce positive effects in multiple test systems for different genetic endpoints, particularly gene mutations and structural chromosome aberrations, and in tests performed *in vivo,* which generally are supported by those performed *in vitro*. This mode of action is addressed in more detail in Section 2.3.5 of EPA's cancer guidelines (U.S. EPA, 2005).

above) indicate higher cancer risks resulting from a given exposure occurring early in life when compared with the same amount of exposure during adulthood. However, chemical-specific data relating to mode of action (e.g., toxicokinetic or toxicodynamic information) may suggest that even though a compound has a mutagenic mode of action, higher cancer risks may not result. Such data should be considered before applying the age-dependent adjustment factors.

If the available, chemical-specific information includes an epidemiologic study of the effects of childhood exposure or an animal bioassay involving early-life exposure (Figure 3, Box 5), then these studies are analyzed to develop risk estimates (i.e., cancer slope factors) that specifically address any potential for differential potency in early lifestages. An example is the IRIS assessment of vinyl chloride (U.S. EPA, 2000b; c).

In the absence of early-life studies on a specific chemical under consideration (Figure 3, Box 6), the extrapolation from the point of departure to lower doses employs linear extrapolation (see Section 3.3.1 of the U.S. EPA [2005] cancer guidelines). This choice is based on mode-of-action data indicating that mutagens can give rise to cancers with an apparently low-dose linear response. Adjustments to the resultant risk estimates are specified with regard to childhood exposures. This approach is adopted because risk estimates based on an average daily exposure prorated over a lifetime do not consider the potential for higher cancer risks from early-life exposure.

The adjustments described below reflect the potential for early-life exposure to make a greater contribution to cancers appearing later in life. The 10-fold adjustment represents an approximation of the weighted geometric mean tumor incidence ratio from juvenile or adult exposures in the repeated dosing studies (see Table 8). This adjustment is applied for the first 2 years of life, when toxicokinetic and toxicodynamic differences between children and adults are greatest (Ginsberg et al., 2002; Renwick, 1998). Toxicokinetic differences from adults, which are greatest at birth, resolve by approximately 6 months to 1 year, while higher growth rates extend for longer periods. The 3-fold adjustment represents an intermediate level of adjustment that is applied after 2 years of age through <16 years of age. This upper age limit represents middle adolescence following the period of rapid developmental changes in puberty and the conclusion of growth in body height in NHANES data (Hattis et al., 2005). Efforts to map the approximate start of mouse and rat bioassays (i.e., 60 days) to equivalent ages in humans ranged from 10.6 to 15.1 years (Hattis et al., 2005). Data are not available to calculate a specific dose-response adjustment factor for the 2 to <16-year age range, so EPA selected the 3-fold

adjustment because it reflects a midpoint, i.e., approximately half the difference between 1 and 10 on a logarithmic scale ($10^{1/2}$), between the 10-fold adjustment for the first two years of life and no adjustment (i.e., 1-fold) for adult exposure. EPA also recognizes that exposures occurring near the end of life may have little effect on lifetime cancer risk, but lacks adequate data at present to provide an adjustment for this "wasted dose" effect. Similarly, since most of the studies involved only one latency period, the potential effect of early-life exposure on latency for the observed tumors could not be evaluated. The lack of data on effect on latency also limited the types of analyses that could be performed, e.g., more complex dose-response functions, such as multi-stage or clonal expansion models, could not be evaluated. Thus, the potential effects of early-life exposures on latency were not evaluated. Finally, as the adjustment factors are derived from a weighted geometric mean of the data evaluated, these adjustment will both over-estimate and under-estimate the potential potency for early-life exposure for chemicals with a mutagenic mode of action for carcinogenesis. An examination of the data in the tables demonstrates that some of the ratios were less than one, while others exceeded 10. For this reason, the Supplemental Guidance emphasizes that chemical-specific data should be used in preference to these default adjustment factors whenever such data are available.

The following adjustments represent a practical approach that reflects the results of the preceding analysis, which concluded that cancer risks generally are higher from early-life exposure than from similar exposure durations later in life:

- For exposures before 2 years of age (i.e., spanning a 2-year time interval from the first day of birth up until a child's second birthday), a 10-fold adjustment.

- For exposures between 2 and <16 years of age (i.e., spanning a 14-year time interval from a child's second birthday up until their sixteenth birthday), a 3-fold adjustment.

- For exposures after turning 16 years of age, no adjustment.

Clearly other age groups, such as an age group experiencing pubertal changes in physiology, or approximately ages 9 - 15, may experience changes in biological processes that could lead to modifications in the susceptibility to the effects of some carcinogens, depending on the mode of action. This Supplemental Guidance focuses on carcinogens with a mutagenic mode

of action. For any mode of action, the Agency is interested in identifying lifestages that may be particularly sensitive or refractory for carcinogenesis, and believes that the mode of action framework as described by EPA's cancer guidelines (U.S. EPA, 2005), is an appropriate mechanism for elucidating these lifestages. In general, the Agency's analyses of lifestages that may be susceptible will depend on three factors: (1) establishing the mode of action for carcinogenesis; (2) using knowledge about the biological and toxicological key events in that mode of action that are likely to be affected by lifestages; and (3) the availability, or development, of data that allow analysis of the effects of chemicals acting by that mode of action during the relevant ages. For each mode of action evaluated, therefore, the various age groupings determined to be at a differential risk, which may differ significantly from those proposed for the mutagenic mode of action, are expected to be evaluated independently of other modes of action. When data, including well established mode of action data, are available that allow specific evaluation of lifestage differences in toxicokinetics or toxicodynamics that would lead to lesser or greater susceptibility from early-life exposures to carcinogens, then those data should be used, as generally discussed in EPA's cancer guidelines (U.S. EPA, 2005), in preference to the default procedures described in this Supplemental Guidance.

The 10-fold and 3-fold adjustments in slope factor are to be combined with age-specific exposure estimates when estimating cancer risks from early life exposure to carcinogens that act through a mutagenic mode of action. It is important to emphasize that these adjustments are combined with corresponding age-specific estimates of exposure to assess cancer risk. For example, for a 70-year lifetime, where there are data showing negligible exposure to children, the estimated cancer risk from childhood exposure would be also negligible and the lifetime cancer risk would be reduced to that resulting from the relevant number of years of adult exposure (in the absence of specific information, 55 years). Where there are data (measured or modeled) for childhood exposures, the age-group specific exposure values are used along with the corresponding adjustments to the slope factor. Where there are no relevant data or models for childhood exposures and only lifetime average exposure data are available, the lifetime exposure data are used with the adjustments to the slope factor for each age segment.

It is recognized that, when the exposure is fairly uniform over a lifetime, the effect of these adjustments on estimated lifetime cancer risk are small relative to the overall uncertainty of

such estimates. These adjustments can be applied when estimating the cancer risk resulting from childhood exposure. These adjustments are applied when developing risk estimates from conventional animal bioassays or epidemiologic studies of effects of adult exposure. Some examples follow in the next section.

The Agency has also carefully considered both the advantages and disadvantages to extending the default potency adjustment factors to carcinogenic chemicals for which the mode of action remains unknown. It is the Agency's long-standing science policy position that use of the linear low-dose extrapolation approach (without further adjustment) provides adequate public health conservatism in the absence of chemical-specific data indicating differential early-life susceptibility. At the present time, therefore, EPA is recommending these age-dependent adjustment factors only for carcinogens acting through a mutagenic mode of action based on a combination of analysis of available data and the above-mentioned science policy position. In general, the Agency prefers to rely on analyses of data, rather than general defaults. When data are available for a susceptible lifestage, they should be used directly to evaluate risks for that chemical and that lifestage on a case-by-case basis. In this analysis, the data for non-mutagenic carcinogens, when the mode of action is unknown, were judged to be too limited and the modes of action too diverse to use this as a category for which a general default adjustment factor approach can be applied.

6 COMBINING LIFESTAGE DIFFERENCES IN EXPOSURE AND DOSE-RESPONSE WHEN ASSESSING CARCINOGEN RISK - SOME EXAMPLES FOR CARCINOGENS THAT ACT THROUGH A MUTAGENIC MODE OF ACTION

It is important for the risk assessor to consider lifestage differences in both exposure and dose-response when assessing cancer risk resulting from early-life exposures. As discussed in Section 5, age dependent adjustments factors (ADAFs) in dose response (i.e., slope factors) are combined with age specific exposure estimates when assessing cancer risks. This is a departure from the way cancer risks have historically been based upon the premise that risk is proportional to the daily average of lifetime dose. This Supplemental Guidance recommends an integrative approach that can be used to assess total lifetime risk resulting from lifetime or less-than-lifetime exposure during a specific portion of a lifetime.

The following examples can help demonstrate how to apply this guidance by integrating potential lifestage differences in exposure and/or dose-response (potency), and also demonstrate what the resulting impacts are on calculated risks. These hypothetical examples consider risks from both lifetime, as well as less-than-lifetime oral exposures. Risks associated with inhalation exposure to carcinogens that act via a mutagenic mode of action are calculated in similar fashion by applying the appropriate ADAF(s) along with the corresponding inhalation unit risk estimate, using pertinent estimates of exposure concentration.

Note again, ADAFs are only to be used for agents with a mutagenic mode of action for carcinogenesis when chemical-specific data are absent. For all modes of action, when chemical-specific data are available for early-life exposure, those data should be used.

6.1 CALCULATING LIFETIME RISKS ASSOCIATED WITH LIFETIME EXPOSURES

Example 1: Consider a scenario of exposure to a carcinogen with a **nonmutagenic** mode of action. Suppose the oral cancer slope factor derived from a typical animal study (i.e., where dosing begins after puberty) is estimated to be 2 per mg/kg-d, and the exposure rate remains constant throughout life at 0.0001 mg/kg-d (this is equivalent to saying the daily average of lifetime dose rate is equal to 0.0001 mg/kg-d). The risk from lifetime exposure is calculated by multiplying the slope factor and the exposure rate:

$$\text{Risk} = (2 \text{ per mg/kg-d}) \times (0.0001 \text{ mg/kg-d})$$

$= \quad 2 \times 10^{-4}$

Example 2: Now consider the same exposure scenario for a carcinogen with a **mutagenic** mode of action for which the oral cancer slope factor, derived from a typical animal study where dosing begins after puberty, is also estimated to be 2 per mg/kg-d. In this case, ADAFs are used, as follows.

a. To calculate lifetime risk for a population with average life expectancy of 70 years, sum the risk associated with each of the three relevant time periods:

- Risk during the first 2 years of life (where the ADAF = 10);
- Risk for ages 2 through < 16 (ADAF = 3); and
- Risk for ages 16 until 70 years (ADAF = 1).

Thus, risk equals the sum of:

- Risk for birth through < 2 yr = (2 per mg/kg-d) x 10 (ADAF) x (0.0001 mg/kg-d) x 2yr/70yr
  $= 0.6 \times 10^{-4}$
- Risk for ages 2 through < 16 = (2 per mg/kg-d) x 3 (ADAF) x (0.0001 mg/kg-d) x (13yr/70yr)
  $= 1.1 \times 10^{-4}$
- Risk for ages 16 until 70 = (2 per mg/kg-d) x 1 (ADAF) x (0.0001 mg/kg-d) x (55yr/70yr)
  $= 1.6 \times 10^{-4}$

Risk $= 0.6 \times 10^{-4} + 1.1 \times 10^{-4} + 1.6 \times 10^{-4}$

$= 3.3 \times 10^{-4}$

b. If exposure varies with age, then such differences are also included. Now suppose the same example as immediately above, except that exposure for ages 1 through <12 was twice as high as exposure for all other ages. In this case, sum the risk associated with each of the five relevant time periods in which exposure rates and/or potencies (slope

factors) vary:

Risk equals the sum of:

- Risk for birth through < 1 yr (1yr) = (2 per mg/kg-d) x 10 (ADAF) x 0.0001 mg/kg-d x 1yr/70yr
  $= 0.3 \times 10^{-4}$
- Risk for ages 1 through < 2 (1yr) = (2 per mg/kg-d) x 10 (ADAF) x 0.0002 mg/kg-d x 1yr/70 yr
  $= 0.6 \times 10^{-4}$
- Risk for ages 2 through < 12 (10yr) = (2 per mg/kg-d) x 3 (ADAF) x 0.0002 mg/kg-d x 10yr/70yr
  $= 1.7 \times 10^{-4}$
- Risk for ages 12 through < 16 (4yr) = (2 per mg/kg-d) x 3 (ADAF) x 0.0001 mg/kg-d x 4yr/70yr
  $= 0.3 \times 10^{-4}$
- Risk for ages 16 until 70 years (55yr) = (2 per mg/kg-d) x 1 (ADAF) x 0.0001 mg/kg-d x 55yr/70yr
  $= 1.6 \times 10^{-4}$

Risk $= 0.3 \times 10^{-4} + 0.6 \times 10^{-4} + 1.7 \times 10^{-4} + 0.3 \times 10^{-4} + 1.6 \times 10^{-4}$
$= 4.5 \times 10^{-4}$

6.2 CALCULATING LIFETIME RISKS ASSOCIATED WITH LESS THAN LIFETIME EXPOSURES

If exposure only occurs for a limited number of years (for example, consider a family that lives near a source of exposure for a five-year period of time before moving away), it is critical to combine lifestage differences in exposure and dose-response for the relevant time interval. The examples presented below demonstrate how adjusting potency and/or exposure can affect the assessment of cancer risk.

Example 3: If exposure to a carcinogen with a mutagenic mode of action with an oral slope factor equal to 2 per mg/kg-d occurs during adulthood for only 5 years, the daily average of lifetime dose is time weighted to apportion risk for the number of years of exposure by a factor of 5/70:

$$\text{Risk} = (2 \text{ per mg/kg-d}) \times (0.0001 \text{ mg/kg-d}) \times (5\text{yr}/70\text{yr})$$
$$= 1.4 \times 10^{-5}$$

Example 4: If this 5-year exposure occurs during childhood, the risk calculations are adjusted to consider the potential for higher potency from early-life exposure. Assessors should remember that the age dependent adjustment factors for carcinogens with a mutagenic mode of action are applied only to exposure periods occurring up to age 16.

a. For a child exposed between ages 5 and 10, only a 3-fold ADAF is applied because the exposure occurs entirely between ages 2 and <16 years:

$$\text{Risk} = 3 \text{ (ADAF)} \times (2 \text{ per mg/kg-d}) \times (0.0001 \text{ mg/kg-d}) \times (5 \text{ yr}/70 \text{ yr})$$
$$= 4.3 \times 10^{-5}$$

b. For an exposure between ages 13 and <18, a 3-fold ADAF is applied only to the 3-year portion occurring before age 16:

Risk equals the sum of:

- Risk for ages 13 through < 16 (3yr) $= 3 \text{ (ADAF)} \times (2 \text{ per mg/kg-d}) \times (0.0001 \text{ mg/kg-d}) \times (3 \text{ yr}/70 \text{ yr})$
  $= 2.6 \times 10^{-5}$
- Risk for ages 16 through < 18 (2yr) $= 1 \text{ (ADAF)} \times (2 \text{ per mg/kg-d}) \times (0.0001 \text{ mg/kg-d}) \times (2 \text{ yr}/70 \text{ yr})$
  $= 0.6 \times 10^{-5}$

$$\text{Risk} = 2.6 \times 10^{-5} + 0.6 \times 10^{-5}$$

$= 3.2 \times 10^{-5}$

c. For a child exposed from birth through age 5, different ADAFs are applied to the periods before and after age 2:

Risk equals the sum of:

- Risk for birth through < 2 (2yr) $= 10\ (ADAF) \times (2\ per\ mg/kg\text{-}d) \times (0.0001\ mg/kg\text{-}d) \times (2\ yr/70\ yr)$
  $= 5.7 \times 10^{-5}$
- Risk for ages 2 through < 5 (3yr) $= 3\ (ADAF) \times (2\ per\ mg/kg\text{-}d) \times (0.0001\ mg/kg\text{-}d) \times (3\ yr/70\ yr)$
  $= 2.6 \times 10^{-5}$

Risk $= 5.7 \times 10^{-5} + 2.6 \times 10^{-5}$
$= 8.3 \times 10^{-5}$

Example 5: Lifetime risk calculations based on less-than-lifetime exposure to a carcinogen with a mutagenic mode of action include any lifestage changes in potency as well as exposure. In this example, again consider a scenario of 5 years of exposure to a carcinogen with a mutagenic mode of action, but suppose that the exposure rate is found to vary from 0.0002 mg/kg-d during the first 2 years of life, to 0.0001 mg/kg-d during the last 3 years.

a. For a child exposed between birth and age 5, sum the risk associated with the two relevant time periods:

Risk equals the sum of:

- Risk for birth through < 2 (2yr) = 10 (ADAF) x (2 per mg/kg-d) x (0.0002 mg/kg-d) x (2 yr/70 yr)
  $= 11.4 \times 10^{-5}$
- Risk for ages 2 through < 5 (3yr) = 3 (ADAF) x (2 per mg/kg-d) x (0.0001 mg/kg-d) x (3 yr/70 yr)
  $= 2.6 \times 10^{-5}$

Risk $= 11.4 \times 10^{-5} + 2.6 \times 10^{-5}$
$= 1.4 \times 10^{-4}$

b. For comparison, a similar risk calculation for 5 years of exposure later in life (after age 16) in which the first 2 years of exposure are double that of the next 3 years are carried out without any adjustment for potency:

Risk equals the sum of:

- Risk for first 2 years of adult exposure = 1 (ADAF) x (2 per mg/kg-d) x (0.0002 mg/kg-d) x (2yr/70yr)
  $= 1.1 \times 10^{-5}$
- Risk for final 3 years of adult exposure = 1 (ADAF) x (2 per mg/kg-d) x (0.0001 mg/kg-d) x (3yr/70yr)
  $= 0.9 \times 10^{-5}$

Risk $= 1.1 \times 10^{-5} + 0.9 \times 10^{-5}$
$= 2 \times 10^{-5}$

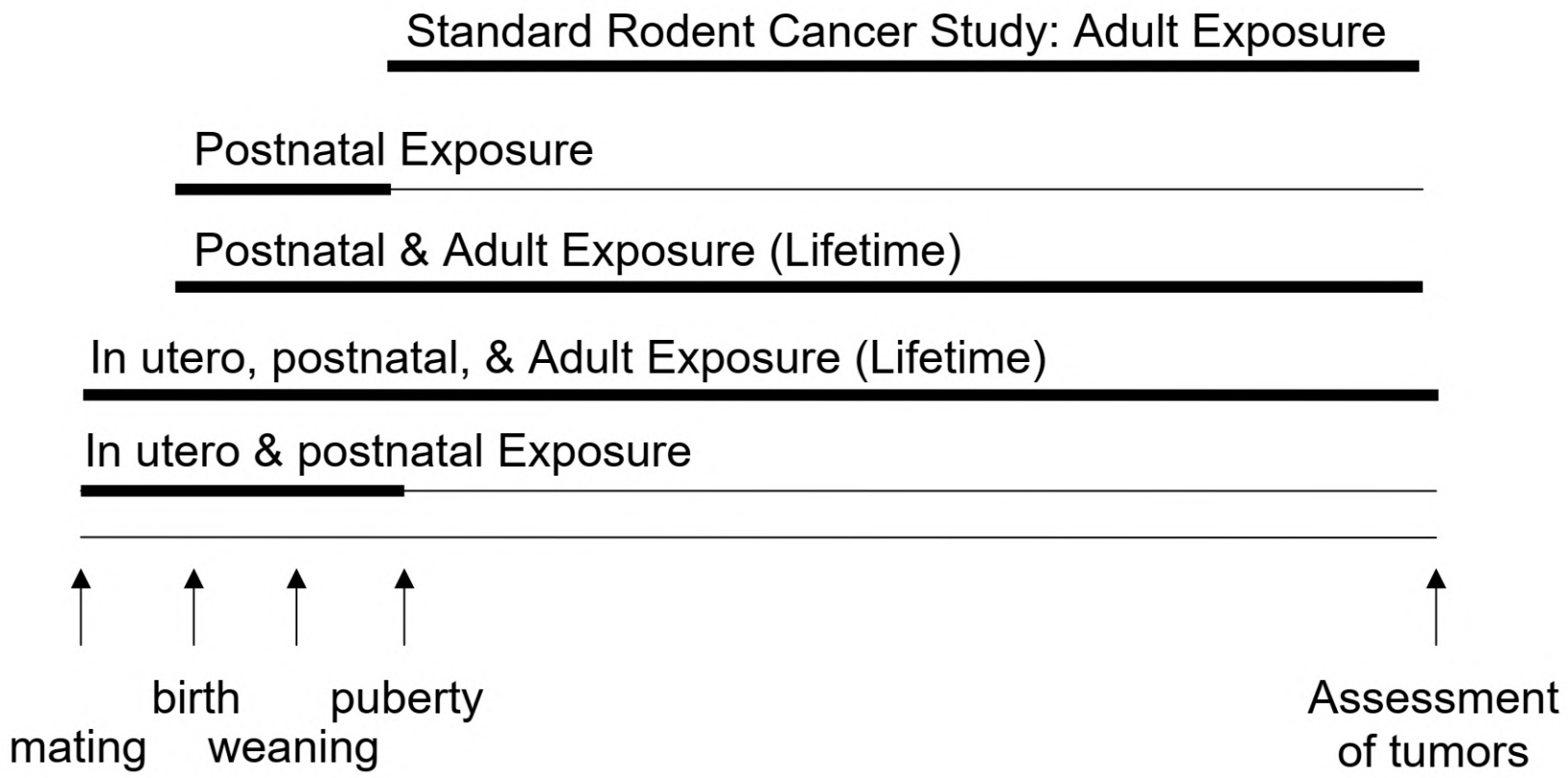

Figure 1. Study designs.

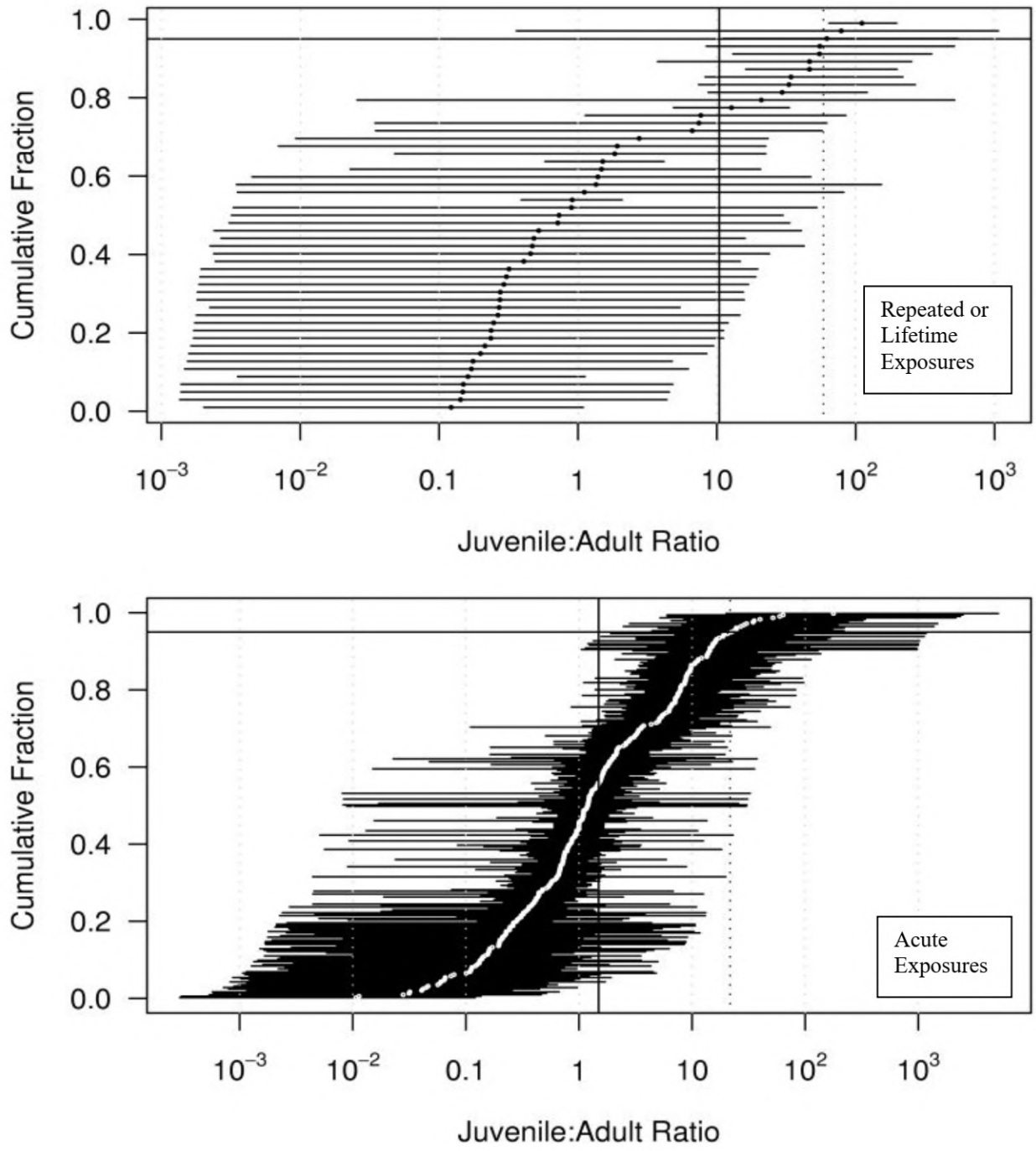

Figure 2: Posterior, unweighted geometric means and 95% confidence intervals for the ratios of juvenile to adult cancer potency for carcinogens acting primarily through a mutagenic mode of action. The top panel is for repeated and lifetime exposure studies (geometric mean in black), the bottom panel is for acute exposure studies mutagens (geometric mean in white). The horizontal lines to the left and right of each geometric mean correspond to 95% confidence limits. The vertical dark line represents the inverse-variance weighted geometric mean of the posterior geometric means. The horizontal dark line represents the 95th percentile of the unweighted distribution, with the vertical, dotted line establishing it value.

Figure 3. Flow chart for early-life risk assessment using mode of action framework

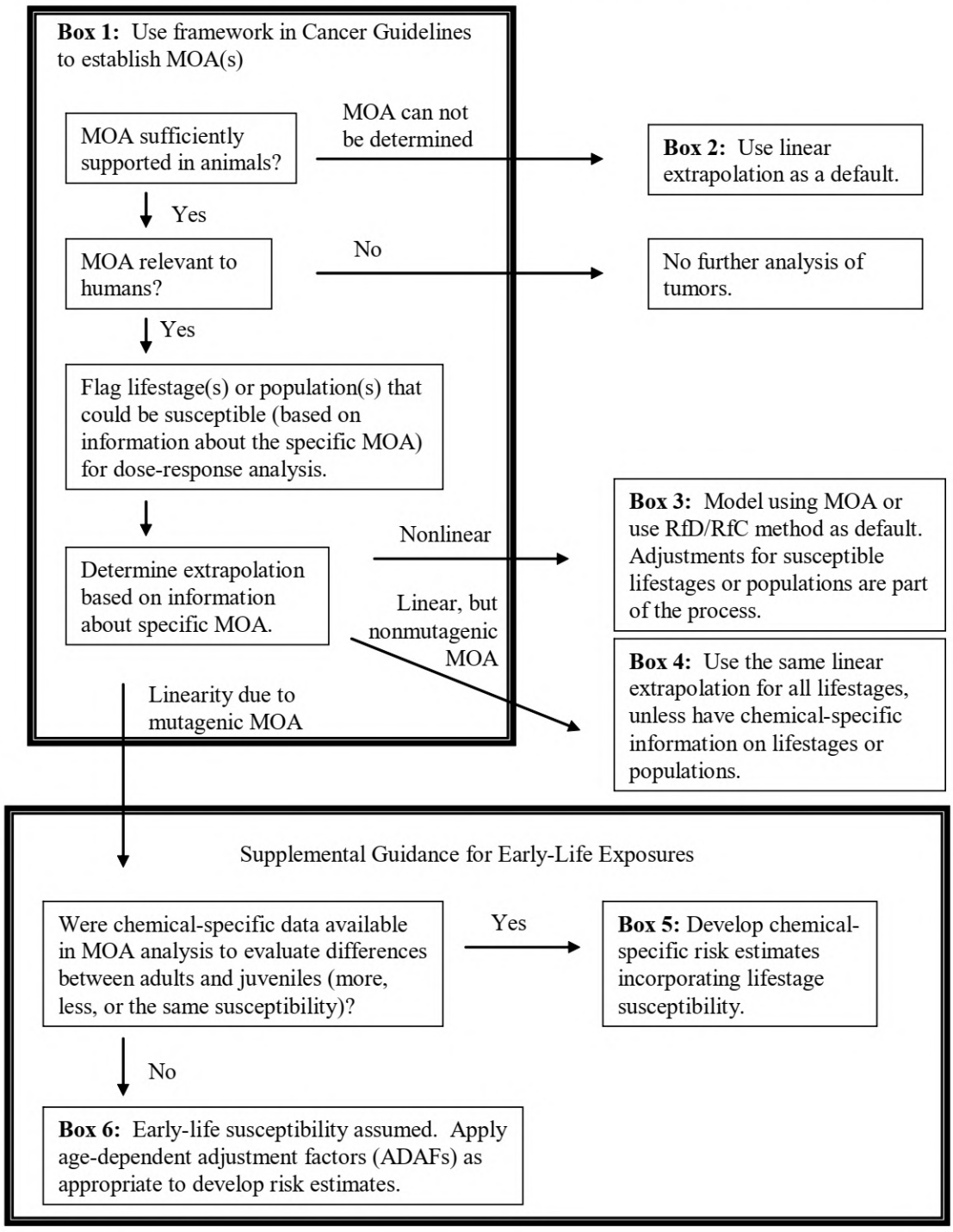

Table 1a. Chemicals that have been found to have carcinogenic effects from prenatal or postnatal exposure in animals as identified in different review articles

Chemical name	Review articles including prenatal and postnatal exposure					Chemicals selected for quantitative analysis
	Fujii (1991)	McClain et al. (2001)	Anderson et al. (2000)	Della Porta and Terracini (1969)	Other literature	
4-Acetylaminobiphenyl (AAB)	X					
4-Aminoazobenzene (AB)	X					
3-Amino-1,4,-dimethyl-5H-pyrido[4,3-b]indole (Trp-P-1)	X					
2-Aminodipyridol[1,2-a:3',2'-d]imidazole (Glu-P-2)	X					
2-Amino-6-methyldipyridol[1,2-a:3',2'-d]imidazole (Glu-P-1)	X					
3-Amino-1-methyl-5H-pyrido[4,3-b]indole (Trp-P-2)	X					
Amitrole						X
Arsenic					X	
5-Azacytidine			X			
3'-Azido-3'-deoxythymidine (AZT)			X			
Azoxymethane			X			
Benz[*a*]anthracene				X		
Benzidine			X			X
Benzo[*a*]pyrene (BaP)	X			X		X
1-(4'Bromophenylazo)-1-phenyl-1-hydroperoxymethane (BPH)	X					
N-Butyl-N-(3-carboxypropyl)nitrosamine (BCPN)	X					
N-Butyl-N-(3 hydroxbutyl)nitrosamine (BBN)	X					
Butylnitrosourea (BNU)	X					
Cyclophosphamide		X				
Dibenz[*a,h*]anthracene (DBA)				X		X
Dibutylnitrosamine (DBN)	X					
Dichlorodiphenyltrichloroethane (DDT)						X
Dieldrin						X
2-Diethylaminoethyl-2,2-dephenylvalerate hydrochloride (SKF 525A)	X					

Table 1a. Chemicals that have been found to have carcinogenic effects from prenatal or postnatal exposure in animals as identified in different review articles (continued)

Chemical name	Review articles including prenatal and postnatal exposure					Chemicals selected for quantitative analysis
	Fujii (1991)	McClain et al. (2001)	Anderson et al. (2000)	Della Porta and Terracini (1969)	Other literature	
Diethylnitrosamine (DEN)	X		X			X
Diethylstilbesterol (DES)			X			
4-Dimethylaminoazobenzene				X		
1,2-Dimethylhydrazine (DMH)	X					
7,12-Dimethylbenz[*a*]anthracene (DMBA)	X		X	X		X
Dimethylnitrosamine (DMN)	X		X	X		X
5',5'-Diphenylhydantoin (DPH)						X
Estradiol	X	X				
6-Ethoxy-2,2,4-trimethyl-1,2-dihydroquinoline (Santoquin)	X					
Ethylene thiourea (ETU)						X
Ethyl methane sulphonate				X		
Ethylnitrosobiuret			X			
Ethylnitrosourea (ENU)			X			X
N-2-Fluorenylacetamide (FAA)	X			X		
Genistein					X	
3-Hydroxyl-4-acetylaminobiphenyl (N-OH-AAB)	X					
N-2-Hydroxy-N-2-fluorenylacetamide (N-OH-FAA)	X					
2-Hydroxypropyl-propylnitrosamine			X			
9-Methylanthracene				X		
Methyl-2-benzylhydrazine			X			
Methylcholanthrene			X	X		
3-Methyl-4-dimethylaminoabenzene (3'ME-DAB)	X					
4-(Methylnitrosoamino)-1-(3-pyridyl)-1-butanone (NNK)			X			
Methylnitrosourea (NMU)			X			
Methylnitrosourethane			X			
1-Methyl-3-nitro-1-nitrosoguanidine (MNNG)	X					

Table 1a. Chemicals that have been found to have carcinogenic effects from prenatal or postnatal exposure in animals as identified in different review articles (continued)

Chemical name	Review articles including prenatal and postnatal exposure					Chemicals selected for quantitative analysis
	Fujii (1991)	McClain et al. (2001)	Anderson et al. (2000)	Della Porta and Terracini (1969)	Other literature	
2-Naphthylamine				X		
2-Naphthylhydroxyamine				X		
Nickel acetate			X			
N-Nitrosobuylamine			X			
4-Nitroquinoline-1-oxide			X	X		
N-Nitrosomethyl(2-oxopropyl)amine			X			
2-Oxopropyl-propylnitrosamine			X			
1-Phenyl-3,3',-dimethylhydrzine			X			
1-Phenyl-3,3,-dimethyltriazene			X			
Polybrominated biphenyls (PBBs)						X
Safrole (3,4-methylenedioxyally benzene)	X		X			X
Soot	X					
Sterigmatocystin	X					
Tamoxifen					X	
1,3,5-Trimethyl-2,4,6-tris[3,5-di-tert-butyl-4-hydroxybenzyl]benzene (Ionox 33)	X					
Urethane (ethyl carbamate)			X	X		X
Vinyl chloride						X

Table 1b. List of chemicals considered in this analysis. (These are chemicals for which both early-life and adult exposure are reported in the same animal experiment.)

Chemical	References	Study type	Mutagenic mode of action
Amitrole	Vesselinovitch (1983)	Repeat dosing	
Benzidine	Vesselinovitch et al. (1975b)	Repeat dosing	X
Benzo[*a*]pyrene (BaP)	Vesselinovitch et al. (1975a)	Acute exposure	X
Dibenzanthracene (DBA)	Law (1940)	Acute exposure	X
Dichlorodiphenyltrichloroethane (DDT)	Vesselinovitch et al. (1979)	Repeat dosing Lifetime exposure	
Dieldrin	Vesselinovitch et al. (1979)	Repeat dosing Lifetime exposure	
Diethylnitrosamine (DEN)	Peto et al. (1984)	Lifetime exposure	X
	Vesselinovitch et al. (1984)	Acute exposure	
Dimethylbenz[*a*]anthracene (DMBA)	Meranze et al. (1969)	Acute exposure	X
	Pietra et al. (1961)	Acute exposure	
	Walters (1966)	Acute exposure	
Dimethylnitrosamine (DMN)	Hard (1979)	Acute exposure	X
Diphenylhydantoin, 5,5- (DPH)	Chhabra et al. (1993b)	Repeat dosing Lifetime exposure	
Ethylnitrosourea (ENU)	Naito et al. (1981)	Acute exposure	X
	Vesselinovitch et al. (1974)	Acute exposure	
	Vesselinovitch (1983)	Acute exposure	
Ethylene thiourea (ETU)	Chhabra et al. (1992)	Repeat dosing Lifetime exposure	
3-Methylcholanthrene (3-MU)[a]	Klein (1959)	Repeat dosing	X
Methylnitrosourea (NMU)	Terracini and Testa (1970) Terracini et al. (1976)	Acute exposure Acute exposure	X
Polybrominated biphenyls (PBBs)	Chhabra et al. (1993a)	Repeat dosing Lifetime exposure	
Safrole	Vesselinovitch et al. (1979)	Repeat dosing Lifetime exposure	X
Urethane	Chieco-Bianchi et al. (1963) Choudari Kommineni et al. (1970) De Benedictis et al. (1962) Fiore-Donati et al. (1962)	Acute exposure Acute exposure Acute exposure Acute exposure	X
	Klein (1966)	Acute exposure Lifetime exposure	
	Liebelt et al. (1964)	Acute exposure	
	Rogers (1951)	Acute exposure	
Vinyl chloride (VC)	Maltoni et al. (1984)	Repeat dosing	X

[a] Formerly known as 20-methylcholanthrene.

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
Amitrole	Mice ($B6C3F_1$)	liver	Control	None	Control: 0 ppm	N/A	90 weeks	1/98 (1%)	0/96 (0%)	Incidences are mice with adenomas or carcinomas.	Vesselinovitch (1983)
			Gestation day 12	Diet, to mothers	500 ppm	Gestation day 12 to delivery		6/74 (8%)[b]	0/83 (0%)[b]		
			Newborn	Diet, to mothers	500 ppm	Birth until weaning		10/45 (22%)[b]	0/55 (0%)[b]		
			At weaning	Diet, to offspring	500 ppm	From weaning to 90 weeks		20/55 (36%)[b]	9/49 (18%)[b]		
Benzidine	Mice ($B6C3F_1$)	liver	Control	None	Control: 0 ppm	N/A	90 weeks	1/98 (1%)	0/100 (0%)	Higher sensitivity in males during perinatal period, in females during adulthood. Incidences are mice with adenomas or carcinomas.	Vesselinovitch et al. (1975b) Vesselinovitch et al. (1979a)
			Gestation day 12	Diet, to mothers	150 ppm	Gestation day 12 to delivery		17/55 (31%)[c]	2/62 (3%)[d]		
			Newborn	Diet, to mothers	150 ppm	Birth until weaning		62/65 (95%)[c]	2/43 (5%)[d]		
			At weaning	Diet, to offspring	150 ppm	From weaning to 90 weeks		22/50 (44%)[c]	47/50 (94%)[c]		
			Gestation day 12	Diet, to mothers	150 ppm	Gestation day 12 until weaning		49/49 (100%)[c]	12/48 (25%)[c]		
			Gestation day 12	Diet, to mothers	150 ppm	Gestation day 12 until 90 weeks		50/50 (100%)[c]	47/50 (94%)[c]		
DDT Dichlorodiphenyl-trichloroethane	Mice ($B6C3F_1$)	liver	Control	None	Control: 0 ppm	N/A	90 weeks	1/50 (2%)	—		Vesselinovitch et al. (1979b)
			Week 1	Gavage, daily	230 µg	Weeks 1–4		5/49 (10%)[d]	—		
			Week 5	Diet, daily	150 ppm	Weeks 5–90		8/49 (16%)[d]	—		
			Week 1	Gavage, daily until 4 weeks, then in diet	230 µg 150 ppm (diet)	Weeks 1–90		10/50 (20%)[c]	—		

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
Dieldrin	Mice ($B6C3F_1$)	liver	Control	None	Control: 0 ppm	N/A	90 weeks	1/58 (2%)	—		Vesselinovitch et al. (1979b)
			Week 1	Gavage, daily	12.5 µg	Weeks 1–4		3/46 (7%)[b]	—		
			Week 5	Diet, daily	10 ppm	Weeks 5–90		7/60 (12%)[b]	—		
			Week 1	Gavage, daily until 4 weeks, then in diet	12.5 µg 10 ppm	Weeks 1–90		21/70 (30%)[a]	—		
DEN[e] Diethylnitrosamine	Rats (Colworth)	liver	Control		Control	N/A		29/384 (8%)		Highest tumor rate when dosed at earlier ages. Incidents are rats with adenomas or carcinomas.	Peto et al. (1984)
			Week 3	Diet (in drinking water), daily	16 different doses combined[f]	From week 3 until death	6 months–3 years	105/180 (58%)[b]			
			Week 6			From week 6 until death		714/1440 (50%)[b]			
			Week 20			From week 20 until death		76/180 (42%)[b]			
		esophagus	Control		Control	N/A		0/384 (0%)			
			Week 3	Diet (in drinking water), daily	16 different doses combined[g]	From week 3 until death		77/180 (43%)[b]			
			Week 6			From week 6 until death		663/1440 (46%)[b]			
			Week 20			From week 20 until death		88/180 (49%)[b]			

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
DPH Diphenylhydantoin, 5,5-	Rats (F344/N)	liver	Control	Control	0 ppm	N/A	2 years	0/50 (0%)	0/50 (0%)	In rats, perinatal exposure ranged from 63 to 630 ppm, and adult exposures ranged from 240 to 2,400 ppm. In mice, perinatal exposure ranged from 21 to 210 ppm. Adult exposure ranged from 30 to 300 ppm in males and 60 to 600 ppm in females. Tumor incidences are animals with adenomas or carcinomas.	Chhabra et al. (1993b)
			Perinatal	Diet, daily	630 ppm	Perinatal through 8 weeks		1/50 (2%)[d]	0/49 (0%)[d]		
			8 weeks		800 ppm	8 weeks–2 years		2/50 (4%)[d]	1/50 (2%)[d]		
			8 weeks		2,400 ppm	8 weeks–2 years		4/50 (8%)[d]	1/50 (2%)[d]		
			Perinatal		630–800	Perinatal through 2 years		1/49 (2%)[d]	0/50 (0%)[d]		
			Perinatal		630–2,400 ppm	Perinatal through 2 years		5/49 (10%)[c]	0/50 (0%)[d]		
	Mice ($B6C3F_1$)	liver	Control	Control male	0 ppm	N/A	2 years	29/50 (58%)			
			Perinatal	Diet, male	210 ppm	Perinatal through 8 weeks		33/50 (66%)[d]			
			8 weeks		100 ppm	8 weeks–2 years		29/49 (59%)[d]			
			8 weeks		300 ppm	8 weeks–2 years		26/49 (53%)[d]			
			Perinatal		210–100 ppm	Perinatal through 2 years		35/49 (71%)[d]			
			Perinatal		210–300 ppm	Perinatal through 2 years		41/50 (82%)[c]			
			Control	Control female	0 ppm	N/A	2 years		5/48 (10.4%)[d]		
			Perinatal	Diet, female	210 ppm	Perinatal through 8 weeks			12/49 (24.5%)[d]		
			8 weeks		200 ppm	8 weeks–2 years			14/49 (28%)[c]		
			8 weeks		600 ppm	8 weeks–2 years			30/50 (60%)[c]		
			Perinatal		210–200 ppm	Perinatal through 2 years			16/50 (32%)[c]		
			Perinatal		210–600 ppm	Perinatal through 2 years			34/50 (68%)[c]		

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
ETU Ethylene thiourea	Rats (F344/N)	thyroid	Control	Control	0 ppm	N/A	2 years	1/49 (2%)	3/50 (6%)	Tumor incidences are animals with adenomas or carcinomas.	Chhabra et al. (1992)
			Perinatal	Diet, daily	90 ppm	Perinatal through 8 weeks		4/49 (8%)[d]	3/50 (6%)[d]		
			8 weeks		83 ppm	8 weeks–2 years		12/46 (26%)[c]	7/44 (16%)[d]		
			8 weeks		250 ppm	8 weeks–2 years		37/50 (74%)[c]	30/49 (61%)[c]		
			Perinatal		90–83 ppm	Perinatal through 2 years		13/50 (26%)[c]	9/47 (19%)[d]		
			Perinatal		90–250 ppm	Perinatal through 2 years		48/50 (96%)	37/50 (74%)		
	Mice ($B6C3F_1$)	liver	Control	Control	0 ppm	N/A	2 years	20/49 (41%)	4/50 (8%)		
			Perinatal	Diet, daily	330 ppm	Perinatal through 8 weeks		13/49 (26.5%)[d]	5/49 (10%)[d]		
			8 weeks		330 ppm	8 weeks–2 years		32/50 (64%)[c]	44/50 (88%)[c]		
			8 weeks		1,000 ppm	8 weeks–2 years		46/50 (92%)[c]	48/50 (96%)[c]		
			Perinatal		330–330 ppm	Perinatal through 2 years		34/49 (69%)[c]	46/50 (92%)[c]		
			Perinatal		330–1,000 ppm	Perinatal through 2 years		47/49 (6%)[c]	49/50 (98%)[c]		
		thyroid	Control	Control	0 ppm	N/A		1/50 (2%)	0/50 (0%)		
			Perinatal	Diet, daily	330 ppm	Perinatal through 8 weeks		1/46 (2%)[d]	1/49 (2%)[d]		
			8 weeks		330 ppm	8 weeks–2 years		1/49 (2%)[d]	2/50 (4%)[d]		
			8 weeks		1,000 ppm	8 weeks–2 years		29/50 (58%)[c]	38/50 (76%)[c]		

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
ETU Ethylene thiourea (continued)			Perinatal		330–330 ppm	Perinatal through 2 years		2/48 (4%)[d]	10/49 (20%)[c]		
			Perinatal		330–1,000 ppm	Perinatal through 2 years		35/49 (71%)[c]	38/50 (76%)[c]		
		pituitary	Control	Control	0 ppm	N/A		0/44 (0%)	11/47 (23%)		
			Perinatal	Diet, daily	330 ppm	Perinatal through 8 weeks		0/42 (0%)[d]	11/48 (23%)[d]		
			8 weeks		330 ppm	8 weeks–2 years		0/42 (0%)[d]	19/49 (39%)[d]		
			8 weeks		1,000 ppm	8 weeks–2 years		8/41 (19.5%)[c]	26/49 (53%)[c]		
			Perinatal		330–330 ppm	Perinatal through 2 years		0/45 (0%)[d]	26/47 (55%)[c]		
			Perinatal		330–1,000 ppm	Perinatal through 2 years		4/39 (10%)[d]	24/47 (51%)[c]		

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death		Tumor incidence		Reference
							M	F	M	F	
3-Methylcholanthrene (formerly known as 20-methylcholanthrene)	Mice (Albino)	liver	Control	gavage, 3× per week	NA	NA	475 days	480 days	3/39 (7.7%)	0/36 (0%)	Klein (1959)
			8 days		0.25 mg/g	10×	311 days	321 days	21/25 (84%)[b]	7/30 (23.3%)[b]	
			90 days		0.25 mg/g	10×	330 days	366 days	1/26 (3.8%)[b]	0/29 (0%)[d]	
		lung	Control		NA	NA	475 days	480 days	17/39 (43.6%)	14/36 (38.9%)	
			8 days		0.25 mg/g	10×	311 days	321 days	25/25 (100%)[b]	28/30 (93.3%)[b]	
			90 days		0.25 mg/g	10×	330 days	366 days	25/26 (96.2%)[b]	27/29 (93.1%)[b]	
		fore-stomach	Control		NA	NA	475 days	480 days	0/39 (0%)	0/36 (0%)	
			8 days		0.25 mg/g	10×	311 days	321 days	12/25 (48%)[b]	12/30 (40%)[b]	
			90 days		0.25 mg/g	10×	330 days	366 days	13/26 (50%)[b]	8/29 (27.6%)[b]	
		skin	Control		NA	NA	475 days	480 days	0/39 (0%)	0/36 (0%)	
			8 days		0.25 mg/g	10×	311 days	321 days	4/25 (16%)[b]	4/30 (13.3%)[b]	
			90 days		0.25 mg/g	10×	330 days	366 days	1/26 (3.8%)[b]	1/25 (4%)[b]	

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
PBBs Polybrominated biphenyls	Rats (F344/N)	liver[g]	Control	Control	0 ppm	N/A	2 years	1/50 (2%)	0/50 (0%)	Findings suggest that combined perinatal and adult exposure increases PBB-related hepatocellular carcinogenicity relative to adult-only exposure in mice and female rats. Apparent association between increasing incidences of MCL and exposure to PBB in male and female rats. Tumor incidences are animals with adenomas or carcinomas.	Chhabra et al. (1993a)
			Perinatal	Diet	10 ppm	Perinatal–8 weeks		5/50 (10%)[d]	0/50 (0%)[d]		
			8 weeks		10 ppm	8 weeks–2 years		12/49 (24%)[c]	12/50 (24%)[c]		
			8 weeks		30 ppm	8 weeks–2 years		41/50 (82%)[c]	39/50 (78%)[c]		
			Perinatal		10–10 ppm	Perinatal–2 years		16/50 (32%)[c]	39/50 (78%)[c]		
			Perinatal		10–30 ppm	Perinatal–2 years		41/50 (82%)[c]	47/50 (94%)[c]		
		Mono-nuclear cell leukemia (MCL)	Control	Control	0 ppm	N/A	2 years	25/50 (50%)	14/50 (28%)		
			Perinatal	Diet	10 ppm	Perinatal–8 weeks		31/50 (62%)[d]	13/50 (26%)[d]		
			8 weeks		10 ppm	8 weeks–2 years		33/50 (66%)[c]	22/50 (44%)[d]		
			8 weeks		30 ppm	8 weeks–2 years		31/50 (62%)[d]	23/50 (46%)[c]		
			Perinatal		10–10 ppm	Perinatal–2 years		37/50 (74%)[c]	27/50 (54%)[c]		
			Perinatal		10–30 ppm	Perinatal–2 years		37/50 (74%)[c]	25/50 (50%)[c]		
	Mice ($B6C3F_1$)	liver[g]	Control	Control	0 ppm	N/A	2 years	16/50 (32%)	5/50 (10%)		
			Perinatal	Diet	30 ppm	Perinatal–8 weeks		40/50 (80%)[c]	21/50 (42%)[c]		
			8 weeks		10 ppm	8 weeks–2 years		48/49 (98%)[c]	42/50 (84%)[c]		
			8 weeks		30 ppm	8 weeks–2 years		48/50 (96%)[c]	47/48 (98%)[c]		
			Perinatal		10 ppm	Perinatal–2 years		46/49 (94%)[c]	44/50 (88%)[c]		
			Perinatal		30–30 ppm	Perinatal–2 years		50/50 (100%)[c]	47/47 (100%)[c]		

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
Safrole	Mice ($B6C3F_1$)	liver	Control	None	None	N/A	90 weeks	3/100 (3%)	0/100 (0%)	Highest tumor rate in males due to preweaning treatment. Highest tumor rate in females due to susceptibility in adulthood. Tumor incidences are mice with adenomas or carcinomas.	Vesselinovitch et al. (1979b)
			Day 12 of gestation	Gavage, to mothers	120 µg/g body weight	4× (days 12, 14, 16, 18)		2/61 (3%)[d]	0/65 (0%)[d]		
			Newborn	Gavage, to mothers, on alternate days	120 µg/g body weight	From birth until weaning		28/83 (34%)[c]	2/80 (3%)[d]		
			At weaning	Gavage, to offspring, 2× weekly	120 µg/g body weight	From weaning until 90 weeks		4/35 (11%)[d]	22/36 (61%)[c]		
			Day 12 of gestation	Gavage, to mothers, alternate days	120 µg/g body weight	From gestation until weaning		22/68 (32%)[b]	1/72 (1%)[b]		
			Day 12 of gestation	Gavage, to mothers, alternate days until weaning; Gavage, to offspring, 2× weekly	120 µg/g body weight	From gestation until 90 weeks		19/37 (51%)[b]	37/46 (80%)[b]		
Urethane	Mice ($B6AF_1/J$)	liver	1 week	gavage	2.5 mg/pup	1×	39–40 weeks	Tumor incidence[a]		No tumor data for controls.	Klein (1966)
								M	F		
								12/37 (33%)[b]	0/40 (0%)[b]		
			1 week		2.5 mg/pup	16× (1× at 1 week; 3× weekly for 5 weeks beginning at 4 wks of age)	39 weeks	11/33 (33%)[b]	0/31 (0%)[b]		
			4 weeks		2.5 mg/pup	15× (3× weekly for 5 weeks beginning at 4 weeks of age)	41 weeks	0/37 (0%)[b]	0/31 (0%)[b]		

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
VC Vinyl chloride	Rats (Sprague-Dawley)	liver angio-sarcoma	Control	Control	0 ppm	N/A	135 weeks	0/22 (0%)	0/29 (0%)	Higher tumor risk when exposed at birth, higher for females.	Maltoni et al. (1984)
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk, 5 weeks	124 weeks	5/18 (28%)[b]	12/24 (50%)[b]		
					10,000 ppm			6/24 (25%)[b]	9/20 (45%)[b]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	3/17 (18%)[b]	10/25 (40%)[b]		
					10,000 ppm			3/21 (14%)[b]	4/25 (16%)[b]		
		zymbal gland	Control	Control	0 ppm	N/A	135 weeks	0/28 (0%)	0/29 (0%)		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk, 5 weeks	124 weeks	1/12 (8%)[b]	1/17 (6%)[b]		
					10,000 ppm			1/17 (6%)[b]	0/17 (0%)[b]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	3/29 (10%)[b]	4/30 (13%)[b]		
					10,000 ppm			10/30 (33%)[b]	6/30 (20%)[b]		
		leukemia	Control	Control	0 ppm	N/A	135 weeks	0/27 (0%)	1/29 (3%)		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk, 5 weeks	124 weeks	N/A	1/7 (14%)[b]		
					10,000 ppm			2/6 (33%)[b]	0/15 (0%)[b]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	N/A	0/29 (0%)[b]		
					10,000 ppm			0/27 (0%)[b]	2/29 (7%)[b]		
		nephro-blastoma	Control	Control	0 ppm	N/A	135 weeks	0/22 (0%)	0/29 (0%)		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk, 5 weeks	124 weeks	0/15 (0%)[b]	0/21 (0%)[b]		
					10,000 ppm			0/19 (0%)[b]	0/17 (0%)[b]		

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
VC Vinyl chloride (continued)			Week 13		6,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	4/18 (22%)[b]	1/26 (4%)[b]		
					10,000 ppm			3/21 (14%)[b]	2/25 (8%)[b]		
		angio-sarcomas: other sites	Control	Control	0 ppm	N/A	135 weeks	0/29 (0%)	0/29 (0%)		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk, 5 weeks	124 weeks	1/15 (7%)[b]	0/21 (0%)[b]		
					10,000 ppm			0/19 (0%)	0/17 (0%)[b]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	1/29 (3%)[b]	2/30 (7%)[b]		
					10,000 ppm			2/30 (7%)[b]	1/30 (3%)[b]		
		angiomas and fibromas: other sites	Control	Control	0 ppm	N/A	135 weeks	0/28 (0%)	2/29 (7%)[b]		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk, 5 weeks	124 weeks	1/15 (7%)[b]	0/21 (0%)[b]		
					10,000 ppm			2/19 (11%)[b]	1/17 (6%)[b]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	2/29 (7%)[b]	2/30 (7%)[b]		
					10,000 ppm			2/29 (7%)[b]	1/29 (3%)[b]		
		hepatoma	Control	Control	0 ppm	N/A	135 weeks	0/19 (0%)	0/28 (0%)		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk, 5 weeks	124 weeks	9/18 (50%)[b]	11/24 (46%)[b]		
					10,000 ppm			13/24 (54%)[b]	7/20 (35%)[b]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	0/10 (0%)[b]	1/17 (6%)[b]		
					10,000 ppm			1/8 (13%)[b]	0/16 (0%)[b]		

Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult repeated exposures (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
VC Vinyl chloride (continued)		skin carcinomas	Control	Control	0 ppm	N/A	135 weeks	0/20 (0%)	1/29 (3%)		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk, 5 weeks	124 weeks	1/10 (10%)[b]	1/14 (7%)[b]		
					10,000 ppm			1/16 (6%)[b]	0/15 (0%)[b]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	0/15 (0%)[b]	2/19 (11%)[b]		
					10,000 ppm			2/13 (15%)[b]	1/21 (5%)[b]		
		neuro-blastoma	Control	Control	0 ppm	N/A	135 weeks	0/22 (0%)	0/29 (0%)		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk, 5 weeks	124 weeks	0/18 (0%)[b]	0/29 (0%)[b]		
					10,000 ppm			0/22 (0%)[b]	0/19 (0%)[b]		
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	2/21 (10%)[b]	1/27 (4%)[b]		
					10,000 ppm			2/22 (9%)[b]	5/26 (19%)[b]		

[a] Where not delineated by gender, data combined by study authors or gender not specified. Where percentages only are given, number of subjects not specified.
[b] Not evaluated by authors.
[c] Significant compared with controls.
[d] Evaluated but not significant compared with controls.
[e] Reported as NDEA (N-nitrosodiethylamine) in the original document.
[f] Results from each dose are not available.
[g] Tumors were adenomas or carcinomas.

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
BaP Benzo[*a*]pyrene	Mice ($B6C3F_1$)	liver	Control	Control	None	N/A	142 weeks	7/100 (7%)	1/100 (1%)	In general, hepatomas developed with significantly higher incidence ($p<0.01$) in mice that were treated within 24 hours of birth or at 15 days of age than they did in similarly treated animals at 42 days of age. + higher for males.	Vesselinovitch et al. (1975a)
			Day 1	i.p.	75 µg/g body weight	1×	86 weeks (m) 129 weeks (f)	26/47 (55%)[b]	3/45 (7%)[b]		
					150 µg/g body weight	1×	81 weeks (m) 121 weeks (f)	51/63 (81%)[b]	8/45 (18%)[b]		
			Day 15	i.p.	75 µg/g body weight	1×	93 weeks (m) 116 weeks (f)	36/60 (60%)[b]	4/55 (7%)[b]		
					150 µg/g body weight	1×	81 weeks (m) 90 weeks (f)	32/55 (58%)[b]	4/55 (7%)[b]		
			Day 42	i.p.	75 µg/g body weight	1×	108 weeks(m)	7/55 (13%)[b]	0/47 (0%)[b]		
					150 µg/g body weight	1×	87 weeks (m)	4/47 (9%)[b]	0/46 (0%)[b]		
	Mice ($C3AF_1$)	liver	Control	Control	None	N/A	142 weeks	8/100 (8%)	1/100 (1%)	+ higher for males. "Age at death" is the average age at which tumors were observed.	
			Day 1	i.p.	75 µg/g body weight	1×	80 weeks (m) 91 weeks (f)	21/62 (34%)[b]	1/45 (2%)[b]		
					150 µg/g body weight	1×	69 weeks (m) 701 weeks (f)	24/52 (46%)[b]	1/56 (2%)[b]		
			Day 15	i.p.	75 µg/g body weight	1×	90 weeks (m) 102 weeks (f)	15/56 (27%)[b]	1/49 (2%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
BaP Benzo[*a*]pyrene (continued)					150 µg/g body weight	1×	77 weeks (m) 62 weeks (f)	12/53 (23%)[b]	1/57 (2%)[b]		
			Day 42	i.p.	75 µg/g body weight	1×		0/30 (0%)[b]	0/32 (0%)[b]		
					150 µg/g body weight	1×	79 weeks (m)	1/32 (3%)[c]	0/40 (0%)[b]		
	Mice ($B6C3F_1$)	lung	Control	Control	Control	N/A	142 weeks	13/100 (13%)	9/100 (9%)	Both sexes developed lung tumors with higher incidence when treated with BaP at birth than at 15 or 42 days of age ($p<0.05$).	
			Day 1	i.p.	75 µg/g body weight	1×	103 weeks (m) 126 weeks (f)	20/47 (43%)[b]	22/45 (49%)[b]		
					150 µg/g body weight	1×	84 weeks (m) 112 weeks (f)	37/63 (59%)[b]	28/45 (62%)[b]		
			Day 15	i.p.	75 µg/g body weight	1×	103 weeks (m) 122 weeks (f)	15/60 (25%)[b]	18/55 (33%)[b]		
					150 µg/g body weight	1×	82 weeks (m) 101 weeks (f)	20/55 (36%)[b]	18/45 (40%)[b]		
			Day 42	i.p.	75 µg/g body weight	1×	119 weeks (m) 131 weeks (f)	20/55 (36%)[b]	12/47 (26%)[b]		
					150 µg/g body weight	1×	95 weeks (m) 118 weeks (f)	18/47 (38%)[b]	8/46 (17%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a] M	Tumors[a] F	Comments	Reference
BaP Benzo[*a*]pyrene (continued)	Mice ($C3AF_1$)	lung	Control	Control	None	N/A	142 weeks	60/100 (60%)	50/100 (50%)	Of the two mouse strains tested, $C3AF_1$ mice developed significantly more tumors than did the $B6C3F_1$ mice ($p<0.001$).	Vesselinovitch et al. (1975a)
			Day 1	i.p.	75 µg/g body weight	1×	78 weeks (m) 82 weeks (f)	58/62 (93%)[b]	42/45 (93%)[b]		
					150 µg/g body weight	1×	70 weeks (m) 73 weeks (f)	48/52 (92%)[b]	52/56 (93%)[b]		
			Day 15	i.p.	75 µg/g body weight	1×	87 weeks (m) 98 weeks (f)	52/56 (93%)[b]	46/49 (94%)[b]		
					150 µg/g body weight	1×	75 weeks (m) 79 weeks (f)	50/53 (94%)[b]	52/57 (91%)[b]		
			Day 42	i.p.	75 µg/g body weight	1×	91 weeks (m) 93 weeks (f)	28/30 (93%)[b]	28/32 (87%)[b]		
					150 µg/g body weight	1×	85 weeks (m) 83 weeks (f)	28/32 (87%)[b]	36/40 (90%)[b]		
DBA Dibenzanthracene	Mice (Caracul × P stock)	lung	Control	Control	None	N/A	228 days	1/31 (3.2%)			Law (1940)
			Day 1	i.p.	4 mg per cm^3 vehicle	1×	181 days	24/24 (100%)[b]			
			2 months	s.c.	4 mg per cm^3 vehicle	1×	189 days	2/29 (6.9%)[b]			

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
DEN Diethylnitrosamine	Mice ($B6C3F_1$)	liver	Control	Control	Vehicle (0.01 mL trioctanoin/g body weight)	4×	142 weeks (m) 137 weeks (f)	7/98 (7%)	1/100 (1%)	Animals treated as newborns and infants developed significantly more liver tumors than animals that were treated as young adults. Newborns and infant females developed liver tumors at a later age than similarly treated males. Incidences for malignant tumors only.	Vesselinovitch et al. (1984)
			Day 1	i.p. (3-, 6- and 6-day intervals)	1.5 µg/g body weight	4×	67 weeks (m) 90 weeks (f)	37/51 (73%)[b]	45/64 (70%)[b]		
					3 µg/g body weight	4×	65 weeks (m) 80 weeks (f)	40/58 (69%)[b]	44/65 (68%)[b]		
			Day 15		1.5 µg/g body weight	4×	86 weeks (m) 117 weeks (f)	41/57 (72%)[b]	40/71 (56%)[b]		
					3 µg/g body weight	4×	76 weeks (m) 96 weeks (f)	48/69 (70%)[b]	46/62 (74%)[b]		
			Day 42		1.5 µg/g body weight	4×	117 weeks (m) 135 weeks (f)	9/49 (18%)[b]	1/47 (2%)[b]		
					3 µg/g body weight	4×	123 weeks (m) 133 weeks (f)	6/38 (16%)[b]	4/57 (7%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
DEN Diethylnitrosamine (continued)	Mice ($C3AF_1$)	liver	Control	Control	Vehicle (0.1 trioctanoin/g body weight)	4×	123 weeks (m) 131weeks (f)	8/99 (8%)	1/97 (1%)	Highest tumor rate when dosed at early ages. Newborns and infant females developed liver tumors at a lower incidence than similarly treated males. + higher for males.	Vesselinovitch et al. (1984)
			Day 1	i.p. (3-, 6- and 6-day intervals)	1.5 µg/g body weight	4×	64 weeks (m) 84 weeks (f)	23/32 (72%)[b]	11/39 (28%)[b]		
					3 µg/g body weight	4×	59 weeks (m) 76 weeks (f)	39/58 (67%)[b]	26/50 (52%)[b]		
			Day 15		1.5 µg/g body weight	4×	82 weeks (m) 102 weeks (f)	22/46 (48%)[b]	8/65 (12%)[b]		
					3 µg/g body weight	4×	74 weeks (m) 94 weeks (f)	35/54 (65%)[b]	22/62 (35%)[b]		
			Day 42		1.5 µg/g body weight	4×	105 weeks (m) 106 weeks (f)	12/56 (22%)[b]	0/53 (0%)[b]		
					3 µg/g body weight	4×	105 weeks (m) 103 weeks (f)	9/57 (16%)[b]	0/56 (0%)[b]		
	Mice ($B6C3F_1$)	lung	Control	Control	Vehicle (0.1 trioctanoin/g body weight)	4×	142 weeks (m) 137 weeks (f)	13/98 (13%)	9/100 (9%)	The mice treated as newborns showed lung tumors earlier than animals exposed at other times. It is not known whether this was due to actual earlier emergence of tumors or	

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
DEN Diethylnitrosamine (continued)			Day 1	i.p. (3-, 6- and 6-day intervals)	1.5 µg/g body weight	4×	70 weeks (m) 91 weeks (f)	29/51 (57%)[b]	49/64 (77%)[b]	to their earlier detection caused by shorter survival.	
					3 µg/g body weight	4×	68 weeks (m) 81 weeks (f)	34/58 (59%)[b]	42/65 (65%)[b]		
			Day 15		1.5 µg/g body weight	4×	87 weeks (m) 115 weeks (f)	51/57 (89%)[b]	61/71 (86%)[b]		
					3 µg/g body weight	4×	77 weeks (m) 97 weeks (f)	51/69 (74%)[b]	53/62 (85%)[b]		
			Day 42		1.5 µg/g body weight	4×	123 weeks (m) 129 weeks (f)	38/49 (78%)[b]	38/47 (81%)[b]		
					3 µg/g body weight	4×	121 weeks (m) 127 weeks (f)	33/38 (87%)[b]	43/57 (75%)[b]		
	Mice ($C3AF_1$)	lung	Control	Control	Vehicle (0.1 trioctanoin/g body weight)	4×	142 weeks (m) 137weeks (f)	60/99 (61%)	50/97 (52%)	Of the two strains, $C3AF_1$ mice developed lung tumors with a higher incidence and multiplicity than $B6C3F_1$ hybrids.	
			Day 1	i.p. (3-, 6- and 6-day intervals)	1.5 µg/g body weight	4×	65 weeks (m) 84 weeks (f)	30/32 (94%)[b]	38/39 (97%)[b]		
					3 µg/g body weight	4×	59 weeks (m) 76 weeks (f)	49/58 (84%)[b]	46/50 (92%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
DEN Diethylnitrosamine (continued)			Day 15		1.5 µg/g body weight	4×	80 weeks (m) 101 weeks (f)	42/46 (91%)[b]	61/65 (94%)[b]		
					3 µg/g body weight	4×	74 weeks (m) 92 weeks (f)	50/54 (93%)[b]	57/62 (92%)[b]		
			Day 42		1.5 µg/g body weight	4×	104 weeks (m) 110 weeks (f)	55/56 (98%)[b]	52/53 (98%)[b]		
					3 µg/g body weight	4×	101 weeks (m) 102 weeks (f)	56/57 (98%)[b]	54/56 (96%)[b]		
	Mice ($B6C3F_1$)	liver	Control	Control	None	N/A	90 weeks	1/98 (1%)	0/96 (0%)	Infant animals of both sexes (Day 15) were more sensitive than similarly exposed adults.	Vesselinovitch and Mihailovich (1983)
			Gestation day 18	i.p.	1.5 µg/g body weight	1×		2/50 (4%)[b]	1/51 (2%)[b]		
			Day 15	i.p. (3-, 6- and 6-day intervals)	1.5 µg/g body weight	4×		47/51 (92%)[b]	60/64 (94%)[b]		
			Day 42		1.5 µg/g body weight	4×		13/49 (26%)[b]	3/47 (6%)[b]		
			Day 1	i.p.	1.5 µg/g body weight	1×	73 weeks	15/59 (25%)[b]	—	At the 1.5-µg dose level, 1-day-old mice developed significantly fewer liver tumors than similarly treated infants (Day 15) ($p<0.025$). Tumor incidence in treated groups versus controls was not evaluated.	Vesselinovitch et al. (1979a)
					5 µg/g body weight	1×		29/45 (64%)[b]	—		
					10 µg/g body weight	1×		24/25 (96%)[b]	—		
			Day 15	i.p.	1.5 µg/g body weight	1×		13/24 (54%)[b]	—		
					5 µg/g body weight	1×		40/54 (74%)[b]	—		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
DEN Diethylnitrosamine (continued)					10 µg/g body weight	1×		25/25 (100%)[b]	—		
DMBA Dimethyl-benz[*a*]anthracene	Rats (Sprague-Dawley)	mammary adeno-sarcoma	Day 20	Gavage	10 mg/100 g body weight	1×	Week 25	—	3/6 (50%)[b]	36 of 42 (86%) animals dosed at age 20 days died soon after. Highest number of tumors per animal was in the 46-day group, with decreasing numbers in the older animals. Animals were sacrificed 22 weeks after treatment.	Russo et al. (1979)
			Day 30		10 mg/100 g body weight	1×	Week 26	—	14/15 (93%)[b]		
			Day 40		10 mg/100 g body weight	1×	Week 27	—	8/9 (89%)[b]		
			Day 46		10 mg/100 g body weight	1×	Week 28	—	8/8 (100%)[b]		
			Day 55		10 mg/100 g body weight	1×	Week 29	—	33/34 (97%)[b]		
			Day 70		10 mg/100 g body weight	1×	Week 32	—	5/8 (63%)[b]		
			Day 140		10 mg/100 g body weight	1×	Week 42	—	10/15 (67%)[b]		
			Day 180		10 mg/100 g body weight	1×	Week 47	—	14/26 (54%)[b]		
	Rats (Wistar)	mammary carcinoma[d]	Control 5–8 weeks	Control	None	N/A	17 months	0/22 (0%)	0/25 (0%)	Highest tumor rate in females exposed at 5–8 weeks. Animals were observed for 16 months following treatment.	Meranze et al. (1969)
			Control 26 weeks	Control	None	N/A	20 months	0/31 (0%)	2/20 (10%)		
			< Week 2	Gavage	0.5–1.0 mg	1×	Week 40–56	0/23 (0%)[b]	4/50 (8%)[b]		
			Week 5–8		15 mg	1×	Week 14–55	0/23 (0%)[b]	14/25 (56%)[b]		
			Week 26		15 mg	1×	Week 32–73	0/34 (0%)[b]	4/26 (15%)[b]		
	Rats (Wistar, castrated)	mammary carcinoma	Week 5–8	Gavage	15 mg	1×	Week 14–55	0/21 (0%)[b]	0/22 (0%)[b]		
			Week 26		15 mg	1×	Week 32–73	0/33 (0%)[b]	0/26 (0%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
DMBA Dimethyl-benz[*a*]anthracene (continued)	Rats (Wistar)	Total tumors	Control 5–8 weeks	Control	None	N/A	17 months	0/22 (0%)	0/25 (0%)	Total tumors includes leukemia.	
			Control 26 weeks	Control	None	N/A	20 months	2/31 (6%)	5/20 (25%)		
			< Week 2	Gavage	0.5–1.0 mg	1×	Week 40–56	16/23 (70%)[b]	36/50 (72%)[b]		
			Week 5–8		15 mg	1×	Week 14–55	7/23 (30%)[b]	16/25 (64%)[b]		
			Week 26		15 mg	1×	Week 32–73	12/34 (35%)[b]	13/26 (50%)[b]		
	Mice (BALB/c)	lung	Control: Day 1	Control s.c.	Aqueous gelatine	1×	40 weeks	0/12 (0%)	7/23 (30%)	15 µg DMBA gave rise to a significantly greater incidence of lung tumors when administered to newborn mice than to suckling or young adults.	Walters (1966)
			Day 1	s.c.	15 µg	1×	40 weeks[f]	14/14 (100%)[b]	24/24 (100%)[b]		
			Week 2–3 (suckling)	s.c.	15 µg	1×	42–43 weeks	12/23 (52%)[b]	16/22 (73%)[b]		
				s.c.	30 µg (60 µg total)	2×	42–43 weeks	14/14 (100%)[b]	24/24 (100%)[b]		
			Adult[e]	s.c.	15 µg	1×	48-49 weeks	6/12 (50%)[b]	15/33 (45%)[b]		
				s.c.	30 µg (60 µg total)	2×	48-49 weeks	9/10 (90%)[b]	21/23 (91%)[b]		
				s.c.	30 µg (180 µg total)	6×	48-49 weeks	12/12 (100%)[b]	13/13 (100%)[b]		
	Mice (Swiss)	lymphoma	Control	Control	None	N/A	31–52 weeks	3/408 (0.7%)		Higher tumor rates at younger age of exposure. Only one treatment group was exposed i.p.; others were exposed by s.c. injection..	Pietra et al. (1961)
			Day 1	i.p.	30–40 µg	1×	13–33 weeks	6/31 (19%)[b]			
			Day 1	s.c.	30–40 µg	1×	12–27 weeks	8/27 (30%)[b]			
			Week 8	s.c.	900 µg	1×	30 weeks	1/13 (8%)[b]			

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a] M	Tumors[a] F	Comments	Reference
DMBA Dimethyl-benz[*a*]anthracene (continued)	Mice (Swiss)	lung	Control	Control	None	N/A	31–52 weeks	4/408 (0.9%)			
			Day 1	i.p.	30–40 µg	1×	13–33 weeks	24/31 (77%)[b]			
			Day 1	s.c.	30–40 µg	1×	12–27 weeks	23/27 (85%)[b]			
			Week 8	s.c.	900 µg	1×	30 weeks	2/13 (15%)[b]			
DMN Dimethyl-nitrosamine	Rats (Wistar)	kidney carcinoma	Day 1	i.p.	20 mg/kg	1×	≥5 months	1/33 (3)[b]		In the neonatal group, the dose was reduced to 20 mg/kg to achieve approximately equivalent numbers of survivors. No control group.	Hard (1979)
			Day 21		30 mg/kg	1×		5/39 (13)[b]			
			Month 1		30 mg/kg	1×		2/33 (6)[b]			
			Month 1.5		30 mg/kg	1×		1/28 (4)[b]			
			Month 2		30 mg/kg	1×		1/26 (4)[b]			
			Month 3		30 mg/kg	1×		10/27 (37)[b]			
			Month 4		30 mg/kg	1×		7/32 (22)[b]			
			Month 5		30 mg/kg	1×		0/14 (0)[b]			
	Rats (Wistar)	kidney adenoma	Day 1	i.p.	20 mg/kg	1×	≥5 months	1/33 (3)[b]			
			Day 21		30 mg/kg	1×		13/39 (33)[b]			
			Month 1		30 mg/kg	1×		11/33 (33)[b]			
			Month 1.5		30 mg/kg	1×		13/28 (48)[b]			
			Month 2		30 mg/kg	1×		11/26 (42)[b]			
			Month 3		30 mg/kg	1×		18/27 (67)[b]			
			Month 4		30 mg/kg	1×		17/32 (53)[b]			
			Month 5		30 mg/kg	1×		6/14 (43)[b]			

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a] M	Tumors[a] F	Comments	Reference
DMN Dimethyl-nitrosamine (continued)	Rats (Wistar)	kidney mesenchymal tumors	Day 1	i.p.	20 mg/kg	1×	≥5 months	8/33 (24)[b]		Mesenchymal tumors were most frequent in the three youngest age groups (z test, $p < 0.001$).	
			Day 21		30 mg/kg	1×		18/39 (46)[b]			
			Month 1		30 mg/kg	1×		23/33 (70)[b]			
			Month 1.5		30 mg/kg	1×		5/28 (19)[b]			
			Month 2		30 mg/kg	1×		2/26 (8)[b]			
			Month 3		30 mg/kg	1×		3/27 (11)[b]			
			Month 4		30 mg/kg	1×		7/32 (22)[b]			
			Month 5		30 mg/kg	1×		0/14 (0)[b]			
	Rats (Wistar)	kidney cortical epithelial tumors	Day 1	i.p.	20 mg/kg	1×	≥5 months	2/33 (6)[b]			Hard (1979)
			Day 21		30 mg/kg	1×		16/39 (41)[b]			
			Month 1		30 mg/kg	1×		12/33 (36)[b]			
			Month 1.5		30 mg/kg	1×		14/28 (52)[b]			
			Month 2		30 mg/kg	1×		11/26 (42)[b]			
			Month 3		30 mg/kg	1×		18/27 (67)[b]			
			Month 4		30 mg/kg	1×		21/32 (66)[b]			
			Month 5		30 mg/kg	1×		6/14 (43)[b]			
	Rats (Wistar)	Total tumors	Day 1	i.p.	20 mg/kg	1×	≥5 months	11/33 (33)[b]			
			Day 21		30 mg/kg	1×		25/39 (64)[b]			
			Month 1		30 mg/kg	1×		25/33 (76)[b]			
			Month 1.5		30 mg/kg	1×		17/28 (63)[b]			
			Month 2		30 mg/kg	1×		13/26 (50)[b]			
			Month 3		30 mg/kg	1×		18/27 (67)[b]			
			Month 4		30 mg/kg	1×		22/32 (69)[b]			
			Month 5		30 mg/kg	1×		7/14 (50)[b]			

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a] M	Tumors[a] F	Comments	Reference
ENU Ethylnitrosourea	Rats	nervous system	Day 1	Injection	20 mg/kg	1×		100%[b]		Susceptibility to neuro-oncogenic effect declined with increasing age.	Maekawa and Mitsumori (1990)
			Day 30	Injection	20 mg/kg	1×		61%[b]			
	Mice ($B6C3F_1$)	liver	Control	Control	None	N/A	90 weeks	1/98 (1%)	0/96 (0%)	Both male and female mice were responsive to exposure during prenatal and infant life.	Vesselinovitch (1983)
			Gestation day 18	i.p.	60 µg/g body weight	1×		28/52 (54%)[b]	18/49 (37%)[b]		
			Day 15		60 µg/g body weight	1×		41/50 (82%)[b]	28/51 (55%)[b]		
			Day 42		60 µg/g body weight	1×		10/50 (20%)[b]	5/50 (10%)[b]		
	Rats (Wistar)	nerve tissue	Control	Control	None	N/A	4–7 months	0/16 (0%)	0/10 (0%)	Highest tumor rate seen when exposed during gestation or soon after birth. Statistically significant decrease in tumor incidence with increasing age of exposure.	Naito et al. (1981)
			Gestation day 16	i.p.	40 mg/kg	1×		26/26 (100%)[b]	18/18 (100%)[b]		
			Day 1	s.c.	40 mg/kg	1×		12/12 (100%)[g]	16/16 (100%)[g]		
			Week 1		40 mg/kg	1×		12/17 (71%)[b]	18/20 (90%)[b]		
			Week 2		40 mg/kg	1×		10/14 (71%)[b]	14/18 (78%)[b]		
			Week 3		40 mg/kg	1×		6/13 (46%)[b]	5/17 (29%)[b]		
			Week 4		40 mg/kg	1×		8/15 (53%)[b]	2/10 (20%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
ENU Ethylnitrosourea (continued)	Mice ($B6C3F_1$)	lung	Day 1	i.p.	60 µg/g body weight	1×		49/55 (89%)[b]	49/50 (98%)[b]		Vesselinovitch et al. (1974)
			Day 15			1×		50/55 (91%)[b]	47/55 (85%)[b]		
			Day 42			1×		53/59 (90%)[b]	44/51 (86%)[b]		
			Day 1		120 µg/g body weight	1×		36/38 (95%)[b]	54/60 (90%)[b]		
			Day 15			1×		45/49 (92%)[b]	43/50 (86%)[b]		
			Day 42			1×		52/54 (96%)[b]	50/57 (88%)[b]		
	Mice ($C3AF_1$)	lung	Day 1		60 µg/g body weight	1×		46/47 (98%)[g]	51/51 (100%)[g]		
			Day 15			1×		49/49 (100%)[g]	57/59 (97%)[g]		
			Day 42			1×		59/59 (100%)[g]	57/57 (100%)[g]		
			Day 1		120 µg/g body weight	1×		63/64 (98%)[g]	53/57 (93%)[g]		
			Day 15			1×		54/56 (96%)[g]	50/56 (89%)[g]		
			Day 42			1×		59/59 (100%)[g]	48/48 (100%)[g]		
	Mice ($B6C3F_1$)	liver	Day 1	i.p.	60 µg/g body weight	1×		50/54 (93%)[g]	28/43 (65%)[g]		
			Day 15			1×		55/56 (98%)[g]	33/54 (61%)[g]		
			Day 42			1×		12/40 (30%)[b]	6/39 (15%)[b]		
			Day 1		120 µg/g body weight	1×		29/34 (85%)[g]	32/53 (60%)[g]		
			Day 15			1×		45/48 (94%)[g]	29/43 (67%)[g]		
			Day 42			1×		17/49 (35%)[g]	4/50 (8%)[g]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
ENU Ethylnitrosourea (continued)	Mice ($C3AF_1$)	liver	Day 1	i.p.	60 µg/g body weight	1×		42/45 (93%)[g]	19/41 (46%)[g]		
			Day 15			1×		42/50 (84%)[g]	19/48 (40%)[g]		
			Day 42			1×		7/29 (24%)[b]	4/50 (8%)[b]		
			Day 1		120 µg/g body weight	1×		55/62 (89%)[g]	19/45 (42%)[g]		
			Day 15			1×		35/45 (78%)[g]	15/35 (43%)[g]		
			Day 42			1×		8/33 (24%)[b]	3/33 (9%)[b]		
	Mice ($B6C3F_1$)	kidney	Day 1	i.p.	60 µg/g body weight	1×		11/48 (23%)[b]	5/49 (10%)[b]		
			Day 15			1×		6/41 (15%)[b]	7/31 (23%)[b]		
			Day 42			1×		4/40 (10%)[b]	3/37 (8%)[b]		
			Day 1		120 µg/g body weight	1×		10/30 (33%)[g]	14/53 (26%)[b]		
			Day 15			1×		17/37 (46%)[g]	19/49 (39%)[b]		
			Day 42			1×		8/40 (20%)[b]	11/39 (28%)[b]		
	Mice ($C3AF_1$)	kidney	Day 1	i.p.	60 µg/g body weight	1×		7/44 (16%)[b]	6/45 (13%)[b]		
			Day 15			1×		7/41 (17%)[b]	8/46 (17%)[b]		
			Day 42			1×		3/42 (42%)[b]	3/43 (7%)[b]		
			Day 1		120 µg/g body weight	1×		4/52 (7%)[b]	6/29 (21%)[g]		
			Day 15			1×		8/35 (23%)[b]	12/29 (41%)[g]		
			Day 42			1×		6/41 (71%)[b]	3/39 (8%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
ENU Ethylnitrosourea (continued)	Mice (B6C3F1)	Harderian	Day 1		60 µg/g body weight	1×		7/40 (17%)[b]	5/43 (12%)[b]		
			Day 15			1×		10/51 (20%)[b]	17/59 (29%)[b]		
			Day 42			1×		14/50 (28%)[b]	14/45 (31%)[b]		
			Day 1		120 µg/g body weight	1×		9/30 (30%)[g]	6/52 (12%)[b]		
			Day 15			1×		15/41 (37%)[g]	8/31 (26%)[b]		
			Day 42			1×		25/48 (52%)[g]	14/49 (29%)[b]		
	Mice ($C3AF_1$)	Harderian	Day 1		60 µg/g body weight	1×		3/25 (12%)[b]	4/35 (11%)[b]		
			Day 15			1×		1/9 (11%)[b]	6/38 (16%)[b]		
			Day 42			1×		12/48 (25%)[b]	5/33 (15%)[b]		
			Day 1		120 µg/g body weight	1×		3/52 (6%)[b]	1/25 (4%)[b]		
			Day 15			1×		6/46 (13%)[b]	2/52 (4%)[b]		
			Day 42			1×		5/29 (17%)[b]	2/11 (18%)[b]		
	Mice ($B6C3F_1$)	stomach	Day 1		60 µg/g body weight	1×		3/48 (6%)[b]	4/43 (9%)[b]		
			Day 15			1×		10/42 (24%)[g]	7/45 (16%)[b]		
			Day 42			1×		9/51 (18%)[g]	8/36 (22%)[b]		
			Day 1		120 µg/g body weight	1×		2/29 (7%)[b]	9/53 (17%)[b]		
			Day 15			1×		10/35 (29%)[g]	12/33 (36%)[b]		
			Day 42			1×		12/53 (23%)[g]	12/50 (24%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
ENU Ethylnitrosourea (continued)	Mice ($C3AF_1$)	stomach	Day 1		60 µg/g body weight	1×		2/39 (5%)[b]	7/45 (16%)[b]		
			Day 15			1×		7/45 (16%)[g]	7/38 (18%)[b]		
			Day 42			1×		14/55 (25%)[g]	7/49 (14%)[b]		
			Day 1		120 µg/g body weight	1×		8/60 (13%)[b]	9/44 (20%)[b]		
			Day 15			1×		16/51 (31%)[g]	11/42 (26%)[b]		
			Day 42			1×		19/48 (40%)[g]	13/37 (35%)[b]		
	Mice ($B6C3F_1$)	malignant lymphomas	Day 1		60 µg/g body weight	1×		2/55 (4%)[b]	6/52 (12%)[g]		
			Day 15			1×		3/56 (5%)[b]	14/59 (24%)[g]		
			Day 42			1×		9/59 (15%)[b]	17/59 (29%)[g]		
			Day 1		120 µg/g body weight	1×		8/39 (20%)[b]	15/65 (23%)[g]		
			Day 15			1×		14/60 (23%)[b]	17/58 (29%)[g]		
			Day 42			1×		12/59 (20%)[b]	14/60 (23%)[g]		
	Mice ($C3AF_1$)	malignant lymphomas	Day 1		60 µg/g body weight	1×		6/49 (12%)[b]	8/49 (16%)[g]		
			Day 15			1×		3/49 (6%)[b]	13/61 (21%)[g]		
			Day 42			1×		6/60 (10%)[b]	9/55 (16%)[g]		
			Day 1		120 µg/g body weight	1×		3/66 (5%)[b]	10/58 (17%)[g]		
			Day 15			1×		10/56 (18%)[b]	18/60 (30%)[g]		
			Day 42			1×		3/49 (6%)[b]	13/50 (26%)[g]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumor incidence[a]		Comments	Reference
								M	F		
NMU Methylnitrosourea	Mice ($BC3F_1$)	Total tumors	Control	Control	N/A	N/A	60 weeks	1/20 (5%)	0%	Control mice did not exhibit tumors in target sites except a single hepatoma in a male control mouse.	Terracini and Testa (1970)
		lung	Day 1	i.p.	50 µg/g body weight	1×	60 weeks	12/15 (80%)[b]	16/19 (84%)[b]		
			5 weeks		50 µg/g body weight	1×	60 weeks	10/26 (39%)[b]	10/35 (29%)[b]		
		lympho-sarcoma	Day 1		50 µg/g body weight	1×	60 weeks	23/39 (59%)[b]	23/45 (51%)[b]		
			5 weeks		50 µg/g body weight	1×	60 weeks	11/35 (31%)[b]	21/45 (47%)[b]		
		liver	Day 1		50 µg/g body weight	1×	60 weeks	10/12 (83%)[b]	1/17 (6%)[b]		
			5 weeks		50 µg/g body weight	1×	60 weeks	0%[b]	0%[c]		
		kidney	Day 1		50 µg/g body weight	1×	60 weeks	3/15 (20%)[b]	3/18 (17%)[b]		
			5 weeks		50 µg/g body weight	1×	60 weeks	2/21 (10%)[b]	0%[c]		
		fore-stomach	Day 1		50 µg/g body weight	1×	60 weeks	0%[b]	4/17 (24%)[b]		
			5 weeks		50 µg/g body weight	1×	60 weeks	8/22 (36%)[b]	12/18 (67%)[b]		
	Rats (Wistar)	mammary	Day 1	i.p.	50 µg/g body weight	1×	60 weeks	0%[b]	4/14 (29%)[b]	Tumor incidence for control rats was based on previous experiments (Della Porta et al., 1968) and was not specifically reported in this paper.	Terracini and Testa (1970)
			5 weeks		50 µg/g body weight	1×	60 weeks	0%[b]	3/5 (60%)[b]		
		lympho-sarcoma	Day 1		50 µg/g body weight	1×	60 weeks	1/10 (10%)[b]	0%[b]		
			5 weeks		50 µg/g body weight	1×	60 weeks	2/8 (25%)[b]	1/11 (9%)[b]		
		kidney (ana-plastic)	Day 1		50 µg/g body weight	1×	60 weeks	14/18 (78%)[b]	9/13 (69%)[b]		
			5 weeks		50 µg/g body weight	1×	60 weeks	2/5 (40%)[b]	5/12 (42%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumor incidence[a]		Comments	Reference
								M	F		
NMU Methylnitrosourea (continued)		kidney (adenoma)	Day 1		50 µg/g body weight	1×	60 weeks	3/14 (21%)[b]	2/6 (33%)[b]		
			5 weeks		50 µg/g body weight	1×	60 weeks	¼ (25%)[b]	0%[b]		
		forestomach	Day 1		50 µg/g body weight	1×	60 weeks	4/14 (29%)[b]	3/6 (50%)[b]		
			5 weeks		50 µg/g body weight	1×	60 weeks	0%[c]	0%[b]		
		intestine	Day 1		50 µg/g body weight	1×	60 weeks	3/10 (30%)[b]	2/2 (100%)[b]		
			5 weeks		50 µg/g body weight	1×	60 weeks	2/4 (50%)[b]	0%[b]		
	Mice (C3Hf/Dp)	thymus	control	i.p.	NA	NA	120 wks[**]	0/34 (0%)	0/25 (0%)	[*]Age at death from thymic lymphoma reported specifically for some, but not all, dose groups. [**]Control mice were sacrificed at 120 wks. [***]Age of death for all mice in this dose group, regardless of cancer type.	Terracini et al. (1976)
			Day 1		25 µg NMU/g body weight	1×	29 ± 8.4 wks	2/16 (13%)[b]	5/25 (20%)[b]		
			Day 70		25 µg NMU/g body weight	1×	120 wks (M)[***] 100 wks (F)	0/20 (0%)[c]	1/20 (5%)[b]		
			Day 1		50 µg NMU/g body weight	1×	16.5 ± 0.7 wks	16/24 (67%)[b]	30/44 (68%)[b]		
			Day 21		50 µg NMU/g body weight	1×	24.5 ± 2.5 wks	14/44 (32%)[b]	18/38 (47%)[b]		
			Day 70		50 µg NMU/g body weight	1×	31.4 ± 4.4 wks	9/30 (30%)[b]	6/41 (15%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death		Tumor incidence		Reference
							M	F	M	F	
NMU Methylnitrosourea (continued)	Mice (C3Hf/Dp)	extra-thymic lymphoma	control	i.p.	NA	NA	120 weeks	120 weeks	1/34 (3%)	2/25 (8%)	Terracini et al. (1976)
			Day 1		25 µg NMU/g body weight	1×	100 weeks	90 weeks	2/16 (13%)[b]	1/25 (4%)[b]	
			Day 70		25 µg NMU/g body weight	1×	120 weeks	100 weeks	0/20 (0%)[b]	0/20 (0%)[b]	
			Day 1		50 µg NMU/g body weight	1×	70 weeks	80 weeks	0/24 (0%)[b]	0/44 (0%)[b]	
			Day 21		50 µg NMU/g body weight	1×	100 weeks	90 weeks	1/44 (2%)[b]	0/38 (0%)[b]	
			Day 70		50 µg NMU/g body weight	1×	110 weeks	90 weeks	1/30 (3%)[b]	0/41 (0%)[b]	
		lung	control	i.p.	NA	NA	120 weeks	120 weeks	4/34 (12%)	6/25 (24%)	
			Day 1		25 µg NMU/g body weight	1×	100 weeks	90 weeks	7/16 (44%)[b]	13/25 (52%)[b]	
			Day 70		25 µg NMU/g body weight	1×	120 weeks	100 weeks	12/20 (60%)[b]	8/20 (40%)[b]	
			Day 1		50 µg NMU/g body weight	1×	70 weeks	80 weeks	5/24 (21%)[b]	11/44 (25%)[b]	
			Day 21		50 µg NMU/g body weight	1×	100 weeks	90 weeks	23/44 (52%)[b]	15/38 (39%)[b]	
			Day 70		50 µg NMU/g body weight	1×	110 weeks	90 weeks	18/30 (60%)[b]	24/41 (59%)[b]	
		liver	control	i.p.	NA	NA	120 weeks	120 weeks	13/34 (38%)	1/25 (4%)	Terracini et al. (1976)
			Day 1		25 µg NMU/g body weight	1×	100 weeks	90 weeks	9/16 (56%)[g]	2/25 (8%)[b]	
			Day 70		25 µg NMU/g body weight	1×	120 weeks	100 weeks	12/20 (60%)[g]	2/20 (10%)[b]	
			Day 1		50 µg NMU/g body weight	1×	70 weeks	80 weeks	4/24 (17%)[g]	3/44 (7%)[b]	
			Day 21		50 µg NMU/g body weight	1×	100 weeks	90 weeks	21/44 (48%)[g]	1/38 (2.6%)[b]	

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death		Tumor incidence		Reference
							M	F	M	F	
NMU Methylnitrosourea (continued)	Mice (C3Hf/Dp)		Day 70		50 µg NMU/g body weight	1×	110 weeks	90 weeks	8/30 (27%)[g]	2/41 (5%)[b]	
		stomach	control	i.p.	NA	NA	120 weeks	120 weeks	0/34 (0%)	5/25 (20%)	
			Day 1		25 µg NMU/g body weight	1×	100 weeks	90 weeks	2/16 (13%)[b]	10/25 (40%)[b]	
			Day 70		25 µg NMU/g body weight	1×	120 weeks	100 weeks	3/20 (15%)[b]	7/20 (35%)[b]	
			Day 1		50 µg NMU/g body weight	1×	70 weeks	80 weeks	2/24 (8%)[b]	1/44 (2%)[b]	
			Day 21		50 µg NMU/g body weight	1×	100 weeks	90 weeks	19/44 (43%)[b]	9/38 (24%)[b]	
			Day 70		50 µg NMU/g body weight	1×	110 weeks	90 weeks	8/30 (27%)[b]	21/41 (51%)[b]	
		kidney	control	i.p.	NA	NA	120 weeks	120 weeks	0/34 (0%)	0/25 (0%)	Terracini et al. (1976)
			Day 1		25 µg NMU/g body weight	1×	100 weeks	90 weeks	0/16 (0%)[b]	0/25 (0%)[b]	
			Day 70		25 µg NMU/g body weight	1×	120 weeks	100 weeks	0/20 (0%)[b]	0/20 (0%)[b]	
			Day 1		50 µg NMU/g body weight	1×	70 weeks	80 weeks	0/24 (0%)[b]	4/44 (9%)[b]	
			Day 21		50 µg NMU/g body weight	1×	100 weeks	90 weeks	1/44 (2%)[b]	4/38 (11%)[b]	
			Day 70		50 µg NMU/g body weight	1×	110 weeks	90 weeks	5/30 (17%)[b]	7/41 (17%)[b]	

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death		Tumor incidence		Reference
							M	F	M	F	
NMU Methylnitrosourea (continued)	Mice (C3Hf/Dp)	ovary	control	i.p.	NA	NA	120 weeks	120 weeks	NA	3/25 (12%)	
			Day 1		25 µg NMU/g body weight	1×	100 weeks	90 weeks	NA	2/25 (8%)[b]	
			Day 70		25 µg NMU/g body weight	1×	120 weeks	100 weeks	NA	4/20 (20%)[b]	
			Day 1		50 µg NMU/g body weight	1×	70 weeks	80 weeks	NA	0/44 (0%)[b]	
			Day 21		50 µg NMU/g body weight	1×	100 weeks	90 weeks	NA	9/38 (24%)[b]	
			Day 70		50 µg NMU/g body weight	1×	110 weeks	90 weeks	NA	16/41 (39%)[b]	
		mammary	control	i.p.	NA	NA	120 weeks	120 weeks	NA	2/25 (8%)	Terracini et al. (1976)
			Day 1		25 µg NMU/g body weight	1×	100 weeks	90 weeks	NA	1/25 (4%)[b]	
			Day 70		25 µg NMU/g body weight	1×	120 weeks	100 weeks	NA	0/20 (0%)[b]	
			Day 1		50 µg NMU/g body weight	1×	70 weeks	80 weeks	NA	0/44 (0%)[b]	
			Day 21		50 µg NMU/g body weight	1×	100 weeks	90 weeks	1/44 (2%)[b]	0/38 (0%)[b]	
			Day 70		50 µg NMU/g body weight		110 weeks	90 weeks	NA	4/41 (9.8%)[b]	
		uterus or vagina	control	i.p.	NA	NA	120 weeks	120 weeks	NA	1/25 (4%)	
			Day 1		25 µg NMU/g body weight	1×	100 weeks	90 weeks	NA	1/25 (4%)[b]	
			Day 70		25 µg NMU/g body weight	1×	120 weeks	100 weeks	NA	6/20 (30%)[b]	
			Day 1		50 µg NMU/g body weight	1×	70 weeks	80 weeks	NA	0/44 (0%)[b]	
			Day 21		50 µg NMU/g body weight	1×	100 weeks	90 weeks	NA	1/38 (3%)[b]	
			Day 70		50 µg NMU/g body weight		110 weeks	90 weeks		7/41 (17%)[b]	

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
Urethane	Mice (SWR)	lung adenoma	Newborn	s.c.	0.18 mg/g body weight	1×	10 weeks	100%[b]		The average number of tumors per mouse increased linearly with dose.	Kaye and Trainin (1966)
			11–22 weeks	s.c.	0.25 mg/g body weight	1×	23–34 weeks	0%[b]			
	Mice (C3H/f)	liver	Control	Control	None	N/A	493 days (m) 553 days (f)	14/97 (14%)	1/77 (1%)		Liebelt et al. (1964)
			Day 1	i.p.	0.8 mg/g body weight	1×	481 days (m) 434 days (f)	27/30 (90%)[g]	18/39 (46%)[g]		
			8–10 weeks	i.p.	1 mg/g body weight	1×	321 days (m) -	6/25 (24%)[c]	0/32 (0%)[c]		
		lung	Control	Control	None	N/A	493 days (m) 553 days (f)	0/97 (0%)	0/77 (0%)	The number of lung tumors among the controls was not provided.	
			Day 1	i.p.	0.8 mg/g body weight	1×	401 days (m) 408 days (f)	14/30 (46%)[g]	19/39 (48%)[g]		
			8–10 weeks	i.p.	1 mg/g body weight	1×	506 days (m) -	2/25 (8%)[c]	0/32 (0%)[c]		
		reticular tissue	Control	Control	None	N/A	493 days (m) 553 days (f)	2/97 (2%)	6/77 (8%)		
			Day 1	i.p.	0.8 mg/g body weight	1×	285 days (m) 343 days (f)	4/30 (13%)[c]	22/39 (56%)[g]		
			8–10 weeks	i.p.	1 mg/g body weight	1×	- 453 days (f)	0/25 (25%)[c]	4/32 (13%)[c]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a] M	Tumors[a] F	Comments	Reference
Urethane (continued)	Mice (Swiss)	leukemia	Control	Control	None	N/A	8–10 months	1%		Highest tumor rates when dosed at birth. Exposure to newborns was followed by 21.6% leukemia, occurring at a mean age of 105 days.	Fiore-Donati et al. (1962)
			Day 1	s.c.	2 mg in 0.05 mL aqueous solution	1×		13/60 (22%)[b]			
			Day 5		4 mg in 0.05 mL aqueous solution	1×		7/39 (18%)[b]			
			Day 40		20 mg in 0.1 mL aqueous solution	1×		2/63 (3%)[b]			
	Mice (Swiss)	lung adenoma	Control 2 weeks	Control	None	N/A	9 weeks	0/15 (0%)	—	The proportion of animals with adenomas decreased steadily with age of exposure.	Rogers (1951)
			Control 4 weeks	Control	None	N/A	11 weeks	0/14 (0%)	—		
			Control 6 weeks	Control	None	N/A	13 weeks	1/15 (7%)	—		
			Control 8 weeks	Control	None	N/A	15 weeks	2/15 (13%)	—		
			Control 10 weeks	Control	None	N/A	17 weeks	0/15 (0%)	—		
			2 weeks	i.p.	1 mg/g body weight	1×	9 weeks	24/24 (100%)[b]	—		
			4 weeks	i.p.	1 mg/g body weight	1×	11 weeks	23/25 (92%)[b]	—		
			6 weeks	i.p.	1 mg/g body weight	1×	13 weeks	22/25 (88%)[b]	—		
			8 weeks	i.p.	1 mg/g body weight	1×	15 weeks	21/25 (84%)[b]	—		
			10 weeks	i.p.	1 mg/g body weight	1×	17 weeks	19/25 (76%)[b]	—		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors[a]		Comments	Reference
								M	F		
Urethane (continued)	Mice (Swiss)	lung adenoma	3 weeks	i.p.	0.25 mg/g body weight	1×	12 weeks	16/19 (84%)[b]	—		
					0.5 mg/g body weight	1×	12 weeks	16/20 (80%)[b]	—		
					1 mg/g body weight	1×	12 weeks	18/20 (90%)[b]	—		
			8 weeks	i.p.	0.25 mg/g body weight	1×	17 weeks	4/17 (24%)[b]	—		
					0.5 mg/g body weight	1×	17 weeks	15/16 (94%)[b]	—		
					1 mg/g body weight	1×	17 weeks	18/18 (100%)[b]	—		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumor incidence[a]		Comments	Reference
								M	F		
Urethane (continued)	Mice (Swiss)	liver	Control	Control	N/A	N/A	360–720 days	10/227 (4.4%)	4/222 (8.22%)		Chieco-Bianchi et al. (1963)
			Day 1	s.c.	1 mg/g body weight	1×	180 days	1/20 (5%)[g]	0/20 (0%)[c]		
			Day 1	s.c.	1 mg/g body weight	1×	240 days	2/17 (12%)[g]	0/12 (0%)[c]		
			Day 1	s.c.	1 mg/g body weight	1×	300 days	5/18 (28%)[g]	0/16 (0%)[c]		
			Day 1	s.c.	1 mg/g body weight	1×	360 days	11/20 (55%)[g]	0/23 (0%)[c]		
			Day 1	s.c.	1 mg/g body weight	1×	420 days	13/15 (87%)[g]	2/22 (9%)[g]		
			Day 1	s.c.	1 mg/g body weight	1×	480 days	17/23 (74%)[c]	2/25 (8%)[c]		
			Day 5	s.c.	1 mg/g body weight	1×	420 days	9/13 (69.2%)[b]	2/11 (18.2%)[b]		
			Day 20	s.c.	1 mg/g body weight	1×	420 days	1/13 (8%)[b]	0/16 (0%)[b]		
			Day 40	s.c.	1 mg/g body weight	1×	420 days	0/11 (0%)[b]	0/9 (0%)[b]		
	Mice (Swiss)	skin	Control	Control	N/A	N/A	180–550 days	30/712 (4.21%)		Croton oil treatment initiated at 40 days of age.	Chieco-Bianchi et al. (1963)
			Day 1	s.c.	1 mg urethane/g body weight; 5% croton oil	single dose urethane, croton oil applied 2×/week for 10 mos	660 days	26/59 (44.1%)[g]			

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumor incidence[a]		Comments	Reference
								M	F		
Urethane (continued)			Day 40	s.c.	1 mg urethane/g body weight; 5% croton oil	single dose urethane, croton oil applied 2×/week for 10 mos	700 days	8/41 (19.5%)[b]			
	Mice ($B6AF_1/J$)	liver	Control	gavage	N/A	N/A	71 weeks	1/25 (4%)	0/25 (0%)		Klein (1966)
			Day 1		1 mg/g body weight	1×	66 weeks	9/20 (45%)[g]	9/26 (35%)[g]		
			Day 7		1 mg/g body weight	1×	67 weeks	20/22 (91%)[g]	20/26 (77%)[g]		
			Day 14		1 mg/g body weight	1×	68 weeks	16/20 (80%)[g]	10/23 (43%)[g]		
			Day 21		1 mg/g body weight	1×	69 weeks	13/23 (57%)[g]	1/20 (5%)[g]		
			Day 28		1 mg/g body weight	1×	70 weeks	4/24 (17%)[g]	1/20 (5%)[g]		
		lung	Control	gavage	1 mg/g body weight	1×	71 weeks	9/25 (36%)	6/25 (24%)		
			Day 1		1 mg/g body weight	1×	66 weeks	20/20 (100%)[b]	25/26 (96%)[b]		
			Day 7		1 mg/g body weight	1×	67 weeks	22/22 (100%)[b]	26/26 (100%)[b]		
			Day 14		1 mg/g body weight	1×	68 weeks	19/20 (95%)[b]	19/23 (83%)[b]		
			Day 21		1 mg/g body weight	1×	69 weeks	23/23 (100%)[b]	19/20 (95%)[b]		
			Day 28		1 mg/g body weight	1×	70 weeks	24/24 (100%)[b]	20/20 (100%)[b]		
	Mice ($B6AF_1/J$)	Harderian gland	Control	gavage	1 mg/g body weight	1×	71 weeks	0/25 (0%)	0/25 (0%)		Klein (1966)
			Day 1		1 mg/g body weight	1×	66 weeks	0/20 (0%)[c]	1/26 (4%)[b]		

Table 3. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure (continued)

Chemical	Species (strain)	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumor incidence[a]		Comments	Reference
								M	F		
Urethane (continued)			Day 7		1 mg/g body weight	1×	67 weeks	0/22 (0%)[c]	1/26 (4%)[b]		
			Day 14		1 mg/g body weight	1×	68 weeks	0/20 (0%)[c]	2/23 (9%)[b]		
			Day 21		1 mg/g body weight	1×	69 weeks	1/23 (4%)[b]	0/20 (0%)[c]		
			Day 28		1 mg/g body weight	1×	70 weeks	0/24 (0%)[c]	0/20 (0%)[c]		
		forestomach	Control	gavage	1 mg/g body weight	1×	71 weeks	0/25 (0%)	1/25 (4%)		
			Day 1		1 mg/g body weight	1×	66 weeks	0/20 (0%)[c]	3/26 (12%)[b]		
			Day 7		1 mg/g body weight	1×	67 weeks	1/22 (5%)[b]	1/26 (4%)[b]		
			Day 14		1 mg/g body weight	1×	68 weeks	1/20 (5%)[b]	4/23 (17%)[b]		
			Day 21		1 mg/g body weight	1×	69 weeks	0/23 (0%)[c]	1/20 (5%)[b]		
			Day 28		1 mg/g body weight	1×	70 weeks	2/24 (8%)[b]	1/20 (5%)[b]		

[a] Where not delineated by gender, data combined by study authors or gender not specified. Where percentages only are given, number of subjects not specified.
[b] Not evaluated by authors.
[c] Evaluated but not significant compared with controls.
[d] Study also included mammary fibroadenomas and fibromas as well as other types of cancers.
[e] 8–9 weeks old.
[f] Includes survivors up to 40 weeks only.
[g] Significant compared with controls.

i.p. = intraperitoneal injection; s.c. = subcutaneous injection

Table 4. Ratio of early-life to adult cancer potencies for studies with repeated exposures of juvenile and adult animals to carcinogens with a mutagenic mode of action*

Compound	Species (strain)	Sex	Dose	Tumor	Unweighted geometric mean	2.5%	Median	97.5%	Reference
Benzidine	Mice ($B6C3F_1$)	male		liver	111	64	**110**	198	Vesselinovitch et al. (1975b)
		female		liver	0.16	0.004	**0.22**	1.1	
3-MU 3-Methylcholanthrene (formerly known as 20-methylcholanthrene)	Mice (Albino)	male	0.25 mg/g	hepatoma	33	7.4	**30**	268	Klein (1959)
		female	0.25 mg/g	hepatoma	7.7	1.1	**7.1**	85	
		male	0.25 mg/g	forestomach	0.91	0.39	**0.91**	2.1	
		female	0.25 mg/g	forestomach	1.5	0.58	**1.5**	4.2	
		male	0.25 mg/g	skin	1.8	0.048	**2.1**	22	
		female	0.25 mg/g	skin	1.5	0.023	**1.8**	21	
Safrole	Mice ($B6C3F_1$)	male		liver	47	16	**44**	198	Vesselinovitch et al. (1979b)
		female		liver	0.12	0.002	**0.18**	1.1	
VC Vinyl chloride	Rats (Sprague-Dawley)	male	6,000 ppm	liver-angiosarcoma	6.7	0.035	**9.8**	57	Maltoni et al. (1984)
		male	10,000 ppm	liver-angiosarcoma	7.4	0.035	**11**	62	
		female	6,000 ppm	liver-angiosarcoma	13	4.9	**13**	33	
		female	10,000 ppm	liver-angiosarcoma	30	8.7	**29**	121	
		male	6,000 ppm	zymbal gland	0.73	0.0032	**1.1**	30	
		male	10,000 ppm	zymbal gland	0.27	0.0022	**0.4**	5.4	
		female	6,000 ppm	zymbal gland	0.48	0.0027	**0.7**	16	
		female	10,000 ppm	zymbal gland	0.15	0.0014	**0.19**	4.5	
		male	10,000 ppm	leukemia	21	0.026	**37**	514	
		female	6,000 ppm	leukemia	1.3	0.0035	**1.7**	153	
		female	10,000 ppm	leukemia	0.29	0.0019	**0.35**	17	
		male	6,000 ppm	nephroblastomas	0.15	0.0014	**0.19**	4.8	
		male	10,000 ppm	nephroblastomas	0.17	0.0015	**0.21**	6.2	
		female	6,000 ppm	nephroblastomas	0.28	0.0018	**0.33**	16	
		female	10,000 ppm	nephroblastomas	0.24	0.0017	**0.29**	11	
		male	6,000 ppm	angiosarcomas-other sites	0.9	0.0033	**1.26**	53	
		male	10,000 ppm	angiosarcomas-	0.25	0.0017	**0.30**	12	

Table 4. Ratio of early-life to adult cancer potencies for studies with repeated exposures of juvenile and adult animals to mutagenic chemicals (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Unweighted geometric mean	2.5%	Median	97.5%	Reference
				other sites					
VC Vinyl chloride (continued)		female	6,000 ppm	angiosarcomas-other sites	0.24	0.0017	**0.29**	11	
		female	10,000 ppm	angiosarcomas-other sites	0.32	0.0019	**0.38**	20	
		male	6,000 ppm	angiomas & fibromas-other sites	0.72	0.0031	**1.0**	33	
		male	10,000 ppm	angiomas & fibromas-other sites	1.4	0.0045	**2.36**	47	
		female	6,000 ppm	angiomas & fibromas-other sites	0.27	0.0018	**0.33**	16	
		female	10,000 ppm	angiomas & fibromas-other sites	0.52	0.0024	**0.63**	41	
		male	6,000 ppm	hepatoma	62	11	**58**	543	
		male	10,000 ppm	hepatoma	34	8.2	**32**	218	
		female	6,000 ppm	hepatoma	55	13	**51**	352	
		female	10,000 ppm	hepatoma	55	8.4	**53**	513	
		male	6,000 ppm	skin carcinomas	1.1	0.0035	**1.5**	82	
		male	10,000 ppm	skin carcinomas	0.41	0.0024	**0.56**	15	
		female	6,000 ppm	skin carcinomas	0.46	0.0024	**0.59**	24	
		female	10,000 ppm	skin carcinomas	0.31	0.0019	**0.37**	19	
		male	6,000 ppm	neuroblastoma	0.21	0.0016	**0.26**	9.5	
		male	10,000 ppm	neuroblastoma	0.20	0.0016	**0.24**	8.5	
		female	6,000 ppm	neuroblastoma	0.27	0.0018	**0.32**	15	
		female	10,000 ppm	neuroblastoma	0.14	0.0014	**0.18**	4.4	

* The 2.5% and 97.5% are percentiles of the posterior distribution. For a Bayesian distribution, these percentiles function in a manner similar to the 95% confidence limits for other types of statistical analyses.

Table 5. Ratio of early-life to adult cancer potencies for studies with repeated exposures of juvenile and adult animals to chemicals with a nonmutagenic mode of action*

Compound	Species (strain)	Sex	Dose	Tumor	Ratio of juvenile to adult potency				Reference
					Unweighted geometric mean	2.5%	Median	97.5%	
Amitrole	Mice ($B6C3F_1$)	male	NA	liver	13	5.1	**14**	30	Vesselinovitch (1983)
		female	NA	liver	0.14	0.0013	**0.18**	3.9	
DDT	Mice ($B6C3F_1$)	male	NA	liver	1.3	0.0044	**2.5**	25	Vesselinovitch et al. (1979a)
Dieldrin	Mice ($B6C3F_1$)	male	NA	liver	0.75	0.0031	**1.2**	27	Vesselinovitch et al. (1979a)
DPH	Rats (F344/N)	male	630	liver	0.4	0.0024	**0.54**	16	Chhabra et al. (1993b)
		female	630	liver	0.24	0.0017	**0.29**	12	
	Mice ($B6C3F_1$)	male	210	liver	1.5	0.0040	**2.4**	71	
		female	210	liver	1.3	0.0056	**2.6**	15	
ETU	Rats (F344/N)	male	90	thyroid	0.37	0.0029	**0.61**	5.4	Chhabra et al. (1992)
		female	90	thyroid	0.23	0.0018	**0.3**	7.0	
	Mice ($B6C3F_1$)	male	330	liver	0.091	0.0011	**0.12**	1.9	
		female	330	liver	0.057	0.0010	**0.081**	0.65	
		male	330	thyroid	0.41	0.0022	**0.52**	25	
		female	330	thyroid	0.4	0.0024	**0.55**	16	
		male	330	pituitary	0.32	0.0019	**0.38**	22	
		female	330	pituitary	0.24	0.0018	**0.32**	6.9	
PBB	Rats (F344/N)	male	10	liver	0.59	0.0041	**1.1**	6.6	Chhabra et al. (1993a)
		female	10	liver	0.063	0.0009	**0.079**	1.2	
		male	10	mononuclear cell leukemia	0.79	0.0035	**1.4**	18	
		female	10	mononuclear cell leukemia	0.21	0.0017	**0.28**	6.0	
	Mice ($B6C3F_1$)	male	30	liver	3.9	1.9	**3.9**	7.5	
		female	30	liver	1.0	0.37	**1.05**	2.1	

* The 2.5% and 97.5% are percentiles of the posterior distribution. For a Bayesian distribution, these percentiles function in a manner similar to the 95% confidence limits for other types of statistical analyses.

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action*

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
BaP*	Mice ($B6C3F_1$)	male	75 µg/kg	liver	1 day	9.3	2.9	**8.4**	55	Vesselinovitch et al. (1975a)
					15 days	11	3.5	**9.6**	61	
		female	75 µg/kg		1 day	1.2	0.0083	**1.6**	31	
					15 days	1.7	0.015	**2.1**	36	
		male	150 µg/kg		1 day	29	8.2	**26**	194	
					15 days	15	4.1	**13**	109	
		female	150 µg/kg		1 day	8.8	1.4	**8.1**	94	
					15 days	1.2	0.0082	**1.6**	30	
	Mice ($C3AF_1$)	male	75 µg/kg	liver	1 day	11	2.1	**10**	112	
					15 days	7.5	1.1	**7.0**	83	
		female	75 µg/kg		1 day	0.2	0.0018	**0.26**	9.1	
					15 days	0.2	0.0017	**0.24**	8.5	
		male	150 µg/kg		1 day	14	3.0	**12.8**	130	
					15 days	3.6	0.11	**3.8**	49	
		female	150 µg/kg		1 day	0.2	0.0017	**0.24**	8.8	
					15 days	0.2	0.0017	**0.24**	8.7	
	Mice ($B6C3F_1$)	Male	75 µg/kg	lung	1 day	1.2	0.45	**1.2**	3.4	
					15 days	0.2	0.0046	**0.31**	1.4	
		female	75 µg/kg	lung	1 day	2.8	1.096	**2.7**	9.5	
					15 days	1.4	0.41	**1.4**	5.1	
		Male	150 µg/kg	lung	1 day	2.2	1.0	**2.1**	5.4	
					15 days	0.8	0.2	**0.82**	2.3	
		female	150 µg/kg	lung	1 day	7.9	2.6	**7.2**	43	
					15 days	3.7	1.1	**3.4**	22	
	Mice ($C3AF_1$)	male	75 µg/kg	lung	1 day	1.2	0.47	**1.2**	3.2	
					15 days	1.1	0.43	**1.08**	3.1	

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
BaP* (continued)		female	75 µg/kg	lung	1 day	1.6	0.66	**1.55**	4.0	
					15 days	1.6	0.71	**1.63**	4.2	
		male	150 µg/kg	lung	1 day	1.5	0.57	**1.5**	5.0	
					15 days	1.9	0.71	**1.8**	6.0	
		female	150 µg/kg	lung	1 day	1.3	0.61	**1.3**	2.9	
					15 days	1.2	0.54	**1.1**	2.6	
DBA	Mice			lung		178	20	**143**	5100	Law (1940)
DEN**	Mice ($B6C3F_1$)	male	6 µg/kg	liver	1 day	9.0	3.5	**8.3**	37	Vesselinovitch et al. (1984)
					15 days	8.9	3.5	**8.2**	36	
		female	6 µg/kg	liver	1 day	35	9.1	**31**	239	
					15 days	25	6.3	**226**	175	
		male	12 µg/kg	liver	1 day	9.6	3.3	**8.8**	50	
					15 days	9.8	3.4	**8.9**	51	
		female	12 µg/kg	liver	1 day	16	5.9	**15**	67	
					15 days	19	7.1	**18**	79	
	Mice ($C3AF_1$)	male	6 µg/kg	liver	1 day	7.3	2.9	**6.9**	26	
					15 days	3.5	1.4	**3.3**	13	
		female	6 µg/kg	liver	1 day	17	3.2	**16**	166	
					15 days	6.4	0.86	**6.0**	73	
		male	12 µg/kg	liver	1 day	11	3.7	**9.5**	53	
					15 days	9.8	3.4	**8.9**	50	
		female	12 µg/kg	liver	1 day	40	8.5	**36**	340	
					15 days	25	5.0	**22**	221	
	Mice ($B6C3F_1$)	male	6 µg/kg	lung	1 day	0.5	0.27	**0.52**	0.93	
					15 days	1.6	0.95	**1.6**	2.7	
		female	6 µg/kg	lung	1 day	0.9	0.54	**0.89**	1.5	
					15 days	1.2	0.76	**1.2**	2.0	

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
DEN** (continued)		male	12 µg/kg	lung	1 day	0.4	0.21	**0.40**	0.73	
					15 days	0.7	0.39	**0.66**	1.1	
		female	12 µg/kg	lung	1 day	0.7	0.44	**0.73**	1.2	
					15 days	1.4	0.88	**1.4**	2.3	
	Mice ($C3AF_1$)	male	6 µg/kg	lung	1 day	0.7	0.22	**0.67**	1.7	
					15 days	0.5	0.21	**0.56**	1.3	
		female	6 µg/kg	lung	1 day	1.1	0.45	**1.1**	2.5	
					15 days	0.7	0.36	**0.74**	1.5	
		male	12 µg/kg	lung	1 day	0.3	0.084	**0.33**	0.76	
					15 days	0.6	0.26	**0.62**	1.4	
		female	12 µg/kg	lung	1 day	0.7	0.35	**0.75**	1.6	
					15 days	0.7	0.37	**0.75**	1.5	
DMBA#	Rats (Wistar)	male		total	2 vs 5–8 wks	3.3	1.3	**3.2**	10	Meranze et al. (1969)
					2 vs 26 wks	3.2	1.3	**3.1**	9.7	
		female		total	2 vs 5–8 wks	1.3	0.68	**1.3**	2.5	
					2 vs 26 wks	3.3	1.2	**3.0**	16	
				mammary	2 vs 5–8 wks	0.0	0.0012	**0.056**	0.26	
					2 vs 26 wks	0.2	0.0023	**0.29**	5.3	
					5 vs 26 wks	7.1	1.8	**6.4**	55	
	Mice (Balb/c)	male	15 µg	lung	1 day	30	2.8	**22**	1482	Walters (1966)
					15–19 days	1.0	0.28	**1.0**	3.5	
		male	30 µgx2	lung	15–19 days	14	1.056	**10**	978	
		female	15 µg	lung	1 day	60	6.0	**46**	2350	
					15–19 days	3.1	0.51	**3.0**	22	
		female	30 µgx2	lung	15–19 days	15	1.2	**11**	1004	
	Mice (Swiss)			lymphoma		2.7	0.60	**2.5**	19	Pietra et al. (1961)
				lung		9.1	2.9	**8.7**	40	

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
DMN***	Rats (Wistar)		3 wks	total	1 month	0.7	0.41	**0.73**	1.3	Hard (1979)
					1.5 months	1.1	0.58	**1.1**	2.1	
					2 months	1.5	0.75	**1.5**	3.0	
					3 months	0.9	0.50	**0.94**	1.8	
			24 hr		1 month	0.3	0.13	**0.28**	0.6	
					1.5 months	0.4	0.18	**0.42**	0.9	
					2 months	0.6	0.24	**0.56**	1.3	
					3 months	0.4	0.16	**0.36**	0.78	
			1 month		1.5 months	1.5	0.80	**1.52**	3.0	
					2 months	2.0	1.0	**2.0**	4.2	
					3 months	1.3	0.69	**1.3**	2.5	
ENU	Mice ($B6C3F_1$)	male		liver		7.8	3.9	**7.7**	18	Vesselinovitch (1983)
		female				7.1	2.9	**6.9**	21	
	Rats (Wistar)	male		nerve tissue	1 day	27	2.5	**20**	1374	Naito et al. (1981)
					1 week	1.6	0.61	**1.6**	4.6	
					2 weeks	1.6	0.58	**1.6**	4.8	
					3 weeks	0.7	0.12	**0.72**	2.3	
		female			1 day	64	6.0	**50**	2488	
					1 weeks	9.6	2.6	**8.9**	59	
					2 weeks	6.2	1.6	**5.7**	40	
					3 weeks	0.7	0.0090	**0.89**	8.9	
	Mice ($B6C3F_1$)	male	60 µg/g	lung	1	1.0	0.60	**1.0**	1.7	Vesselinovitch et al. (1974)
					15	1.1	0.66	**1.1**	1.8	
		female	60 µg/g	lung	1	2.1	1.17	**2.1**	4.1	
					15	1.0	0.60	**1.0**	1.7	
		male	120 µg/g	lung	1	1.0	0.60	**1.0**	1.7	

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
					15	1.1	0.66	**1.0**	1.8	
ENU (continued)		female	120 µg/g	lung	1	2.1	1.2	**2.1**	4.1	
					15	1.0	0.60	**1.0**	1.7	
	Mice ($C3AF_1$)	male	60 µg/g	lung	1	8.7	2.7	**8.0**	48	
					15	52	5.2	**39**	2141	
		female	60 µg/g	lung	15	0.7	0.32	**0.72**	1.6	
		male	120 µg/g	lung	1	0.9	0.38	**0.92**	2.2	
					15	0.7	0.28	**0.67**	1.6	
		female	120 µg/g	lung	1	0.5	0.24	**0.54**	1.2	
					15	0.4	0.18	**0.42**	0.92	
	Mice ($B6C3F_1$)	male	60 µg/g	liver	1	8.8	4.2	**8.5**	22	
					15	14	6.2	**14**	37	
		female	60 µg/g	liver	1	6.3	2.6	**6.1**	18	
					15	5.6	2.4	**5.4**	16	
		male	120 µg/g	liver	1	5.2	2.5	**5.1**	11	
					15	7.6	3.9	**7.5**	17	
		female	120 µg/g	liver	1	11	4.1	**11**	46	
					15	14	4.9	**13**	55	
	Mice ($C3AF_1$)	male	60 µg/g	liver	1	12	4.7	**11**	43	
					15	8.1	3.2	**7.6**	29	
		female	60 µg/g	liver	1	7.5	2.6	**7.0**	32	
					15	4.8	1.8	**4.6**	18	
		male	120 µg/g	liver	1	9.8	4.1	**9.3**	32	
					15	6.6	2.7	**6.3**	23	
		female	120 µg/g	liver	1	5.4	1.7	**5.0**	25	
					15	5.4	1.7	**5.1**	25	
	Mice ($B6C3F_1$)	male	60 µg/g	kidney	1	2.2	0.73	**2.1**	8.0	
					15	1.2	0.29	**1.2**	5.1	

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
		female	60 µg/g	kidney	1	0.7	0.024	**0.85**	5.9	
					15	2.6	0.61	**2.5**	15	
ENU (continued)		male	120 µg/g	kidney	1	1.7	0.65	**1.7**	4.4	
					15	2.6	1.14	**2.6**	6.4	
		female	120 µg/g	kidney	1	0.9	0.37	**0.87**	2.0	
					15	1.4	0.67	**1.4**	3.2	
	Mice ($C3AF_1$)	male	60 µg/g	kidney	1	1.8	0.17	**1.9**	15	
					15	2.0	0.25	**2.0**	16	
		female	60 µg/g	kidney	1	1.0	0.016	**1.3**	13	
					15	2.1	0.16	**2.2**	20	
		male	120 µg/g	kidney	1	0.2	0.0029	**0.24**	1.5	
					15	1.5	0.38	**1.5**	5.9	
		female	120 µg/g	kidney	1	2.3	0.17	**2.4**	20	
					15	7.1	1.8	**6.5**	47	
	Mice ($B6C3F_1$)	male	60 µg/g	Harderian	1	0.3	0.018	**0.41**	1.4	
					15	0.5	0.075	**0.52**	1.4	
		female	60 µg/g	Harderian	1	0.1	0.0025	**0.16**	0.74	
					15	0.8	0.35	**0.84**	2.0	
		male	120 µg/g	Harderian	1	0.4	0.13	**0.42**	0.96	
					15	0.6	0.26	**0.57**	1.2	
		female	120 µg/g	Harderian	1	0.1	0.0030	**0.18**	0.85	
					15	0.7	0.17	**0.77**	2.1	
	Mice ($C3AF_1$)	male	60 µg/g	Harderian	1	0.1	0.0023	**0.20**	1.3	
					15	0.1	0.0016	**0.18**	1.8	
		female	60 µg/g	Harderian	1	0.4	0.019	**0.52**	2.5	
					15	0.8	0.15	**0.85**	3.4	
		male	120 µg/g	Harderian	1	0.1	0.0010	**0.086**	1.0	
					15	0.3	0.0050	**0.40**	2.8	

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
		female	120 µg/g	Harderian	1	0.1	0.0012	**0.094**	1.2	
					15	0.1	0.0012	**0.081**	0.90	
ENU (continued)	Mice ($B6C3F_1$)	male	60 µg/g	stomach	1	0.3	0.0091	**0.34**	2.4	
					15	1.9	0.61	**1.82**	8.7	
		female	60 µg/g	stomach	1	0.2	0.0083	**0.26**	1.1	
					15	0.2	0.0072	**0.24**	1.0	
		male	120 µg/g	stomach	1	0.2	0.0059	**0.20**	0.90	
					15	1.2	0.50	**1.2**	2.9	
		female	120 µg/g	stomach	1	0.6	0.19	**0.60**	1.5	
					15	1.6	0.67	**1.6**	3.7	
	Mice ($C3AF_1$)	male	60 µg/g	stomach	1	0.0	0.0009	**0.063**	0.51	
					15	0.3	0.023	**0.41**	1.3	
		female	60 µg/g	stomach	1	0.8	0.085	**0.89**	3.5	
					15	1.1	0.19	**1.1**	4.5	
		male	120 µg/g	stomach	1	0.2	0.010	**0.19**	0.56	
					15	0.7	0.32	**0.70**	1.5	
		female	120 µg/g	stomach	1	0.4	0.14	**0.46**	1.2	
					15	0.6	0.24	**0.64**	1.5	
NMU	Mice ($BC3F_1$)	male	50 µg/g	lung adenomas	1	3.4	1.3	**3.3**	9.3	Terracini and Testa (1970)
		female	50 µg/g	lung adenomas	1	6.3	2.4	**6.0**	23	
		male	50 µg/g	lymphosarcoma	1	2.5	1.1	**2.4**	6.4	
		female	50 µg/g	lymphosarcoma	1	1.1	0.49	**1.1**	2.4	
		male	50 µg/g	hepatoma	1	35	6.5	**32**	324	
		female	50 µg/g	hepatoma	1	0.3	0.0023	**0.39**	13	
		male	50 µg/g	renal adenoma	1	0.9	0.0093	**1.2**	13	
		female	50 µg/g	renal adenoma	1	1.3	0.0081	**1.7**	33	
		male	50 µg/g	forestomach	1	0.0	0.0006	**0.039**	0.52	
		female	50 µg/g	forestomach	1	0.1	0.0027	**0.15**	0.69	

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
	Mice (C3Hf/Dp)	male	25 µg/g	thymic lymphoma	1	1.9	0.048	**2.1**	23	
NMU (continued)		female	25 µg/g	thymic lymphoma	1	1.2	0.0089	**1.5**	30	
		male	25 µg/g	lung adenomas	1	1.0	0.013	**1.2**	11	
		female	25 µg/g	lung adenomas	1	0.4	0.018	**0.46**	1. 7	
		male	25 µg/g	liver tumor	1	0.2	0.0016	**0.21**	4.6	
		female	25 µg/g	liver tumor	1	0.3	0.0026	**0.39**	4.4	
		male	25 µg/g	Stomach	1	0.5	0.0045	**0.67**	6.8	
		female	25 µg/g	Stomach	1	0.3	0.0046	**0.43**	3.8	
				ovarian	1	0.1	0.0014	**0.17**	3.5	
				uterine/vaginal	1	8.6	1.1	**8.1**	97	
		male	50 µg/g	thymic lymphoma	1	7.9	3.1	**7.4**	30	
		female	50 µg/g	thymic lymphoma	1	3.1	1.3	**3.0**	7.8	
		male	50 µg/g	lung adenomas	1	0.04	0.0008	**0.058**	0.45	
		female	50 µg/g	lung adenomas	1	0.1	0.0012	**0.084**	0.53	
		male	50 µg/g	liver tumor	1	0.2	0.0021	**0.33**	7.8	
		female	50 µg/g	liver tumor	1	0.1	0.0011	**0.13**	4.5	
		male	50 µg/g	Stomach	1	0.01	0.0003	**0.013**	0.12	
		female	50 µg/g	Stomach	1	0.1	0.0022	**0.15**	0.96	
				ovarian	1	0.0	0.0003	**0.014**	0.14	
				uterine/vaginal	1	0.0	0.0005	**0.034**	0.46	
		male	50 µg/g	thymic lymphoma	21	4.3	1. 6	**4.1**	17	
		female	50 µg/g	thymic lymphoma	21	1.0	0.39	**1.0**	2.6	
		male	50 µg/g	lung adenomas	21	0.1	0.0022	**0.22**	1.1	
		female	50 µg/g	lung adenomas	21	0.7	0.30	**0.75**	1.7	

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
		male	50 µg/g	liver tumor	21	0.1	0.0013	**0.15**	4.3	
		female	50 µg/g	liver tumor	21	0.9	0.0051	**1.4**	23	
NMU (continued)		male	50 µg/g	stomach	21	0.1	0.001	**0.08**	0.64	
		female	50 µg/g	stomach	21	1.8	0.77	**1.8**	4.7	
				ovarian	21	0.0	0.0007	**0.055**	0.97	
				uterine/vaginal	21	1.7	0.59	**1.7**	6.4	
Urethane	Mice (Swiss)	male	1 mg/g	liver	1	24	4.4	**21**	220	Chieco-Bianchi et al. (1963)
		female	1 mg/g	liver	1	0.4	0.0044	**0.54**	13	
		male	1 mg/g	liver	5	14	2.4	**13**	137	
		female	1 mg/g	liver	5	1.2	0.017	**1.4**	26	
		male	1 mg/g	liver	20	0.2	0.0018	**0.28**	10	
		female	1 mg/g	liver	20	0.1	0.0011	**0.12**	4.8	
		both	1 mg/g	skin	1	0.2	0.0027	**0.32**	5.4	
Urethane + croton oil	Mice (Swiss)	both	1 mg/g	skin	1	2.9	1.2	**2.8**	8.2	
Urethane	Rats (MRC Wistar-derived)	male/ female	16%×6	neurilemmomas	1	0.2	0.0028	**0.33**	4.5	Choudari Kommineni et al. (1970)
		male/ female	16%×6	neurilemmomas	28	0.4	0.0045	**0.51**	6.3	
		male/ female	16%×6	liver	1	7.9	1.4	**7.1**	82	
		male/ female	16%×6	liver	28	0.2	0.0026	**0.4**	11.7	
		male/ female	16%×6	thyroid	1	0.0	0.0006	**0.039**	0.67	
		male/ female	16%×6	thyroid	28	0.1	0.0011	**0.1**	1.5	
	Mice (Swiss)	male/ female	1 mg/g	lung	1	15	1.2	**11**	997	De Benedictis et al. (1962)
	Mice (Swiss)			leukemia		6.7	1.7	**6.1**	45	Fiore-Donati et al.

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
						5.1	1.1	**4.7**	38	(1962)
Urethane (continued)	Mice ($B6AF_1/J$)	male	1 mg/g	liver	21	5.1	1.4	**4.7**	30	Klein (1966)
		female	1 mg/g	liver	21	0.2	0.0019	**0.26**	6.0	
				Harderian gland	1	0.3	0.0021	**0.33**	11	
					7	0.3	0.0021	**0.33**	11	
					14	0.6	0.0044	**0.85**	20	
		male	1 mg/g	Harderian gland	21	0.3	0.0024	**0.41**	13	
		male	1 mg/g	forestomach	1	0.1	0.0009	**0.079**	1.9	
		female	1 mg/g	forestomach	1	0.4	0.0028	**0.49**	11	
		male	1 mg/g	forestomach	7	0.1	0.0017	**0.19**	3.5	
		female	1 mg/g	forestomach	7	0.1	0.0013	**0.16**	5.0	
		male	1 mg/g	forestomach	14	0.2	0.0018	**0.21**	3.9	
		female	1 mg/g	forestomach	14	0.8	0.0056	**1.1**	18	
		male	1 mg/g	forestomach	21	0.1	0.0008	**0.072**	1.7	
		female	1 mg/g	forestomach	21	0.2	0.0015	**0.2**	6.3	
				lung	1	1.0	0.36	**0.95**	2.5	
		male	1 mg/g	lung	14	0.8	0.26	**0.8**	2.3	
		female	1 mg/g	lung	14	0.4	0.16	**0.45**	1.1	
					21	0.9	0.31	**0.86**	2.4	
	Mice (C3H/f)	male	1 mg/g	liver	1	14	4.0	**12**	81	Liebelt et al. (1964)
		female	1 mg/g	liver	1	16	3.2	**15**	155	
		male	1 mg/g	lung	1	5.9	1.7	**5.6**	28	
		female	1 mg/g	lung	1	22	4.5	**20**	203	
		male	1 mg/g	reticular tissue	1	2.0	0.023	**2.3**	38	
		female	1 mg/g	reticular tissue	1	8.6	2.3	**7.7**	60	
	Mice (Swiss)		1 mg/g	pulmonary adenomas	2 vs 4 weeks	14	1.1	**10.1**	965	Rogers (1951)

Table 6. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to carcinogens with a mutagenic mode of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Day	Ratio of juvenile to adult potency				Reference
						Unweighted geometric mean	2.5%	Median	97.5 %	
			1 mg/g	pulmonary adenomas	2 vs 6 weeks	16	1.3	**11.3**	1025	
Urethane (continued)			1 mg/g	pulmonary adenomas	2 vs 8 weeks	19	1.6	**13.3**	1126	
			1 mg/g	pulmonary adenomas	2 vs 10 weeks	21	1.9	**14.5**	1168	
			0.25 mg/g	adenomas	3 vs 8 weeks	7.1	2.3	**6.7**	29	
			0.5 mg/g	adenomas	3 vs 8 weeks	0.7	0.29	**0.67**	1.6	
			1.0 mg/g	adenomas	3 vs 8 weeks	0.7	0.28	**0.68**	1.6	

* The 2.5% and 97.5% are percentiles of the posterior distribution. For a Bayesian distribution, these percentiles function in a manner similar to the 95% confidence limits for other types of statistical analyses.

Table 7. Ratio of early-life to adult cancer potencies for studies with lifetime exposures starting with juvenile and adult animals to carcinogens with mutagenic or nonmutagenic modes of action*

Compound	Species (strain)	Sex	Dose	Tumor	Unweightedg eometric mean	2.5%	Median	97.5%	Reference
Mutagenic compounds									
DEN	Rats (Colworth)		multiple	liver	2.8	0.0093	**5.6**	23	Peto et al. (1984)
				esophagus	0.18	0.0015	**0.23**	4.8	
Safrole	Mice ($B6C3F_1$)	male		liver	50	3.7	**50**	253	Vesselinovitch et al. (1979b)
		female		liver	4.0	0.007	**4.0**	23	
Urethane	Mice ($B6AF_1/J$)	male	2.5 mg/pup	liver	79	0.36	**102**	1,064	Klein (1966)
		female	2.5 mg/pup	liver	0.47	0.0022	**0.55**	42	
Nonmutagenic compounds									
DDT	Mice ($B6C3F_1$)			liver	23	0.0023	**0.58**	23	Vesselinovitch et al. (1979a)
Dieldrin	Mice ($B6C3F_1$)			liver	91	0.014	**14**	91	Vesselinovitch et al. (1979a)
DPH	Rats (F344/N)	male	630:800	liver	0.31	0.0019	**0.37**	18	Chhabra et al. (1993b)
			630:2,400	liver	0.36	0.0021	**0.45**	17	
		female	630:800	liver	0.33	0.0019	**0.39**	21	
			630:2,400	liver	0.33	0.0019	**0.39**	21	
	Mice ($B6C3F_1$)	male	210:100	liver	0.71	0.0028	**0.93**	49	
			210:300	liver	14	0.03	**23**	214	
		female	210:200	liver	0.32	0.002	**0.42**	13	
			210:600	liver	0.35	0.0023	**0.53**	8.8	
ETU	Rats (F344/N)	male	90:83	thyroid	0.23	0.0017	**0.3**	7.3	Chhabra et al. (1992)
			90:250	thyroid	9.1	1.1	**10.5**	27	
		female	90:83	thyroid	0.37	0.0021	**0.46**	19	
			90:250	thyroid	0.61	0.0034	**1.1**	10	

Table 7. Ratio of early-life to adult cancer potencies for studies with lifetime exposures starting with juvenile and adult animals to carcinogens with mutagenic or nonmutagenic modes of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Unweighted geometric mean	2.5%	Median	97.5%	Reference
ETU (continued)	Mice ($B6C3F_1$)	male	330:330	liver	0.37	0.0022	**0.5**	14	
			330:1,000	liver	0.48	0.0027	**0.75**	12	
		female	330:330	liver	0.33	0.0023	**0.5**	7.8	
			330:1,000	liver	0.42	0.0025	**0.65**	11	
		male	330:330	thyroid	0.44	0.0022	**0.52**	34	
			330:1,000	thyroid	0.63	0.0035	**1.12**	10	
		female	330:330	thyroid	5.2	0.011	**10**	108	
			330:1,000	thyroid	0.18	0.0016	**0.24**	4.2	
		male	330:330	pituitary	0.40	0.0021	**0.47**	32	
			330:1,000	pituitary	0.18	0.0015	**0.22**	5.7	
		female	330:330	pituitary	0.21	0.0016	**0.26**	10	
			330:1,000	pituitary	0.27	0.0019	**0.36**	9.0	
PBB	Rats (F344/N)	male	10:10	liver	0.39	0.0023	**0.56**	13	Chhabra et al. (1993a)
			10:30	liver	0.18	0.0016	**0.25**	4.3	
		female	10:10	liver	36	15	**36**	86	
			10:30	liver	3.1	0.023	**4.6**	22	
		male	10:10	mononuclear cell leukemia	0.51	0.0025	**0.69**	23	
		male	10:30	mononuclear cell leukemia	0.77	0.0031	**1.1**	35	
		female	10:10	mononuclear cell leukemia	0.54	0.0026	**0.74**	24	
		female	10:30	mononuclear cell leukemia	0.34	0.0021	**0.45**	15	
	Mice ($B6C3F_1$)	male	30:30	liver	8.9	0.015	**12.2**	1,076	
		female	30:30	liver	4.4	0.0075	**6.2**	786	
		male	10:10	liver	0.15	0.0014	**0.2**	3.9	

Table 7. Ratio of early-life to adult cancer potencies for studies with lifetime exposures starting with juvenile and adult animals to carcinogens with mutagenic or nonmutagenic modes of action (continued)

Compound	Species (strain)	Sex	Dose	Tumor	Unweighted geometric mean	2.5%	Median	97.5%	Reference
		female	10:10	liver	0.29	0.0021	**0.43**	7.0	

* The 2.5% and 97.5% are percentiles of the posterior distribution. For a Bayesian distribution, these percentiles function in a manner similar to the 95% confidence limits for other types of statistical analyses.

Table 8. Summary of quantitative estimates of ratio of early-life to adult cancer potencies

Dose	Tissue	Number of chemicals	Inverse-weighted geometric mean ratio	Unweighted Minimum	Unweighted Maximum	Number of ratios	Percentage >1
Chemicals with mutagenic mode of action							
Repeated		4	10.5	0.12	111	45	42
Lifetime		3	8.7	0.18	79	6	67
	Combined repeated and lifetime	**6**	**10.4**	**0.12**	**111**	**51**	**45**
Acute	**Combined**	11	1.5	0.01	178	268	55
	Forestomach	3	0.076	0.01	1.9	32	16
	Harderian	2	0.48	0.06	0.8	20	0.0
	Kidney	2	1.6	0.17	7.1	18	78
	Leukemia	1	5.9	5.1	6.7	2	100
	Liver	5	8.1	0.10	40	70	77
	Lung	7	1.1	0.04	178	77	56
	Lymph	2	1.8	1.1	2.7	3	100
	Mammary (wk 5 vs wk 26)	1	7.1	NA	NA	1	100
	Mammary (wk 2 vs wk 5–8 or 26)	1	0.071	NA	NA	2	0
	Nerve	2	2.3	0.24	64	8	75
	Nerve (Day 1 comparison)	2	10	0.24	64	3	67
	Ovarian	1	0.033	0.01	0.13	3	0
	Reticular tissue	1	6.5	1.96	8.6	2	100
	Thymic lymphoma	1	2.8	1.01	7.9	6	100
	Thyroid	1	0.05	0.03	0.08	2	0
	Uterine/vaginal	1	1.6	0.03	8.6	3	67
	Day 1	7	1.7	0.01	178	127	55
	Day 15	3	1.5	0.06	52	74	65
Chemicals with nonmutagenic mode of action							
Repeated		6	2.2	0.06	13	22	27
Lifetime		5	3.4	0.15	36	38	21

Table 9. Excess Relative Risk (ERR) estimates for cancer incidence from Life Span Study (Japanese survivors)[a]

Site	Average ERR at 1 Sv	
	<20[b]	>20[b]
Stomach	0.74	0.24
Colon	0.62	0.7
Liver	1.3	0.31
Lung	0.57	1.1
Bone and connective tissue	11	0.42
Skin	5.4	0.39
Breast	3.3	0.98
Urinary bladder	0.71	0.79
Leukemia	6.1	3.7

[a] Information extracted from tables in UNSCEAR, Annex I (2000).
[b] Age at exposure.

Table 10. Excess Relative Risk (ERR) estimates for incidence of thyroid cancer from Life Span Study[a]

Age at exposure	Average ERR at 1 Sv (No. cases)
0–9 yr	10.25 (24)
10–19 yr	4.5 (35)
20–29 yr	0.10 (18)
>30 yr	0.04 (55)

[a] Information extracted from tables in UNSCEAR, Annex I (2000).

Table 11. Coefficients for the Revised Methodology mortality risk model (from U.S. EPA, 1999)[a]

Cancer type	Risk model type[b]	Age group				
		0–9	10–19	20–29	30–39	40+
Male:						
Stomach	R	1.223	1.972	2.044	0.3024	0.2745
Colon	R	2.290	2.290	0.2787	0.4395	0.08881
Liver	R	0.9877	0.9877	0.9877	0.9877	0.9877
Lung	R	0.4480	0.4480	0.0435	0.1315	0.1680
Bone	A	0.09387	0.09387	0.09387	0.09387	0.09387
Skin	A	0.06597	0.06597	0.06597	0.06597	0.06597
Breast	R	0.0	0.0	0.0	0.0	0.0
Ovary	R	0.0	0.0	0.0	0.0	0.0
Bladder	R	1.037	1.037	1.037	1.037	1.037
Kidney	R	0.2938	0.2938	0.2938	0.2938	0.2938
Thyroid	A	0.1667	0.1667	0.1667	0.1667	0.1667
Leukemia	R	982.3	311.3	416.6	264.4	143.6
Female:						
Stomach	R	3.581	4.585	4.552	0.6309	0.5424
Colon	R	3.265	3.265	0.6183	0.8921	0.1921
Liver	R	0.9877	0.9877	0.9877	0.9877	0.9877
Lung	R	1.359	1.359	0.1620	0.4396	0.6047
Bone	A	0.09387	0.09387	0.09387	0.09387	0.09387
Skin	A	0.06597	0.06597	0.06597	0.06597	0.06597
Breast	R	0.7000	0.7000	0.3000	0.3000	0.1000
Ovary	R	0.7185	0.7185	0.7185	0.7185	0.7185
Bladder	R	1.049	1.049	1.049	1.049	1.049
Kidney	R	0.2938	0.2938	0.2938	0.2938	0.2938
Thyroid	A	0.3333	0.3333	0.1667	0.1667	0.1667
Leukemia	R	1,176	284.9	370.06	178.8	157.1

[a] The coefficients were derived using several models applied to data from A-bomb survivors and selected medical exposures.

[b] A = absolute risk with coefficient units of 10^{-4} $(Gy\ y)^{-1}$; R= relative risk with coefficient units of Gy^{-1}.

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Exhibit E

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Volume I: Human Health Evaluation Manual
(Part F, Supplemental Guidance for Inhalation Risk Assessment)

Final

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LIST OF ACRONYMS

µg	Microgram
µm	Micrometer
ADAF	Age Dependent Adjustment Factor
AT	Averaging Time
ATSDR	Agency for Toxic Substances and Disease Registry
BMCL	Benchmark Concentration, Lower confidence limit
BMD	Benchmark Dose
BW	Body Weight
CA	Contaminant Concentration in Air
CERCLA	Comprehensive Environmental Response, Compensation, and Liability Act
CSF	Cancer Slope Factor
DAF	Dosimetric Adjustment Factor
ED	Exposure Duration
EC	Exposure Concentration
EF	Exposure Frequency
EPA	Environmental Protection Agency
ER	Extra-respiratory
ET	Exposure Time
ETh	Extrathoracic
F_r	Fractional Deposition in region r
F_{total}	Total particle deposition in respiratory tract
$H_{b/g\text{-}animal}$	Animal Blood:Gas Partition Coefficient
$H_{b/g\text{-}human}$	Human Blood:Gas Partition Coefficient
HEAST	Health Effects Assessment Summary Table
HEC	Human Equivalent Concentration
HI	Hazard Index
HQ	Hazard Quotient
ICRP	International Commission for Radiological Protection
IR	Inhalation Rate
IRIS	Integrated Risk Information System
IUR	Inhalation Unit Risk
kg	Kilogram
LEC_{10}	Lower limit on Effective Concentration, using a 10 percent response level
LOAEL	Lowest Observable Adverse Effect Level
ME	Microenvironment
MF	Modifying Factor
mg	Milligram
MOA	Mode of Action
MRL	Minimal Risk Level
MW	Molecular Weight
NCEA	National Center for Environmental Assessment
NOAEL	No Observable Adverse Effect Level
ORD	Office of Research and Development
OSRTI	Office of Superfund Remediation and Technology Innovation

LIST OF ACRONYMS (CONT.)

OSWER	Office of Solid Waste and Emergency Response
PBPK	Physiologically Based Pharmacokinetic
POD	Point of Departure
ppm	Parts Per Million
PPRTV	Provisional Peer Reviewed Toxicity Value
PRG	Preliminary Remediation Goal
PU	Pulmonary
Q-alv	Alveolar ventilation rate
QSAR	Quantitative Structure-Activity Relationship
RAGS	Risk Assessment Guidance for Superfund
RBC	Risk-Based Concentration
RfC	Reference Concentration
RfD	Reference Dose
RGDR	Regional Gas Dose Ratio
RDDR	Regional Deposited Dose Ratio
RME	Reasonable Maximum Exposure
SA	Surface Area
SSL	Soil Screening Level
STSC	Superfund Health Risk Technical Support Center
TB	Tracheobronchial
TOT	Total Respiratory System
UF	Uncertainty Factor
V_e	Minute Volume

1. INTRODUCTION

The Environmental Protection Agency's (EPA's) Superfund Program has updated its approach for determining risk from inhaled chemicals to be consistent with the inhalation dosimetry methodology described in *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry* (USEPA, 1994; hereafter, the *Inhalation Dosimetry Methodology*).[1] This document provides Superfund site risk assessors with guidance that should help more consistently address the *Inhalation Dosimetry Methodology*.

This document outlines recommended processes consisting of a series of steps as well as recommended equations for EPA Regions to consider when estimating inhalation exposure and risk at Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) sites. This guidance is intended to provide a recommended methodology for consistently addressing the inhalation pathway in risk assessments for Superfund sites.

Some of the statutory provisions described in this document contain legally binding requirements. However, this document does not substitute for those provisions or regulations, nor is it a regulation itself. Thus, it cannot impose legally binding requirements on EPA, States, or the regulated community, and may not apply to a particular situation based upon the circumstances. Any decisions regarding a particular remedy selection decision will be made based on the statute and regulations, and EPA decisionmakers retain the discretion to adopt approaches on a case-by-case basis that differ from this guidance where appropriate. EPA may change this guidance in the future.

1.1 Background

EPA's *Risk Assessment Guidance for Superfund (RAGS), Part A* (USEPA, 1989; hereafter, *RAGS, Part A*) outlined a previously recommended approach for conducting site-specific baseline risk assessments for inhaled contaminants.[2] According to the original RAGS approach, the inhalation exposure estimate was typically derived in terms of a chronic, daily "air intake" (mg/kg-day) using the following general approach. The intake of the chemical was estimated as a function of the concentration of the chemical in air (CA), inhalation rate (IR), body weight (BW), and the exposure scenario. Age-specific values for BW and IR were used when evaluating childhood exposures. Table 1 presents the *RAGS, Part A* equation for calculating intake for inhalation exposure. Inhalation toxicity values were "converted" into similar units for the risk quantification step. Cancer risk was estimated by multiplying the chronic daily intake of the chemical from the air by the "inhalation cancer slope factor" (CSF_i); the Hazard Quotient (HQ) for non-cancer effects was estimated by dividing the intake of the chemical by an "inhalation reference dose" (RfD_i).[3]

The approach outlined in *RAGS, Part A* was developed before EPA issued the *Inhalation Dosimetry Methodology*, which describes the Agency's refined recommended approach for interpreting

[1] The *Inhalation Dosimetry Methodology* can be found at the following web address: http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=71993.

[2] See sections 6.6.3, 7.2.3, 7.3.3, and 8.2 of *RAGS, Part A*.

[3] EPA defines an HQ in *RAGS, Part A* as: "The ratio of a single substance exposure level over a specified time period (e.g., subchronic) to a reference dose (RfD) for that substance derived from a similar exposure period" (USEPA, 1989).

inhalation toxicity studies in laboratory animals or studies of occupational exposures of humans to airborne chemicals. Under the *Inhalation Dosimetry Methodology*, the experimental exposures are typically extrapolated to a Human Equivalent Concentration (HEC), and a reference concentration (RfC) is typically calculated by dividing the HEC by uncertainty factors (UFs). As described in the Agency's *Guidelines for Cancer Risk Assessment* (USEPA, 2005a), the HEC developed in accordance with the *Inhalation Dosimetry Methodology* typically is also used in developing an inhalation unit risk (IUR) for cancer risk assessment (which may also be called an inhalation cancer slope factor).[4] The procedure that was used to calculate the published RfC or IUR is described in the Integrated Risk Information System (IRIS) profile or other toxicological reference document for a chemical.

TABLE 1
RAGS, PART A EQUATION DESCRIBING THE ESTIMATION OF INHALATION EXPOSURE

Equation	Location in RAGS, Part A
Intake (mg/kg-d) = CA x (IR/BW) x (ET x EF x ED)/AT	Exhibit 6-16, Page 6-44
Key: CA (mg/m^3) = contaminant concentration in air; IR (m^3/hr) = inhalation rate; BW (kg) = body weight; ET (hours/day) = exposure time; EF (days/year) = exposure frequency; ED (years) = exposure duration; and AT (days) = averaging time (period over which exposure is averaged).	

The Superfund Program has updated its inhalation risk paradigm to be compatible with the *Inhalation Dosimetry Methodology*, which represents the Agency's current methodology for inhalation dosimetry and derivation of inhalation toxicity values.[5] This document recommends that when estimating risk via inhalation, risk assessors should use the concentration of the chemical in air as the exposure metric (e.g., mg/m^3), rather than inhalation intake of a contaminant in air based on IR and BW (e.g., mg/kg-day).

1.2 Purpose and Scope

The intake equation described above (*RAGS, Part A*, Exhibit 6-16) is not consistent with the principles of EPA's *Inhalation Dosimetry Methodology* because the amount of the chemical that reaches the target site is not a simple function of IR and BW. Instead, the interaction of the inhaled contaminant with the respiratory tract is affected by factors such as species-specific relationships of exposure concentrations (ECs) to deposited/delivered doses and physiochemical characteristics of the inhaled contaminant. The *Inhalation Dosimetry Methodology* also considers the target site where the toxic effect occurs (e.g., the respiratory tract or a location in the body remote from the portal-of-entry) when applying dosimetric adjustments to experimental concentrations (USEPA, 1994). Therefore, this *RAGS, Part A* equation is not recommended for estimating exposures to inhaled contaminants.

[4] The phrase "inhalation cancer slope factor," as used in this guidance, refers generally to the risk per a measure of inhalation exposure. Inhalation exposure in cancer bioassays or occupational studies from which slope factors may be derived is most commonly expressed as an exposure concentration (e.g., µg agent/m^3 air). Please note that this differs from past use of the phrase "inhalation cancer slope factor" or "CSF_i" by the Superfund program to refer to a cancer slope expressed as an "inhalation intake" (e.g., *RAGS, Part A* (USEPA, 1989)).

[5] For additional information about the Superfund program's adoption of the *Inhalation Dosimetry Methodology*, please refer to the summary of a 2003 Superfund workshop on inhalation risk assessment: http://www.epa.gov/oswer/riskassessment/pdf/finalinhalationriskworkshop.pdf.

The purpose of this document is to provide a recommended approach for developing the information necessary to assist risk assessment and risk management decision-making at waste sites involving potential risks from inhalation exposures.[6, 7] This includes providing equations that may be used in conducting baseline risk assessments and in calculating risk-based concentrations (RBCs). It is intended that *RAGS, Part F* will replace those portions of *RAGS, Part A*, which addressed inhalation risk.

1.3 Effects on Other Office of Superfund Remediation and Technology Innovation Guidance

EPA recommends that the intake equation presented in *RAGS, Part A* (USEPA, 1989, Exhibit 6-16) should no longer be used when evaluating risk from the inhalation pathway. Implementation of a risk assessment approach consistent with the *Inhalation Dosimetry Methodology* will also affect the following guidance documents: *RAGS, Part B*, Section 3.3: Volatilization and Particulate Emission Factors (USEPA, 1991); and the Office of Solid Waste and Emergency Response's (OSWER's) *Draft Guidance for Evaluating the Vapor Intrusion to Indoor Air Pathway from Groundwater and Soils* (USEPA, 2002a; hereafter the *Vapor Intrusion Guidance*). EPA no longer recommends using the equations in Section 3.3 of *RAGS, Part B* nor the inhalation toxicity values generated using simple route-to-route extrapolation, such as those presented in the 2002 draft *Vapor Intrusion Guidance* and related documents.[8]

This guidance does not affect the equations pertaining to risk from inhaled chemicals in the *Soil Screening Guidance* (USEPA, 1996), Section 2.4, or the *Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites* (USEPA, 2002b), Sections 4.2.3, 5.3.2 and Appendix B, other than to clarify that the IURs and RfCs used in the equations are based on continuous exposure (24 hours per day). If the exposure scenario of interest is less than 24 hours per day, the scenario-specific exposure time (ET) in hours per day should be used in the equations and the averaging time should be in units of hours (see Equations 6 and 8 in this document). *RAGS, Part D* (USEPA, 2001) is also not affected by *RAGS, Part F*, as it includes sufficient flexibility to accommodate the revisions described in this guidance. In addition, the screening values presented on the "Regional Screening Levels for Chemical Contaminants at Superfund Sites" screening level/preliminary remediation goal table are consistent with *RAGS, Part F* (USEPA, 2008a).[9] Readers can contact EPA headquarters with questions about the compatibility of specific Superfund documents with *RAGS, Part F*.

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[6] Note that the assessment of risk from inhaled nanoparticles is outside the scope of this document.

[7] If a site contains asbestos contamination, risk assessors should contact EPA's Technical Review Workgroup for Metals and Asbestos for assistance.

[8] Related documents include the *Johnson and Ettinger (1991) Model for Subsurface Vapor Intrusion into Buildings* spreadsheet models (http://www.epa.gov/oswer/riskassessment/airmodel/johnson_ettinger.htm) and the accompanying *User's Guide for Evaluating Subsurface Vapor Intrusion into Buildings* (USEPA, 2004a).

[9] This table can be found on EPA Regions 3, 6, and 9 websites (http://www.epa.gov/reg3hwmd/risk/human/rb-concentration_table/index.htm; http://www.epa.gov/earth1r6/6pd/rcra_c/pd-n/screen.htm; and http://www.epa.gov/region09/waste/sfund/prg/index.html).

2. BACKGROUND ON DERIVATION OF INHALATION TOXICITY VALUES

For all exposure routes, there are generally two approaches for deriving toxicity values. One involves the derivation of a reference value (e.g., RfC or RfD), while the other involves derivation of a predictive cancer risk estimate (e.g., an oral or inhalation CSF, such as an IUR). For the inhalation route, both approaches rely on EPA's *Inhalation Dosimetry Methodology* for the extrapolation of experimental concentrations to HECs. This extrapolation is described in Section 2.1 and its subsections. The approaches for deriving a toxicity value from the HEC are described in Sections 2.2 and 2.3 and differ depending on the type of toxicity value (e.g., RfC, IUR). This information is provided for background purposes only. **The procedures outlined in Section 2 are typically performed by IRIS chemical managers or by inhalation toxicologists at the National Center for Environmental Assessment's (NCEA's) Superfund Health Risk Technical Support Center (STSC) rather than as part of a baseline risk assessment.**

2.1 Application of Inhalation Dosimetry

The *Inhalation Dosimetry Methodology* recognizes a hierarchy of approaches that can be used for determining the HEC that is used to derive the RfC or IUR. Generally, the preferred approach is to use physiologically-based pharmacokinetic (PBPK) models.[10] With sufficient data, a PBPK model is capable of calculating the amount of the chemical that reaches the target organ in an animal from any exposure scenario and then estimating what human exposure would result in this same amount of chemical reaching the target organ (i.e., the HEC). PBPK models can also be used to derive continuous ECs from human and animal studies with less-than-continuous exposures. Because constructing a valid PBPK model is an information-intensive process that typically requires substantial chemical-specific data, this approach has rarely been used (USEPA, 2004b); an example can be found in the IRIS file for vinyl chloride (USEPA, 2000a). In cases where a complete PBPK model is not available, an intermediate model relying on certain chemical-specific data may be used (USEPA, 1994).[11]

If the database to support the preferred approach is inadequate, an alternative approach, called the Default Chemical Category-Specific Method can be used. This method incorporates the use of limited or categorical chemical-specific and physiological information. The default method is discussed below, followed by the procedures outlined in the *Inhalation Dosimetry Methodology* for deriving the RfC and IUR as they apply to the interpretation of animal and human data.

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[10] EPA defines PBPK models in the IRIS glossary as a model that estimates the dose to a target tissue or organ by taking into account the rate of absorption into the body, distribution among target organs and tissues, metabolism, and excretion (USEPA, 2008b). For further information about PBPK modeling, please refer to *Approaches for the Application of Physiologically Based Pharmacokinetic Models and Supporting Data in Risk Assessment* (USEPA, 2006a).

[11] The *Inhalation Dosimetry Methodology* recognizes the existence of alternate approaches in addition to the two presented in this guidance. The PBPK approach is generally preferred. In the absence of such a model, alternate models may be more optimal than the default approach when default assumptions or parameters can be replaced by more detailed, biologically-motivated descriptions or actual data, respectively. For instance, a model may be considered more optimal if it incorporates chemical or species-specific information or if it accounts for mechanistic determinants. See Table 3-6 in the *Inhalation Dosimetry Methodology* for more details on the hierarchy of approaches (EPA, 1994, page 3-40).

2.1.1 Default Approach - Extrapolation from Experimental Animal Data

The default method involves a two-step procedure that uses limited or categorical chemical-specific and physiological information to calculate the HEC. First, the chosen point of departure (POD) from the experimental data for a chemical is adjusted to derive a concentration intended to represent an equivalent dose under conditions of continuous exposure (7 days a week, 24 hours a day).[12] In the second step, this concentration is then multiplied by a Dosimetric Adjustment Factor (DAF) to generate the HEC. Further details on each step are outlined below.

2.1.1.1 Duration Adjustment to Continuous Exposure

Most of the inhalation studies of laboratory animals used to derive RfCs and IURs involve an exposure regimen of four to six hours per day, five to seven days per week, for 13 weeks or more (equivalent to 10 percent or more of the lifetime of the animal). The POD concentration from an animal study is mathematically adjusted to reflect an equivalent dose under conditions of continuous exposure.[13] Adjustment of duration to a continuous exposure scenario is regularly applied as a default procedure to studies with repeated exposures but not to single-exposure inhalation toxicity studies in animals (USEPA, 1994). Operationally, this is accomplished by applying a *c* x *t* product (where "*c*" is concentration, and "*t*" is duration of exposure) for both the number of hours in a daily exposure period and the number of days per week that the exposure is experienced. For example, if exposure in a particular study was 6 hours per day, 5 days per week, the experimental exposure is multiplied by 6/24 x 5/7 to calculate an equivalent continuous exposure. The general equation provided in the *Inhalation Dosimetry Methodology* (USEPA, 1994, Equation 4-2) for calculating duration-adjusted exposure levels in mg/m^3 for experimental animals is presented below.

$NOAEL_{[ADJ]}$ = E x D x W **(Equation 1)**

Where:

$NOAEL_{[ADJ]}$ (mg/m^3) = the NOAEL or analogous exposure level obtained with an alternate approach (e.g., LOAEL, LEC_{10}), adjusted for duration of experimental regimen;
E (mg/m^3) = the NOAEL or analogous exposure level observed in the experimental study;
D (h/h) = number of hours exposed/24 hours; and
W (days/days) = number of days of exposure/7days.

Using the example above, the assumption is that the product of *c* x *t*, not concentration alone, is associated with the toxicity observed. This is roughly equivalent to implying that if an effect occurs from a chemical at an exposure of 6 hours per day at 40 parts per million (ppm), that same effect will

[12] Examples of PODs include the no-observed-adverse-effect level (NOAEL); the lowest-observed-adverse-effect level (LOAEL); Benchmark Concentration, Lower confidence limit (BMCL); and the Lower limit on an Effective Concentration using a 10 percent response level (LEC_{10}). For definitions of the various PODs, please refer to the IRIS glossary (http://www.epa.gov/ncea/iris/help_gloss.htm).

[13] Continuous exposure refers to 24 hours per day, 7 days per week.

occur at an exposure of 24 hours per day at 10 ppm.[14] Note that this adjustment always produces a lower concentration value than that administered to experimental animals. Thus, as stated in *A Review of the Reference Dose and Reference Concentration Processes* (hereafter, the *RfD/RfC Review*), application of this procedure results in an automatic margin of protectiveness for chemicals for which concentration alone may be the more appropriate dose metric, and it reflects the maximum dose for chemicals for which total or cumulative dose is the appropriate measure (USEPA, 2002c). If a different procedure is used to calculate the continuous exposure, it should be fully discussed in the relevant technical support document for the chemical (e.g., IRIS profile, Provisional Peer Reviewed Toxicity Values (PPRTVs) Assessment). For additional discussion, including the uncertainties associated with this approach, see Section 4.3.2 of the *Inhalation Dosimetry Methodology* and Section 4.4.2.1 of the *RfD/RfC Review* (USEPA, 2002c).

2.1.1.2 Dosimetric Adjustment to Human Equivalent Concentration

Typically, the adjusted POD concentration from the animal study is next converted to an HEC using the following equation (USEPA, 1994, Equation 4-3):

$NOAEL_{[HEC]} = NOAEL_{[ADJ]} \times DAF$ **(Equation 2)**

Where:

$NOAEL_{[HEC]}$ (mg/m^3) = the NOAEL or analogous exposure level obtained with an alternate approach, dosimetrically adjusted to an HEC;

$NOAEL_{[ADJ]}$ (mg/m^3) = the NOAEL or analogous exposure level obtained with an alternate approach, adjusted for duration of experimental regimen; and

DAF = Dosimetric Adjustment Factor for the specific site of effects (e.g., respiratory tract region or extra-respiratory).

The DAF is typically based on ratios of animal and human physiologic parameters. The specific DAF used depends on the nature of the contaminant (e.g., particle or gas) and the target site where the toxic effect occurs (e.g., respiratory tract or a location in the body remote from the portal-of-entry). For example, the DAF can be based on either the Regional Gas Dose Ratio (RGDR), for gases with respiratory effects, or the Regional Deposited Dose Ratio (RDDR) for particles.

Table 2 provides information on the site of effects for the different chemical types. It also lists the physiologic parameters considered when calculating the DAF for specific regions of the body.[15] In addition, the table provides references to the equations from the *Inhalation Dosimetry Methodology* used in deriving the DAFs. Figure 1 provides a schematic of the human respiratory tract, illustrating each of the different regions.

[14] This assumption is based on Haber's Law, which states that "the incidence and/or severity of an adverse health effect depends on the total exposure to a potentially toxic substance. Total exposure (*K*) is the concentration of the substance (*c*) times the duration time of exposure (*t*), (i.e., *c* x *t*=*K*)" (Gaylor, 2000).

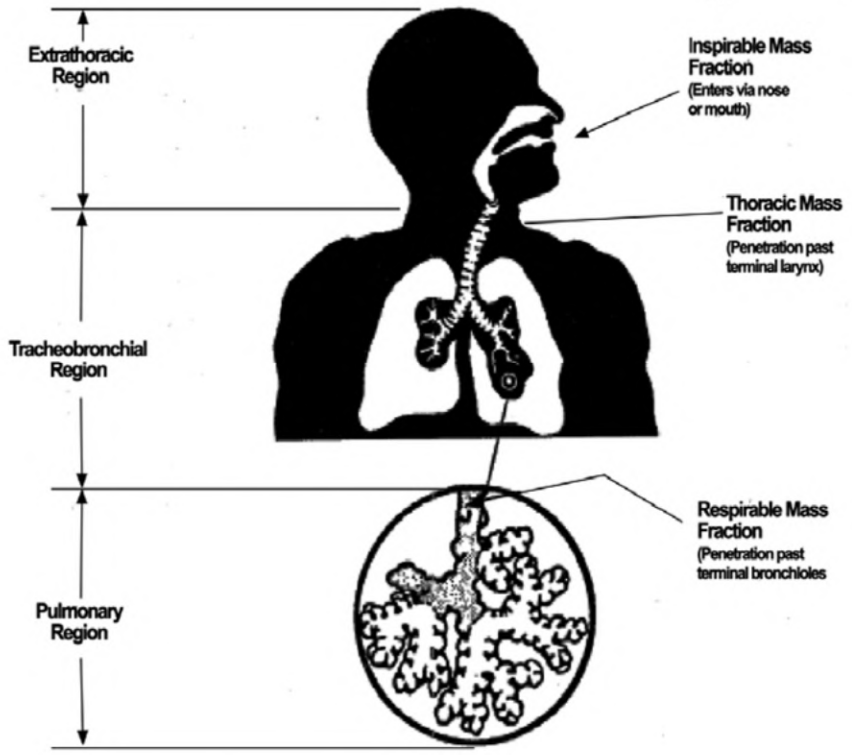
[15] The three main regions of the respiratory tract include the following: 1) Extrathoracic (includes nose, mouth, nasopharynx, oropharynx, laryngopharynx, and larynx); 2) Tracheobronchial (includes trachea, bronchi, and bronchioles); and 3) Pulmonary (includes respiratory bronchioles, alveolar ducts, alveolar sacs and the alveoli).

TABLE 2
CONTAMINANT PROPERTIES AND DOSIMETRIC ADJUSTMENT FACTORS[a]

Chemical Type	Site of Effects	Parameters Considered in Derivation of DAF for Regions of the Body[b]	DAF Equation Numbers in Inhalation Dosimetry Methodology[c]
Category 1 Gases (e.g., acrolein, hydrogen fluoride, chlorine)	Respiratory	-Minute volume (ETh, TB) -Surface area (ETh, TB, PU) -Mass transport coefficient (TB, PU) -Fraction of inhaled chemical penetrating the respiratory region (PU) -Alveolar ventilation rate (PU)	4-18 (ETh), 4-21 & 4-22 (TB), 4-28 (PU)
Category 2 Gases (e.g., acetonitrile, xylene, propanol, isoamyl alcohol)	Respiratory and Remote	-Mass transport coefficients (ETh, TB) -Blood:gas partition coefficient (ET, TB, ER) -Cardiac output (ETh, TB, ER) -Alveolar ventilation rate (PU) -Surface Area (PU) -Minute volume (ER)	4-18 (ETh), 4-21 & 4-22 (TB), 4-28 (PU), 4-48 (ER)[d,e]
Category 3 Gases (e.g., benzene, styrene)	Remote	Blood:gas partition coefficient (ER)	4-48[d]
Particles	Respiratory and Remote	-Minute volume (TOT, ER) -Surface area (TOT) -Fractional deposition of particle (TOT, ER) -Body weight (ER) -Inhaled concentration (ER)	4-14 (TOT), 4-15 (ER)

[a] Due to the complexities inherent in evaluating the health effects associated with exposure to gases, no definitive or comprehensive list of Category 1, 2, or 3 gases is available. Risk assessors should consult with an inhalation toxicologist in order to classify a specific gas as Category 1, 2, or 3, since there is overlap between the sites of effects and the parameters considered in deriving the DAF for different regions of the respiratory tract.
[b] Additional discussion of the terms used in this table can be found in the *Inhalation Dosimetry Methodology*.
[c] The *Inhalation Dosimetry Methodology* provides equations for deriving DAFs for the different contaminant categories. The equations listed in this table are the default equations for each specific region in the body.
[d] This refers to Equation 4-48 that is found on page 4-60 of the *Inhalation Dosimetry Methodology*.
[e] The equations presented for Category 2 gases in the *Inhalation Dosimetry Methodology* contain errors. Therefore, this table refers to the equations for Category 1 and 3 gases, which are expected to cover respiratory and remote effects from Category 2 gases.
Acronyms: ETh = Extrathoracic; TB = Tracheobronchial; PU = Pulmonary; ER = Extra-respiratory; TOT = Total respiratory system.

FIGURE 1
HUMAN RESPIRATORY TRACT



Source: EPA (1994), Figure 3-1, Page 3-5.

Category 1 gases are highly water-soluble and/or are rapidly irreversibly reactive in the respiratory tract (e.g., acrolein, hydrogen fluoride, chlorine). They do not significantly accumulate in the blood, and therefore their effects are usually exclusively respiratory (USEPA, 1994). The DAF for Category 1 gases consists of an RGDR and is based on the animal to human ratio of the minute volume (V_e) divided by the surface area (SA) of the region of the respiratory tract where the effect occurs.[16] See Appendix A, Sections 1, 2, and 3 of this guidance for examples of specific Category 1 DAF equations.

[16] For the purposes of this document, the V_e is defined as the total ventilation per minute and equals the product of the tidal volume (the air volume entering or leaving the lungs with a single breath) and the respiratory frequency.

Category 3 gases are relatively water-insoluble and are unreactive in the respiratory tract (e.g., benzene, styrene). Their toxicity is generally at sites remote to the respiratory tract (USEPA, 1994). The DAF for Category 3 gases is based on the ratio of the animal blood:gas partition coefficient ($H_{b/g\text{-}animal}$) and the human blood:gas partition coefficient ($H_{b/g\text{-}human}$). See Appendix A, Section 4 of this guidance for an example of a Category 3 DAF equation.

Category 2 gases are moderately water-soluble and may be rapidly reversibly reactive or moderately to slowly irreversibly reactive in respiratory tract tissue (e.g., acetonitrile, xylene, propanol, isoamyl alcohol). These gases have potential for significant accumulation in the blood, so they can exhibit both respiratory and remote toxicity (USEPA, 1994). The DAF for respiratory effects of Category 2 gases consists of an RGDR and is based on the animal to human ratio of the V_e and the SA of the region of the respiratory tract where the effect occurs, as for Category 1 gases. The DAF for extra-respiratory (ER) effects of a Category 2 gas is based on the ratio of the $H_{b/g\text{-}animal}$ and the $H_{b/g\text{-}human}$, as for Category 3 gases.

Particles also vary by solubility and reactivity. However, the default equations used to estimate the predicted regional deposition fractions for particles are based on non-soluble, non-hygroscopic particles (USEPA, 1994, Section 4.3.5.3). The DAF for a particle causing an effect in the respiratory tract is the $RDDR_r$. The $RDDR_r$ is based on the animal to human ratio of the V_e and the fractional deposition of the particle in that region (F_r), divided by the SA_r of the region where the effect occurs. This derivation, from the *Inhalation Dosimetry Methodology,* conservatively assumes that 100 percent of the deposited dose remains in the respiratory tract; clearance mechanisms are not considered. The DAF for a particle causing an ER effect, the $RDDR_{ER}$, is based on the animal to human ratio of the V_e and the total deposition of the particle in the entire respiratory tract (F_{total}), divided by BW (USEPA, 1994). The $RDDR_{ER}$ assumes that 100 percent of the deposited dose in the entire respiratory tract is available for uptake into the systemic circulation. See Appendix A, Section 5 for examples of specific particle DAF equations.

2.1.2 Default Approach - Extrapolation from Human Occupational Data

When human data are available to derive an RfC, duration adjustments are often required to account for differences in exposure scenarios (e.g., extrapolation from an 8 hour/day occupational exposure to a continuous chronic exposure). The default approach recommended by the *Inhalation Dosimetry Methodology* for adjusting the POD concentration (e.g., the no observable adverse effect level (NOAEL)) obtained from human study data is provided below in Equation 3 (USEPA, 1994, Equation 4-49).[17,18]

[17] If sufficient data are available, a PBPK model or intermediate approach using chemical-specific information may be employed in preference to the default method for extrapolating human occupational data to an HEC.

[18] EPA's IRIS glossary defines an adverse effect as the following: "A biochemical change, functional impairment, or pathologic lesion that affects the performance of the whole organism, or reduces an organism's ability to respond to an additional environmental challenge" (USEPA, 2008b).

$NOAEL_{[HEC]}$ = NOAEL x (VEho/VEh) x 5 days/7 days **(Equation 3)**

Where: $NOAEL_{[HEC]}$ (mg/m^3) = the NOAEL or analogous exposure level obtained with an alternate approach, dosimetrically adjusted to an ambient HEC;
NOAEL (mg/m^3) = occupational exposure level (time-weighted average over an 8-hour exposure period);
VEho = human occupational default minute volume over 8 hours (10 m^3); and
VEh = human ambient default minute volume over 24 hours (20 m^3).

2.2 Derivation of the Inhalation Unit Risk

The default approach for determining predictive cancer risk recommended by EPA's *Guidelines for Carcinogen Risk Assessment* (USEPA, 2005a; hereafter, *Cancer Guidelines*) is a linear extrapolation from exposures observed in the animal or human occupational study.[19] This approach involves drawing a straight line from the POD to the origin. The default linear extrapolation approach is generally considered to be conservatively protective of public health, including sensitive sub-populations (USEPA, 2005a). The slope of this line is commonly called the slope factor, and when the units are risk per $\mu g/m^3$, it is also called the IUR. EPA defines an IUR in the IRIS glossary as "the upper-bound excess lifetime cancer risk estimated to result from continuous exposure to an agent at a concentration of 1 $\mu g/m^3$ in air" (USEPA, 2008b). Equation 4 below presents a linear extrapolation from a POD of 10 percent response (LEC_{10}).[20]

$IUR = 0.1/LEC_{10[HEC]}$ **(Equation 4)**

Where: IUR $(\mu g/m^3)^{-1}$ = Inhalation Unit Risk; and
$LEC_{10[HEC]}$ ($\mu g/m^3$) = the lowest effective concentration using a 10 percent response level, dosimetrically adjusted to an HEC.

2.3 Derivation of the Reference Concentration

EPA defines an RfC in the IRIS glossary as "an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious effects during a lifetime" (USEPA, 2008b). The RfC is derived after a review of the health effects database for a chemical and identification of the most sensitive and relevant endpoint along with the principal study or studies demonstrating that endpoint. EPA Chemical Managers use UFs to account for recognized

[19] According to the *Cancer Guidelines*, "[a] nonlinear approach should be selected when there are sufficient data to ascertain the mode of action [MOA] and conclude that it is not linear at low doses and the agent does not demonstrate mutagenic or other activity consistent with linearity at low doses" (USEPA, 2005a, page 3-22). In addition, [l]inear extrapolation should be used when there are MOA data to indicate that the dose-response curve is expected to have a linear component below the POD" (USEPA, 2005a, page 3-21). This information will appear on the IRIS profile or other toxicological information source for a chemical. Chemicals with a mutagenic MOA are thought to pose a higher risk during early life. Procedures for assessing cancer risk from these chemicals are outlined in Section 5.1.

[20] The POD used in Equation 4 is an LEC_{10}, which is the lower 95 percent confidence limit on the concentration corresponding to a 10 percent response rate (i.e., the EC_{10}). Other PODs may be substituted for this value, which could be associated with alternative response levels (e.g., 1 percent, 5 percent).

uncertainties in the extrapolations from the experimental data conditions to an estimate appropriate to the assumed human scenario (USEPA, 1994). See Table 3 for a description of the standard UFs. The formula used for deriving the RfC from the HEC is provided below.

$RfC = NOAEL_{[HEC]}/(UF)$[1] **(Equation 5)**

Where: RfC (mg/m^3) = Reference Concentration
$NOAEL_{[HEC]}$ (mg/m^3) = The NOAEL or analogous exposure level obtained with an alternate approach, dosimetrically adjusted to an HEC; and
UF = Uncertainty factor(s) applied to account for the extrapolations required from the characteristics of the experimental regimen.

[1] Some toxicological information sources for RfCs will incorporate an additional factor to account for deficiencies in the available data set, called a modifying factor (MF). In 2002, however, EPA published the *RfD/RfC Review,* which recommended that the use of MFs be discontinued because their purpose is "sufficiently subsumed in the general database UF" (USEPA, 2002c, page xviii). Therefore, RfCs published subsequent to this document will not include MFs.

TABLE 3
THE USE OF UNCERTAINTY FACTORS IN DERIVING AN INHALATION REFERENCE CONCENTRATION

Standard UFs	Processes Considered in the UF Purview
H = Human to sensitive human: Extrapolation of valid experimental results from studies using prolonged exposure to average healthy humans. Intended to account for the variation in sensitivity among the members of the human population.	-Pharmacokinetics/Pharmacodynamics -Sensitivity[2] -Differences in body weight (age, obesity) -Concomitant exposures -Activity pattern -Does not account for idiosyncrasies
A = Animal to human: Extrapolation from valid results of long-term studies on laboratory animals when results of studies of human exposure are not available or are inadequate. Intended to account for the uncertainty in extrapolating laboratory animal data to the case of average healthy humans.	-Pharmacokinetics/Pharmacodynamics -Relevance of laboratory animal model -Species sensitivity
S = Subchronic to chronic: Extrapolation from less-than-chronic exposure results on laboratory animals or humans when there are no useful long-term human data. Intended to account for the uncertainty in extrapolating from less than chronic NOAELs to chronic NOAELs.	-Accumulation/Cumulative damage -Pharmacokinetics/ Pharmacodynamics -Severity of effect -Recovery -Duration of study -Consistency of effect with duration
L = LOAEL to NOAEL: Derivation from a LOAEL instead of a NOAEL. Intended to account for the uncertainty in extrapolating from LOAELs to NOAELs.	-Severity -Pharmacokinetics/Pharmacodynamics -Slope of dose-response curve -Trend, consistency of effect -Relationship of endpoints -Functional vs. histopathological evidence -Exposure uncertainties
D = Incomplete to complete data: Extrapolation from valid results in laboratory animals when the data are "incomplete." Intended to account for the inability of any single laboratory animal study to adequately address all possible adverse outcomes in humans.[1]	-Quality of critical study -Data gaps -Power of critical study/supporting studies -Exposure uncertainties

[1] The *RfD/RfC Review* indicates that this UF accounts for the potential for deriving an underprotective RfD/RfC as a result of an incomplete characterization of the chemical's toxicity or if the existing data suggest that a lower reference value might result if additional data were available (considering both the lacking and available data for particular organ systems as well as life stage) (USEPA, 2002c).
[2] The *RfD/RfC Review* also stresses that susceptible populations and life stages are accounted for with this UF (USEPA, 2002c).
Source: USEPA, 1994, Table 4-9, page 4-77.

3. CHARACTERIZING EXPOSURE

3.1 Introduction

This section describes an approach for characterizing exposure in a baseline risk assessment that is consistent with the *Inhalation Dosimetry Methodology*. The approach involves the estimation of exposure concentrations (ECs) for each receptor exposed to contaminants via inhalation in the risk assessment. ECs are time-weighted average concentrations derived from measured or modeled contaminant concentrations in air at a site, adjusted based on the characteristics of the exposure scenario being evaluated.[21,22]

Equations for estimating ECs are provided below. This document does not provide default input values for the exposure parameters referenced in these equations. EPA recommends the use of site-specific exposure values consistent with the exposure pathways and receptors at a site wherever practicable and appropriate. If a risk assessor opts to rely on default exposure input values, current Superfund-supported values may be found at the exposure assessment portion of the Superfund website: (http://www.epa.gov/oswer/riskassessment/superfund_hh_exposure.htm).

3.2 Estimating Exposure Concentrations for Assessing Cancer Risks

The estimation of an EC when assessing cancer risks characterized by an IUR involves the CA measured at an exposure point at a site as well as scenario-specific parameters, such as the exposure duration and frequency.[23] The EC typically takes the form of a CA that is time-weighted over the duration of exposure and incorporates information on activity patterns for the specific site or the use of professional judgment. The equation for estimating an EC for use with an IUR is presented below.

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[21] The default method for deriving inhalation toxicity values also involves calculating time-weighted ECs, as discussed in Sections 2.1.1.1 and 2.1.2.

[22] The ECs in this document are in units of $\mu g/m^3$. Inhalation toxicity values presented on IRIS are typically expressed in units of $\mu g/m^3$ or mg/m^3, which are mass units. Some regulatory contexts require the use of volumetric units such as ppm. The conversion from mass units to volumetric units depends on the molecular weight (MW) of the material as well as the ambient temperature and atmospheric pressure. To convert from ppm to mg/m^3, the following equation can be used: $\frac{ppm \times MW}{V} = mg/m^3$; where MW is the molecular weight of the gas and V is the volume of 1 gram molecular weight of the airborne contaminant. This is derived by the formula V = RT/P; where R is the ideal gas constant, T is the temperature in Kelvin (K = 273.16 + T°C) and P is the pressure in mm Hg. The value of R is 62.4 when T is in Kelvin, (K = 273.16 + T°C), the pressure is expressed in units of mm Hg and the volume is in liters. The value of R differs if the temperature is expressed degrees Fahrenheit (°F) or if other units of pressure are used (e.g., atmospheres, kilopascals).

[23] ECs are typically based on either estimated (i.e., modeled) or measured contaminant concentrations in air.

EC = (CA x ET x EF x ED)/AT **(Equation 6)**

Where: EC ($\mu g/m^3$) = exposure concentration;
CA ($\mu g/m^3$) = contaminant concentration in air;
ET (hours/day) = exposure time;
EF (days/year) = exposure frequency;
ED (years) = exposure duration; and
AT (lifetime in years x 365 days/year x 24 hours/day) = averaging time

3.3 Estimating Exposure Concentrations for Calculating Hazard Quotients

When estimating ECs for non-cancer or cancer hazards characterized by an HQ, risk assessors should match each exposure scenario at a site to the appropriate EC equation, based on the scenario duration and frequency of exposure.[24] Figure 2 presents a flowchart to assist risk assessors with this process and provides recommended equations that can be used to estimate the EC for each type of scenario.[25] As shown in Figure 2, the recommended process for estimating ECs to be used in calculating an HQ involves the following three steps: 1) assess the duration of the exposure scenario; 2) assess the exposure pattern of the exposure scenario; and 3) estimate the scenario-specific EC.

3.3.1 Step 1: Assess Duration

The first step in the recommended process of estimating an EC for use in calculating an HQ involves assessing the duration of the exposure scenario at a site. Step 1 in Figure 2 indicates that the risk assessor first should decide whether the duration of the exposure scenario is generally acute, subchronic, or chronic. Toxicologists have long been aware that effects from a single or short-term exposure can differ markedly from effects resulting from repeated exposures. The response by the exposed person depends upon factors such as whether the chemical accumulates in the body, whether it overwhelms the body's mechanisms of detoxification or elimination, or whether it produces irreversible effects (Eaton & Klaassen, 2001). Therefore, ideally, the chemical-specific elements of metabolism and kinetics, reversibility of effects, and recovery time should be considered as part of this recommended process when defining the duration of a site-specific exposure scenario.

[24] Traditionally, the HQ approach was limited to non-cancer hazard assessment. However, the HQ approach may also be appropriate for carcinogens with a non-linear mode of action. The 2005 *Cancer Guidelines* state the following on this subject: "For cases where the tumors arise through a nonlinear mode of action, an oral reference dose or an inhalation reference concentration, or both, should be developed in accordance with EPA's established practice for developing such values … this approach expands the past focus of such reference values (previously reserved for effects other than cancer) to include carcinogenic effects determined to have a nonlinear mode of action" (USEPA, 2005a; page 3-24).

[25] Figure 2 was developed for the evaluation of inhalation exposures. While the concepts presented in this flowchart may be useful for assessing other exposure routes (e.g., oral or dermal), these other routes are beyond the scope of this document, and therefore, are not explicitly considered. Caution should be used when using Figure 2 to evaluate other exposure routes, as considerations beyond those outlined in the flowchart may apply (e.g., time to reach steady state for dermal exposures).

To the extent possible, exposure durations (EDs) evaluated in a site-specific risk assessment should be consistent with the ED represented by the toxicity value. However, frequencies or durations of human exposures often are not as clearly defined as those in animal studies with controlled exposures, particularly for intermittent exposures. For example, the emission of some volatile chemicals into the ambient air may vary with temperature and season, providing fluctuating exposures for humans living near the source. Therefore, risk assessors should use best professional judgment to determine if the ED in a given scenario is reasonably similar to the duration associated with the toxicity value. Risk assessors should describe the uncertainties associated with their choice of toxicity value in the risk characterization section of the risk assessment (see Section 9.2.2 of this document). For situations where duration-appropriate toxicity values are not available, please follow the procedures outlined in Section 4.2 and Appendix C of this document.

The specific definition for each exposure duration category may vary depending on the source of the toxicity value being used. For Tier 1 toxicity values obtained from EPA's IRIS database, acute exposures are defined as lasting 24 hours or less; subchronic exposures are defined as repeated exposures by the oral, dermal, or inhalation route for more than 30 days, up to approximately 10 percent of the human lifespan; and chronic exposures are defined as repeated exposures for more than approximately 10 percent of the human lifespan (USEPA, 2008b).[26, 27]

After deciding which duration the exposure scenario most closely matches, risk assessors should then proceed to Step 2, following the path of the selected duration. Note that if an acute duration is selected, risk assessors should proceed directly to Step 3 to estimate an acute EC for each acute exposure period.

3.3.2 Step 2: Assess Exposure Pattern

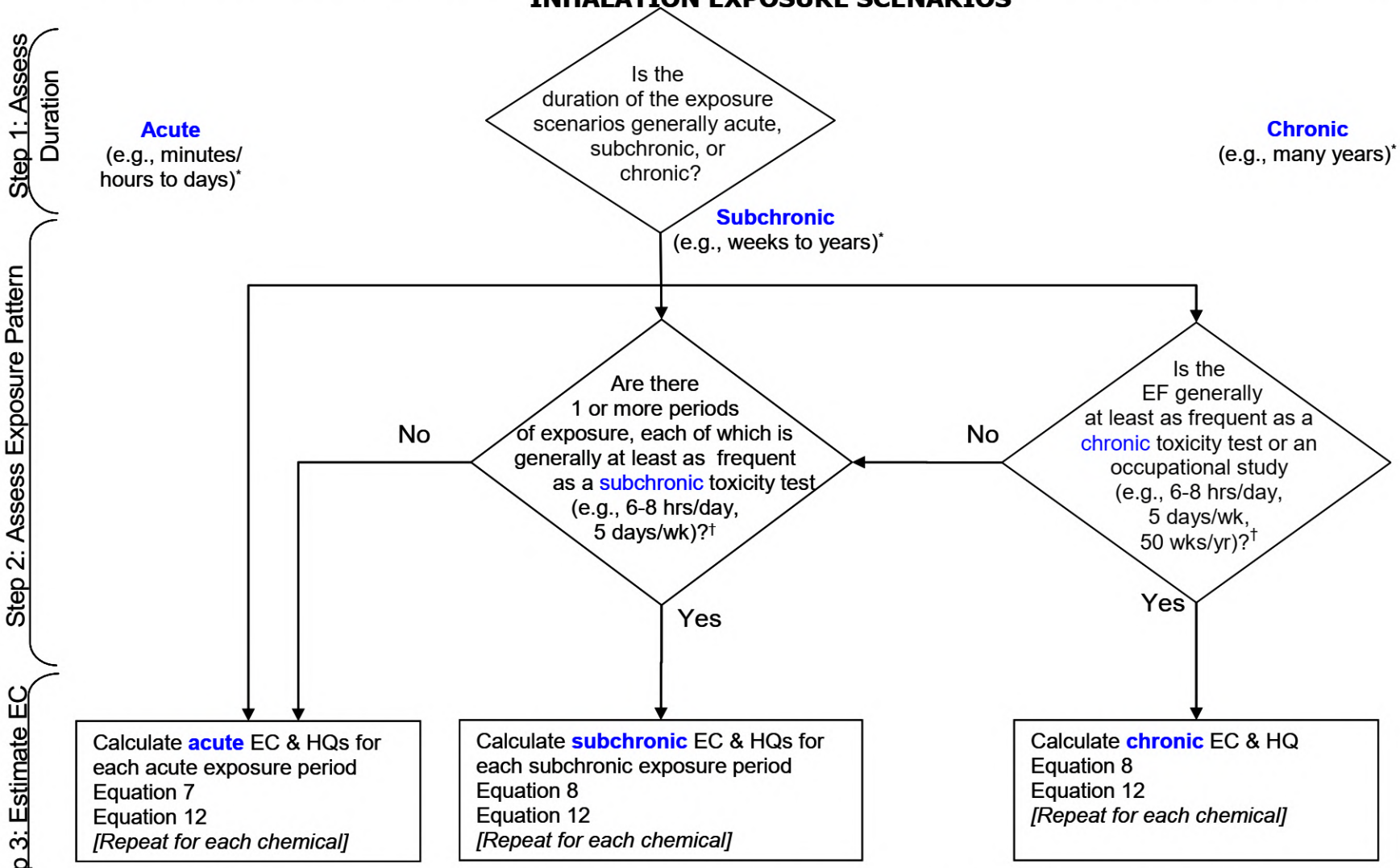
Step 2 of the recommended process for estimating an EC for use in a hazard quotient involves assessing the exposure pattern for each exposure scenario at a site. This entails comparing the exposure time and frequency at a site to that of a typical subchronic or chronic toxicity test.[28]

[26] Note that other sources of toxicity values may define exposures differently. For example, the Agency for Toxic Substances and Disease Registry (ATSDR) (which publishes Minimal Risk Levels (MRLs)) defines acute exposures as occurring from one to 14 days, intermediate exposures as greater than 14 to 364 days, and chronic exposures as 365 days or longer. However, the toxicity values are based on the same underlying toxicological concepts described in this section.

[27] Exposures with a duration lasting between 24 hours and 30 days should be treated as subchronic for the purposes of this document.

[28] Exposure regimens vary from study to study. Risk assessors should use best professional judgment to determine if the exposure pattern in a given scenario is reasonably similar to a typical regimen for a subchronic or chronic study.

FIGURE 2
RECOMMENDED PROCEDURE FOR DERIVING EXPOSURE CONCENTRATIONS AND HAZARD QUOTIENTS FOR INHALATION EXPOSURE SCENARIOS



* The specific definition for each duration category may vary depending on the source of the toxicity value being used. For Tier 1 toxicity values obtained from IRIS:
acute exposures are defined as those lasting 24 hours or less;
subchronic exposures are defined as repeated exposures for more than 30 days, up to approximately 10 percent of the life span in humans; and
chronic exposures are defined as repeated exposures for more than approximately 10 percent of the life span in humans (EPA, 2008b).
For the purposes of this document, short-term exposures, defined by the IRIS glossary as repeated exposures for more than 24 hours, up to 30 days, should be treated as subchronic.

† Exposure regimens vary from study to study. Risk assessors should use best professional judgment to determine if the exposure pattern in a given scenario is reasonably similar to a typical regimen for a chronic or subchronic study.

For exposure scenarios with a subchronic duration, risk assessors should follow the center path on the flowchart. Step 2 in this path asks whether there are one or more periods of exposure, each of which is generally as frequent as a subchronic toxicity test (e.g., 6-8 hours per day, 5 days per week). If the exposure scenario matches this description, risk assessors should proceed to Step 3 and estimate a subchronic EC for each subchronic exposure period. However, if the exposure pattern contains periods that are significantly shorter and/or involve significantly less frequent exposures than indicated in the flow chart, risk assessors should derive acute ECs for each of these exposure periods. If it is difficult to determine whether a specific exposure scenario is best modeled as a subchronic exposure or as a series of independent acute exposures, due to uncertainty in the time required to return to baseline following exposure, risk assessors may want to derive ECs using both approaches.

If the exposure scenario has a chronic duration, risk assessors should follow the right hand path on the flowchart. Step 2 in this path asks whether the exposure frequency (EF) is generally as frequent as a chronic animal toxicity test or a human occupational study (e.g., 6-8 hours per day, 5 days per week, for 50 weeks per year). If the exposure scenario matches this description, risk assessors should proceed to Step 3 and estimate a single chronic EC. However, if the scenario differs significantly from this pattern, risk assessors should proceed to the second question under the subchronic duration path and proceed as outlined above.

3.3.3 Step 3: Estimate Exposure Concentration

Step 3 of the recommended process involves estimating the EC for the specific exposure scenario based on the decisions made in Steps 1 and 2. For acute exposures, the EC is equal to the CA. Risk assessors can estimate an acute EC for each acute exposure period at a site using Equation 7. For longer-term exposures, risk assessors should take into consideration the exposure time, frequency, and duration for each receptor being evaluated as well as the period over which the exposure is averaged (i.e., the averaging time (AT)) to arrive at a time-weighted EC. If there are one or more exposure periods that are generally as frequent as a subchronic toxicity test, risk assessors should use Equation 8 to estimate a subchronic EC for each of these exposure periods. (Exposure periods with significantly less frequency should be treated as acute exposures.) If the exposure pattern is generally as frequent as a chronic toxicity test of an occupational study, risk assessors should use Equation 8 to estimate a single chronic EC for the duration of the exposure.

Acute Exposures

EC = CA **(Equation 7)**

Where: EC ($\mu g/m^3$) = exposure concentration;
CA ($\mu g/m^3$) = contaminant concentration in air;

Chronic or Subchronic Exposures

EC = (CA x ET x EF x ED)/AT **(Equation 8)**

Where:
EC ($\mu g/m^3$) = exposure concentration;
CA ($\mu g/m^3$) = contaminant concentration in air;
ET (hours/day) = exposure time;
EF (days/year) = exposure frequency;
ED (years) = exposure duration; and
AT (ED in years x 365 days/year x 24 hours/day) = averaging time

Note: If the duration of the exposure period is less than one year, the units in the above equation can be changed to the following: EF (days/week); ED (weeks/exposure period); and AT (hours/exposure period).

It is important to use the EC equation that most closely matches the exposure pattern and duration at a site. For instance, if the exposure pattern at a site consists of a series of short (e.g., 4-hour) periods of high exposure separated by several days of no exposure, the approach outlined above recommends estimating an acute EC for each acute exposure period. If the chronic EC equation (Equation 8) were to be used instead, the result would be an average EC value that may lead to an underestimate of risk since the inhaled concentrations could be higher than acute toxicity values during periods of exposure.

3.4 Estimating Exposure Concentrations in Multiple Microenvironments

When detailed information on the activity patterns of a receptor at a site is available, risk assessors can use these data to estimate the EC for either non-carcinogenic or carcinogenic effects. The activity pattern data describe how much time a receptor spends, on average, in different microenvironments (MEs), each of which may have a different contaminant concentration level.[29] By combining data on the contaminant concentration level in each ME and the activity pattern data, the risk assessor can calculate a time-weighted average EC for a receptor. Because activity patterns (and hence, MEs) can vary over a receptor's lifetime, EPA recommends that risk assessors pursuing the ME approach first calculate a time-weighted average EC for each exposure period characterized by a specific activity pattern (e.g., separate ECs for a school-aged child resident and a working adult resident). These exposure period-specific ECs can then be combined into a longer term or lifetime average EC by weighting the EC by the duration of each exposure period. The following sections further explain these two steps.

3.4.1 Using Microenvironments to Estimate an Average Exposure Concentration for a Specific Exposure Period

The ME approach can be used to estimate an average EC for a particular exposure period during which a receptor has a specified activity pattern. As a simplified example, a residential receptor may

[29] EPA defines a microenvironment in *Air Quality Criteria for Particulate Matter: Volume II* as a defined space that can be treated as a well-characterized, relatively homogeneous location with respect to pollutant concentration for a specified time period (e.g., rooms in homes, restaurants, schools, offices, inside vehicles, or outdoors) (USEPA, 2004b).

be exposed to a higher concentration of a contaminant in air in the bathroom for 30 minutes per day while showering, and exposed to a lower concentration in the rest of the house for the remaining 23.5 hours per day. In this case, risk assessors can use the CA value experienced in each ME weighted by the amount of time spent in each ME to estimate an average EC for the period of residency in that house using Equation 9.[30] This approach may also be used to address exposures to contaminants in outdoor and indoor environments at sites where both indoor and outdoor samples have been collected or where the vapor intrusion pathway has been characterized.

$$EC_j = \sum_{i=1}^{n} (CA_i \times ET_i \times EF_i) \times ED_j / AT_j \qquad \textbf{(Equation 9)}$$

Where:
EC_j ($\mu g/m^3$) = average exposure concentration for exposure period j;
CA_i ($\mu g/m^3$) = contaminant concentration in air in ME i;
ET_i (hours/day) = exposure time spent in ME i;
EF_i (days/year) = exposure frequency for ME i;
ED_j (years) = exposure duration for exposure period j; and
AT_j (hours) = averaging time = ED_j x 24 hours/day x 365 days/year.

3.4.2 Estimating an Average Exposure Concentration Across Multiple Exposure Periods

To derive an average EC for a receptor over multiple exposure periods, the average EC from each period (as calculated above in Equation 9) can be weighted by the fraction of the total exposure time that each period represents, using Equation 10. For example, when estimating cancer risks, the risk assessor may calculate a lifetime average EC where the weights of the individual exposure periods are the duration of the period, ED_j, divided by the total lifetime of the receptor. Alternatively, when estimating an HQ, risk assessors can use Equation 10 to calculate less-than-lifetime average ECs across multiple exposure periods. In that case, the AT will equal the sum of the individual EDs for all of the exposure periods.

$$EC_{LT} = \sum_{i=1}^{n} (EC_j \times ED_j) / AT \qquad \textbf{(Equation 10)}$$

Where:
EC_{LT} ($\mu g/m^3$) = long-term average exposure concentration;
EC_j ($\mu g/m^3$) = average exposure concentration of a contaminant in air for exposure period j;
ED_j (years) = duration of exposure period j; and
AT (years)[1] = averaging time.

[1] When evaluating cancer risk, the AT is equal to lifetime in years. When evaluating non-cancer hazard, the AT is equal to the sum of the EDs for each exposure period.

[30] If one or more MEs involve acute exposures, risk assessors should conduct a supplemental analysis comparing the CA for each of those MEs to a corresponding acute toxicity value to ensure that receptors are protected from potential acute health effects.

4. SELECTING APPROPRIATE TOXICITY VALUES

After characterizing the exposure scenarios and estimating ECs for each receptor at a site, the risk assessor should select appropriate inhalation toxicity values for each inhaled contaminant. For estimating cancer risks, this typically involves identifying and evaluating available published cancer potency estimates. For estimating HQs, this typically involves identifying and evaluating reference values that match the characterization of the exposure scenario from Figure 2 (i.e., acute, subchronic, or chronic reference values).

This section provides guidance for the selection of toxicity values appropriate for assessing risk under inhalation exposure scenarios. It describes sources for the most current inhalation data and provides guidance for proceeding when published inhalation toxicity data are not available.

4.1 Sources for Inhalation Toxicity Data

The OSWER Directive, *Human Health Toxicity Values in Superfund Risk Assessment* (USEPA, 2003), provides a recommended hierarchy of toxicological data sources to guide risk assessors when selecting appropriate toxicity values. This document sets out a recommended three-tiered framework for selecting human toxicity values. Tier 1 consists of EPA's IRIS, Tier 2 consists of EPA's PPRTVs, and Tier 3 includes other toxicity values as recommended by NCEA, such as the California EPA toxicity values, the Agency for Toxic Substances and Disease Registry's (ATSDR's) Minimal Risk Levels (MRLs), and Health Effects Assessment Summary Table (HEAST) toxicity values. Priority in Tier 3 should be given to sources that are the most current and those that are peer reviewed. Consultation with the Superfund Headquarters office is recommended regarding the use of Tier 3 values for Superfund response decisions when the contaminant appears to be a risk driver for the site.

The most up-to-date information on Superfund-supported cancer potency estimates and chronic and subchronic cancer and non-cancer reference values for inhaled contaminants are available on the Superfund risk assessment website (www.epa.gov/oswer/riskassessment/superfund_toxicity.htm). Superfund-recommended sources for acute non-cancer toxicity values can be found at www.epa.gov/oswer/riskassessment/superfund_acute.htm.[31]

In situations where the desired reference value (e.g., acute, subchronic, chronic) is not available, risk assessors may use a reference value based on the next longer duration of exposure as a conservative estimate that would be protective for a shorter-term ED (USEPA, 2002c). For example, if a risk assessor determines that an ED at a site is subchronic, but no subchronic toxicity value is available, a chronic RfC can be used to assess hazard.

EPA recommends that toxicity values published in Superfund-supported sources should generally be used in the risk equations presented in this guidance, without modification. This includes IURs on IRIS that were calculated from oral values using a default ventilation rate and BW (see Appendix B for a list of these chemicals). It is not generally appropriate to make adjustments to these values

[31] In selecting an acute toxicity value, risk assessors should consider the duration associated with their estimate of exposure (e.g., a 1-hour versus a 24-hour air sample). Use of a toxicity value specified for a longer duration than that of the exposure estimate may overestimate hazard, while the use of a shorter duration acute reference value may underestimate hazard.

based on IR and BW using the intake equation, because the amount of the chemical that reaches the target site through the inhalation pathway is not a simple function of these parameters (see Section 1.2). Use of the toxicity values listed in Appendix B should be noted in the uncertainty section of the risk assessment (see Section 9).

4.2 Recommended Procedures for Assessing Risk in the Absence of Inhalation Toxicity Values

The following section provides guidance on recommended procedures for situations where inhalation toxicity values are not available in any of the toxicity data sources described in Section 4.1.

If RfC and IUR values are not available for an inhaled contaminant, risk assessors should first contact NCEA's STSC for guidance.[32] Risk assessors working on Superfund sites can contact STSC to determine whether a provisional peer-reviewed toxicity value (PPRTV) exists for a contaminant; if not, the risk assessor, in cooperation with the appropriate EPA Regional office may request that STSC develop a PPRTV document or that STSC develop an inhalation toxicity value as a "consult". The latter would be specific to the site in question only. Additional information on STSC's current process for developing alternative toxicity values is described in Appendix C.

If STSC indicates that no quantitative toxicity information for the inhalation route is available, the risk assessor should conduct a qualitative evaluation of this exposure route. The risk assessor should discuss in the uncertainty section of the risk assessment report the implications of not quantitatively assessing risks due to inhalation exposures to chemicals lacking inhalation toxicity data. See the section on Risk Characterization (Section 9) in this guidance for more information.

Performing simple route-to-route extrapolation without the assistance of STSC is generally not appropriate because hazard may be misrepresented when data from one route are substituted for another without any consideration of the pharmacokinetic differences between the routes (USEPA, 1998). The following circumstances, outlined in the *Inhalation Dosimetry Methodology* (page 4-6), are specific examples of situations when route-to-route extrapolation from oral toxicity values might not be appropriate, even for use during screening:

- When groups of chemicals are expected to have different toxicity by the two routes – for example, metals, irritants, and sensitizers;
- When a first-pass effect by the respiratory tract is expected;
- When a first-pass effect by the liver is expected;
- When a respiratory tract effect is established, but dosimetry comparison cannot be clearly established between the two routes;
- When the respiratory tract was not adequately studied in the oral studies; and
- When short-term inhalation studies, dermal irritation, in vitro studies, or characteristics of the chemical indicate the potential for portal-of-entry effects at the respiratory tract, but studies themselves are not adequate for inhalation toxicity value development.

[32] All contact with STSC should be performed by an EPA regional risk assessor. States and other entities should first contact their EPA regional risk assessor with questions on inhalation toxicity values. Regional risk assessors can then contact STSC on their behalf.

The *Cancer Guidelines* (USEPA, 2005a) includes the following statement regarding route-to-route extrapolation:

> "When a qualitative extrapolation can be supported, quantitative extrapolation may still be problematic due to the absence of adequate data. The differences in biological processes among routes of exposure (oral, inhalation, dermal) can be great because of, for example, first-pass effects and different results from different exposure patterns. There is no generally applicable method for accounting for these differences in uptake processes in a quantitative route-to-route extrapolation of dose-response data in the absence of good data on the agent of interest. Therefore, route-to-route extrapolation of dose data relies on a case-by-case analysis of available data" (page 3-10).

5. ESTIMATING RISKS

This section provides updated equations recommended for estimating excess cancer risks and HQs from inhaled contaminants of concern at Superfund sites. Please see Section 8.2.1 of *RAGS, Part A* for further information about how to interpret calculated excess cancer risks and HQs.

5.1 Cancer Risks Characterized by an Inhalation Unit Risk

The excess cancer risk for a receptor exposed via the inhalation pathway can be estimated with the following equation:

Risk = IUR x EC **(Equation 11)**

Where: IUR $(\mu g/m^3)^{-1}$ = Inhalation Unit Risk; and
EC $(\mu g/m^3)$ = exposure concentration (See Equation 6).

When estimated ECs are above the POD used for the low dose extrapolation described in Section 2.3, a linear concentration-response relationship may not hold.[33] In such situations, the risk assessor should not use toxicity values developed through low dose extrapolation techniques. Instead, the risk assessor may report semi-quantitative risk estimates (e.g., risks are greater than 10^{-2}) or estimate risk using the original model underlying the toxicity value, which can be found in the technical support document for the value (e.g., IRIS profile, PPRTV Assessment).

When estimating cancer risks for children, risk assessors should be aware of chemicals that pose a higher risk of cancer when exposure occurs during early life. If evidence exists suggesting differences in risk across age groups for a chemical, this typically will be considered in the derivation of the toxicity value and described in the chemical's technical support document.

[33] Reviews of chemical-specific IRIS files indicate that the risk level corresponding to the concentration level above which the IUR should not be used often falls at or near 10^{-2}. However, this risk level varies by chemical and, therefore, risk assessors should refer to the toxicity value's technical support document for information on the concentration range for which the IUR was intended to be used.

Chemicals that have been determined to cause cancer by a mutagenic mode of action (MOA) are thought to pose a higher risk during early life. An EPA-recommended procedure exists for assessing risks from these chemicals. Figure 3 summarizes the recommendations of the *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* (USEPA, 2005b; hereafter *Supplemental Cancer Guidelines*) on how to adjust childhood risk calculations to account for chemicals with a mutagenic MOA for carcinogenicity. Please refer to the *Supplemental Cancer Guidelines* (USEPA, 2005b) for a list of chemicals with a mutagenic MOA that were used in the development of that document.

In addition, EPA's website for the "Handbook for Implementing the Supplemental Cancer Guidance at Waste and Cleanup Sites" contains an up-to-date list of chemicals that EPA has determined to have a mutagenic MOA (http://www.epa.gov/oswer/riskassessment/sghandbook/index.htm). As chemicals receive new assessments for mutagenicity, this information will appear in the IRIS profile or PPRTV assessment.

FIGURE 3
GUIDANCE ON ASSESSING RISK FROM EARLY-LIFE EXPOSURES FOR CHEMICALS ACTING BY A MUTAGENIC MODE OF ACTION FOR CARCINOGENICITY

If a chemical has been determined to cause cancer by a mutagenic MOA, it is possible that exposures to that chemical in early-life may result in higher lifetime cancer risks than a comparable duration adult exposure.

In risk assessments of exposure to chemicals for which a mutagenic MOA for carcinogenicity has been determined by EPA and a linear low-dose extrapolation performed, one of the following generally pertains:

1) If chemical-specific data on susceptibility from early-life exposures were available for derivation of CSFs, those slope factors are used for risk characterization, and Age Dependent Adjustment Factors (ADAFs) are not applied.
2) If chemical-specific data on susceptibility from early-life exposures were not available, the ADAFs are applied in calculating or estimating risks associated with early-life exposures (USEPA, 2005c).

If the latter case applies, the *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* (USEPA, 2005b) recommends the following default ADAFs be applied in risk assessments:

- 10-fold adjustment for exposures during the first 2 years of life;
- 3-fold adjustment for exposures from ages 2 to <16 years of age; and
- No adjustment for exposures after turning 16 years of age.

In such cases, Equation 11 can be altered to include the ADAFs in the following way:

$$Risk = (IUR \times EC_{<2} \times ADAF_{<2}) + (IUR \times EC_{2\text{-}16} \times ADAF_{2\text{-}16}) + (IUR \times EC_{>16})$$

Sources: USEPA, 2005b and USEPA, 2005c.
Note: All communications and factsheets pertaining to the implementation of the 2005 *Cancer Guidelines* can be found at www.epa.gov/osa/spc/cancer_guidelines.htm.

5.2 Hazard Quotients

The HQ for the inhalation pathway can be calculated with the following general equation:

HQ = EC/(Toxicity Value[1] x 1000 µg/mg) **(Equation 12)**

Where: HQ (unitless) = Hazard Quotient;
EC ($\mu g/m^3$) = exposure concentration (See Equations 7 or 8);
Toxicity Value (mg/m^3) = Inhalation toxicity value (e.g., RfC) that is appropriate for the exposure scenario (acute, subchronic, or chronic).

[1] Risk assessors should refer to the flowchart (Figure 2) to select an appropriate inhalation toxicity value for the exposure scenario at a site in order to calculate the HQ.

6. EXAMPLE EXPOSURE SCENARIOS

This section of the guidance includes examples of the types of exposure scenarios risk assessors may encounter when evaluating inhalation exposures at waste sites. Each scenario includes sample values for exposure parameters and reviews the process of estimating the EC and risks for cancer and other health effects. These examples are provided for illustrative purposes only and are not representative of every exposure scenario that could be encountered at a site. Furthermore, risk assessors should use site-specific values for exposure parameters if practicable when estimating ECs and risk levels or HQs. This would typically require some information on activity patterns for the specific site or the use of professional judgment. If default values are to be used for certain exposure parameters, please consult the Superfund website for up-to-date information on Superfund-recommended default exposure parameters.[34]

6.1 Residential Receptor

An example of a residential scenario could consist of inhalation exposure for up to 24 hours per day, up to 350 days per year for 6 to 30 years. When estimating cancer risk for this type of scenario, Equation 6 is recommended to calculate an EC and Equation 11 is recommended to estimate risk. For estimating hazard quotients for cancer or non-cancer effects, this scenario can be evaluated using the steps outlined in Figure 2. The duration of this scenario ranges from 6 to 30 years, which can be considered chronic (because it consists of repeated exposures for approximately 10 percent of a receptor's lifespan). The frequency of this scenario is generally as frequent as a chronic toxicity test and therefore Equation 8 is recommended to derive a chronic EC and Equation 12 with a chronic toxicity value is recommended to calculate an HQ. If information about multiple MEs is available, risk assessors should proceed according to Section 3.4 to estimate ECs to use in estimating cancer risks or HQs.

When assessing the risk under the residential scenario for children, the risk assessor should keep in mind that exposure parameters, specifically those related to activity patterns (e.g., exposure time, frequency, and duration) may be different for children and adults at the same site. For example, due

[34] http://www.epa.gov/oswer/riskassessment/superfund_hh_exposure.htm.

to outdoor play patterns, children may spend more time near the source of contamination than adults, and thus would have higher exposure time and/or exposure frequency values than adults living in the same location.[35] For indoor vapor intrusion from the subsurface, very young children might be more highly exposed due to substantial time spent indoors.

Beyond the consideration of activity patterns, MEs, and chemicals with a mutagenic MOA for carcinogenicity (as described in Section 5.1), no additional adjustments to account for specific child receptors should be made to the default values. Appendix A of this document is intended to illustrate that the use of default values sufficiently covers age-related variation in DAF or HEC values derived using the EPA *Inhalation Dosimetry Methodology's* default approach.

6.2 Commercial-Industrial/Occupational Receptor

An example of a commercial-industrial or occupational inhalation exposure scenario could be characterized by full-time workers (e.g., 8 hours per day, 5 days per week) in an indoor setting, such as an office building, exposed via vapor intrusion of subsurface contamination on a daily basis for 5 to 25 years. When estimating cancer risk for this type of scenario, Equation 6 is recommended to calculate an EC and Equation 11 is recommended to estimate risk. Following the flowchart in Figure 2, the duration and exposure pattern of this scenario would typically be considered chronic. Therefore, Equation 8 is recommended to derive a chronic EC and Equation 12 is recommended (with a chronic RfC) when calculating an HQ for cancer or non-cancer effects. If information about multiple MEs is available, risk assessors should proceed according to Section 3.4 when deriving ECs to use in estimating cancer risks or HQs. Exposure parameters should be adjusted to consider the exposure time, frequency and duration for this scenario, which may differ from a residential scenario. Risk assessors should also use appropriate exposure parameters for outdoor workers who, similar to children, may spend more time near a source of contamination than indoor workers.

6.3 Construction Worker

One example of a construction worker scenario could involve a long-term project (1-2 years) with workers exposed regularly to contaminant vapors and fugitive dust (8 hours per day, 5 days per week). When estimating cancer risk for this type of scenario, Equations 6 and 11 are recommended to calculate an EC and the risk estimate, respectively. Following the flowchart in Figure 2, the duration of this exposure scenario would typically be considered subchronic. In addition, this exposure is generally as frequent as a subchronic toxicity test. Therefore, Equation 8 is recommended to derive a subchronic EC, and Equation 12 is recommended for use with a subchronic toxicity value to calculate the HQ. If information about multiple MEs is available, risk assessors should proceed according to Section 3.4 when deriving ECs to use in estimating cancer risks or HQs.

6.4 Trespasser/Recreational Receptor

An example trespasser/recreational scenario could consist of an exposure of 1 to 2 hours per day, for 100 days per year or less. When estimating cancer risk for this type of scenario, Equations 6 and 11

[35] For additional information about early-lifestage age groups to consider when assessing children's exposure to environmental contaminants, please consult EPA's *Guidance on Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants* (EPA, 2005d).

are recommended to calculate an EC and the risk estimate, respectively. Following the steps in Figure 2 for cancer or non-cancer effects characterized by an RfC, each exposure period should be assessed separately because this exposure lasts only one to two hours each day for an average of two days per week. Therefore, Equation 7 is recommended to derive acute ECs for each exposure period. In addition, Equation 12 is recommended for use with an acute toxicity value to calculate HQs for each exposure period.

7. TARGET CONCENTRATIONS FOR SCREENING ANALYSIS OF INHALATION PATHWAYS

For purposes of this guidance, risk-based screening levels are values that may be compared to the contaminant concentration in air to help risk assessors identify potential contaminants of concern. Screening levels can also be calculated for comparison with samples from source media at a site, such as soil. Screening levels are generally not appropriate for use as clean-up levels; they are intended to aid in initial evaluation of contaminants and exposure pathways of concern prior to proceeding with a baseline risk assessment.[36] If contaminant concentrations in air exceed the risk-based screening levels appropriate for the receptor population of interest, risk assessors should gather site-specific information to determine the need for any remedial action. The following sections outline a recommended approach for calculating screening levels in air as well as source media.

7.1 Target Contaminant Concentrations in Air

The equations recommended for estimating ECs and risk (Equations 6 through 12) can be used to calculate target contaminant concentrations in air by following the four steps outlined below in Table 4.[37]

If air samples from a site are found to be below the target concentration, the risk assessor can generally conclude that this pathway does not pose an unacceptable level of risk from the contaminant. If the concentrations are found to exceed the screening levels, the risk assessor should evaluate the inhalation pathway further by gathering additional site-specific data on contaminant levels, site conditions, and receptor characteristics.

7.2 Screening Levels for Other Media

Inhalation risk-based screening levels may also be calculated for media other than air, including soils, tap water, soil gas, and ground water. The soil gas and ground water values may be derived specifically to address concerns about vapor intrusion from subsurface contamination into indoor spaces.

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[36] EPA regions, states, or other agencies may support unique screening levels for specific purposes that may differ from the method presented in this document. Generally, when using screening levels it is important that risk assessors understand the target risks, toxicity, and exposure assumptions as well as migration-attenuation assumptions on which they are based, and to apply them for their intended use.

[37] Target contaminant concentrations in air calculated according to the procedure outlined in this document are generally protective for direct inhalation exposures. This process should not be used to calculate concentrations in air to be protective of indirect exposures (e.g., ingestion of crops contaminated through air delivery or vapor phase transfer, ingestion of livestock or fish contaminated indirectly through air deposition or vapor phase transfer).

TABLE 4 RECOMMENDED PROCEDURE FOR CALCULATING RISK-BASED SCREENING CONCENTRATIONS FOR CONTAMINANTS IN AIR		
	Cancer Risk-Based	**Hazard-Based**[1]
Step 1: Select Target Levels	Select target cancer risk (e.g., 1 x 10^{-6}).	Select target HQ (e.g., 1).
Step 2: Identify Toxicity Value[2]	Identify inhalation cancer potency value (e.g., IUR). If none exists, proceed with hazard-based screening level calculation.	Identify inhalation reference value (e.g., RfC) to match exposure scenario (acute, subchronic, or chronic). If none exist, proceed with cancer screening level calculation.
Step 3: Calculate CA	Using target cancer risk from Step 1 along with the receptor- and scenario-specific exposure parameter values, calculate CA; the following equation is recommended: CA = (AT x Target Risk)/(IUR x ET x EF x ED)	Using target HQ from Step 1 along with the receptor- and scenario-specific exposure parameter values, calculate CA; the following equation is recommended: CA = (AT x Target HQ x RfC x 1000 µg/mg)/(ET x EF x ED)
Step 4: Select Screening Concentration	Select minimum of predicted cancer risk- and hazard-based values as screening concentrations.[3] Repeat for each receptor/scenario combination of interest.	

[1] Hazard-based screening concentrations are typically derived from reference values such as RfCs. These values may be available for non-cancer effects but may include cancer, if a nonlinear MOA is thought to operate for a chemical.
[2] If no inhalation toxicity value is available for a chemical, contact STSC for further direction on how to proceed.
[3] Screening levels estimated from the equations presented in Step 3 could yield concentrations that exceed the maximum possible vapor concentration for a chemical. In such cases, it may be useful to calculate the maximum possible vapor concentration of the pure contaminant at the temperature of interest, using the following formula: C_{max} = S x H x 10^3 L/m^3, where S = solubility at 25° C (or temperature of interest) and H (unitless) = Henry's Law Constant at 25° C (or temperature of interest). This equation is based on an established relationship (see, for example, Schwartzenbach et al. 1993), that allows the Henry's Law Constant to be estimated as the ratio of a compound's vapor pressure and aqueous solubility for compounds that are slightly to moderately soluble in water. When the dimensionless Henry's Law constant, H, is used, the relationship described above can be used to calculate the vapor concentration of a saturated solution of a given compound, assuming equilibrium between the vapor and aqueous phases.

7.2.1 Soil Screening Levels

When evaluating risk in a source medium, such as soil, it is typically possible to calculate screening levels for that medium that are expected to be protective of inhalation exposures based on the expected transfer of a contaminant from the source medium to the air. Soil Screening Levels (SSLs) can be described as "risk-based soil concentrations derived for individual chemicals of concern from standardized sets of equations. These equations combine EPA chemical toxicity data with parameters defined by assumed future land uses and exposure scenarios, including receptor characteristics and potential exposure pathways" (USEPA, 2002b). These SSLs may be used for screening analyses and may serve as the basis for the development of Preliminary Remediation Goals (PRGs). Refer to the *Soil Screening Guidance* (USEPA, 1996) and the *Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites* (USEPA, 2002b) for recommended equations that can be used to calculate SSLs for volatilization of chemicals from soil to air and for particulate emissions.

7.2.2 Tap Water Screening Values

Contaminated tap water may pose risk by the inhalation route if the contaminants present are volatile. Screening levels can be calculated for tap water that account for inhalation exposures resulting from the household use of water (e.g., showering, laundering, dishwashing). Risk assessors should consult their local EPA regional risk assessor for direction on how to calculate appropriate screening levels for tap water.

7.2.3 Soil Gas or Ground Water Screening Values for Vapor Intrusion

If there is concern at a site about the possibility of migration of vapor-forming chemicals from contaminated soil gas or ground water into the indoor air of overlying buildings ("vapor intrusion"), screening values can be calculated for these media. Risk assessors should first follow the procedure outlined in Section 7.1 and Table 4 to calculate a risk-based target concentration for the contaminant in air.

For the calculation of a soil gas screening-level concentration, the target air concentration is then divided by an assumed screening-level attenuation factor. The attenuation factor (the ratio of indoor air divided by subsurface source concentration) represents the factor by which subsurface vapor concentrations migrating into indoor air spaces are reduced due to a variety of attenuating mechanisms.

For the calculation of a ground water screening-level concentration, the target air concentration is divided by an assumed screening-level attenuation factor, and the resulting soil gas concentration is converted to a corresponding ground water concentration, assuming equilibrium between the aqueous and vapor phases at the water table.

Risk assessors should consult their local EPA regional risk assessor for direction on how to calculate appropriate screening levels for soil gas and ground water when vapor intrusion is an issue at a site.

8. DEVELOPING AGGREGATE AND CUMULATIVE RISK ESTIMATES

EPA's current approach to estimating cumulative risk or hazard at a site from multiple chemicals, set forth in *RAGS, Part A* (USEPA, 1989), is not affected by the *Inhalation Dosimetry Methodology* and therefore is not being updated at this time. In addition, the aggregation of risks and hazards across multiple exposure routes should remain unchanged. The recommended approaches for aggregating risk and hazard estimates are outlined below.

8.1 Estimating Cumulative Risks and Hazards Across Multiple Chemicals

The recommended method for estimating cumulative risk and hazard at a site from exposure to multiple chemicals is described in *RAGS, Part A*, Section 8.2.2. This method is based on the default approaches described in *Guidelines for the Health Risk Assessment of Chemical Mixtures* (USEPA, 1986). Additional information on this method was subsequently published in the *Supplementary Guidance for Conducting Health Risk Assessment of Chemical Mixtures* (USEPA, 2000b). The recommended methods to use with quantitative cancer risk estimates as well as with HQs are outlined below.

8.1.1 Cancer Risks

When evaluating predicted cancer risks from multiple contaminants, risk assessors should estimate the cancer risk for each substance and then sum these risks. This yields an estimate of total cancer risk, which represents the cumulative predicted cancer risk for the chemicals at a site.

Risk assessors should note, however, that this recommended method assumes "independence of action by the compounds involved (i.e., that there are no synergistic or antagonistic chemical interactions and that all chemicals produce the same effect, i.e., cancer)" (USEPA, 1989). In addition, this simple additive approach is generally most appropriate for total cancer risks less than 0.1. If these assumptions are incorrect, over- or under-estimation of actual multiple-substance risk could result (USEPA, 1989).

8.1.2 Hazard Quotients

When the evaluation involves multiple chemicals assessed via HQs, risk assessors typically first calculate the HQ for each substance, and then sum the individual HQ values. This generally yields an estimated hazard index (HI) for the multiple chemicals assessed via a hazard-based approach. Separate HIs should be calculated for each type of exposure period (i.e., chronic, subchronic, acute). If an HI is greater than 1, it is generally appropriate to derive separate HIs for each target organ of concern (for more information, see *RAGS, Part A*, page 8-14).[38] When multiple acute exposures are present at a site, risk assessors should evaluate each acute exposure event separately. Hazards from multiple chemicals generally should be summed only when the exposures to these chemicals occur simultaneously.[39]

8.2 Aggregating Risk and Hazard Quotients Across Exposure Routes

Guidance for combining the multi-chemical risk estimates and hazard quotients across exposure pathways is described in *RAGS, Part A*, Section 8.3 (USEPA, 1989). In order to determine whether risks or HIs should be combined across exposure pathways, risk assessors should first identify reasonable exposure pathway combinations. Then, risk assessors should examine whether it is likely that the same individuals would consistently face the reasonable maximum exposure (RME) by more than one pathway.

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[38] This recommended method assumes that "the dose for each individual component is at a level at which effects are not expected to occur, be observable, or be of concern; however, when the doses are combined, effects of concern may be expected or observed in response to the higher dose level of the mixture" (EPA, 2000b, page 12). Another assumption of the HI approach is that the compounds induce the same effect by the same mechanism of action. Therefore, "application of the HI equation to a number of compounds that are not expected to induce the same type of effects or that do not act by the same mechanism, although appropriate as a screening-level approach, could overestimate the potential for effects" (EPA, 1989, page 8-14). This is generally less of a concern if one to two substances are responsible for driving the HI above 1.

[39] In cases where a single chemical is present at a site and receptors are exposed through a series of acute exposure events, the highest single EC should be compared to an acute reference value of the appropriate duration to assess hazard.

The recommended approach for estimating excess cancer risk from exposure via multiple routes is to first estimate cancer risk from each exposure pathway and then sum across the multiple routes.[40]

For the effects assessed via a reference value, risk assessors should calculate the HI for each exposure pathway and sum across the multiple routes. Separate total HIs should be calculated for each type of exposure period (i.e., chronic, subchronic or acute). If the HI exceeds one, there may be concern for potential adverse effects and risk assessors should consider deriving separate HIs for each target organ of concern.

9. RISK CHARACTERIZATION

Risk characterization is the final, summarizing step in conducting a risk assessment. Generally, the purpose of the risk characterization section of a report is to:[41]

- Describe the key findings of the risk assessment in a transparent manner, including identifying hazard, characterizing the dose-response relationship, and describing receptor exposures;
- Identify and describe the scientific and policy assumptions used in the assessment;
- Characterize uncertainties in results; and
- Provide an overall conclusion about the risks present at a site (USEPA, 2000c).

A well-crafted risk characterization section puts risk calculations into context for risk managers so that they may effectively weigh and interpret risk assessment results (i.e., it is the interface between risk assessment and risk management). A few of the key issues and uncertainties involved in calculating risks from inhalation exposures are outlined below.

9.1 Highly Exposed or Susceptible Populations and Life Stages

EPA recommends that the risk characterization portion of the risk assessment explain any particular susceptibilities to inhaled toxicants or potential for increased inhalation exposures among the various receptor groups at a site.[42] We discuss below two possible examples, children and worker receptors, though this discussion could apply to other receptor characteristics as well (e.g., age, disease, gender, genetic characteristics).

9.1.1 Children

One population group that could potentially be more highly exposed to inhalation exposures at a site is children. As discussed in Section 6.2, exposure parameters related to activity patterns (e.g., exposure time, frequency, and duration) and MEs, may vary across age groups. For example, due to outdoor play patterns, children may spend more time near the source of contamination than adults,

[40] Note that this approach is generally most appropriate for total cancer risks of less than 0.1 (EPA, 1989).

[41] For specific information on the format of risk characterizations, refer to *Elements to Consider when Drafting EPA Risk Characterizations* (EPA, 1995c).

[42] EPA's IRIS glossary defines susceptibility as the following: "Increased likelihood of an adverse effect, often discussed in terms of relationship to a factor that can be used to describe a human subpopulation (e.g., life stage, demographic feature, or genetic characteristic)" (EPA, 2008b).

and thus would have higher exposure time and/or exposure frequency values than adults living in the same location. Therefore, it is important to carefully describe site-specific exposures to children, and assumptions made in risk calculations.[43]

If chemical-specific data on susceptibility to the toxic effects from early life exposures are available, these data are considered when developing toxicity values that specifically address differential toxicity to the young (e.g., vinyl chloride) (USEPA, 2005c). Toxicity values derived using the default approach from the *Inhalation Dosimetry Methodology* are developed for the human population as a whole, including sensitive subgroups. Therefore, as described in Section 6 of Appendix A, no quantitative adjustment of toxicity values derived using the default approach in the *Inhalation Dosimetry Methodology* is recommended for specific age groups to account for different ventilation rates or body weights of specific age groups.

When evaluating risk to carcinogenic chemicals with a demonstrated mutagenic MOA but which lack chemical-specific information on susceptibility from early life exposures, EPA recommends a quantitative adjustment of the toxicity value to account for early life susceptibility, as described in the *Supplemental Cancer Guidelines* (see USEPA, 2005b & 2005c; and Section 5.1 of this guidance for further information).

9.1.2 Workers

Workers could have increased exposure under certain occupational scenarios. Some outdoor workers might spend more time near a source of contamination in the course of their job and this should be reflected in adjustments to the exposure parameters (e.g., ET, Exposure Frequency (EF), and ED) describing the worker exposure scenario. Toxicity values derived using the *Inhalation Dosimetry Methodology* are developed for the human population as a whole, including sensitive populations and life stages. In the default *Inhalation Dosimetry Methodology* approach, typical variation in IRs between periods of high activity and rest is considered. However, if workers have especially high levels of exertion with correspondingly high ventilation rates, these workers could be at the upper end of the risk range, particularly if they are exposed to Category 1 gases, which have direct effects in the respiratory tract. This implication should be recognized in the risk characterization section.

9.2 Uncertainties in Inhalation Risk Assessment

This guidance recommends including an assessment of the key uncertainties that may significantly impact risk estimates for inhaled chemicals. This should ensure transparency, clarity, reasonableness and consistency in risk assessments, as recommended by EPA's *Policy for Risk Characterization* (USEPA, 1995a). Other sources of uncertainty may be present and other EPA documents provide guidance on characterizing uncertainty in risk the assessment process (USEPA, 1992, 1995a, 1995b, 1995c, 1997a, 1997b). Key uncertainties related to inhalation risk assessment, which is the focus of this section, include the development of ECs, choice of toxicity value, lack of quantitative toxicity information via inhalation, and the approach to estimating and aggregating risks. According to EPA's *Guidance for Risk Characterization*, the discussion of uncertainty "should reflect the type and complexity of the risk assessment, with the level of effort for analysis and discussion of uncertainty

[43] For additional information on children's health risk assessment, please consult *A Framework for Assessing Health Risks of Environmental Exposures to Children* (EPA, 2006b).

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corresponding to the level of effort for the assessment" (USEPA, 1995b). Therefore, risk assessors should provide a qualitative and/or quantitative evaluation of key uncertainties pertaining to inhalation risk, and their impact on the outcome of the assessment, consistent with the level of effort of the specific risk assessment.

9.2.1 Development of Exposure Concentrations

As described in Section 3 of this guidance, with the exception of acute exposures, time-weighted averages are typically used to represent intermittent or variable inhalation exposures to receptors at a site. This recommended approach is consistent with the duration adjustment approach (based on Haber's Law) that is generally used in deriving the toxicity values (see Section 2.1.1.1 for further information). As mentioned in Section 3, when evaluating situations in which the exposure is long-term, yet there are short periods of significantly higher exposure, those periods should also be assessed using appropriate short-term toxicity values. This ensures that periods of much higher exposure can be appropriately assessed and not "diluted out" in the assessment of longer-term exposure.

When information on multiple MEs exists at a site, risk assessors may choose to estimate ECs as outlined in Section 3.4. However, this typically requires sufficient time-activity information of receptors at a site to accurately determine the time spent in each ME. Incomplete or low quality data on time-activity pattern may introduce uncertainty into the estimation of the ECs for MEs. Risk assessors should describe the quality and completeness of these data.

The recommended method for determining the CA at a site can potentially introduce uncertainty into the EC calculations. For instance, if contaminant concentrations in air are measured, risk assessors should consider uncertainties related to how well the set of air samples available at a site represents the duration and time period being assessed as well as measurement uncertainty related to the methods and equipment used. In addition, risk assessors should describe any potential confounding of indoor air samples by other sources of contaminants (e.g., household products). If contaminant concentrations in air are modeled, (e.g., by EPA's spreadsheet models for vapor intrusion) risk assessors should address model-related uncertainties and their potential impact on the estimate of contaminant concentrations in air. Considerations of particle size at the site versus particle size used to derive the toxicity value are also important.

9.2.2 Toxicity Assessment

Section 4.1 of this document indicates that some IURs on IRIS were developed through extrapolation from oral CSFs (see Appendix B of this document). The use of toxicity values derived through simple route-to-route extrapolation introduces additional uncertainty into risk calculations. Therefore, risk assessors should indicate when extrapolated IURs are used and should characterize the potential impact of the uncertainty associated with using these values, if known.

Section 4.2 and Appendix C of this guidance recommends contacting STSC to help identify appropriate toxicity values for conducting a risk assessment at Superfund sites in the absence of published inhalation toxicity values. If STSC is unable to recommend a toxicity value, risk assessors should acknowledge the resulting uncertainty in risk associated with the chemical(s) lacking inhalation toxicity data. If STSC provides risk assessors with a toxicity value based on a PBPK

model, model uncertainty should be discussed. In addition, if STSC provides risk assessors with one or more structurally analogous chemicals, risk assessors can use toxicity data for these chemicals to help characterize the potential magnitude of the inhalation risk associated with the chemical(s) lacking data. In this case, risk assessors should acknowledge the uncertainty associated with relying on toxicity data for analogous chemicals to characterize risk at the site.

Risk assessors should also acknowledge chemicals that lack duration-appropriate toxicity values and discuss the potential impacts of substituting alternative toxicity values for HQ calculations. For instance, if the ED is determined to be subchronic but no subchronic inhalation RfC or analogous toxicity value is available for that chemical, the risk assessor should address the uncertainty associated with calculating an HQ using a toxicity value for a different duration, such as chronic, or the impact of not quantifying those risks. In addition, if risk assessors use an acute toxicity value that does not match the duration of the acute exposure being assessed, the possibility of under or overestimating hazard should be discussed.

When conducting a screening-level risk assessment using screening values such as those described in Section 7, it is important to further evaluate and clearly describe the quality and uncertainties associated with the inhalation toxicity values used in the risk assessment if measured sample contaminant concentrations at a site exceed these screening values.

9.2.3 Estimating Cancer Risks

For high exposures, for example those within the range of epidemiological studies (usually those predicted to have risks greater than 10^{-2}), the IUR derived from the linear extrapolation below the range of observation is generally not appropriate for use (see Section 5.1 of this document for further information).[44] Risk assessors should provide specific information in the risk characterization describing how these high exposures were addressed in the risk assessment. For instance, if a risk assessor chose to provide a semi-quantitative approach (e.g., indicating that risks are above 10^{-2}), this should be indicated, along with a description of the uncertainties involved in not fully quantifying risk associated with exposure to this chemical. If a risk assessor chose to use the original model in the IRIS file or other technical background document, the risk characterization section should include a description of any uncertainties in the model used and could contain examples of the risks estimated.

9.2.4 Estimating Risk and Hazard from Multiple Chemicals and Exposure Pathways

Risk assessors should also describe uncertainties involved in aggregating risk and hazard across multiple chemicals and exposure pathways. For instance, the approaches described in Section 8 of this document are associated with several assumptions (e.g., independence of action and doses for individual compounds at levels not expected to be of concern). If these assumptions are not met, aggregation may not be appropriate. This should be fully described in the risk characterization section and any uncertainties involved in the lack of quantitative information should be indicated.

[44] Also refer to Section 8.2.1 of *RAGS, Part A* for further discussion of this topic (EPA, 1989, page 8-6).

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APPENDIX A

APPENDIX A

ANALYSIS OF DEFAULT APPROACH FOR HEC DERIVATION AS COMPARED TO POPULATION- AND LIFESTAGE-SPECIFIC CALCULATIONS

NOTE: The Agency's inhalation dosimetry methodology (USEPA, 1994; hereafter, "the *Inhalation Dosimetry Methodology"*) is a technical report that describes the derivation of human equivalent concentrations (HECs) from animal (or human) studies, as well as the other steps involved in developing a chronic Reference Concentration (RfC). This appendix is included to illustrate the HEC derivation using the *Inhalation Dosimetry Methodology*'s default approach (with the recommended default values for humans), and to also illustrate the impact of substituting alternate age- and activity-specific human values into the default calculations. The default approach is employed for chemicals for which more chemical-specific dosimetric and pharmacokinetic data are not available, thus precluding the use of more advanced models for deriving the HEC. The calculations in this appendix do not represent a refined or optimal model for assessing intra-human variability (e.g., age- and activity-specific risks), and are not intended to imply that risk assessors should deviate from the *Inhalation Dosimetry Methodology* by substituting alternate values into the default calculations. Age-specific data are limited. Because of these limitations, the calculations made for different ages and exposure groups in this appendix are not recommended for use in quantitative risk assessment (i.e., they are only for the purpose of illustration), but may be useful in discussions of uncertainty and variability associated with the default approach.

It is also noted that, as of this writing, the Agency is involved in a routine reevaluation of scientific advancements in the field, with consideration of the need for improvement to the *Inhalation Dosimetry Methodology*. Any revisions will consider current understanding of inhalation dosimetry and differences across and within species, as well as the Agency's risk assessment needs. In order to transparently and quantitatively address children's inhalation dosimetry and risk assessment, this guidance document will be updated (on-line) when Agency methodology updates are available that are specific to early life. Until that time, the 1994 *Inhalation Dosimetry Methodology* is the appropriate Agency methodology.

INTRODUCTION

This appendix consists of examples and discussions illustrating the current default chemical category-specific approach to inhalation dosimetry for the various categories of gases and particles as described in *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry* (USEPA, 1994; hereafter, the *Inhalation Dosimetry Methodology*). This default inhalation dosimetry approach is used to convert toxicological and epidemiological study data to an HEC that can then be used to derive chronic RfCs for the human population (inclusive of susceptible populations and life stages, such as children) and also in the development of Inhalation Unit Risks (IURs) (USEPA, 2005). The default approach does not rely on age- or activity-specific values for physiological parameters when calculating HECs; however the default approach has been designed by EPA to derive reference values that are protective across the entire population.

The appendix includes six sections. Sections 1 through 3 address Category 1 gases. These sections provide example calculations for Category 1 highly reactive, high water solubility gases that are typically absorbed in the upper airways, exhibiting adverse effects in the extrathoracic (ETh), tracheobronchial (TB), and pulmonary (PU) regions of the respiratory tract, respectively. These examples include comparisons of HEC calculations based on default parameters with those derived using age- and activity-specific parameters for the respiratory region affected. Section 4 addresses Category 3 low reactivity, limited water solubility gases that exhibit systemic effects outside the respiratory tract. Section 5 addresses changes in particle deposition in the respiratory tract across age groups. The conclusions are summarized in Section 6.

When reviewing the examples, please note the following:

- An RfC derived using the *Inhalation Dosimetry Methodology* is defined as "an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime" (USEPA, 2008).

- All examples in this appendix are based on the *Inhalation Dosimetry Methodology*. EPA is committed to periodically reviewing and updating the *Inhalation Dosimetry Methodology* to ensure that it reflects the current state of the science and that it yields toxicity values that sufficiently cover potential age- and activity-related variation in inhalation exposure. A review and update is currently underway.

- The examples in this appendix are all based on calculating HECs from a point of departure (POD) for non-cancer effects (e.g., a No Observed Adverse Effect Level (NOAEL), Lowest Observed Adverse Effect Level (LOAEL), or Benchmark Concentration, Lower confidence limit (BMCL)). These calculations could also be performed in an identical manner for carcinogens using a POD for cancer risk estimate derivation (e.g., a Lower limit on the Effective Concentration (LEC) value).

- The default animal and human values for minute volume (V_e) and surface area (SA) used in these examples were obtained from *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry* (USEPA, 1994).[45] The age- and activity-specific V_e values were obtained from the International Commission on Radiological Protection (ICRP) Publication 66, *Human Respiratory Tract Model for Radiological Protection* (ICRP, 1994).[46] Age-specific SA values used in Examples 1 and 2 were calculated using scaled estimates for the mass and thickness of respiratory region-specific target tissue from ICRP (1994); Values for Example 3 were calculated from an allometric scaling equation presented in a publication by Zeltner et al. (1987). EPA's Office of Research and Development (ORD) selected these data following review of the available physiological data for the age groups indicated in the examples.

- Chemical-specific data from the Integrated Risk Information System (IRIS) file for acrolein were used in the ETh example (Example 1). However, the other two examples, which focus on effects in the TB and PU regions, respectively, use hypothetical data for the POD because there are currently no chemicals on IRIS exhibiting Critical Effects (for RfC derivation) in those regions.[47] The conclusions of these two examples are unaffected by the use of hypothetical data because the results are driven by the values of parameters that are not chemical-specific (i.e., SA and V_e).

[45] The minute volume is the total ventilation per minute and equals the product of the tidal volume (the air volume entering or leaving the lungs with a single breath) and the respiratory frequency.

[46] For further information on inhalation rates in humans under different scenarios, refer to Chapter 5 of EPA's *Exposure Factors Handbook* (EPA, 1997).

[47] Hypothetical examples for the TB and PU regions were included in this appendix because currently no RfCs for gases on IRIS are calculated based on animal studies showing health effects occurring in these regions of the respiratory system

1. EXAMPLE 1: CATEGORY 1 GAS, EXTRATHORACIC EFFECTS, ACROLEIN

The Dosimetric Adjustment Factor (DAF) for a Category 1 gases, the Regional Gas Dose Ratio (RGDR), is based on the animal to human ratio of the V_e divided by the SA of the region of the respiratory tract where the effect occurs. For acrolein, the effect occurs in the ETh region. The DAF is typically calculated using the following equation (USEPA, 1994, Equation 4-18):

$$RGDR_{ETh} = \frac{\left(\frac{V_e}{SA_{ETh}}\right)_{animal}}{\left(\frac{V_e}{SA_{ETh}}\right)_{human}} = \frac{\frac{0.14\,L/min}{15\,cm^2}}{\frac{13.8\,L/min}{200\,cm^2}} = 0.14 \qquad \textbf{(Equation A-1)}$$

The default *Inhalation Dosimetry Methodology*-recommended values for the V_e and SA_{ETh} of the Wistar rat (the animal in the principal study for acrolein) are 0.14 L/min (0.20 m^3/day) and 15 cm^2, respectively (USEPA, 1994). EPA's default human values are 13.8 L/min (20 m^3/day) for V_e and 200 cm^2 for SA_{ETh} (USEPA, 1994). The RGDR for the ETh region ($RGDR_{ETh}$) was calculated using these values for the rat and the human as shown in Equation A-1. In the laboratory animal study on acrolein, the LOAEL adjusted for continuous exposure ($LOAEL_{[ADJ]}$) of 0.16 mg/m^3 (USEPA, 2003) is used as the point of departure. The $LOAEL_{[HEC]}$ is the $LOAEL_{[ADJ]}$ multiplied by the $RGDR_{ETh}$.

To illustrate any potential age- or activity-related variation in the $LOAEL_{[HEC]}$ that might result from using human parameter values other than the defaults, scaled estimates for the mass and thickness of ETh target tissue from ICRP (1994) at different ages are used to calculate the SA_{ETh} values in Table A-1. Age- and activity-related V_e reported in ICRP (1994) are based on daily time-budgeted reference values. Table A-1 shows little variation in the resultant $LOAEL_{[HEC]}$ across the groups in this example. The default procedure produces the lowest $LOAEL_{[HEC]}$ value in Table A-1 and is, therefore, sufficient to cover all of these groups.

TABLE A-1 COMPARISON OF THE HEC-DEFAULT (EPA, 1994) WITH EXAMPLE $LOAEL_{[HEC]}$ VALUES FOR HUMANS OF DIFFERENT AGES AND ACTIVITY PATTERNS FOR THE EXTRATHORACIC REGION					
	Total $V_{e\ (human)}$ (L/min)[a]	$SA_{ETh\ (human)}$ (cm^2)[b]	$(V_e/SA_{ETh})_{human}$ (L/min-cm^2)	$RGDR_{ETh}$	$LOAEL_{[HEC]}$ (mg/m^3)
Outdoor Worker, Male	17.5	470	0.037	0.25	0.04
Sedentary Worker, Male	15.4	470	0.033	0.28	0.04
Sedentary Worker, Female	12.6	407	0.031	0.30	0.05
15 Year-Old Male	14.0	439	0.032	0.29	0.05
15 Year-Old Female	10.9	397	0.027	0.35	0.06
10 Year-Old	10.6	293	0.036	0.26	0.04
5 Year-Old	6.1	198	0.031	0.30	0.05
1 Year-Old	3.6	97.1	0.037	0.25	0.04
3 Month-Old	2.0	65.8	0.030	0.31	0.05
HEC - Default	13.8	200	0.069	0.14	0.02
[a] These values are from the ICRP publication, Tables 8, 27, B.16a, B.16b and B.17 (ICRP, 1994). [b] These values are from the ICRP publication, Tables 1 and 5 (ICRP, 1994).					

2. EXAMPLE 2: CATEGORY 1 GAS, TRACHEOBRONCHIAL EFFECTS, HYPOTHETICAL CHEMICAL

The DAF for a Category 1 gas or vapor exhibiting effects in the TB region is based on the animal to human ratio of the V_e divided by the SA of the TB region for each species. The DAF is typically calculated using the following equation:

$$RGDR_{TB} = \frac{\left(\frac{V_e}{SA_{TB}}\right)_{animal}}{\left(\frac{V_e}{SA_{TB}}\right)_{human}} = \frac{\frac{0.14\ L/min}{22.5\ cm^2}}{\frac{13.8\ L/min}{3200\ cm^2}} = 1.4 \qquad \textbf{(Equation A-2)}^{48}$$

This example assumes that the hypothetical chemical has been tested on Wistar rats and therefore utilizes the EPA animal default values for that strain. The V_e value used is 0.14 L/min (0.20 m^3/day) and the default SA_{TB} is 22.5 cm^2 (USEPA, 1994). EPA's default human values are 13.8 L/min (20 m^3/day) for V_e and 3200 cm^2 for SA_{TB} (USEPA, 1994). The RGDR for the TB region ($RGDR_{TB}$) is calculated using these values for the rat and the human, as shown in Equation A-2. The example also assumes a NOAEL adjusted for continuous exposure ($NOAEL_{[ADJ]}$) of 0.16 mg/m^3 as the point of departure. The $NOAEL_{[HEC]}$ is the $NOAEL_{[ADJ]}$ multiplied by the $RGDR_{TB}$.

Table A-2 shows little variation across age and activity groups in the $NOAEL_{[HEC]}$. The variation from the default (less than a factor of 2) is less than the default value of 10 used for the uncertainty factor for intraspecies variability when deriving the RfC. Application of the normal procedure for

[48] This equation is the reduced, default version of Equation 4-19 of the *Inhalation Dosimetry Methodology*. Equation 4-19 is reduced to this form consistent with the derivation of the reduced form of the RGDR equation of extrathoracic effects described in section 4.3.6.1 and Appendix I of the *Inhalation Dosimetry Methodology*.

determining the RfC will accommodate the observed variation. In addition, RfCs and IURs are developed for chronic exposure and will generally involve an exposure for multiple years.

TABLE A-2
COMPARISON OF THE HEC-DEFAULT (EPA, 1994) WITH EXAMPLE $LOAEL_{[HEC]}$ VALUES FOR HUMANS OF DIFFERENT AGES AND ACTIVITY PATTERNS FOR THE TRACHEOBRONCHIAL REGION

	Total $V_{e\ (human)}$ (L/min)[a]	$SA_{TB\ (human)}$ (cm^2)[b]	$(V_e/SA_{TB})_{human}$ (L/min-cm^2)	$RGDR_{TB}$	$NOAEL_{[HEC]}$ (mg/m^3)
Outdoor Worker M	17.5	2660	0.0066	0.94	0.15
Sedentary Worker M	15.4	2660	0.0058	1.1	0.18
Sedentary Worker F	12.6	2640	0.0048	1.3	0.21
15 year M	14.0	2520	0.0056	1.1	0.18
15 year F	10.9	2250	0.0048	1.3	0.21
10 Year	10.6	1830	0.0058	1.1	0.18
5 Year	6.1	1340	0.0046	1.4	0.22
1 Year	3.6	857	0.0042	1.5	0.24
3 Months	2.0	712	0.0028	2.2	0.35
HEC-default	13.8	3200	0.0043	1.4	0.22

[a] These values are from the ICRP publication, Tables 8, 27, B.16a, B.16b and B.17 (ICRP, 1994).
[b] These values are from the ICRP publication, Tables 1 and 5 (ICRP, 1994).

3. EXAMPLE 3: CATEGORY 1 GAS, PULMONARY EFFECTS, HYPOTHETICAL CHEMICAL

The DAF for a Category 1 gas or vapor with an effect in the PU region is based on the animal to human ratio of the alveolar ventilation rate (Q-alv) divided by the SA of the PU region (SA_{PU}) for each species. The Q-alv is approximately equal to the V_e multiplied by 0.7. This adjustment accounts for the anatomic/physiologic deadspace in the PU region, making the Q-alv equivalent to the amount of inspired air available for gas exchange (West, 2000). The DAF for this region of the respiratory tract is typically calculated using the following equation:

$$RGDR_{PU} = \frac{\left(\frac{Q-alv}{SA_{PU}}\right)_{animal}}{\left(\frac{Q-alv}{SA_{PU}}\right)_{human}} = \frac{\frac{0.1\,L/min}{0.34\,m^2}}{\frac{9.7\,L/min}{54\,m^2}} = 1.6 \qquad \textbf{(Equation A-3)}^{49}$$

This example assumes that the hypothetical chemical has been tested on Wistar rats and therefore utilizes the EPA animal default values for that strain. The V_e valued used is 0.14 L/min (0.20 m^3/day), which when multiplied by 0.7, yields a Q-alv of 0.1 L/min. The example uses the EPA default rat SA_{PU} of 0.34 m^2 (USEPA, 1994). EPA's default human values are 13.8 L/min (20

[49] This equation is the reduced, default version of Equation 4-23 of the *Inhalation Dosimetry Methodology*. Equation 4-23 is reduced to this form consistent with the derivation of the reduced form of the RGDR equation of extrathoracic effects described in section 4.3.6.1 and Appendix I of the *Inhalation Dosimetry Methodology*.

m^3/day) for V_e (which yields a Q-alv of 9.7 L/min) and 54 m^2 for SA_{PU} (USEPA, 1994). The RGDR for the PU region ($RGDR_{PU}$) is calculated using these values for the rat and the human, as shown in Equation A-3. The example also assumes a $NOAEL_{[ADJ]}$ of 0.16 mg/m^3 as the point of departure. The $NOAEL_{[HEC]}$ is the $NOAEL_{[ADJ]}$ multiplied by the $RGDR_{PU}$.

Table A-3 below provides the Q-alv values for humans based on the daily time-budgeted V_e for different ages and activity levels from the ICRP publication (1994). SA data for the PU region in the ICRP publication are estimated using an allometric scaling model fitted to data from a morphometric analysis of SA_{PU} in a sample of seven children (ranging in age from 26 days to 5 years) and eight adults (Zeltner et al., 1987). ORD selected the Zeltner analysis for this example because these SA_{PU} data are based on empirical morphometric measurements of human lungs as opposed to scaled estimates determined from lung models (such as those done by Yu and Xu, 1987 or Yu and Yoon, 1991). In addition, the children and adult SA_{PU} values calculated in the Zeltner analysis are supported by several independent studies that measured SA_{PU} in children (Langston et al., 1984) or in adults using similar morphometric techniques (Crapo et al., 1982 & 1983; Stone et al., 1992; Mercer et al., 1994).

Table A-3 shows little variation in the resultant $NOAEL_{[HEC]}$ across the groups in this example. The default procedure produces the lowest $NOAEL_{[HEC]}$ value in Table A-3 and is, therefore, sufficient to cover all of these groups.

TABLE A-3

COMPARISON OF THE HEC-DEFAULT (EPA, 1994) WITH EXAMPLE $LOAEL_{[HEC]}$ VALUES FOR HUMANS OF DIFFERENT AGES AND ACTIVITY PATTERNS FOR THE PULMONARY REGION

	Total V_e (L/min)[a]	$Q\text{-}alv_{(human)}$ (L/min)[b]	$SA_{PU\ (human)}$ (m^2)	$(Q\text{-}alv/SA_{PU})_{human}$ (L/min-m^2)	$RGDR_{PU}$	$NOAEL_{HEC}$ (mg/m^3)
Outdoor Worker, Male	17.5	12	139	0.088	3.3	0.53
Sedentary Worker, Male	15.4	11	139	0.078	3.7	0.59
Sedentary Worker, Female	12.6	8.8	114	0.077	3.8	0.61
15 Year-Old Male	14.0	9.8	108	0.091	3.2	0.51
15 Year-Old Female	10.9	7.6	100	0.076	3.8	0.61
10 Year-Old	10.6	7.4	62.0	0.12	2.4	0.38
5 Year-Old	6.1	4.3	37.3	0.11	2.6	0.42
1 Year-Old	3.6	2.5	18.5	0.14	2.1	0.34
3 Month-Old	2.0	1.4	11.0	0.13	2.2	0.35
HEC-Default	13.8	9.7	54.0	0.18	1.6	0.26

[a] These values are from the ICRP publication, Tables 8, 27, B.16a, B.16b and B.17 (ICRP, 1994).
[b] These values are from Zeltner et al. (1987).

4. CATEGORY 3 GASES

The DAF for a Category 3 gas or vapor is based on the ratio of the animal blood:gas partition coefficient to the human blood:gas partition coefficient and is typically calculated using the following equation:

$$DAF = \frac{(H_{b/g})_{animal}}{(H_{b/g})_{human}} \qquad \textbf{(Equation A-4)}$$

The blood:gas partition coefficient is primarily determined by the solubility of the gas in an aqueous medium as well as the protein and lipid content of the blood. There is little reason to suspect that the blood:gas partition coefficient for a non-metabolized chemical will vary greatly across the human population. The limited data available indicate no difference in the blood:gas partition coefficient with age for methylene chloride in mice (Thomas et al., 1996), and for sevoflurane, isoflurane, and halothane in humans (Malviya and Lerman, 1990). Two studies examining the solubility of volatile anesthetics (isoflurane, enflurane, halothane, and methoxyflurane) in the blood and body tissues found higher blood:gas partition coefficients in adults compared with children (Lerman, et al., 1984 & 1986). Any variability in the blood:gas partition coefficient with age is expected to be less than the default value of 10 used for the uncertainty factor for intraspecies variability when deriving the RfC. Any variability in the blood:gas partition coefficient with age is also not expected to cause a large overestimate or underestimate in the calculated cancer risk.

Because of the limited data available, the *Inhalation Dosimetry Methodology* makes the science policy decision to use a value of one for the ratio of the partition coefficients when the animal to human ratio exceeds one or when the animal or human value is unknown. At this time, all chemicals on IRIS for which both human and animal data are available have an animal to human ratio of partition coefficient greater than 1.[50] Therefore, the default assumption of one is a conservative approach that is not likely to underestimate the chemical-specific DAF.

5. PARTICLE DEPOSITION ACROSS AGE GROUPS

The DAF for a particle causing an effect in the respiratory tract, the Regional Dose Deposition Ratio ($RDDR_r$), is based on the animal to human ratio of the V_e and the fractional deposition of the particle in that region (F_r), divided by the surface area of the region where the effect occurs (SA_r) (USEPA, 1994). Inherent in this derivation is the assumption that 100 percent of the deposited dose remains in the respiratory tract and any clearance mechanisms are not considered. The $RDDR_r$ is typically calculated using the following equation:

$$RDDR_r = \frac{\left(\frac{V_e}{SA_r} \times F_r\right)_{animal}}{\left(\frac{V_e}{SA_r} \times F_r\right)_{human}} \qquad \textbf{(Equation A-5)}$$

[50] While 1,4-dioxane has not yet been evaluated on IRIS, it provides an exception to this statement, in that the blood:gas partition coefficient is 2750 for mice, 1850 for rats, and 3650 for humans, yielding an animal to human ratio of 0.75 for mice and 0.51 for rats (Reitz et al., 1990).

The DAF for a particle causing an extra-respiratory (ER) effect, the $RDDR_{ER}$, is based on the animal to human ratio of the V_e and the total deposition of the particle in the entire respiratory tract (F_{total}), divided by body weight (BW) (USEPA, 1994). The $RDDR_{ER}$ assumes that 100 percent of the deposited dose in the entire respiratory tract is available for uptake into the systemic circulation. The following general equation can be used to estimate the $RDDR_{ER}$:

$$RDDR_{ER} = \frac{\left(\frac{V_e}{BW} \times F_{total}\right)_{animal}}{\left(\frac{V_e}{BW} \times F_{total}\right)_{human}} \qquad \textbf{(Equation A-6)}$$

The information on particle deposition in various age groups is quite limited. A discussion of the current state of the science can be found in the *Air Quality Criteria for Particulate Matter Volume II*, Section 6.2.3.2 (USEPA, 2004; hereafter, *PM Criteria Document*).

Experimental and modeling results are summarized in Table A-4. The results for experimental studies are mixed, some suggesting higher deposition in children and others finding no difference across age groups. Bennett and Zeman (1998) and Schiller-Scotland et al. (1994) found no difference between total deposition of particles in the respiratory tract of children (aged 7 to14 and 6 to12, respectively) and adults for 1 to 2 micrometer particles. Schiller-Scotland et al. did find two- to three-fold higher total particulate deposition in 6 to 12 year olds for particles of 2 to 3 micrometers in size. In addition, Bennett et al. (1997) found that deposition in the ETh region was 50 percent greater in children than adults. The *PM Criteria Document* concludes that "these...studies ...do not provide unequivocal evidence for significant differences in deposition between adults and children" (USEPA, 2004, page 6-29). The document notes, however, that children may have higher activity levels and higher associated minute ventilation per lung size, potentially causing a greater size-specific dose of particles to the lung.

Modeled results suggest a higher deposition of particles in the TB region of children when compared to adults, depending on the particle size (Xu and Yu (1986); Hofmann et al. (1989); Musante and Martonen (1999); Phalen and Oldham (2001); Asgharian et al. (2004); Jarabek et al. (2005); Ginsberg et al. (2005)). Mixed results again are found in modeling studies for total deposition and deposition in other respiratory regions. In general, where differences are observed in either experimental or modeled studies, variability in deposition between age groups has been reported to be most often in the range of 1- to 3-fold greater for children than for adults, but ranging from equivalency or less up to 7-fold greater.[51]

[51] A modeling analysis examining deposition fraction per unit area at various airway generations of the lung as a function of age for various particle sizes (ranging from 0.01 to 10 μm) reported comparisons between a 3-month old and 21-year old that ranged from equivalency up to a 14-fold difference in this metric for some specific airway generations (Asgharian et al., 2004).

TABLE A-4
PARTICLE DEPOSITION ACROSS AGE GROUPS

Study	Particle Size	Results
		Experimental Studies
Becquemin et al. (1991)	Various	Nasal deposition higher in adults (up to 1.8-fold higher at rest and up to 3.4-fold higher during exercise) than children – meaning that thoracic airways of children are less protected than those of adults.
Bennett et al. (1997)	4.5 µm	-ETh deposition of particles 50 percent greater in children (higher for younger ages). -No significant difference in total respiratory tract deposition.
Bennett and Zeman (1998)	1-2 µm	No difference between 7-14 year olds and adults in total deposition of particles in the respiratory tract.
Schiller-Scotland et al. (1994)	1-2 µm	No difference between 6-12 year olds and adults in total deposition of particles in the respiratory tract.
	2-3 µm	Two- to three-fold higher total deposition of particles in 6-12 year olds versus adults.
		Modeled Studies
Asgharian et al. (2004)	0.01-10 µm	-Up to 1.2-fold higher total deposition in 3 month olds compared to adults in the TB region. -Up to 1.5-fold higher total deposition in 8 year olds compared to adults in the alveolar region. Total deposition higher in adults than 3 and 23 month olds (up to 2-fold). -Estimates of deposition fraction per unit area at various airway generations of the lung and various particle sizes highest for 3 month olds compared to adults (up to 14-fold). Higher deposition also seen for 23 month olds (up to 5-fold) and 8 year olds (up to 3-fold) compared with adults. No difference in deposition in 14 year olds compared to adults.
Cheng et al. (1995)	0.0046-0.2 µm	Nasal casts of children's airways found increased deposition efficiency for ultrafine particles with decreasing age, suggesting that young children may receive a higher dose of ultrafine particles to the upper airways.
Ginsberg et al. (2005)	0.001-10 µm	-Higher deposition in 3 month olds compared with adults for coarse and fine particles in the upper TB (up to 2-fold) and PU (up to 4-fold) regions. -Higher deposition in adults in the lower TB region.
Hoffmann et al. (1989)	1-2 µm	-1.5- to 2-fold higher total deposition in the TB region for particles in resting 8 year olds versus adults. -40-50 percent lower total deposition of particles in 8 year olds under conditions of exercise.
Jarabek et al. (2005)	0.3-6 µm	-Retained mass in the TB region normalized to regional SA was compared across age groups. -Up to 2-fold lower deposition in 3 month olds compared to adults. -Up to 2-fold higher deposition in 3 year olds and 14 year olds compared to adults.
Musante and Martonen (1999)	0.25-5 µm	-Total deposition was generally higher in children (ages 7, 22, 48, and 98 months) than adults (e.g., total lung deposition in 48-month olds was 38 percent higher than adults for 1µm particles). -TB deposition monotonically decreased as a function of age (i.e., younger children had increased TB deposition). -PU deposition greatest in the 48 and 98-month children.
Musante and Martonen (2000)	2 µm	3-fold higher deposition of particles in the PU region for 7 month olds versus adults.
Oldham et al. (1997)	Various	Airway models of trachea and bronchial airways showed total deposition in children (ages 4 and 7) greater than adult (up to approximately 7-fold higher for 4 year olds compared to adults for 4.5 µm particles).
Phalen and Oldham (2001)	0.1-10 µm	-No difference in total deposition of particles in 2 year olds versus adults. -Somewhat higher (13-81 percent; depending on particle size) deposition of particles in the TB region. -Lower deposition of particles in the PU region.
Xu and Yu (1986)	Various	Increased total deposition (up to 1.5-fold higher) in children aged 6 months, 2 years, and 8 years compared with adults for particles of varying sizes.

6. CONCLUSIONS

The examples and discussions included in this appendix suggest that the *Inhalation Dosimetry Methodology's* default approaches for derivation of the HEC for Category 1 gases with effects in the ETh, TB, and PU regions and for Category 3 gases typically are sufficient to cover variation across human age- and activity-level groups. The process for deriving an RfC from the HEC includes applying an uncertainty factor (UF) to account for within-species variability, adding further protection. When deriving an IUR for a carcinogen, UFs are not used. However the procedures for estimating an IUR incorporate conservative assumptions that would likely accommodate the degree of variation observed in these examples.

Experimental and modeling results for particles suggest the potential for small differences in deposition of particles in the respiratory tract as a function of age. The assumption that 100 percent of the deposited dose is available for uptake into the systemic circulation (for remote acting toxicants), or for activity in the respiratory tract (for local toxicity) is likely to result in an overestimation of dose to the target tissue. Any small variation in deposition among age groups should be considered against the potential magnitude of such overestimation. These differences in calculated deposition are small relative to the default 10-fold UF that accounts for intra-species variability in the derivation of the RfC. In addition, RfCs and IURs are developed for chronic exposure and will generally involve an exposure for multiple years. No additional correction of the toxicity values for these age groups is needed when the RfC or IUR is used in a risk assessment. Calculations in these examples are based on empirical data from sources listed and referenced in ICRP Publication 66 (ICRP, 1994). While ORD selected the ICRP values as the best estimates for these examples, other published values for V_e and SA exist. The use of alternate values may change the $LOAEL_{[HEC]}$ calculated for the various populations and life stages and may show more or less variability in results across the age and activity groups. In addition, the examples for the TB and PU regions are based on a hypothetical chemical, since currently no RfCs for gases on IRIS are calculated based on animal studies showing health effects occurring in these regions of the respiratory system. Given the parameter values used in the default method for calculating the HEC, it is likely that the process would yield results sufficient to cover populations and life stages with varying activities and physiologic characteristics.

Note that the available data, albeit limited, generally support these conclusions. As recommended by the Reference Dose (RfD)/RfC Technical Panel (USEPA, 2002), EPA has been exploring issues involving dose to the young from inhalation exposures, both theoretically and experimentally as well as further considering the existing animal-to-human extrapolation procedures described in current methodologies (e.g., USEPA, 1994). This is especially important because of the significant developmental changes that occur in the lung from birth well into adolescence (Pinkerton and Joad, 2000). The review and updating of these methodologies will be based on the best available science.

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APPENDIX B

APPENDIX B

CHEMICALS ON IRIS WITH EXTRAPOLATED INHALATION UNIT RISKS

Table B-1 contains chemicals on the Environmental Protection Agency's (EPA's) Integrated Risk Information System (IRIS) with Inhalation Unit Risk (IUR) values calculated by extrapolation using the default ventilation rate and body weight from the oral Cancer Slope Factor (CSF). These chemicals cause tumors remote from the respiratory tract. Also listed is the year EPA verified the cancer assessment. The list was compiled in September 2008.

EPA recommends that extrapolated IURs should be used with risk Equations 6 and 11 in the main document without additional modification for calculation of cancer risk by the inhalation route of exposure. It is generally not appropriate to make adjustments based on ventilation rate and body weight using the intake equation, because the amount of the chemical that reaches the target site of the chemical through the inhalation pathway is not a simple function of the inhalation rate and body weight. Risk assessors should outline the uncertainties involved in using extrapolated IURs in the risk characterization section of the risk assessment.

TABLE B-1 CHEMICALS WITH EXTRAPOLATED INHALATION UNIT RISKS ON IRIS	
Chemical	**Year of Verification**
Acrylamide[1]	1988
Aldrin	1987
Aramite	1991
Azobenzene	1988
Bromoform	1989
Chlordane	1997
Chloroform[1]	1987
DDT	1987
1,2-Dichloroethane	1986
Dieldrin	1987
1,2-Diphenylhydrazine	1986
Heptachlor	1987
Heptachlor epoxide	1987
Hexachlorobenzene	1989
Hexachlorobutadiene[1]	1986
Alpha-hexachlorocyclohexane	1986
Beta-hexachlorocyclohexane	1986
Technical-hexachlorocyclohexane	1986
Hexachlorodibenzo-p-dioxin mixture	1987
Hexachloroethane	1986
N-nitroso-di-n-butylamine	1986
N-nitrosodiethylamine	1986
N-nitrosodimethylamine	1986
N-nitrosopyrrolidine	1986
Polychlorinated biphenyls	1996
1,1,2,2-Tetrachloroethane	1986
1,1,1,2-Tetrachloroethane	1988
Toxaphene	1987
1,1,2-Trichloroethane	1986
2,4,6-Trichlorophenol	1989
[1] Note that this chemical's IUR is currently under review.	

APPENDIX C

APPENDIX C

STSC's PROCESS FOR DERIVING ALTERNATIVE INHALATION TOXICITY VALUES

If Reference Concentration (RfC) and/or Inhalation Unit Risk (IUR) values for an inhaled contaminant are not available from the sources in the Environmental Protection Agency's (EPA's) Office of Solid Waste and Emergency Response (OSWER) hierarchy, risk assessors should first contact the National Center for Environmental Assessment's (NCEA's) Superfund Health Risk Technical Support Center (STSC) for guidance.[52] Risk assessors working on Superfund sites can contact STSC to determine whether a provisional peer-reviewed toxicity value (PPRTV) exists for a contaminant; if not, the risk assessor, in cooperation with the appropriate EPA Regional office may request that STSC develop a PPRTV document or that STSC develop an inhalation toxicity value as a "consult." The latter would be specific to the site in question only.

As a first choice, if human or whole animal studies exist providing a suitable No Observable Adverse Effect Level (NOAEL)/Lowest Observable Adverse Effect Level (LOAEL) or Point of Departure (POD) from a Benchmark Dose (BMD) analysis, this data normally will be used by STSC to develop an inhalation toxicity value. If, in addition, a suitable human inhalation physiologically based pharmacokinetic (PBPK) model exists that can be utilized to refine the dose metric to the target organ, then this information generally will be included in developing an inhalation toxicity value.

If no appropriate whole animal or human studies exist, but an appropriate peer reviewed human inhalation PBPK model exists that has been validated by experimental results, then STSC usually will attempt to derive an inhalation toxicity value from this model. If none exists, but a suitable PBPK animal inhalation models exists, STSC may attempt developing a human model and deriving an inhalation value.

PBPK modeling quantitatively describes the absorption/metabolism/distribution and elimination of the chemical from a point of entry (oral, inhalation, dermal) to the target organ(s). In some cases, an oral PBPK model can be extrapolated to the inhalation pathway, but care must be taken to consider direct pulmonary effects that may not be evident by oral dosing.

As a next approach, STSC typically will evaluate development of an inhalation toxicity value using a suitable surrogate chemical based on a quantitative structure-activity relationship (QSAR) model with structural selection criteria and solubility/toxicity considerations. STSC may evaluate possible surrogate chemicals based on several available structural models and provide a comparison. Selection of the appropriate surrogate may depend on the weight of evidence of these models.

[52] All contact with STSC should be performed by an EPA regional risk assessor. States and other entities should first contact their EPA regional risk assessor with questions on inhalation toxicity values. Regional risk assessors can then contact STSC on their behalf.

If STSC uses any of the methods for developing toxicity values other than from human or whole animal data, the value normally will be presented as a "screening" value with the caveat that it should not be used as a risk driver for a site without consultation with the STSC. The uncertainties associated with using toxicity values derived through PBPK modeling or QSAR, or with using a surrogate value should be described in the risk characterization portion of the risk assessment (see Section 9). Risk assessors are discouraged from performing simplistic route-to-route extrapolations from oral data using default assumptions about Inhalation Rate (IR) and body weight (BW).[53]

[53] If STSC indicates that no quantitative toxicity information for the inhalation route is available, the risk assessor should conduct a qualitative evaluation of this exposure route. The risk assessor should discuss in the uncertainty section of the risk assessment report the implications of not quantitatively assessing risks due to inhalation exposures to chemicals lacking inhalation toxicity data. See the section on Risk Characterization (Section 9) in the main text of this guidance for more information.

Exhibit F

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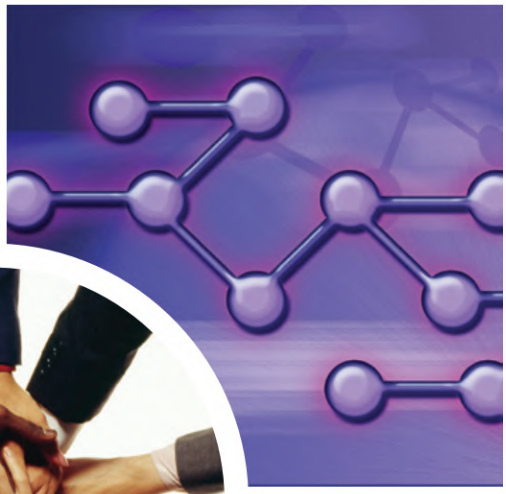
Interim Guidance on

Human Health Risk Assessment for Short-Term Exposure to Carcinogens at Contaminated Sites











Federal Contaminated Sites Risk Assessment in Canada

Canada

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Également disponible en français sous le titre :
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FEDERAL CONTAMINATED SITES RISK ASSESSMENT IN CANADA

Interim Guidance on

Human Health Risk Assessment for Short-Term Exposure to Carcinogens at Contaminated Sites

2013
Prepared by:
Contaminated Sites Division
Safe Environments Directorate

TR 4803

REC 6468

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PREFACE

The Federal Contaminated Sites Action Plan (FCSAP) is a program of the Government of Canada designed to achieve improved and continuing federal environmental stewardship as it relates to contaminated sites located on federally owned or operated properties. Guidance documents on human health risk assessment (HHRA) prepared by the Contaminated Sites Division of Health Canada in support of the FCSAP are available on our website and may also be obtained by contacting the Contaminated Sites Division at *cs-sc@hc-sc.gc.ca*.

This interim guidance document provides additional direction for custodial departments with respect to amortization of short-term exposure to carcinogens at contaminated sites. It is of particular importance at remote sites or sites that are accessed infrequently. The guidance is intended to be advisory in nature and will be updated periodically on the basis of revisions to current expertise, applicable standards and recommendations received from stakeholders. Readers are advised to consult with Health Canada, Contaminated Sites Division, to confirm that they are using the most recent version available on the Health Canada website and that the use of HHRAs is reflective of current and best practices. This document is not to be considered a substitute for the guidance of a qualified professional practitioner.

Work and opinions from various consultants, academics and governmental agencies were used to create this guidance. In particular, Angela Li-Muller, Margaret Yole, Norm Healey and Sanya Petrovic of Health Canada are recognized for their contribution.

Health Canada requests that any questions, comments, criticisms, suggested additions or revisions to the document be directed to the following: Contaminated Sites Division, Safe Environments Directorate, Health Canada, 269 Laurier Avenue West, 4th floor, Address Locator: 4904A, Ottawa, ON K1A 0K9. Email: *cs-sc@hc-sc.gc.ca*.

See also: *www.hc-sc.gc.ca/ewh-semt/contamsite/index-eng.php*.

ABBREVIATIONS AND ACRONYMS

A-D	Armitage-Doll
ADAF	age-dependent adjustment factors
AF	absorption factor
ASF	age sensitivity factor
BHT	butylated hydroxytoluene
BW	body weight
C	concentration
CalEPA	California Environmental Protection Agency
CSD	Contaminated Site Division
DES	diethylstibesterol
DMBA	dimethylbenzanthracene
DNA	deoxyribonucleic acid
DQRA	detailed quantitative risk assessment
ED	exposure duration
ED_{01}	maximum likelihood estimate of the dose corresponding to a 1% additional cancer risk
ER	exposure rate
FCSAP	Federal Contaminated Sites Action Plan
HC	Health Canada
HHRA	human health risk assessment
ILCR	incremental lifetime cancer risk
IR	intake rate
LADD	lifetime average daily dose
LMS	linearized multistage
LOAEL	lowest observed adverse effect level
MVK	Moolgavkar-Venzon-Knudson
NOAEL	no observed adverse effect level
PAHs	polycyclic aromatic hydrocarbons
PBBs	polybrominated biphenyls
PBPK	physiologically based pharmacokinetic
PQRA	preliminary quantitative risk assessment
SF	slope factor
TC	tolerable concentration
TDI	tolerable daily intake
TRV	toxicological reference value
UR	unit risk
US EPA	United States Environmental Protection Agency

EXECUTIVE SUMMARY

This document provides guidance for application at federal contaminated sites funded under the Federal Contaminated Sites Action Plan (FCSAP). It is considered to be interim and is based on an assessment of the current scientific literature. The document does not represent the opinion of Health Canada outside the application of federal contaminated sites funded under the FCSAP.

The current approach to evaluating health risks associated with human exposure to carcinogens at contaminated sites focuses on incremental lifetime cancer risks. The approach to cancer risk assessment varies according to the mode of action at the tumour site in question. Unless there is evidence to support a threshold mode of action, the current approach assumes a linear dose-response relationship at low doses (i.e. non-threshold). The incremental lifetime cancer risk (ILCR) is calculated as a product of the lifetime daily dose (or concentration) and the toxicological reference value (TRV), expressed as cancer slope factor (or inhalation unit risk).

A threshold approach can be applied when there are sufficient data to ascertain the mode of action at the tumour site in question and to conclude that the dose-response relationship is not linear at low doses. For these carcinogenic effects, the TRVs are expressed as tolerable daily intakes (TDIs) or concentrations (TCs), the intakes or concentrations to which it is believed that a person can be exposed daily over a lifetime without deleterious effects. Human exposure is compared with these TRVs, where appropriate, to determine health risks.

Characterization of human cancer risks usually makes use of TRVs that have been derived from epidemiological or toxicological studies with comparable exposure patterns. TRVs for carcinogens are often based on the results of animal studies in which the animals were exposed on a daily basis throughout their adult lifespan. Exposures at contaminated sites may mirror these exposure patterns, but in some circumstances exposures may occur over a period of time much shorter than the lifetime of the exposed individual. In a short-term exposure scenario, short-term exceedance (or excursion) above chronic average daily exposure could occur as a result of variation in intake rates or daily fluctuation in chemical concentrations in environmental media. As a result, the health risks of short-term exposure often need to be addressed.

For contaminated site risk assessments, the current practice of characterizing ILCR associated with less-than-lifetime exposures to carcinogens that act via a non-threshold mode of action involves averaging the short period of exposure over a lifetime to calculate the lifetime average daily dose (LADD). Several issues regarding this practice of averaging the exposure have been raised:

- There is a potential for underestimating cancer risks with the practice of time-averaging of exposures (LADD).
- Variability in sensitivity among different lifestages may not be fully considered.

In addition, depending on the magnitude of exposure, carcinogenic agents may elicit other, chronic and short-term non-cancer health effects as a result of short-term exposures. At present, these effects are often not evaluated.

The Contaminated Sites Division (CSD) will continue to review information related to risk assessments for carcinogenic agents, including short-term exposure and dose averaging.

Cancer Risk Assessment: Non-Threshold Carcinogenic Effects

A literature review was conducted to evaluate whether averaging short-term exposure over a lifetime would be adequate to estimate cancer risk using cancer slope factors derived from chronic animal studies. Both theoretical studies using mathematical models of carcinogenesis and empirical studies involving exposure during discrete age windows suggest that exposures in early lifestages are usually associated with a higher risk of carcinogens acting through a mutagenic mode of action. It was concluded that application of age-dependent adjustment factors to the cancer slope factor with exposure averaged over a lifetime can provide a generally conservative estimate of lifetime cancer risks. As an interim measure, the United States Environmental Protection Agency (EPA) approach has been adopted as a default recommendation for contaminated site risk assessments.

The ILCR can be estimated by summing the risk from each discrete exposure period. For non-threshold carcinogens acting through a mutagenic mode of action, it is recommended that age-dependent adjustment factors (ADAFs) be applied to the cancer slope factor (or inhalation unit risk) with exposure averaged over a lifetime to account for the sensitivity of the age-specific exposure period. We have developed default ADAFs by adjusting the US EPA's ADAFs to be consistent with the age groups recommended by CSD. These default factors can be applied when age-specific cancer slope factors (or inhalation unit risks) or chemical-specific data are not available.

When exposure periods do not match the CSD's age groupings, CSD recommends that the US EPA's ADAFs be applied. For example, if exposure occurs only between 7 months and less than 2 years of age, the adjustment factor of 10 applies. Likewise, if exposure occurs only between 12 and < 16 years of age, the ADAF of 3 applies. When chemical-specific data are available for a susceptible lifestage, these data can be used directly to evaluate risks for the chemical and the lifestage on a case-by-case basis.

Recommended interim adjusted age-dependent adjustment factors (ADAFs) for cancer risk assessment at contaminated sites for carcinogenic effects via a mutagenic mode of action

Lifestage	Age	Adjusted age-dependent adjustment factor (ADAF)[a]
Infant	0–6 months	10
Toddler	7 months–4 years	5[b]
Child	5–11 years	3
Teenager	12–19 years	2[c]
Adult	20+	1

[a] US EPA (2005 a, b), except as noted.

[b] $ADAF_{7\ mo–4\ yr} = (ADAF_{0-<2} * D_{7\ mo–1} / D_{7\ mo–4}) + (ADAF_{2–4} * D_{2–4} / D_{7\ mo–4}) = 10 * 1.5/4.5 + 3 * 3/4.5 = 5$, and D_i = exposure duration in years

[c] $ADAF_{12–19} = (ADAF_{12-<16} * D_{12–15} / D_{12–19}) + (ADAF_{16+} * D_{16–19} / D_{12–19}) = 3 * 4/8 + 1 * 4/8 = 2$, and D_i = exposure duration in years

When the mode of action is unknown or the burden of proof for a threshold mode of action has not been met, CSD recommends a non-threshold approach to cancer risk estimation. If chemical-specific data are available on quantitative differences between early lifestages and adults, an analysis of the differences could be used to adjust risk estimates for early life exposures. Otherwise, CSD does not recommend extending the default age-dependent potency adjustment factors to these carcinogenic effects. This position would be analogous to recommending a default ADAF of 1 for all lifestages.

Cancer Risk Assessment: Threshold Carcinogenic Effects

At this time, the CSD does not recommend a default age-specific adjustment for carcinogenic effects determined to have a non-linear dose-response relationship (i.e. threshold) at low doses. Adjustment can be made on a chemical-specific basis if supported by experimental data. These substances would be included in an HHRA using a TDI (or a TC in the case of inhalation exposure).

The CSD recommends that dose averaging for short-term exposure for these types of carcinogenic effects be performed in the same way as for substances with threshold non-carcinogenic effects. It is important that dose averaging should not underestimate the potential for threshold carcinogenic effects. Without a sound basis for doing so (i.e. it cannot be a default assumption), the human health risk assessor should not simply mathematically spread out a short-term dose over a longer period and conclude that the short-term dose is toxicologically equivalent to a lower dose over the long period. Instead, exposure should be averaged over the total actual exposure period and compared with the appropriate TRV. A scientific rationale is required to support any proposed amortization (dose averaging beyond actual exposure period) to ensure that short-term risks are not underestimated. This analysis needs to be done on a chemical-specific basis.

Assessment of Potential Non-Cancer Health Effects from Short-Term Exposure

For short-term exposure, carcinogenic agents may elicit other, chronic and short-term non-cancer health effects, depending on the magnitude of exposure. Short-term effects can be evaluated for potential critical receptors/lifestages[1] using short-term TRVs where available (either from other regulatory agencies or derived from literature values as per the Health Canada, 2010, detailed quantitative risk assessment [DQRA] guidance) and when applicable to the exposure scenarios. If short-term TRVs are not available, such evaluation can be conducted on the basis of relevant dose-response information from toxicity studies. It is also important to consider whether the short-term exposure might elicit early biological key events that might progress to health effects at a later date.

[1] Including relevant receptors/lifestages with the highest exposure and receptors/lifestages associated with specific sensitivity to the toxicity of the contaminants.

1.0 INTRODUCTION

1.1 Current Cancer Risk Assessment Approach

Health Canada's Contaminated Sites Division (CSD) has a current risk assessment approach for carcinogenic effects that assumes a linear dose-response relationship at low doses (non-threshold) unless there are adequate data to ascertain a mode of action that is consistent with a non-linear dose-response relationship at low doses (i.e. threshold). This approach is particularly relevant for agents that are mutagenic[2] and DNA reactive. The incremental lifetime cancer risk is calculated as a product of the lifetime daily dose and cancer slope factor.

A threshold approach can be applied when there are sufficient data to ascertain the mode of action at the tumour site in question and to conclude that the dose-response relationship is not linear at low doses. Such a carcinogenic agent usually has not been shown to demonstrate mutagenic or other properties consistent with linearity at low doses. Endocrine disruption, cell proliferation, cytotoxicity and receptor-binding are some examples of a non-linear mode of action. For these carcinogenic effects, the CSD risk assessment approach assumes a non-linear dose-response relationship at low doses. The toxicological reference value (TRV) is derived by applying an uncertainty factor to a benchmark dose or benchmark concentration (if available)—a NOAEL (no observed adverse effect level) or a LOAEL (lowest observed adverse effect level)—as appropriate to establish a tolerable daily intake (TDI) or concentration (TC), i.e. the intake or concentration to which it is believed that a person can be exposed daily over a lifetime without deleterious effects.

In many cases, non-carcinogenic effects rather than carcinogenicity may be the main determinant of health risk from long-term exposure to the threshold carcinogenic agent. For example, the developmental effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin occur at lower exposure levels than those required for carcinogenicity and have been used to establish the TRV.

1.2 Issues Related to Less-Than-Lifetime Exposure to Carcinogens at Contaminated Sites

Short-term exposure to carcinogens at contaminated sites may be associated with activities that occur over a relatively short period of time, such as seasonal activities like camping, occasional visits to a remote site and certain occupational activities, e.g. construction and underground service installation. As a result, short-term health risks need to be addressed.

The significance of exposure to contaminants is best characterized by comparison with TRVs derived from epidemiological or toxicological studies with comparable exposure patterns (i.e. short-term exposure compared with TRVs derived from a short-term study). Otherwise, significant uncertainty could be introduced into risk characterization.

TRVs for carcinogens are often based on the results of animal studies in which the animals were exposed on a daily basis throughout their adult lifespan. Exposures to human receptors at a contaminated site may mirror this pattern of exposure, but more often exposure occurs for only a portion of the lifetime or may be intermittent. Exposures at a contaminated site may occur during childhood or in utero, lifestages not represented in standard cancer bioassays.

The current practice of characterizing incremental lifetime cancer risks (ILCR) associated with less-than-lifetime exposures to non-threshold carcinogens involves averaging the short period of exposure over a lifetime to calculate the lifetime average daily dose (LADD). The following issues related to dose averaging (sometimes referred to as dose amortization) have been raised when exposures occur over a short time frame:

1. There is a potential for underestimating cancer risks with the calculation of a LADD associated with a short exposure period.
2. The possibility of acute/subchronic non-cancer effects due to elevated exposures has not been considered and may be relevant when the exposure is elevated above the LADD over a subchronic period. For example, the physiological response will be different following a large short-term exposure as compared with the same exposure averaged over a longer period.
3. Variability in sensitivity among different lifestages may not have been fully considered. For example, the prenatal and neonatal periods, childhood, adolescence, and peri-menopausal and senior lifestages, as well as genetic predisposition, are currently not included in standard adult animal bioassays for deriving estimates of cancer potency.

This document provides a background discussion on each of these issues and presents interim guidance and supporting rationales.

[2] A carcinogen acts via a mutagenic mode of action if the carcinogen or its metabolite is DNA-reactive or has the ability to bind to the DNA. Mutagenicity is "the induction of permanent, transmissible changes in the amount, chemical properties or structures of the genetic material. In most cases, mutation involves changes in DNA structure that either have no effect or cause harm" (USEPA, 2005b; Schoeny, 2011).

1.3 Practice of Dose Averaging

Dose averaging refers to the practice of time averaging a short period of exposure or several intermittent short-duration exposure(s) over a longer duration. This practice is also referred to as exposure amortization. It assumes toxicity to be linearly proportional to the magnitude and duration of exposure. For example, it assumes an exposure of 365 µg/kg bw-day for 1 day, 36.5 µg/kg bw-day for 10 days and 1 µg/kg bw-day for 365 days to be toxicologically equivalent, which could be untrue. The risk for the shorter-term exposure could be underestimated. With this practice, daily exposures that exceed the maximum chronic acceptable daily dose (either a TDI or a risk-specific dose) may be incorrectly considered acceptable because they occur for only a short period of time. In the case of threshold carcinogens, this practice raises questions about the magnitude by which the TDI can be exceeded and for what duration before unacceptable chronic health risks (including carcinogenicity) are possible or expected. For non-threshold carcinogens, the practice raises the question of whether a high dose over a short period results in the same lifetime cancer risk as the same total dose over a lifetime. Also at issue is whether the short-term exposure could elicit adverse acute/subchronic non-carcinogenic health effects.

The answers to these questions, in part, depend on the following:

- when (at what lifestage) the excess exposure is expected to occur;
- whether there are any specific sensitivities associated with that lifestage; and
- whether these sensitivities have been accounted for (perhaps through application of uncertainty factors) in the TRV.

2.0 DOSE AVERAGING FOR NON-THRESHOLD CARCINOGENIC EFFECTS

The current practice of characterizing incremental cancer risks associated with less-than-lifetime exposures involves averaging the short period of exposure over a lifetime to calculate the LADD. This practice assumes that the overall incremental cancer risk is a function of the total dose received and is independent of the exposure pattern: a high dose of a carcinogen received over a short period is assumed to be equivalent to the corresponding total dose spread over a lifetime (US EPA, 1986). However, this practice is not based on firm scientific evidence or principles (Hrudey, 1998), and the US EPA (1986) has acknowledged that the approach is fraught with uncertainty; it recommends that risk assessments include a qualitative discussion of the uncertainty of this assumption.

Various groups of scientists have expressed concern that the LADD approach could underestimate cancer risk (Kodell et al., 1987, Chen et al., 1988; Murdoch et al., 1992; US EPA, 2005a; Halmes et al., 2000); the summary of some of these studies is presented in Table 2. In addition, the age at which short-term exposure occurs could influence cancer risk, as different lifestages may vary in susceptibility (Drew et al., 1983; Crump and Howe, 1984; Ginsberg, 2003; US EPA, 2005a, 2005b; Hattis et al., 2004, 2005).

The uncertainty of the practice was identified as an issue "under review" in Health Canada's (2004) guidance on Human Health Preliminary Quantitative Risk Assessment for contaminated sites. Since that publication, Health Canada's CSD has commissioned a series of contractor reports from consulting and academic experts (Brand, 2004; GlobalTox International Consultants, 2005; Wilson Scientific Consulting Inc., 2006; Orr, 2007; Al-Zoughool and Krewski, 2008) to aid in the decision-making on this issue.

Table 2.1 Summary of modelling studies that compare cancer risks from short-term exposure with those from lifetime-equivalent exposure (extent of under/overestimation reported quantitatively for short-term adult exposure only)

Reference	Study type	Qualitative assessment	Range of most likely predicted LADD underestimate to overestimate of risk	Maximum predicted underestimate (overestimate) of risk
Murdoch et al., 1992	Theoretical modelling for 30-day exposures of astronauts aged 25 to 45 to hypothetical carcinogens inside the space station. Both A-D[a] multistage and MVK[b] models were used.	LADD may underestimate or overestimate risks.	–2 to +6 fold (A-D multistage model); –2 to +7 fold (MVK model)	–2 (+33) fold (A-D multistage model); –1.4 (+63) fold (MVK model)
Kodell et al., 1987	The A-D multistage model was used to model intermittent exposure to a hypothetical carcinogen starting at age 0, 10, 20 and 50 for 1, 10 and 20 years. The ratio of excess risk for intermittent dosing relative to predicted excess risk based on LADD was calculated.	LADD underestimates risk maximally when the number of cancer stages is assumed to be 6, the 1st stage is dose-dependent and exposure occurs during years 1–10 of life.	–3 to +14 fold	–3 (> $+10^5$) fold
Chen et al., 1988	The MVK model was used to calculate the ratio of excess risk for short-term exposure to a hypothetical carcinogen to predicted excess risk associated with underlying assumptions of LADD, with various input parameters, including duration of exposure and start time of exposure.	LADD underestimates risk maximally with early-stage carcinogen and exposure early in life.	–2 to +13 fold (initiator); –4.5 to +13 fold (completer); –9 to +9 fold (promoter)	–2 (> +100) fold (initiator); –5 (> +25) fold (completer); –77 (+100) fold (promoter)

[a] Armitage-Doll

[b] Moolgavkar-Venzon-Knudson

2.1 Dose Averaging for Less-Than-Lifetime Adult-Only Exposures

The issue of dose averaging can be confounded by the potential for varied susceptibility among different lifestages. The TRV developed from studies involving adult-only exposure (e.g. occupational studies) may be inadequate to account for earlier sensitive lifestages, especially when short-duration, high-magnitude exposure is experienced during these sensitive time windows. For this reason, less-than-lifetime exposure occurring only during the adult lifestage is addressed first. In this case, the only issue leading to the potential underestimate of health risk is assumed to be the mathematical manipulation of the level of exposure. For example, daily occupational exposures occurring 5 days per week for 48–52 weeks per year are amortized to the equivalent daily dose over 7 days per week for 52 weeks per year (resulting in a lower calculated daily exposure). Amortization of this magnitude is common, as TRVs are often derived from epidemiological studies based in occupational environments. Similarly, animals are dosed 5 days per week in some toxicity studies.

Two general lines of inquiry have been explored to determine the extent to which time averaging may over or underestimate cancer risks in adult-only exposures:

1. Evidence from animal bioassays or epidemiological studies in which the cancer risks estimated from short-term exposures are compared with those derived from adult lifetime exposures.
2. Comparison of the cancer risk estimates from short-term exposures with those derived for lifetime exposures at the LADD-equivalent dose using generally accepted mathematical models of carcinogenesis.

2.1.1 Dose Averaging Implications from Adult Animal Bioassays

Standard carcinogenicity bioassays involve near-lifetime exposures; however, exposures of very limited duration may also result in tumour formation. A literature review by Calabrese and Blain (1999) found 426 chemicals from a broad range of chemical classes that could induce cancer after a single administration in a large number of animal models. Most of these chemicals, if not all, were found to be genotoxic. Thirty nine percent caused more tumours, 22% caused fewer tumours, and the remaining 39% showed similar tumourigenic responses when the carcinogen was administered as a single dose as compared with the same dose fractionated over a lifetime. However, Calabrese and Blain (1999) and others (Ginsberg, 2003) did not consider varied lifestage susceptibility when analyzing the available data, which involved a single exposure at different lifestages (i.e. fetal, neonatal).

Stop-exposure studies (summarized in Table 2.2) illustrate the influence of exposure schedule and duration on cancer risk. Exposures were stopped after only a portion of the animal's lifespan, and the animals were observed long enough to measure tumour development.

Table 2.2 Summary of studies comparing cancer risks from short-term (adult-only) exposure with those from lifetime-equivalent exposure (with same total dose)[a]

Reference	Study type	Qualitative assessment	Range of most likely predicted LADD underestimate to overestimate of risk	Maximum predicted underestimate (overestimate) of risk
	Animal experiments			
Halmes et al., 2000	Animal stop-exposure—data from 11 National Toxicology Program studies (adult animals—male rats or mice). Cancer potency was estimated using 2-year continuous bioassay data with or without inclusion of stop-exposure data.	Tumour responses in the stop-exposure experiment were underpredicted by continuous exposure data at 34/59 tumour sites for 6/11 chemicals, and overpredicted at 2/59 tumour sites for 2/11 chemicals. Prediction was accurate for 26/59 tumour sites for 9/11 chemicals.	Undefined	Undefined
		Inclusion of stop-exposure data in ED_{01}[b] estimation (as compared with using continuous bioassay data alone) led to a decrease for 63% of the chemical/tumour/site combinations and an increase for 17% of the chemical/site combinations, mostly within one order of magnitude. 15% (of all tumour sites examined) showed a greater than 10-fold decrease (greater risk or potency) in ED_{01}, implying a higher risk with shorter exposure.	Undefined	Undefined
		The "equivalent averaging times"[c] for the stop-exposures were generally longer than the actual exposure durations but less than 104 weeks for 12 of the 14 dose groups for which this comparison was made. The median "equivalent averaging time" for all the groups was 62 weeks, indicating that averaging stop-exposure duration over a lifetime (LADD) would underestimate the risk by a median factor of 2.	–5 to +2 fold	–5 (+2) fold

Table 2.2 – cont'd ➜

Reference	Study type	Qualitative assessment	Range of most likely predicted LADD underestimate to overestimate of risk	Maximum predicted underestimate (overestimate) of risk
Drew et al., 1983	Animals exposed to constant concentrations of vinyl chloride (adult animals—rats, 2 strains of mice, hamsters) by inhalation. Animal age at the start of exposure and exposure duration were varied among different exposure groups.	For most of the animal species studied, exposure from months 2–8 of life produced higher tumour frequency than exposure at later lifestages for the same duration (8–14, 14–20 or 20–26 months of age), possibly because animals died before a potential tumour could be expressed in the latter groups.	Undefined	Undefined
Hattis et al., 2004	Animals—rats and mice exposed to four types of ionizing radiation at different stages of life	On the basis of a total of 138 group tumour incidence observations, dosage delivered to older animals (6–12 or 19–21 months old) appeared to be 3 fold less effective than a similar dosage delivered to young adult animals (3–3.5 months), suggesting greater sensitivity during early adulthood.	Undefined	Undefined
	Epidemiological studies			
Hauptmann et al., 2000	Case-control study of lung cancer and smoking in adults (4300 cases). The effect of smoking pattern on lung cancer risk was examined using a linear model taking into consideration that different exposure periods vary in their contribution to the overall cancer risk.	The number of cigarettes smoked within 5–15 years prior to patient interview strongly determined lung cancer risk; the number smoked more than 20 years earlier contributed minimally to risk. The pattern corresponds to an observed decrease in risk corresponding to the time since smoking cessation. Authors concluded that use of cumulative or average dose may not be appropriate for estimating lung cancer risk.	Undefined	Undefined
Hauptmann et al., 2002	Pooled data from two German case-control studies (2652 cases) on asbestos and lung cancer were assessed in terms of various exposure metrics.	The results suggested that cancer risk increased for 5–15 years after exposure and then declined. Other studies have indicated a 20–40 year latency period for asbestos-induced lung cancer. Dose averaging over a lifetime would underestimate the risk for people whose remaining lifespan is greater than the latency period and would overestimate the risk for people whose remaining lifespan is shorter than the latency period.	Undefined	Undefined

Table 2.2 – cont'd ➜

Reference	Study type	Qualitative assessment	Range of most likely predicted LADD underestimate to overestimate of risk	Maximum predicted underestimate (overestimate) of risk
Elwood et al., 1985; Elwood, 1992	Histories of exposure to sun of 595 patients with malignant melanoma in Western Canada were examined in a case-control study.	Significant increase in risk was correlated with summer vacation and recreational activities with intense sun exposure. A moderate amount of total occupational exposure (likely from intermittent seasonal exposure) increased the risk; further increased exposure (> 200 whole body equivalent hours of exposure per season associated with long continuous exposure) had no effect or resulted in decreased risk (for men). At the same total sun exposure, the relative risk of melanoma from short-term intermittent recreational exposure exceeded long-term occupational exposure by up to 2 fold.	+1 to –2 fold	–2(+1)

[a] Adapted from Tables 4.5-1 and 4.5-2 in Orr (2007); edited to exclude studies in which juvenile exposures were compared with adult exposures.

[b] ED_{01} is the maximum likelihood estimate of the dose corresponding to a 1% additional cancer risk.

[c] Equivalent averaging time is the length of time over which stop-exposure doses have to be averaged so that the observed response falls exactly on the fitted dose-response curve developed from the continuous exposure (i.e. 104 weeks) data.

Halmes et al. (2000) evaluated cancer data from 12 similar United States National Toxicology Program animal bioassays in which both chronic lifetime and stop-exposure dosing protocols (using male rats except for 1,3-butadiene, to which male mice were exposed) were followed. The Weibull Model was fitted first to the chronic data only and then to the combined chronic and stop-exposure data adjusted to average lifetime exposure. Tumours developed following exposure to 11 chemicals (acting through different modes of action), some at multiple sites, totalling 59 chemical/site combinations. The same response rate was observed for 44% of the chemical/tumour site combinations. However, for 46% of the chemical/tumour site combinations, the response rate was higher in the stop-exposure groups than the chronic lifetime exposure groups. About 5% showed a lower response in the stop-exposure groups than the chronic lifetime exposure groups. Therefore, the assumption of equivalent cancer risk at equivalent total doses (i.e. that the product of concentration and time is constant independent of the exposure pattern) was incorrect at least half of the time. Combining stop-exposure and continuous exposure data in ED_{01}[3] estimation showed varied effect. Inclusion of responses from the stop-exposure groups led to a decrease in the ED_{01} (greater risk or potency) for 63% of the chemical/tumour/site combinations and an increase in the ED_{01} (lesser risk or potency) for 17% of the chemical/site combinations, mostly within one order of magnitude. While the overall change was less than 2-fold (in either direction) for 36% of the tumour sites examined, approximately 15% (of all tumour sites examined) showed a greater than 10-fold decrease (greater risk or potency) in ED_{01}, implying a higher risk with shorter exposure. The largest reduction was 102-fold for lymphomas following 1,3-butadiene exposure.

Halmes et al. (2000) also evaluated dose averaging by determining the "equivalent averaging time". Equivalent averaging time is the length of time over which stop-exposure doses have to be averaged so that the observed response falls exactly on the fitted dose-response curve developed from the continuous exposure (i.e. 104 weeks) data. This method of evaluation has a direct implication for cancer risk assessment. The stop-exposure studies exposed animals for varying durations that ranged from 13 weeks to 66 weeks. For most endpoints, the "equivalent averaging times" were generally longer than the actual exposure durations but less than 104 weeks for 12 of the 14 dose groups for which this comparison was made. The median "equivalent averaging time" for all the groups was 62 weeks, indicating that averaging the stop-exposure dose over a lifetime (i.e. LADD) would underestimate cancer risk by a median factor of 2 (ranging from an overestimation of 2-fold to an underestimation of 5-fold).

In addition to duration-related variability (i.e. short-term versus long-term exposures), carcinogenic sensitivity may not be constant throughout the adult period. On the basis of their analysis of animal (rats and mice) experimental data involving four different types of ionizing radiation, Hattis et al. (2004) demonstrated that the dosage delivered to older animals (6–12 months or 19–21 months old) appeared to be several-fold less effective than a similar dosage delivered to young adults (3–3.5 months old), suggesting greater sensitivity for exposures in early adulthood.

In summary, experimental data with animals suggest that averaging short-term exposure over a lifetime results in uncertainties and may overestimate or underestimate the risk when exposure occurs during adulthood. The level of underestimation or overestimation is generally within an order of magnitude for the substances studied. However, many carcinogens found at contaminated sites have not been studied in this manner.

2.1.2 Dose Averaging Implications from Adult Exposures in Epidemiological Studies

The available epidemiological data on the effect of exposure patterns on cancer risks (summarized in Table 2.2) are limited, lung and skin cancer being the most frequently studied.

A review (Wilson Scientific Consulting Inc., 2006) of the literature on cancer risk from smoking indicates a general scientific consensus that cancer risk decreases for individuals who quit smoking when compared with those who continue to smoke, the extent of the reduction lessening as the age of quitting increases. The review concluded that an appreciable amount of cancer risk is removed 10 years after smoking cessation. However, although smoking reduction may also lead to reduced lung cancer risk, the conclusion did not consider the intensity of smoking or the age of the smoker. Smoking is a unique activity that involves inhaling a high dose of a mixture of carcinogenic and non-carcinogenic chemicals, which include irritants and pharmacologically active levels of nicotine. The effects of both psychological and physical addiction as well as other socioeconomic factors may not have been accounted for in the analyses. Therefore, the exposure–risk relationship observed for smoking may not be applicable to carcinogens and exposures typical of contaminated sites. In addition, the available analysis of the smoking data lacks a quantitative comparison of the cancer risks predicted by LADD and alternative approaches with the observed cancer risks as a function of smoking intensity (dose) and duration.

Hauptmann et al. (2002) investigated lung cancer risk associated with occupational exposure to asbestos in two German case-control studies. The data suggest that an individual's lung cancer risk increased for 5–15 years after exposure and then declined. The risk declined to about one-half after more than 20 years from the final exposure. When individual risks were modelled and compared, the risk was higher and peaked earlier at high exposure rates as

[3] Maximum likelihood estimate of the dose corresponding to a 1% additional cancer risk.

compared with lower exposure rates (5 fiber-yrs/yr for 5 years versus 0.5 fiber-yrs/yr over 50 years). The result suggests that dose averaging over a lifetime would underestimate the risk, especially for people whose remaining lifespan is longer than the latency period. On the other hand, the risk would be overestimated for people whose remaining lifespan is shorter than the latency period.

Case control studies of the incidence of melanoma or basal cell carcinoma involving patients 20–79 years of age with a recent diagnosis in Western Canada (Elwood et al., 1985) found an individual's total dose alone did not determine cancer risk, as the intensity of exposure also played a role. Activities that likely involved more intense sun exposure (vacation and recreation) conferred a greater level of risk (by up to 2-fold) than if the same dose had been achieved by predominantly occupational exposure. A moderate amount of occupational sun exposure (likely from intermittent seasonal exposure) increased the risk, but further increase in exposure (typical of chronic occupational exposure) either had no effect or resulted in decreased risk (for men) (Elwood, 1992). Other major studies showed a similar pattern following intermittent exposures, although results from the northern hemisphere studies are more definitive than from Australian studies (Kricker et al., 1995), partly because the total dose received in Australia is so much greater (Elwood, 1992).

The limited human data associated with short-term or intermittent exposure support the notion that averaging short-duration or intermittent exposure over a longer time period may not be appropriate for predicting cancer risk.

2.1.3 Theoretical Cancer Modelling Studies of Less-Than-Lifetime Exposure

Mathematical models of cancer, such as the A-D multistage model and MVK model (the latter model is also known as the two stage birth-death-mutation model), are generally compatible with the current understanding of the mechanism of carcinogenesis. The A-D multistage model assumes cancer to be the end result of a normal cell going through a finite number (e.g. k) of irreversible independent transitions (stages) that must take place in a specific order (Armitage, 1985; Al-Zoughool and Krewski, 2008). The MVK model assumes that the clonal expansion of cancer involves two discrete phases: initiation (due to genetic damage) and malignant conversion with progression (Al-Zoughool and Krewski, 2008). Although these models have not been validated (United Kingdom Department of Health, 2004), they have been used to describe the age-dependent rate of cancer formation and to explore the extent to which the LADD approach could over or underestimate cancer risk resulting from less-than-lifetime exposure scenarios (Kodell et al., 1987; Murdoch and Krewski, 1988; Chen et al., 1988; Murdoch et al., 1992, Al-Zoughool and Krewski, 2008). These analyses may provide insight into the upper bound estimate of the level of over or underestimation of the risk.

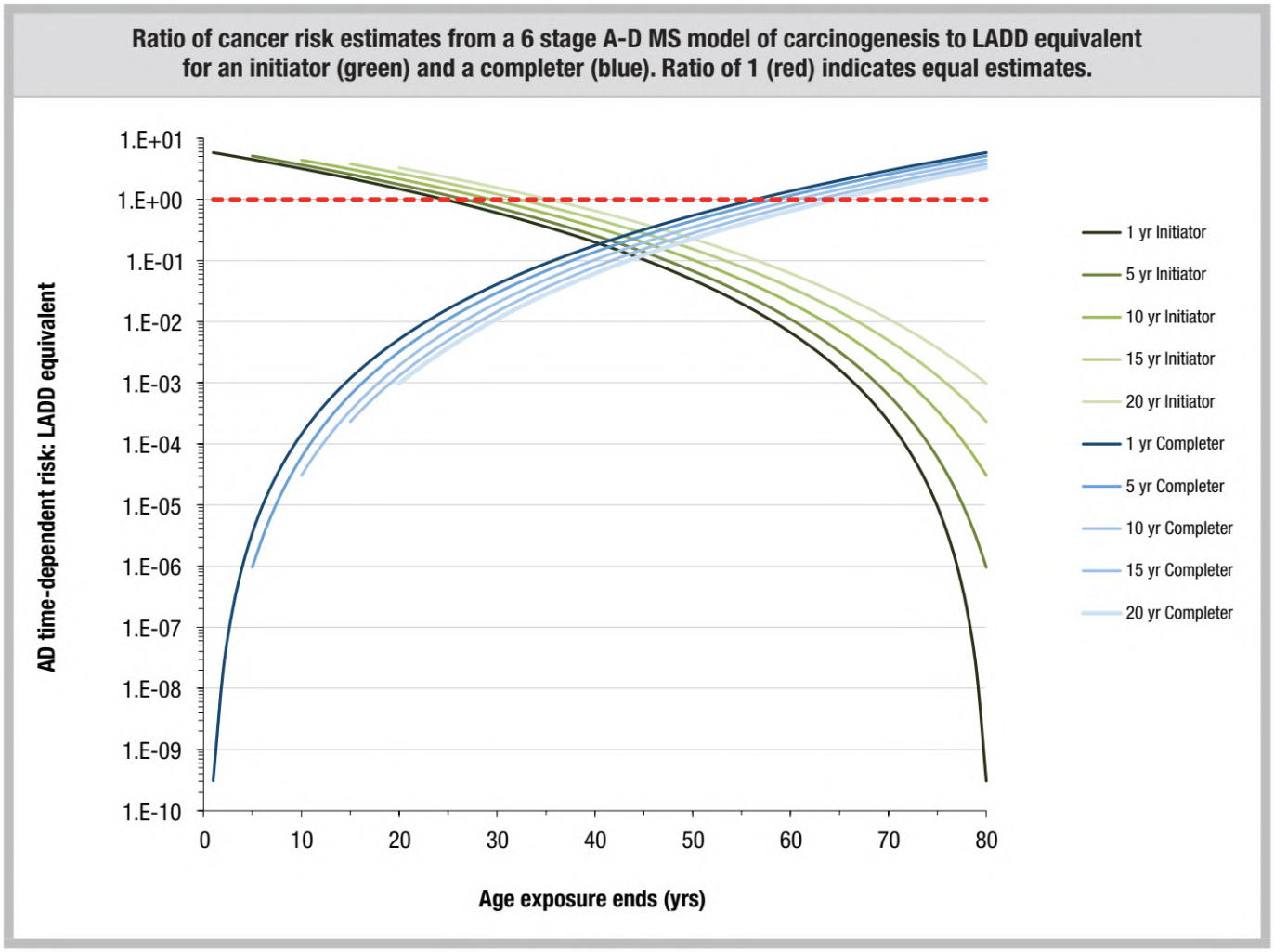
Using the A-D multistage time-to-tumour model, a number of publications (Murdoch et al., 1992; Al-Zoughool and Krewski, 2008; Kodell et al., 1987) have demonstrated the propensity of LADD to over or underestimate cancer risk under certain exposure scenarios. The theoretical upper bound of underestimation by the LADD approach was also estimated. The consensus is that the LADD approach can over or underestimate cancer risks for less-than-lifetime exposures depending on the exposure. The greatest extent of underestimation was postulated for two general scenarios: short-term exposures in early life to initiators (carcinogens that increase the rate of the first stage of carcinogenesis) and short-term exposures late in life to completers (carcinogens that increase the rate of the last stage of carcinogenesis, Chen et al., 1988). In both cases, LADD can underestimate cancer risk by up to a factor of 6. When short-duration exposure occurs in an adult's mid-life period, the extent of underestimation is less than 2- to 3-fold. Depending on the mode of action, cancer risk from short-term exposure may also be overestimated by up to several orders of magnitude.

The relationships between the prevalence and magnitude of potential under and overestimates of cancer risk using the LADD approach are illustrated in Figure 2.1. This figure compares the relative risk estimates generated using a 6-stage A-D multistage model (to estimate cancer risks for time-dependent exposure patterns) with those calculated using an "equivalent" LADD (a time-weighted average dose assuming constant lifetime exposure). The value of 1 on the Y axis represents equivalent risk estimates. Values greater than 1 represent cases in which LADD underestimates cancer risks relative to the time-dependent risk model, and values smaller than 1 represent cases in which LADD overestimates those risks. The figure illustrates that, except for the specific cases discussed above, the LADD is more likely to overestimate cancer risk, and the magnitude of potential overestimation is much greater than the magnitude of underestimation.

It is important to note that the difference in cancer risk estimates between the models is dependent on the number of stages considered in the A-D multistage model, which stage is affected and the age at first exposure. Figure 2.1 illustrates a comparison using the 6-stage A-D multistage model and an assumption that only one stage (i.e. first or last stage) is dose-related. The difference between the models in cancer risk estimates will be smaller if one uses a lower number of cancer stages in the A-D multistage model. The modelled cancer risk estimates become approximately equivalent with a 2-stage A-D model (assuming carcinogenesis has only two stages).

The results from the MVK model generally parallel those from the A-D multistage model exercises (Chen et al., 1988; Murdoch et al., 1992). The model predicts LADD may over or underestimate cancer risks depending on the cell growth rate, time of first exposure, duration of exposure and the type of carcinogen. The maximum underestimate of risk reported by Chen et al. (1988) using the LADD approach would occur with early-life, shorter exposures to an initiator (maximum 7-fold underestimate) or with longer duration, late-life exposures to a completer (maximum 4.5-fold underestimate). When exposure takes place during mid-life, the degree to which LADD can underpredict cancer risk (up to 2-fold) for initiators using the MVK model is generally quite comparable with the A-D multistage model prediction (Chen et al., 1988; Murdoch et al., 1992).

Figure 2.1 Relative cancer risk estimates for various ages and durations of adult exposure calculated using a 6-stage Armitage-Doll multistage (MS) model for estimating cancer risks for time-dependent exposure patterns versus lifetime average daily dose (LADD). Only one stage was assumed to be dose-related in the modelling, the first stage for "initiators" and the last (or kth) stage for "completers". A value of 1 on the Y axis (indicated by the red horizontal dotted line) represents equivalent risk estimates. Values greater than 1 represent cases in which LADD underestimates cancer risks, and values smaller than 1 represent cases in which LADD overestimates risks.



2.1.4 Summary for Dose Averaging for Less-Than-Lifetime Adult Exposure

Evidence from animal experiments, epidemiological studies and theoretical modelling studies supports the conclusion that exposure pattern has an effect on lifetime cancer risk. Averaging less-than-lifetime exposure over a lifetime using LADD may underestimate or overestimate cancer risks, depending on the timing of exposure and the mode of action of the carcinogen. The degree of underestimation seems generally to be confined to within an order of magnitude and is approximately 2-fold for short exposure during all but the very late stages of adulthood. Theoretical modelling predicts up to a 6-fold underestimation of risk for exposure to a completer only late in life; however, most chemicals act through multiple mechanisms, and few exclusive completers have been identified. The original multistage A-D model assumes that cancer incidence increases with age at a constant rate. The review by Al-Zoughool and Krewski (2008) indicates that this assumption does not apply to the incidence of prostate and breast cancers, which increase until age 40 and 50 and decline thereafter; the incidence of most cancer types declines after the age of 80. The multistage model may therefore overestimate cancer rates in the elderly, and LADD may not underpredict cancer risk from less-than-lifetime exposure to (theoretical) completers late in life as much as the model suggests.

Overall, the limited evidence currently available suggests dose averaging over a lifetime (LADD) overestimates as frequently as it underestimates cancer risk for short-term exposure. However, for adult exposures to mutagenic carcinogens (e.g. initiators), the underestimation of cancer risk is insignificant in most cases. Adjustment to correct for underestimation of cancer risk resulting from using the LADD approach for less-than-lifetime exposures in adults is therefore not recommended (i.e. the status quo is maintained).

2.2 Dose Averaging for Less-Than-Lifetime Early-Life Exposure

Cancer slope factors are generally derived from adult human epidemiological studies or standard chronic adult rodent bioassays. The US EPA (2005a) conducted a comprehensive review of cancer risk associated with early-life exposure to determine whether specific age-dependent adjustments of adult cancer slope factors were needed when assessing cancer risk from early-life exposure.

The review found limited cancer epidemiological data involving childhood exposure to radiation and chemotherapeutic agents. A review of available animal studies (Barton et al., 2005; Chhabra et al., 1993; Peto et al., 1984; Vesselinovitch et al., 1979) indicated that early-life exposures (i.e. perinatal) usually resulted in a higher tumour incidence later in life than standard adult-only exposures.

These findings are consistent with the current understanding of biological processes involved in carcinogenesis and are supported by other reviews (McConnell, 1992; Miller et al., 2002; US EPA, 1996), which found the following:

- Tumours usually occur at the same sites following either perinatal or adult exposure.
- Perinatal exposure followed by adult exposure usually increases the percentage of treated animals bearing tumour or reduces the latency period before tumours are observed as compared with adult-only exposures.

The US EPA (2005a) identified several factors that may contribute to increased susceptibility to carcinogens in early life:

- Differences in the capacity to metabolize and clear chemicals at different ages can result in larger or smaller internal doses of the active agent(s), either increasing or decreasing risk (Ginsberg et al., 2002; Renwick, 1998).
- More frequent cell division during development can result in enhanced fixation of mutations because of the reduced time available for repair of DNA lesions, and clonal expansion of mutant cells results in a larger population of mutants (Slikker et al., 2004).
- Some embryonic cells, such as brain cells, lack key DNA repair enzymes.
- Some components of the immune system are not fully functional during development (Holladay and Smialowicz, 2000; Holsapple et al., 2003).
- Hormonal systems operate at different levels during different lifestages (Anderson et al., 2000).
- Induction of developmental abnormalities can result in a predisposition to carcinogenic effects later in life (Anderson et al., 2000; Birnbaum and Fenton, 2003; Fenton and Davis, 2002).
- While tumour promotion processes can be very dependent upon the duration of promotion, initiation processes can occur in relatively brief periods.
- Most tumours take extended periods to develop, which means that damage occurring earlier in life is more likely to result in tumours before death than would exposures that occur later in life.

The US EPA (2005a) compared the cancer potencies from early-life exposure with the cancer potencies from adult exposure in repeated (continuous) dosing studies taken from the published literature. Studies included in the analysis involved a) exposure of animals either only during the juvenile or adult period and followed through adulthood to assess tumour incidence; or b) exposure of animals beginning either in the juvenile or adult period, but once begun continuing through life. Cancer potencies were estimated by fitting the one-hit model, or a restricted form of the Weibull model, to the data for each age group. The analysis for the six carcinogens

(benzidine, diethylnitrosamine, 3-methylcholanthrene, safrole, urethane and vinyl chloride) with a mutagenic mode of action is most informative. The results indicate that the early lifestages can be, but are not always, much more susceptible to cancer development than when exposure occurs in the adult lifestage. The ratio of tumour incidence from early life to adult exposure varies by chemical, sex and species with the weighted geometric mean ratio estimated at 10.4.

The US EPA (2005a) performed a similar analysis of acute dosing studies (which generally compared a single exposure during the juvenile period with identical or similar exposure in adult animals). The results[4] supported the concept that early-lifestage exposure to carcinogenic chemicals with a mutagenic mode of action leads to increased tumour incidence when compared with adult exposure of a similar dose and duration.

On the basis of the analysis involving repeated (continuous) dosing studies, the US EPA (2005a) recommended adjusting the adult cancer slope factor by a factor of 10 for exposures to mutagenic carcinogens occurring during the first 2 years of life. Pharmacokinetic and pharmacodynamic differences between children and adults are greatest during the first 2 years of life (World Health Organization, 2006), which corresponds to the period of birth to weaning in laboratory rodents (Hattis, 2005; WHO, 2006).

The US EPA (2005a) considered the available data insufficient to calculate a specific adjustment factor for the period from 2 through 15 years of age, which represents middle adolescence and follows the period of rapid developmental changes during puberty. The US EPA therefore selected a 3-fold adjustment as it is the geometric mean between the 10-fold adjustment for the first 2 years of life and a unity adjustment for adult exposure. The US EPA recommends that these default age-dependent adjustment factors be applied only when chemical-specific data on early-life exposure are absent.

Although the limited data for carcinogens with a non-mutagenic mode of action (e.g. hormonally mediated) suggest increased susceptibility when exposure occurs perinatally, the US EPA (2005a) considered the data inadequate to derive a generic adjustment of cancer response. More research is needed, particularly because it was observed that tumours arising from hormonally active chemicals appeared to involve different sites when exposure occurred during early life versus adulthood.

The California Environmental Protection Agency (CalEPA, 2009) released its findings on a similar study it undertook to address age-related cancer. This study compared cancer potencies (estimated by applying the linearized multistage [LMS] model to the dose-response data from animal experiments) from early-life exposures (exposed during the prenatal, postnatal or juvenile period) with exposure at an older age, preferably during adulthood. CalEPA used the full distribution of the cancer slope to derive the ratios of cancer potencies from early-life to adult exposures with adjustment for time to manifest tumour (i.e. to account for the longer available time the young animals had from exposure to tumour development). Each chemical was represented by a single distribution based on cancer potencies estimated from one or more studies and from all tumour sites.

The medians of the postnatal age sensitivity factor (ASF), estimated from data on 18 carcinogens (55 distributions), and the juvenile ASF, estimated from data on 5 carcinogens (7 distributions), were reported as 13.5 and 4.5 respectively. Because of the limited database and the broad distributions of results for different chemicals, CalEPA found no basis for specifying a default ASF with greater than half-log precision (i.e. values of 1, 3, 10, 30, etc). Further, rodents are born at a stage of maturity that approximates that of a third-trimester human foetus. Therefore, in the absence of chemical-specific data, CalEPA recommended applying a default ASF of 10 for the third trimester to age 2 years (totalling 2.25 years) and a factor of 3 for ages 2 through 15 years to account for potential higher sensitivity during early lifestages. While the same values were selected by US EPA (2005a) to be applied only to carcinogens with a mutagenic mode of action, CalEPA will apply these factors to all carcinogens. CalEPA (2009) included in its analysis three non-genotoxic carcinogens and found evidence that early life is a susceptible time for a carcinogen thought to act through a non-mutagenic mode of action, e.g. diethylstilbestrol (DES). CalEPA's rationale for not restricting ASF to chemicals acting via a mutagenic mode of action includes the potential problems of defining "mutagenic mode of action" when applied narrowly and the possibility of carcinogens with multiple modes of action that dominate at different lifestages (CalEPA, 2009).

2.3 Dose Averaging for Prenatal Exposure (Transplacental Carcinogenesis)

A number of agents are suspected to be transplacental carcinogens, i.e. in utero exposure to these agents leads to cancer development later in life, involving either a mutagenic or a non-mutagenic mode of action. Most data are from animal studies, such as those involving DES, genistein, tamoxifen, polycyclic aromatic hydrocarbons (PAHs), polybrominated biphenyls, polychlorinated dibenzo-p-dioxins (dioxin; reviewed in Birnbaum and Fenton, 2003), arsenic (Waalkes et al., 2004) and nitrosamines (Mohr et al., 1983). In humans, only radiation and DES have been shown to cause cancer following in utero exposures (Anderson et al., 2000; Barton et al., 2005; and Birnbaum and Fenton, 2003). Other chemicals suspected to be transplacental carcinogens

[4] Based on acute dosing carcinogenic data for eight chemicals with a mutagenic mode of action: benzo[a]pyrene, dibenzanthracene, diethylnitrosamine, dimethylbenzanthracene, dimethylnitrosamine, ethylnitrosourea, methylnitrosourea, urethane.

on the basis of human data include aflatoxin B1 and the hormones used for assisted reproduction (in vitro fertilization). These substances are not typically found at federal contaminated sites; moreover, for many substances that are found at contaminated sites, the data on transplacental carcinogenesis are available only from animal studies.

Some chemicals may be acting as initiators following in utero exposures or prezygotic exposure of the male parent, with cancer formed only upon subsequent postnatal promotion and/or additional exposures (i.e. in utero exposure creates altered susceptibility to cancer later in life). This effect has been seen experimentally with various chemicals, including dioxin/dimethylbenzantracene (DMBA; Brown et al., 1998), 3-methylcholanthrene/butylated hydroxytoluene (Gressani et al., 1999), genistein or atrazine/DMBA (Hilakivi-Clarke et al., 1999; Fenton and Davis, 2002) and N-methyl-N-nitrosourea or PAHs/phenobarbital (Diwan et al., 1989). In utero initiation/postnatal promotion has been demonstrated in humans only for DES and radiation (Yamasaki et al., 1992).

The prenatal to adult cancer potency ratio has not been considered in the US EPA (2005a) supplemental guidance. The CalEPA (2009) has conducted a probabilistic analysis of the prenatal to adult potency ratio. The prenatal age window showed an increased sensitivity to the majority of the 14 carcinogens (22 potency ratio distributions) analyzed. The median of the prenatal ASF distribution was 2.9. However, because of the limited database and the considerable variability in available data, no recommendation on a default adjustment factor was proposed for prenatal exposures in the first and second trimesters. As rodents are born at a stage of maturation similar to that of a third-trimester human foetus, the trimester is included in the default ASF of 10 proposed for up to 2 years of age (i.e. total duration of 2.25 years). No other major regulatory agency has a default position for adjustment of risk calculations for prenatal exposures. While CalEPA (2009) illustrated how an ASF of 10 can be applied when the daily exposure (mg/kg-d) is known, the agency has not provided sample risk calculations for human exposure from known environmental concentrations.

Physiologically based pharmacokinetic (PBPK) modeling of transplacental transfer could theoretically better define the magnitude of increased susceptibility in the foetus. However, validated PBPK models are unlikely to become available in the near future, as the necessary data for modelling and reliable markers of foetal exposure are lacking, and the models themselves require further refinement (Anderson et al., 2000). Efforts to advance knowledge on issues such as the temporal profile and gene polymorphism in enzymes involved in carcinogen activation/detoxification and DNA repair enzymes in the foetus would facilitate development of better PBPK models. More work with animal models is needed to identify transplacental carcinogens and their mechanism of action, including interaction with target genes.

2.4 Dose Averaging for Less-Than-Lifetime Exposure during Puberty

Mutagenic carcinogens are generally more effective in rapidly dividing tissues. The higher rates of cell division provide more opportunities for carcinogens to interact with DNA and less time for DNA repair prior to cell division, which results in increased probability of initiation activity. During puberty, there is dramatic growth in reproductive and other related organs, including some parts of the brain, potentially making them more susceptible to mutagenic carcinogens acting at those sites.

Changes in physiological and biological processes during puberty could also alter susceptibility to the effects of some non-mutagenic carcinogens (e.g. endocrine-disrupting chemicals). On the basis of its analysis of the limited available data, the US EPA Science Advisory Board (US EPA, 2004) concluded that altered sensitivity to the development of cancer may occur when exposure takes place during puberty as compared with other exposure time windows.

3.0 PROPOSED INTERIM MEASURE FOR HUMAN HEALTH RISK ASSESSMENT FOR LESS-THAN-LIFETIME EXPOSURE TO CANCER-CAUSING AGENTS AT CONTAMINATED SITES

The CSD provides this interim guidance with regard to HHRA of carcinogenic agents, including short-term exposure and dose averaging. Risk assessments submitted to CSD should provide a rationale taking into consideration the mode of action at the tumour site in question.

3.1 Assessment of Cancer Risk for Non-Threshold Carcinogenic Effects

3.1.1 Carcinogenic Effects Acting Through a Mutagenic Mode of Action

The US EPA (2005 a, b) provides one of the most comprehensive analyses of the available data related to increased sensitivity when exposure to a carcinogen with a mutagenic mode of action occurs at early lifestages. As an interim measure, CSD has adapted the US EPA approach for contaminated site risk assessments.

The US EPA's default adjustment factor of 10 is supported by LMS modelling studies (Al-Zoughool and Krewski, 2008) indicating that a default factor of 6 should be applied to LADD-based cancer risk estimates for mutagens (i.e. to account for potential increased effectiveness of early-life exposure to an initiator). An additional factor of 1.6 may be applied to slope factors derived from rodent bioassays in which exposure begins in early adulthood (6–8 weeks of age), to give a total adjustment of 10 (6×1.6). This additional factor (1.6) is needed to account for the neonatal/infant period (i.e. from birth to 6–8 weeks of age).

This cancer risk assessment approach takes into account the varying sensitivity of different lifestages to cancer effects. The ILCR is estimated by summing the risk from each discrete exposure period. For non-threshold carcinogens acting through a mutagenic mode of action, it is recommended that ADAFs be applied to the cancer slope factor (or inhalation unit risk) with exposure averaged over a lifetime, to account for the sensitivity of the age-dependent exposure period. This approach can be illustrated by the equations below.

ILCR from oral exposure can be estimated using the following equation:

$$ILCR = \sum_i (LADD_i * SF_i)$$

$$= \sum_i (LADD_i * SF * ADAF_i)$$

Where:
$LADD_i$ = dose received during lifestage i averaged over a lifetime
SF_i = age-specific slope factor
SF = adult cancer slope factor (per mg/kg-d)
$ADAF_i$ = age-dependent adjustment factors for lifestage i

For exposure by inhalation, the following equation applies:

$$ILCR = \sum_i (C_{ai} * TR_i * UR * ADAF_i)$$

Where:
C_{ai} = concentration in air during lifestage i (mg/m^3)
TR_i = fraction of time exposed (yr/80 yr)
UR = adult cancer unit risk (per mg/m^3)
$ADAF_i$ = age-dependent adjustment factors for lifestage i

LADD is defined by the following equation:

LADD (mg/kg-d) = [ER * ED]/Lifetime or

LADD (mg/kg-d) = [C * IR * AF * ED] / [BW* Lifetime]

Where: ER = exposure rate (mg/kg-d)
C = chemical concentration in the media (mg/m^3 or mg/kg)
IR = intake rate of medium (m^3/day or kg/day)
AF = medium-specific absorption factor
ED = exposure duration (days)
BW = body weight (kg)
Lifetime = days in a lifetime = 365 d/yr * 80 yr

$LADD_i$ is defined as the dose received during lifestage i averaged over a lifetime and can be represented by the following equation:

$LADD_i$ (mg/kg-d) = [C_i * IR_i * AF * ED_i] / [BW_i * Lifetime]

Where: C_i = chemical concentration in the media a person is exposed to during lifestagei (mg/m^3/ or mg/kg)
IR_i = intake rate of medium during $lifestage_i$ (m^3/day or kg/day)
AF = medium-specific absorption factor
ED_i = exposure duration during $lifestage_i$ (days)
BW_i = body weight during $lifestage_i$ (kg)
Lifetime = days in a lifetime = 365 d/yr * 80 yr

The US EPA's ADAFs have been adjusted to fit the age groups presented in the PQRA (Health Canada, 2004). Table 3.1 summarizes the default adjusted ADAFs that CSD recommends for contaminated site risk assessments of non-threshold carcinogens with a mutagenic mode of action. These default factors can be applied when age-specific cancer slope factors, age-specific inhalation unit risks or chemical-specific data are not available. In scenarios where exposure periods do not match the CSD's age groups, CSD recommends that the US EPA's ADAFs be applied. For example, if exposure occurs only between 7 months and less than 2 years of age, the adjustment factor of 10 would apply. Likewise, if exposure occurs only between 12 and < 16 years of age, the ADAF of 3 would apply. Worked examples are illustrated in Section 4.

When age-specific cancer slope factors, age-specific inhalation unit risks or chemical-specific data are available for a susceptible lifestage, it is preferable to use these data directly to evaluate risks for the chemical and the lifestage on a case-by-case basis. In these cases, such as vinyl chloride, application of default ADAFs would not be appropriate. The US EPA recommends twice the adult inhalation unit risk to be applied for estimating incremental cancer risk from continuous exposure to vinyl chloride from birth.

For intermittent exposures, the total cancer risk will be the sum of each discrete exposure with lifestage-specific potency and exposure averaged over a lifetime.

Table 3.1 Recommended interim adjusted age-dependent adjustment factors (ADAFs) for cancer risk assessment at contaminated sites for carcinogenic effects via a mutagenic mode of action

Lifestage	Age	Adjusted age-dependent adjustment factor (ADAF)[a]
Infant	0–6 months	10
Toddler	7 months–4 years	5[b]
Child	5–11 years	3
Teenager	12–19 years	2[c]
Adult	20+	1

[a] US EPA (2005 a, b), except as noted.

[b] $ADAF_{7\ mo–4\ yr}$ = ($ADAF_{0–<2}$ * D7 mo-1 / $D_{7\ mo–4}$) + ($ADAF_{2–4}$ * $D_{2–4}$ / $D_{7\ mo–4}$) = 10 * 1.5/4.5 + 3 * 3/4.5 = 5, and D_i = exposure duration in years

[c] $ADAF_{12–19}$ = ($ADAF_{12–<16}$ * $D_{12–15}$ / $D_{12–19}$) + ($ADAF_{16+}$ * $D_{16–19}$ / $D_{12–19}$) = 3 * 4/8 + 1 * 4/8 = 2, and D_i = exposure duration in years

The prenatal period (in utero) may be a sensitive window of exposure for some cancers, and an ADAF of 3 (or 2) may not be sufficient to address increased sensitivity during puberty, but further study is needed to delineate more accurately the magnitude of increased sensitivity. CSD will continue to evaluate the issue as new research data become available and as other regulatory agencies consider this issue. In the interim, CSD recommends addressing the risks associated with mutagenic carcinogen exposure during these lifestages on a case-by-case basis.

To date, among the carcinogens for which CSD provides TRV values, the US EPA (2009, 2011a) has identified carcinogenic PAHs, trichloroethylene and vinyl chloride as acting through a mutagenic mode of action. After a toxicological review, the US EPA (2010) proposed that chromium (VI) is "likely carcinogenic to humans" via the oral route of exposure and hypothesized a mutagenic mode of action for its carcinogenicity. This US EPA report is currently undergoing review (US EPA, 2011b).

3.1.2 Carcinogenic Effects Acting Through an Unknown Mode of Action

For carcinogenic effects with an unknown mode of action or for which the burden of proof for a threshold mode of action has not been met, CSD recommends treating the effect as non-threshold. The mathematical equations used to estimate cancer risk for mutagenic carcinogens can be applied in these situations. If chemical-specific data are available on quantitative differences between early lifestages and adults, an analysis of the differences could be used to adjust risk estimates for early life exposures. Otherwise, CSD does not recommend extending the default age-dependent potency adjustment factors to these carcinogenic effects. This position would be analogous to recommending a default ADAF of 1 for all lifestages.

The non-threshold approach for carcinogenicity risk assessment arises initially from the mechanistic, one-hit model, which assumes that only one-hit is required for the cell to be altered. The role of the body's defence mechanism (e.g. repair, apoptosis), which has an influence on the health outcome, is not considered. CSD considers the use of the linear low-dose extrapolation approach (without further adjustment) to be sufficiently conservative and to provide adequate public health protection for carcinogenic effects with a mode of action that is not mutagenic.

3.2 Assessment of Health Risk from Threshold Carcinogens

The CSD does not recommend a default age-specific adjustment for carcinogenic effects found to have a non-linear dose-response relationship (i.e. threshold) at low doses at this time. An adjustment can be made on a chemical-specific basis if supported by experimental data. These substances would be included in an HHRA using a TDI (or a TC in the case of inhalation exposure).

The CSD recommends that dose averaging for short-term exposure for these types of carcinogenic effects be performed in the same way as for other substances with threshold effects. It is important that dose averaging does not underestimate the potential for threshold carcinogenic effects. Without a sound basis for doing so (i.e. it cannot be a default assumption), the human health risk assessor should not simply mathematically spread out a short-term dose over a long period and conclude that the short-term dose is toxicologically equivalent to a lower dose over the long period. In short, CSD recommends that the exposure be averaged over the total actual exposure period and compared with the appropriate TRV. A scientific rationale is required to support any proposed amortization (dose averaging beyond actual exposure period) to ensure that short-term risks are not underestimated. This analysis needs to be done on a chemical-specific basis.

3.3 Assessment of Health Risk from Non-Cancer Health Effects

For short-term exposure, carcinogenic agents may elicit other chronic and short-term non-cancer health effects, depending on the magnitude of exposure. Short-term effects can be evaluated for potential critical receptors/lifestages[5] using short-term TRVs where available (either from other regulatory agencies or derived from literature values, as per Health Canada, 2010, guidance) and applicable to the exposure scenarios. If short-term TRVs are not available, such evaluation can be conducted according to relevant dose-response information from toxicity studies. It is also important to consider whether the short-term exposure might elicit early biological key events that might progress to health effects at a later date. In many cases, both the short-term and chronic non-carcinogenic effects, rather than carcinogenicity, may be the main determinant of the risk from short-term exposure. For example, keratosis rather than carcinogenicity could drive a risk assessment for exposure to high levels of arsenic in soil (e.g. 100 mg/kg) in a less-than-lifetime exposure scenario.

[5] Including relevant receptors/lifestages with the highest exposure and receptors/lifestages associated with specific sensitivity to the toxicity of the contaminants

4.0 WORKED EXAMPLES

4.1 Assessment of Lifetime Risk Associated with Exposure to a Carcinogen with a Mutagenic Mode of Action

When assessing cancer risk, it is important to consider both the difference in exposure and the increased susceptibility for early lifestages. ADAFs in dose-response (i.e. slope factors) need to be combined with age-specific exposure estimation.

The following examples illustrate how to integrate potential lifestage differences in exposure and susceptibility in risk estimation for both lifetime and less-than-lifetime exposure during a specific period in life. The examples consider risk from oral exposure. Risks associated with inhalation exposure to mutagenic carcinogens can be calculated in a similar manner by applying the appropriate ADAFs with the corresponding inhalation unit risk estimates using appropriate estimates of exposure concentrations.

These calculations assume that the available slope factor does not specifically consider early-life exposure. In the case of carcinogens for which age-specific (and in particular early-life) slope factors are available, these factors should be used instead of adjusting the adult slope factor.

4.1.1 Example 1: Exposure Occurs Over a Lifetime

Consider a scenario of exposure to a hypothetical carcinogen with a mutagenic mode of action present in drinking water. The oral slope factor derived from a typical animal study (i.e. in which dosing begins after puberty) is estimated to be 2 $(mg/kg\text{-}d)^{-1}$. The absorption factor of the carcinogen from drinking water is 1. The carcinogen is present in drinking water at 0.001 mg/L.

To calculate lifetime risk for a population with average life expectancy of 80 years, sum the risk associated with each of the time periods, applying recommended ADAFs to the relevant time periods:

- risk for the infant—first 6 months of life (where ADAF = 10),
- risk for toddler—6 months through 4 years of life (ADAF = 5),
- risk for child—ages 5 through 11 (ADAF = 3),
- risk for teenager—ages 12 through 19 (ADAF = 2) and
- risk for adult—ages 20 to 80 (ADAF = 1)

Thus, the ILCR equals the sum of the various age groups:

- Risk for infant
  = slope factor × ADAF x $LADD_{0–6\ mo}$
  = 2 $(mg/kg\text{-}d)^{-1}$ × 10 × [(0.001 mg/L × 0.3 L/d / 8.2 kg) × 0.5 yr/80yr]
  = 5 x 10^{-6}
- Risk for toddler
  = slope factor × ADAF × $LADD_{7\ mo–4}$
  = 2 $(mg/kg\text{-}d)^{-1}$ × 5 × [(0.001 mg/L × 0.6 L/d / 16.5 kg) × 4.5 yr/80yr]
  = 2 × 10^{-5}
- Risk for children
  = slope factor × ADAF × $LADD_{5–11}$
  = 2 $(mg/kg\text{-}d)^{-1}$ × 3 × [(0.001 mg/L × 0.8 L/d / 32.9 kg) × 7 yr/80yr]
  = 1 × 10^{-5}
- Risk for teenager
  = slope factor × ADAF × $LADD_{12–19}$
  = 2 $(mg/kg\text{-}d)^{-1}$ × 2 × [(0.001 mg/L × 1 L/d / 59.7 kg) × 8 yr/80yr]
  = 8 × 10^{-6}
- Risk for adult
  = slope factor × ADAF × $LADD_{20+}$
  = 2 $(mg/kg\text{-}d)^{-1}$ x 1 × [(0.001 mg/L × 1.5 L/d / 70.7 kg) × 60 yr/80yr]
  = 3 × 10^{-5}

Total ILCR
= 5 × 10^{-6} + 2 × 10^{-5} + 1 × 10^{-5} + 8 × 10^{-6} + 3 × 10^{-5}
= 7 × 10^{-5}

4.1.2 Example 2: Exposure Occurs at Less Than 2 Years of Age

Consider a scenario in which exposure to the same hypothetical carcinogen only takes place for a limited period of time, e.g. in a family that lives near a source of contamination for a short time and then moves away. The exposure may occur with a child aged from 1 to less than 2 years of age. It is important to consider lifestage-specific differences in exposure. The carcinogen has an oral cancer slope factor of 2 $(mg/kg\text{-}d)^{-1}$ derived from a typical animal study, and the concentration in drinking water is 0.001 mg/L.

As this exposure period does not match CSD age groupings, the US EPA's ADAF applies[6].

Risk = slope factor × ADAF × $LADD_{1-<2}$
Risk = 2 $(mg/kg\text{-}d)^{-1}$ × 10 × 0.001 mg/L × 0.6 L/d/16.5 kg × 1 yr/80 yrs
= 9 × 10^{-6}

Thus, the incremental lifetime cancer risk from 1 year of exposure to a carcinogen with a mutagenic mode of action assuming initial exposure at 1 year of age is estimated at 9 × 10^{-6}.

[6] Please note that when the exposure period matches a CSD age grouping, CSD recommends that its ADAFs be used.

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Exhibit G

Technical Support Document for Cancer Potency Factors:

Methodologies for derivation, listing of available values, and adjustments to allow for early life stage exposures.

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EXECUTIVE SUMMARY

The Air Toxics "Hot Spots" Information and Assessment Act (AB 2588, Connelly) was enacted in September 1987. Under this Act, stationary sources of air pollution are required to report the types and quantities of certain substances their facilities routinely release into the air. The goals of the Air Toxics "Hot Spots" Act are to collect emission data, identify facilities having localized impacts, ascertain health risks posed by those facilities, notify nearby residents of significant risks and reduce emissions from significant sources.

The Technical Support Document for Cancer Potency Factors (TSD) contains cancer unit risks and potency factors for 107 of the 201 carcinogenic substances or groups of substances for which emissions must be quantified in the Air Toxics Hot Spots program. These unit risks are used in the cancer risk assessment of facility emissions.

The purpose of this revision to the TSD is to provide updated calculation procedures used to derive the estimated unit risk and cancer potency factors, and to describe the procedures used to consider the increased susceptibility of infants and children compared to adults to carcinogens. This updates cancer risk assessment methods originally laid out in the California Department of Health Services' Guidelines for Chemical Carcinogen Risk Assessment (CDHS, 1985), and more recently summarized in the previous Hot Spots technical support document Part II (OEHHA, 2005a). Summaries of cancer potency factors and the underlying data are provided in Appendices A and B, which are subject to ongoing updates but were not changed as part of the revision process which created this TSD.

The procedures used to consider the increased susceptibility to carcinogens of infants and children as compared to adults include the use of age-specific weighting factors in calculating cancer risks from exposures of infants, children and adolescents, to reflect their anticipated special sensitivity to carcinogens

This document is one part of the Air Toxics Hot Spots Program Risk Assessment Guidelines. The other documents originally included in the Guidelines are Part I: Technical Support Document for the Determination of Acute Toxicity Reference Exposure Levels for Airborne Toxicants; Part III: Technical Support Document for Determination of Noncancer Chronic Reference Exposure Levels; Part IV: Technical Support Document for Exposure Assessment and Stochastic Analysis; Part V: Air Toxic Hot Spots Program Risk Assessment Guidelines. As a part of the same revision process which led to production of this revised TSD on cancer potencies, the original TSDs for Acute and Chronic Reference Exposure Levels have been replaced with a new unified TSD for Acute, 8-hour and Chronic Reference Exposure Levels.

The major changes to the TSD include the following:

- Based on the OEHHA analysis of the potency by lifestage at exposure, OEHHA proposes weighting cancer risk by a factor of 10 for exposures that occur from the third trimester of pregnancy to 2 years of age, and by a factor of 3 for exposures that occur from 2 years through 15 years of age. We intend to apply this weighting factor to all carcinogens,

regardless of purported mechanism of action, unless chemical-specific data exist to the contrary. In cases where there are adequate data for a specific carcinogen of potency by age, we would use the data to make any adjustments to risk.

- OEHHA proposes to use the Benchmark Dose method to compute potency factors rather than the more traditional linearized multistage model (LMS), although the LMS will still be used in some instances. The BMDL model essentially uses an empirical fit to the data (usually best with the multistage model), and then extrapolates with a straight line from the 95% lower confidence limit of the BMD (BMDL) to zero. This method is simpler and does not assume any underlying theoretical mechanisms at the low dose range. The BMDL method results in estimates of potency very similar to those obtained using the LMS method.

- OEHHA will use scaling based on body weight to the ¾ power, rather than to the ⅔ power.

- OEHHA's evaluations of the carcinogenicity of chemicals generally follow the guidelines laid out by IARC for identification and classification of potential human carcinogens, which are described in detail in the most recent revision of the *Preamble* to the IARC monographs series (IARC, 2006).

PREFACE

The Air Toxics "Hot Spots" Information and Assessment Act (AB 2588, Connelly) was enacted in September 1987. Under this Act, stationary sources are required to report the types and quantities of certain substances their facilities routinely release into the air. The goals of the Air Toxics "Hot Spots" Act are to collect emission data, identify facilities having localized impacts, ascertain health risks posed by those facilities, notify nearby residents of significant risks and reduce emissions from significant sources.

The Technical Support Document for Cancer Potency Factors (TSD) contains cancer unit risks and potency factors for 107 of the 201 carcinogenic substances or groups of substances for which emissions must be quantified in the Air Toxics Hot Spots program. These unit risks are used in risk assessment of facility emissions. The TSD provides updated calculation procedures used to derive the estimated unit risk and cancer potency factors, and procedures to consider early-life susceptibility to carcinogens. Summaries of cancer potency factors and the underlying data are provided in Appendices A and B.

In this document, OEHHA is responding to the requirements of the 1999 Children's Environmental Health Protection Act (SB25, Escutia) by revising the procedures for derivation and application of cancer potency factors to take account of general or chemical-specific information which suggests that children may be especially susceptible to certain carcinogens (OEHHA, 2001a). The revised cancer potency derivation procedures described will not be used to impose any overall revisions of the existing cancer potencies, although they do reflect updated methods of derivation. However, individual cancer potency values will be reviewed as part of the ongoing re-evaluation of health values mandated by SB 25, and revised values will be listed in updated versions of the appendices to this document as necessary. The revisions also include the use of weighting factors in calculating cancer risks from exposures of infants, children and adolescents, to reflect their anticipated special sensitivity to carcinogens. Similar legal mandates to update risk assessment methodology and cancer potencies apply to the OEHHA program for development of Public Health Goals (PHGs) for chemicals in drinking water, and Proposition 65 No Significant Risk Levels (NSRLs). The NSRLs may also be revised to reflect concerns for children's health. Revising these numbers will require the originating program to reconsider the value in an open public process. For example, OEHHA would need to release any revised potency factors for public comment and review by the Scientific Review Panel on Toxic Air Contaminants (SRP) prior to adoption under the TAC program. The procedures for outside parties to request reevaluation of cancer potency values by the programs which originated those values are listed in Appendix G.

Appendices A and B provide previously adopted Cal/EPA values which were included in the previous version of the TSD for Cancer Potency Factors (OEHHA, 2005a). Cal/EPA values were developed under the Toxic Air Contaminant (TAC) program, the PHG program, the Proposition 65 program, or in some cases specifically for the Air Toxics Hot Spots program. All the Cal/EPA values are submitted for public comments and external peer review prior to adoption by the program of origin. In the future, new values developed by the Toxic Air Contaminants or Hot Spots programs or other suitable sources will be added as these are approved.

Some U.S. EPA IRIS cancer unit risk values were adopted under the previous versions of these guidelines, and these values will continue to be used unless and until revised by Cal/EPA. U.S. EPA has recently revised its cancer risk assessment guidelines (U.S. EPA, 2005a). Some of the recommended changes in methodology could result in slightly different potency values compared to those calculated by the previous methodology, although in practice a number of the recommendations (for example, the use of ¾ power of the body weight ratio rather than ⅔ power for interspecies scaling) have been available in draft versions of the revised policy for some time and appear in many more recent assessments. U.S. EPA has stated that cancer potency values listed in IRIS will not be revisited solely for the purpose of incorporating changes in cancer potency value calculation methods contained in the revised cancer risk assessment guidelines. U.S. EPA has also issued supplementary guidelines on assessing cancer risk from early-life exposure (U.S. EPA, 2005b).

OEHHA uses a toxic equivalency factor procedure for dioxin-like compounds, including polychlorinated dibenzo-*p*-dioxins, dibenzofurans and polychlorinated biphenyls (PCBs). The Toxicity Equivalency Factor scheme (TEF_{WHO-97}) developed by the World Health Organization/European Center for Environmental Health (WHO-ECEH) is used for determining cancer unit risk and potency values for these chemicals where individual congener emissions are available (Appendix C).

This document is one part of the Air Toxics Hot Spots Program Risk Assessment Guidelines. The other documents originally included in the Guidelines are Part I: Technical Support Document for the Determination of Acute Toxicity Reference Exposure Levels for Airborne Toxicants; Part III: Technical Support Document for Determination of Noncancer Chronic Reference Exposure Levels; Part IV: Technical Support Document for Exposure Assessment and Stochastic Analysis; Part V: Air Toxic Hot Spots Program Risk Assessment Guidelines. As a part of the same revision process which led to production of this revised TSD on cancer potencies, the original TSDs for Acute and Chronic Reference Exposure Levels have been replaced with a new unified TSD for Acute, 8-hour and Chronic Reference Exposure Levels.

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Appendix B. Chemical-specific summaries of the information used to derive unit risk and cancer potency values.

Appendix C. A description of the use of toxicity equivalency factors for determining unit risk and cancer potency factors for polychlorinated dibenzo-*p*-dioxins, dibenzofurans and dioxin-like polychlorinated biphenyls.

Appendix D. A listing of Toxic Air Contaminants identified by the California Air Resources Board.

Appendix E. Descriptions of the International Agency for Research on Cancer (IARC) and U.S. Environmental Protection Agency (U.S. EPA) carcinogen classifications.

Appendix F. An asbestos quantity conversion factor for calculating asbestos concentrations expressed as 100 fibers/m^3 from asbestos concentrations expressed as $\mu g/m^3$.

Appendix G. Procedures for revisiting or delisting cancer potency factors by the program of origin.

Appendix H. Exposure routes and studies used to derive cancer unit risks and slope factors.

Appendix I. "Assessing susceptibility from early-life exposure to carcinogens": Barton *et al.*, 2005 (from *Environmental Health Perspectives)*.

Appendix J. "In Utero and Early Life Susceptibility to Carcinogens: The Derivation of Age-at-Exposure Sensitivity Measures" – conducted by OEHHA's Reproductive and Cancer Hazard Assessment Branch.

INTRODUCTION

The Technical Support Document (TSD) for Describing Available Cancer Potency Factors provides technical information support for the Air Toxics Hot Spots Program Risk Assessment Guidelines. The TSD consists of 12 sections:

1. The TSD introduction.

2. A description of the methodologies used to derive the unit risk and cancer potency values listed in the lookup table.

3. A lookup table containing unit risk and cancer potency values. (Appendix A)

4. Chemical-specific summaries of the information used to derive unit risk and cancer potency values. (Appendix B).

5. A description of the use of toxicity equivalency factors for determining unit risk and cancer potency factors for polychlorinated dibenzo-*p*-dioxins, dibenzofurans and dioxin-like polychlorinated biphenyls (Appendix C).

6. A listing of Toxic Air Contaminants identified by the California Air Resources Board (Appendix D).

7. Descriptions of the International Agency for Research on Cancer (IARC) and U.S. Environmental Protection Agency (U.S. EPA) carcinogen classifications (Appendix E).

8. An asbestos quantity conversion factor for calculating asbestos concentrations expressed as 100 fibers/m^3 from asbestos concentrations expressed as $\mu g/m^3$ (Appendix F).

9. Procedures for revisiting or delisting cancer potency factors by the program of origin (Appendix G).

10. Exposure routes and studies used to derive cancer unit risks and slope factors (Appendix H).

11. "Assessing susceptibility from early-life exposure to carcinogens": Barton *et al*., 2005 (from *Environmental Health Perspectives)* (Appendix I).

12. "In Utero and Early Life Susceptibility to Carcinogens: The Derivation of Age-at-Exposure Sensitivity Measures" – conducted by OEHHA's Reproductive and Cancer Hazard Assessment Branch (Appendix J)

SELECTION OF CANCER POTENCY VALUES

The Office of Environmental Health Hazard Assessment (OEHHA) has developed a number of cancer potencies for use in the Toxic Air Contaminants and Air Toxics Hot Spots programs. This document also provides summaries of cancer potency factors which were originally developed for other California Environmental Protection Agency (Cal/EPA) programs, or by the U.S. EPA. These were reviewed for accuracy, reliance on up-to-date data and methodology, and applicability in the context of the Air Toxics Hot Spots program. Values found appropriate were adopted after public and peer review rather than devoting the resources necessary for a full *de novo* assessment. Thus, cancer potency values (CPF) included in the Technical Support Document (TSD) for Cancer Potency Factors were from the following sources:

1. Toxic Air Contaminant documents

2. Standard Proposition 65 documents

3. U.S.EPA Integrated Risk Information Systems (Office of Health and Environmental Assessment, U.S.EPA)

4. Expedited Proposition 65 documents

5. Other OEHHA assessments , for example for the drinking water program.

All the cancer potency value sources used generally follow the recommendations of the National Research Council on cancer risk assessment (NRC, 1983, 1994). All Cal/EPA program documents undergo a process of public comment and scientific peer review prior to adoption, although the procedures used vary according to the program. The publication procedure for Toxic Air Contaminant documents includes a public comment period and review by the Scientific Review Panel on Toxic Air Contaminants (SRP) before identification of a Toxic Air Contaminant by the Air Resources Board of the California Environmental Protection Agency (Cal/EPA). Furthermore, a petition procedure is available to initiate TAC document review and revision if appropriate because of new toxicity data. Documents developed for the Air Toxics Hot Spots program similarly undergo public comment and peer review by the SRP before adoption by the Director of OEHHA. The standard Proposition 65 document adoption procedure includes a public comment and external peer review by the Proposition 65 Carcinogen Identification Committee. The expedited Proposition 65 document adoption procedure included a public comment period. Risk assessments prepared for development of Public Health Goals (PHGs) for chemicals in drinking water are subject to two public comment periods before the final versions and responses to comments are published on the OEHHA Web site. PHG documents may also receive external peer review. Documents from U.S. EPA's Integrated Risk Information System (IRIS) receive external peer review and are posted on the Internet for public viewing during the external peer review period, and any public comments submitted are considered by the originating office. Additionally, public comment may be solicited during the document posting period. Future preference for use of developed cancer potency factors/unit risks will be done on a case by case basis. Preference will be given to those assessments most relevant to inhalation exposures of the California population, to the most recent derivations using the latest data sets and scientific methodology, and to those having undergone the most open and extensive peer review process.

CANCER RISK ASSESSMENT METHODOLOGIES

This section describes in general the methodologies used to derive the cancer unit risk and potency factors listed in this document. As noted in the Preface to this document, no new cancer unit risks or potency factors were developed for this document. All of the values contained here were previously developed in documents by Cal/EPA or U.S. EPA. Following the recommendations of the National Academy of Sciences (NRC, 1983), Cal/EPA and U.S. EPA have both used formalized cancer risk assessment guidelines, the original versions of which (California Department of Health Services, 1985; U.S. EPA, 1986) were published some time ago. Both these guidelines followed similar methodologies.

In the twenty years since these original guidelines were published there have been a number of advances in the methodology of cancer risk assessment. There have additionally been considerable advances in the quantity of data available not only from animal carcinogenesis bioassays and epidemiological studies, but also from mechanistic studies of carcinogenesis and related phenomena. Some of these advances have been incorporated into newer risk assessments by both agencies on a more or less *ad hoc* basis. There has also been an ongoing effort to provide updated risk assessment guidance documents. In 1995, U.S. EPA released for public comment the "Proposed and Interim Guidelines for Carcinogen Risk Assessment", which was the first of several drafts released for public comment. Many risk assessments appearing since then have used elements of the recommendations contained in that document, in spite of its draft status. A final version of the U.S. EPA's revised cancer risk assessment guidelines has now been released (U.S. EPA, 2005a). Although these new guidelines incorporate a number of substantial changes from their predecessors (U.S. EPA, 1986; 1995), U.S. EPA has stated that cancer potency values listed in IRIS will not be revisited solely for the purpose of incorporating changes in cancer potency value calculation methods.

Cal/EPA has not produced a revised cancer risk assessment guideline document to replace the original version (DHS, 1985). Rather, Cal/EPA has relied on incorporating new data and methodologies as these became available, and described the methods used on a case by case basis in the individual risk assessment documents where these went beyond the original guidance. However, this revision of the TSD for cancer potencies provides a convenient opportunity to summarize the current status of the methodology used by OEHHA for the air toxics programs, and also to highlight points of similarity to, and difference from, the recommendations of U.S. EPA (2005a).

In this document, OEHHA intends to follow the recommendations of the NRC (1994) in describing a set of clear and consistent principles for choosing and departing from default cancer risk assessment options. NRC identified a number of objectives that should be taken into account when considering principles for choosing and departing from default options. These include, "protecting the public health, ensuring scientific validity, minimizing serious errors in estimating risks, maximizing incentives for research, creating an orderly and predictable process, and fostering openness and trustworthiness". The OEHHA cancer risk methodologies discussed in this document are intended to generally meet those objectives cited above.

Hazard Identification

This section will describe: 1) how weight of evidence evaluations are used in hazard evaluation; 2) guidelines for inferring causality of effect; 3) the use of human and animal carcinogenicity data, as well as supporting evidence (*e.g.,* genetic toxicity and mechanistic data); 4) examples of carcinogen identification schemes.

Evaluation of Weight of Evidence

In evaluating the range of evidence on the toxicity and carcinogenicity of a compound, mixture or other agent, a "weight-of-evidence" approach is generally used to describe the body of evidence on whether or not exposure to the agent causes a particular effect. Under this approach, the number and quality of toxicological and epidemiological studies, as well as the consistency of study results and other sources of data on biological plausibility, are considered. Diverse and sometimes conflicting data need to be evaluated with respect to possible explanations of differing results. Consideration of methodological issues in the review of the toxicological and epidemiological literature is important in evaluating associations between exposure to an agent and animal or human health effects. This aspect of the evaluation process has received particular emphasis with respect to epidemiological data, where concerns as to the statistical and biological significance and reliability of the data and the impacts of confounding and misclassification are pressing. Such concerns are also relevant to some extent in the interpretation of animal bioassay data and mechanistic studies. Although the test animals, laboratory environment and characterization of the test agent are usually much better controlled than the equivalent parameters in an epidemiological study, the small sample size can be problematic. In addition, there are uncertainties associated with extrapolation of biological responses from test animal species to humans.

Criteria for Causality

There has been extensive discussion over the last two centuries on causal inference. This has particularly related to epidemiological data, but is also relevant to interpretation of animal studies. Most epidemiologists utilize causal inference guidelines based on those proposed by Bradford Hill (1971). OEHHA has relied on these and on recommendations by IARC (2006), the Institute of Medicine (2004), the Surgeon General's Reports on Smoking (U.S. DHHS, 2004) and standard epidemiologic texts (*e.g.,* Lilienfeld and Lilienfeld, 1980; Rothman and Greenland, 1998). The criteria for determination of causality used by OEHHA have been laid out in various risk assessment documents. The summary below is adapted from the Health Effects section of the document prepared to support the identification of environmental tobacco smoke (ETS) as a Toxic Air Contaminant (OEHHA, 2005b).

1. *Strength of Association*. A statistically significant strong association, which is easier to detect if there is a high relative risk, between a factor and a disease is often viewed as an important criterion for inferring causality because, all other things being equal, a strong and statistically significant association makes alternative explanations for the disease less likely. However, as discussed in Rothman and Greenland (1998), the fact that a relative risk is small in magnitude does not exclude a casual association between the risk factor and the outcome in question. Since it is more difficult to detect (*i.e.*, reach statistical

significance) a small magnitude risk, it is just as likely to indicate causality as a larger magnitude risk.

When assessing all evidence, it is important to consider the strength of the study design (particularly controlling for confounding variables, obtaining an unbiased sample, measurement error) and the level of statistical significance (*i.e.*, the ability to exclude a Type I [false positive] error). The power of the study to detect biologically meaningful effects (*i.e.*, the risk of a Type II [false negative] error) is important in considering studies that do not reach traditional (*i.e.*, $P < 0.05$) statistical significance, particularly if the biological endpoint is serious. If the outcome is serious and the study small (*i.e.*, low power), a larger P value (*e.g.*, $P < 0.10$) may be adequate evidence for identifying an effect.

There are a number of examples of statistically significant, small magnitude associations that are widely accepted as causal, such as causal links between air pollution and cardiovascular/pulmonary mortality and between second-hand smoke exposure and various cancers and heart disease. From a public health perspective, even a small magnitude increase in risk for a common disease can mean large numbers of people affected by the health outcome when exposure is frequent and widespread, as measured by the population attributable risk or attributable fraction. Small magnitude of association must not be confused with statistical significance, which is much more important.

2. *Consistency of Association.* If several investigations find an association between a factor and a disease across a range of populations, geographic locations, times, and under different circumstances, then the factor is more likely to be causal. Consistency argues against hypotheses that the association is caused by some other factor(s) that varies across studies. Unmeasured confounding is an unlikely explanation when the effect is observed consistently across a number of studies in different populations.

   Associations that are replicated in several studies of the same design or using different epidemiological approaches or considering different sources of exposure and in a number of geographical regions are more likely to represent a causal relationship than isolated observations from single studies (IARC, 2006). If there are inconsistent results among investigations, possible reasons are sought, such as adequacy of sample size or control group, methods used to assess exposure, or range in levels of exposure. The results of studies judged to be rigorous are emphasized over those of studies judged to be methodologically less rigorous. For example, studies with the best exposure assessment are more informative for assessing the association between ETS and breast cancer than studies with limited exposure assessment, all else being equal.

3. *Temporality.* Temporality means that the factor associated with causing the disease occurs in time prior to development of the disease. The adverse health effect should occur at a time following exposure that is consistent with the nature of the effect. For example, respiratory irritation immediately following exposure to an irritant vapor is temporally consistent, whereas irritation noted only years later may not be. On the other hand, tumors, noted immediately following exposure, might be temporally inconsistent with a causal relationship, but tumors arising after a latency period of months (in rodents) or years (in rodents or humans) would be temporally consistent.

4. *Coherence and Biological Plausibility.* A causal interpretation cannot conflict with what is known about the biology of the disease. The availability of experimental data or mechanistic theories consistent with epidemiological observations strengthens conclusions of causation. For example, the presence of known carcinogens in tobacco smoke supports the concept that exposure to tobacco smoke could cause increased cancer risk. Similarly, if the mechanism of action for a toxicant is consistent with development of a specific disease, then coherence and biological plausibility can be invoked. It should be noted that our understanding of the biology of disease, and therefore biological plausibility, changes in light of new information which is constantly emerging from molecular biology (including epigenetics), and from new clinical and epidemiological investigations revealing effects influenced by genetic polymorphisms, pre-existing disease, and so forth.

5. *Dose-Response.* A basic tenet of toxicology is that increasing exposure or dose generally increases the response to the toxicant. While dose-response curves vary in shape and are not necessarily always monotonic, an increased gradient of response with increased exposure makes it difficult to argue that the factor is not associated with the disease. To argue otherwise necessitates that an unknown factor varies consistently with the dose of the substance and the response under question. While increased risk with increasing levels of exposure is considered to be a strong indication of causality, absence of a graded response does not exclude a causal relationship (IARC, 2006).

   The dose-response curves for specific toxic effects may be non-monotonic. Under appropriate circumstances, where the dose response shows saturation, the effect of exposures could be nearly maximal, with any additional exposure having little or no effect. In some instances, a response is seen strongly in susceptible subpopulations, and the dose-response is masked by mixing susceptible and non-susceptible individuals in a sample. Further, there are examples of U-shaped or inverted U-shaped dose-response curves, (*e.g.*, for endocrine disrupters) (Almstrup et al., 2002; Lehmann et al., 2004). Finally, timing of exposure during development may mask an overall increase in risk with increasing dose.

6. *Specificity.* Specificity is generally interpreted to mean that a single cause is associated with a single effect. It may be useful for determining which microorganism is responsible for a particular disease, or associating a single carcinogenic chemical with a rare and characteristic tumor (*e.g.*, liver angiosarcoma and vinyl chloride, or mesothelioma and asbestos). However, the concept of specificity is not helpful when studying diseases that are multifactorial, or toxic substances that contain a number of individual constituents, each of which may have several effects and/or target sites.

7. *Experimental evidence.* While experiments are often conducted over a short period of time or under artificial conditions (compared to real-life exposures), experiments offer the opportunity to collect data under highly controlled conditions that allow strong causal conclusions to be drawn. Experimental data that are consistent with epidemiological results strongly support conclusions of causality. There are also "natural experiments" that can be studied with epidemiological methods, such as when exposure of a human population to a substance declines or ceases; if the effect attributed to that exposure decreases, then there is evidence of causality. One example of this is the drop in heart disease death and lung cancer risk after smoking cessation.

It should be noted that the causal criteria are guidelines for judging whether a causal association exists between a factor and a disease, rather than hard-and-fast rules. Lilienfeld and Lilienfeld (1980) note that "*In medicine and public health, it would appear reasonable to adopt a pragmatic concept of causality. A causal relationship would be recognized to exist whenever evidence indicates that the factors form part of the complex of circumstances that increases the probability of the occurrence of disease and that a diminution of one or more of these factors decreases the frequency of that disease. After all, the reason for determining the etiological factors of a disease is to apply this knowledge to prevent the disease.*" Rothman and Greenland (2005) discuss the complexities of causation and the use of rules and deductive methods in causal inference. They also concur with Bradford Hill and others that a determination of causality is a pragmatic conclusion rather than an absolute verdict, and advocate that these criteria should be seen as "*deductive tests of causal hypotheses".*

Data Sources

Human studies: epidemiology, ecological studies and case reports

The aim of a risk assessment for the California Air Toxics programs is to determine potential impact on human health. Ideally therefore, the hazard identification would rely on studies in humans to demonstrate the nature and extent of the hazard. However, apart from clinical trials of drugs, experimental studies of toxic effects in human subjects are rarely undertaken or justifiable. Pharmacokinetic studies using doses below the threshold for any toxic effect have been undertaken for various environmental and occupational agents, but are not usually regarded as appropriate for suspected carcinogens.

The human data on carcinogens available to the risk assessor therefore mostly consist of epidemiological studies of existing occupational or environmental exposures. It is easier to draw reliable inferences in situations where both the exposures and the population are substantial and well-defined, and accessible to direct measurement rather than recall. Thus, many important findings of carcinogenicity to humans are based on analysis of occupational exposures. Problems in interpretation of occupational epidemiological data include simultaneous exposure to several different known or suspected carcinogens, imprecise quantification of exposures and confounding exposures such as active or passive tobacco smoking. The historical database of occupational data has a bias towards healthy white adult males. Thus, the hazard analysis of these studies may not accurately characterize effects on women, infants, children or the elderly, or on members of minority ethnic groups. Nevertheless, the analysis of occupational epidemiological studies, including meta-analyses, has proved an important source for unequivocal identification of human carcinogens.

Epidemiological evidence may also be obtained where a substantial segment of a general population is exposed to the material of interest in air, drinking water or food sources. Rigorous cohort and case-control studies may sometimes be possible, in which exposed individuals are identified, their exposure and morbidity or mortality evaluated, and compared to less exposed but otherwise similar controls. More often at least the initial investigation is a cross-sectional study, where prevalence of exposures and outcomes is compared in relatively unexposed and exposed populations. Such studies are hypothesis-generating, but are important sources of information

nevertheless, and can often also justify more costly and labor-intensive follow-up cohort and/or case-control studies.

The clinical medical literature contains many case reports where a particular health outcome is reported along with unusual exposures that might have contributed to its occurrence. These reports typically describe a single patient or a small group, and have no statistical significance. They are nevertheless useful as indications of possible associations that deserve follow-up using epidemiological methods, and as supporting evidence, addressing the plausibility of associations measured in larger studies.

Animal studies

Although the observation of human disease in an exposed population can provide definitive hazard identification, adequate data of this type are not always available. More often, risk estimates have to be based on studies in experimental animals, and extrapolation of these results to predict human toxicity. The animals used are mostly rodents, typically the common laboratory strains of rat and mouse.

Rats and mice have many similarities to humans. Physiology and biochemistry are similar for all mammals, especially at the fundamental levels of xenobiotic metabolism, DNA replication and DNA repair that are of concern in identifying carcinogens. However, there are also several important differences between rodents and humans. Rodents, with a short life span, have differences in cell growth regulation compared to longer-lived species such as the human. For instance, whereas laboratory investigations have suggested that mutations in two regulatory genes (*e.g.,* H-ras and p-53) are sometimes sufficient to convert a rodent cell to a tumorigenic state, many human cancers observed clinically have seven or eight such mutations. In addition, cultured normal human cells have a very stable karyotype, whereas cultured rodent cells facilely undergo tetraploidization and then aneuploidization in cell culture. Further, cultured human cells senesce and rarely undergo spontaneous immortalization (frequency is 10^{-7} or less), whereas cultured rodent cells facilely undergo immortalization at frequencies on the order of 10^{-3}. The use of genomics to study chemical carcinogenesis is relatively new, but the differences at present appear to be a matter of degree rather than kind.

Differences in regulation of cell division are another likely reason for variation between species in the site of action of a carcinogen, or its potency at a particular site. A finding of carcinogenesis in the mouse liver, for instance, is a reasonably good indicator of potential for carcinogenesis at some site in the human, but not usually in human liver (Huff, 1999). The mouse liver (and to a lesser extent that of the rat) is a common site of spontaneous tumors. It is also relatively sensitive to chemical carcinogenesis. The human liver is apparently more resistant to carcinogenesis; human liver tumors are unusual except when associated with additional predisposing disease, such as hepatitis B or alcoholic cirrhosis, or exposure to aflatoxin B1, or simultaneous exposure to hepatitis B virus and aflatoxin B1. Conversely, other tumor sites are more sensitive in the human than in experimental animals. Interspecies variation in site and sensitivity to carcinogenesis may also arise from differences in pharmacokinetics and metabolism, especially for carcinogens where metabolic activation or detoxification is important. This variability may cause important differences in sensitivity between individuals in a diverse population such as humans. Variability

between individuals in both susceptibility and pharmacokinetics or metabolism is probably less in experimental animal strains that are bred for genetic homogeneity.

Animal carcinogenesis studies are often designed to maximize the chances of detecting a positive effect, and do not necessarily mimic realistic human exposure scenarios. Thus extrapolation from an experimentally accessible route to that of interest for a risk assessment may be necessary. Even for studies by realistic routes such as oral or inhalation, doses may be large compared to those commonly encountered in the environment, in order to counter the limitation in statistical power caused by the relatively small size of an animal experiment. Whereas the exposed population of an epidemiological study might number in the thousands, a typical animal study might have fifty individuals per exposure group. With this group size any phenomenon with an incidence of less than about 5% is likely to be undetectable. Statistically significant results may be obtained even with groups as small as ten animals per dose group, when incidence of a tumor that is rare in the controls approached 100% in a treated group. The consensus experimental design for animal carcinogenesis studies, which has evolved over the last 50 years of investigation, is represented by the protocol used by the U.S. National Toxicology Program (NTP) for studies using oral routes (diet, gavage or drinking water) or inhalation. These carcinogenesis bioassays usually involve both sexes of an experimental species, and most often two species. NTP has standardized the use of the C57BlxC3H F_1 hybrid mouse, and the Fischer 344 rat as the standard test species, although NTP has announced plans to substitute use of the Wistar Han rat for the Fischer 344 rat. There is now an extensive database of background tumor incidences, normal physiology, biochemistry, histology and anatomy for these strains, which aids in the interpretation of pathological changes observed in experiments. Nevertheless, there is enough variation in background rates of common tumors that the use of concurrent controls is essential for hazard identification or dose-response assessment. "Historical control" data are mainly used to reveal anomalous outcomes in the concurrent controls. The fact that a significantly elevated incidence of a tumor relative to the concurrent control group is within the range of historical controls at that site for the test sex and strain is not necessarily grounds for dismissing the biological significance of the finding.

Groups of fifty animals of each sex and species are used, with control groups, and several dose groups, the highest receiving the maximum tolerated dose (MTD). Recent study designs have emphasized the desirability of at least three dose levels covering a decade with "logarithmic" spacing (*i.e.* MTD, 1/2 MTD or 1/3 MTD, and 1/10 MTD). This extended design is aimed at providing better dose-response information, and may contribute important additional information, such as mechanistic insights, for the hazard identification phase.

Supporting evidence: genetic toxicity, mechanistic studies

Investigators have developed additional data sources that can support or modify the conclusions of animal carcinogenesis bioassays, and provide information on mechanisms of action of agents suspected of being carcinogenic based on epidemiological studies or animal bioassays.

Genetic damage in exposed organisms includes both gene mutations (point or frameshift), and larger scale effects such as deletions, gene amplification, sister-chromatid exchanges, translocations and loss or duplication of segments or whole chromosomes. These genetic effects of chemical exposures are deleterious in their own right. In addition, since carcinogenesis results from somatic mutations and similar genetic alterations, agents that cause genetic damage generally

have carcinogenic potential. Conversely, many known carcinogens are also known to be genotoxic, although there is also a significant class of carcinogens that are not directly genotoxic according to the usual tests. These latter agents presumably work by some other mechanism, such as methylation of tumor suppressor genes or demethylation of cellular proto-oncogenes, although recent genetic studies have shown that even tumors induced by these agents may show mutations, deletions or amplification of growth regulatory genes.

Experimental procedures to demonstrate and measure genetic toxicity may involve exposure of intact animals, and examination of genetic changes in, for example, bone marrow cells (or cells descended from these, *e.g.,* the micronucleus test, which detects remnants of chromosomal fragments in immature erythrocytes), mutations in flies (*Drosophila)*, or appearance of color spots in the coat of mice. However, many tests have employed single celled organisms or mammalian cells in culture. The best known of these tests is the *Salmonella* reverse mutation assay, popularly known as the Ames test after its inventor. This is representative of a larger class of tests for mutagenic activity in prokaryotic organisms (bacteria), which necessarily only look at gene-level mutations. Similar tests in eukaryotic microorganisms (yeasts, *Aspergillus*) and cultured mammalian cells also detect chromosomal effects. Many tests using microorganisms *in vitro* involve addition of activating enzymes (*e.g.,* liver postmitochondrial supernatant – "S9") to mimic the metabolism of promutagenic chemicals *in vivo*. Another type of test examines the induction in mammalian cells of morphological transformation or anchorage-independent growth. These two chemically induced, *in vitro* changes are considered two of the many changes that fibroblastic cells must undergo on their route to neoplastic transformation (tumorigenicity). These various genetic tests contribute different information, which may be used to amplify and confirm conclusions drawn from human studies or animal bioassays, or to draw conclusions in the absence of epidemiological or bioassay data. In the latter case they have also been used in prioritizing agents for further evaluation by means of bioassays.

Carcinogen Identification Schemes

Some regulatory programs, such as California's Safe Drinking Water and Toxics Enforcement Act ("Proposition 65") and various activities of the U.S. EPA, require that explicit lists of substances having the potential to act as human carcinogens be maintained. Other such lists are developed by non-regulatory research organizations, such as the U.S. National Toxicology Program and the International Agency for Research on Cancer (IARC), an international program of the World Health Organization. The California air toxics programs do not have any statutory requirement to "identify" carcinogens. The requirement instead is to identify hazardous substances as Toxic Air Contaminants, and to determine whether or not a threshold concentration, below which no adverse effects are expected, is likely to exist:

> ***HEALTH AND SAFETY CODE, Division 26 (Air Resources), § 39660.***
>
> *(2) The evaluation shall also contain an estimate of the levels of exposure that may cause or contribute to adverse health effects. If it can be established that a threshold of adverse health effects exists, the estimate shall include both of the following factors:*
>
> *(A) The exposure level below which no adverse health effects are anticipated.*

> *(B) An ample margin of safety that accounts for the variable effects that heterogeneous human populations exposed to the substance under evaluation may experience, the uncertainties associated with the applicability of the data to human beings, and the completeness and quality of the information available on potential human exposure to the substance. In cases in which there is no threshold of significant adverse health effects, the office shall determine the range of risk to humans resulting from current or anticipated exposure to the substance.*

In practice however this requirement amounts to the need to establish whether or not a substance is carcinogenic. Any such effects are clearly harmful. Whereas the great majority of non-cancer health effects of chemicals are regarded as having a threshold, the default assumption for carcinogens is that there is no threshold (as described below). OEHHA follows the guidelines laid out by IARC for identification and classification of potential human carcinogens, which are described in detail in the most recent revision of the *Preamble* to the IARC monographs series (IARC, 2006). The IARC Monograph series provides evaluations of the carcinogenicity of individual substances or commonly occurring mixtures. The evaluation guidelines used are similar to those used by other scientific or regulatory authorities, including U.S.EPA.

The data inputs to hazard identification for carcinogens are human epidemiological studies, animal bioassays, along with supporting evidence such as mechanistic and genotoxicity data and structure-activity comparisons. IARC also assembles data on the structure and identity of the agent. The list of agents considered includes specific chemicals and also complex mixtures, occupational and lifestyle factors, physical and biological agents, and other potentially carcinogenic exposures.

IARC evaluations determine the quality of evidence for both animal and human evidence as falling into one of four categories: sufficient evidence of carcinogenicity, limited evidence of carcinogenicity, inadequate evidence of carcinogenicity and evidence suggesting lack of carcinogenicity. Stringent requirements for data quality are imposed. In view of their crucial importance, these definitions are quoted directly from the *Preamble* (IARC 2006):

> **"(a) Carcinogenicity in humans**
>
> ***Sufficient evidence of carcinogenicity:*** The Working Group considers that a causal relationship has been established between exposure to the agent and human cancer. That is, a positive relationship has been observed between the exposure and cancer in studies in which chance, bias and confounding could be ruled out with reasonable confidence. A statement that there is *sufficient evidence* is followed by a separate sentence that identifies the target organ(s) or tissue(s) where an increased risk of cancer was observed in humans. Identification of a specific target organ or tissue does not preclude the possibility that the agent may cause cancer at other sites.
>
> ***Limited evidence of carcinogenicity*:** A positive association has been observed between exposure to the agent and cancer for which a causal interpretation is considered by the Working Group to be credible, but chance, bias or confounding could not be ruled out with reasonable confidence.
>
> ***Inadequate evidence of carcinogenicity:*** The available studies are of insufficient quality, consistency or statistical power to permit a conclusion regarding the presence or absence

of a causal association between exposure and cancer, or no data on cancer in humans are available.

Evidence suggesting lack of carcinogenicity: There are several adequate studies covering the full range of levels of exposure that humans are known to encounter, which are mutually consistent in not showing a positive association between exposure to the agent and any studied cancer at any observed level of exposure. The results from these studies alone or combined should have narrow confidence intervals with an upper limit close to the null value (*e.g.,* a relative risk of 1.0). Bias and confounding should be ruled out with reasonable confidence, and the studies should have an adequate length of follow-up. A conclusion of *evidence suggesting lack of carcinogenicity* is inevitably limited to the cancer sites, conditions and levels of exposure, and length of observation covered by the available studies. In addition, the possibility of a very small risk at the levels of exposure studied can never be excluded.

(b) Carcinogenicity in experimental animals

Carcinogenicity in experimental animals can be evaluated using conventional bioassays, bioassays that employ genetically modified animals, and other in-vivo bioassays that focus on one or more of the critical stages of carcinogenesis. In the absence of data from conventional long-term bioassays or from assays with neoplasia as the end-point, consistently positive results in several models that address several stages in the multistage process of carcinogenesis should be considered in evaluating the degree of evidence of carcinogenicity in experimental animals.

The evidence relevant to carcinogenicity in experimental animals is classified into one of the following categories:

***Sufficient evidence of carcinogenicity*:** The Working Group considers that a causal relationship has been established between the agent and an increased incidence of malignant neoplasms or of an appropriate combination of benign and malignant neoplasms in (a) two or more species of animals or (b) two or more independent studies in one species carried out at different times or in different laboratories or under different protocols. An increased incidence of tumours in both sexes of a single species in a well-conducted study, ideally conducted under Good Laboratory Practices, can also provide *sufficient evidence*.

A single study in one species and sex might be considered to provide *sufficient evidence of carcinogenicity* when malignant neoplasms occur to an unusual degree with regard to incidence, site, type of tumour or age at onset, or when there are strong findings of tumours at multiple sites.

***Limited evidence of carcinogenicity*:** The data suggest a carcinogenic effect but are limited for making a definitive evaluation because, *e.g.,* (a) the evidence of carcinogenicity is restricted to a single experiment; (b) there are unresolved questions regarding the adequacy of the design, conduct or interpretation of the studies; (c) the agent increases the incidence only of benign neoplasms or lesions of uncertain neoplastic potential; or (d) the evidence of carcinogenicity is restricted to studies that demonstrate only promoting activity in a narrow range of tissues or organs.

***Inadequate evidence of carcinogenicity*:** The studies cannot be interpreted as showing either the presence or absence of a carcinogenic effect because of major qualitative or quantitative limitations, or no data on cancer in experimental animals are available.

***Evidence suggesting lack of carcinogenicity*:** Adequate studies involving at least two species are available which show that, within the limits of the tests used, the agent is not carcinogenic. A conclusion of *evidence suggesting lack of carcinogenicity* is inevitably limited to the species, tumour sites, age at exposure, and conditions and levels of exposure studied."

IARC utilizes the evaluations of animal and human data, along with supporting evidence including genotoxicity, structure-activity relationships, and identified mechanisms, to reach an overall evaluation of the potential for carcinogenicity in humans. The revised *Preamble* (IARC, 2006) includes a description of the data evaluation criteria for this supporting evidence, and indications as to the situations where the availability of supporting evidence may be used to modify the overall conclusion from that which would be reached on the basis of bioassay and/or epidemiological evidence alone. The overall evaluation is expressed as a numerical grouping, the categories of which are described below, as before by directly quoting IARC (2006):

"Group 1: The agent is *carcinogenic to humans*.

This category is used when there is *sufficient evidence of carcinogenicity* in humans. Exceptionally, an agent may be placed in this category when evidence of carcinogenicity in humans is less than *sufficient* but there is *sufficient evidence of carcinogenicity* in experimental animals and strong evidence in exposed humans that the agent acts through a relevant mechanism of carcinogenicity.

Group 2.

This category includes agents for which, at one extreme, the degree of evidence of carcinogenicity in humans is almost *sufficient*, as well as those for which, at the other extreme, there are no human data but for which there is evidence of carcinogenicity in experimental animals. Agents are assigned to either Group 2A (*probably carcinogenic to humans*) or Group 2B (*possibly carcinogenic to humans*) on the basis of epidemiological and experimental evidence of carcinogenicity and mechanistic and other relevant data. The terms *probably carcinogenic* and *possibly carcinogenic* have no quantitative significance and are used simply as descriptors of different levels of evidence of human carcinogenicity, with *probably carcinogenic* signifying a higher level of evidence than *possibly carcinogenic*.

Group 2A: The agent is *probably carcinogenic to humans*.

This category is used when there is *limited evidence of carcinogenicity* in humans and *sufficient evidence of carcinogenicity* in experimental animals. In some cases, an agent may be classified in this category when there is *inadequate evidence of carcinogenicity* in humans and *sufficient evidence of carcinogenicity* in experimental animals and strong evidence that the carcinogenesis is mediated by a mechanism that also operates in humans. Exceptionally, an agent may be classified in this category solely on the basis of *limited*

evidence of carcinogenicity in humans. An agent may be assigned to this category if it clearly belongs, based on mechanistic considerations, to a class of agents for which one or more members have been classified in Group 1 or Group 2A.

Group 2B: The agent is *possibly carcinogenic to humans*.

This category is used for agents for which there is *limited evidence of carcinogenicity* in humans and less than *sufficient evidence of carcinogenicity* in experimental animals. It may also be used when there is *inadequate evidence of carcinogenicity* in humans but there is *sufficient evidence of carcinogenicity* in experimental animals. In some instances, an agent for which there is *inadequate evidence of carcinogenicity* in humans and less than *sufficient evidence of carcinogenicity* in experimental animals together with supporting evidence from mechanistic and other relevant data may be placed in this group. An agent may be classified in this category solely on the basis of strong evidence from mechanistic and other relevant data.

Group 3: The agent is *not classifiable as to its carcinogenicity to humans.*

This category is used most commonly for agents for which the evidence of carcinogenicity is *inadequate* in humans and *inadequate* or *limited* in experimental animals.

Exceptionally, agents for which the evidence of carcinogenicity is *inadequate* in humans but *sufficient* in experimental animals may be placed in this category when there is strong evidence that the mechanism of carcinogenicity in experimental animals does not operate in humans.

Agents that do not fall into any other group are also placed in this category.

An evaluation in Group 3 is not a determination of non-carcinogenicity or overall safety. It often means that further research is needed, especially when exposures are widespread or the cancer data are consistent with differing interpretations.

Group 4: The agent is *probably not carcinogenic to humans*.

This category is used for agents for which there is *evidence suggesting lack of carcinogenicity* in humans and in experimental animals. In some instances, agents for which there is *inadequate evidence of carcinogenicity* in humans but *evidence suggesting lack of carcinogenicity* in experimental animals, consistently and strongly supported by a broad range of mechanistic and other relevant data, may be classified in this group."

The IARC hazard evaluation system provides a detailed and generally accepted scheme to classify the strength of evidence as to the possible human carcinogenicity of chemicals and other agents. This includes careful consideration of mechanistic data and other supporting evidence, the evaluation of which is also important to inform selection of models or defaults used in dose response assessment, as is described below. The extended consideration of supporting evidence is in fact the primary difference between more recent versions of the guidance from IARC, and also by other organizations including U.S. EPA, and the original versions of that guidance. In fact, the basic criteria for hazard identification based on bioassay and epidemiological data have not

changed substantially in other respects from earlier guidance documents, including that originally published by California (DHS, 1985). Although as noted earlier the California Air Toxics programs do not categorize identified carcinogens, it has generally been the practice to regard any agent with an IARC overall classification in Group 1 or Group 2 as a known or potential human carcinogen. This implies the selection of various policy-based default options, including absence of a threshold in the dose-response curve, unless specific data are available to indicate otherwise. The same basic identification criteria are used by OEHHA scientific staff to determine the appropriate treatment of agents not evaluated by IARC, or for which newer data or revised interpretations suggest that an earlier IARC determination is no longer appropriate.

U.S. EPA has also proposed a scheme for carcinogen hazard identification and strength of evidence classification in their recently finalized Guidelines for Carcinogen Risk Assessment (U.S. EPA, 2005). These principally differ from the IARC guidance in recommending a more extensive narrative description rather than simply a numerical identifier for the identified level of evidence, and also to some degree in the weight accorded to various types of supporting evidence. However, for most purposes they may be regarded as broadly equivalent to the scheme used by IARC, and OEHHA has chosen to cite the IARC (2006) *Preamble* as representing the most up-to-date and generally accepted guidance on this issue.

Dose Response Assessment

The dose-response phase of a cancer risk assessment aims to characterize the relationship between an applied dose of a carcinogen and the risk of tumor appearance in a human. This is usually expressed as a cancer slope factor ["potency" – in units of reciprocal dose - usually $(mg/kg\text{-}body\ weight.day)^{-1}$ or "unit risk" – reciprocal air concentration – usually $(\mu g/m^3)^{-1}$] for the lifetime tumor risk associated with lifetime continuous exposure to the carcinogen at low doses. Cancer potency factors may also be referred to as "cancer slope factors". (As will be described later, additional algorithms may need to be applied to determine risk for specific age groups, or at higher doses where toxicokinetic factors have significant effect.) The basic methodologies recommended in this document are similar to those described by U.S. EPA (2005a) in their Carcinogen Risk Assessment Guidelines. This document therefore refers to U.S. EPA (2005a) for explanation of detailed procedures, and will provide only a brief summary except in cases where OEHHA recommendations are different from or more explicit than those of U.S. EPA.

The following descriptions of methods for dose response assessment, and considerations in their application, apply in principle to the analysis of both animal and human (epidemiological) cancer incidence data. Indeed, the original formulation of the multistage model (Armitage and Doll, 1954) described below was developed based on human cancer incidence. Nevertheless, the number and quality of human cancer incidence datasets are limited. The more complex analyses have usually only been possible for animal experimental data, where the interindividual variability and the exposure conditions can be both measured and controlled. Most commonly, epidemiological studies have necessarily used a form of multivariate analysis to separate the effects of several different variables relating to exposure, demographics and behaviors (*e.g.,* smoking). In these analyses it is usually assumed that the effect measure(s) vary linearly with the exposure: any more complex variance assumptions might exceed the power of the data to determine the required model parameters. However, there are exceptions, especially for occupational studies where the critical exposure is measured as a continuous variable (rather than

just categorical) and where the effect of this exposure is substantial relative to other confounding factors. For example, OEHHA (1998) used a multistage model dealing with both exposure intensity and duration in the analysis of cancer incidence in railroad workers exposure to diesel exhaust (Garshick et al., 1988)

Interspecies Extrapolation

The procedures used to extrapolate low-dose human cancer risk from epidemiological or animal carcinogenicity data are generally health-protective in that they determine an upper confidence bound on the risk experienced by an exposed population. As statistical estimates they cannot be regarded as definite predictions of the risk faced by any one specific individual, who might for a variety of reasons, including individual exposure and susceptibility, experience a risk different from the estimate. The risk assessment procedures used aim to include the majority of variability in the general human population within the confidence bounds of the estimate, although the possibility that some individuals might experience either lower or even no risk, or a considerably higher risk, cannot be excluded. Additionally, differences may exist between the characteristics of the general public and those of studied populations. For example, healthy workers, the subject of most epidemiological studies, are often found to have lower rates of morbidity and mortality than the general population (Wen et al., 1983; Monson, 1986; Rothman and Greenland, 1998). Most human data are derived from studies of largely male adult workers and risk estimates cannot take into account specific physiological factors of women, children, and older populations that may affect the potency of a carcinogen, including early age-at-exposure.

Dose-response assessment based on environmental epidemiological studies may involve evaluation of health impacts at exposure levels within the range of those measured in the study population. However, more usually the source data are studies of occupationally exposed humans or of animals, in which case the exposures in the study are likely to be much higher than those of concern for risk assessments relating to community or ambient exposures. Further, even when extrapolation from animal species to humans is not required, the general population to which the URF is applied may differ in characteristics relative to the occupational population studied. It is therefore necessary to extrapolate from the available data to the population and exposure range of concern, which is done by using a dose-response model derived from the source data. The models used fall into three main classes: mechanistically based models, empirical models and (where data are lacking to support a true data-based model) default assumptions. The factors affecting the dose-response relationships for carcinogenesis may also be divided into those relating to absorption, distribution, metabolism and excretion on the one hand (*i.e.* toxicokinetics), and those relating to the underlying dose-response characteristics of carcinogenesis at the tissue or cellular level (*i.e.* toxicodynamics). In this sense the problem of dose response assessment for carcinogens is similar to that for non-cancer toxic effects. The toxicokinetic models used may in fact be similar for both situations, but the toxicodynamic models are generally different.

Intraspecies Extrapolation and Inter-individual Variability

In estimating the impact of a particular level of exposure to a carcinogen on a target human population, it is necessary to consider the range of susceptibility in the target population. In the present case this is typically defined as the general population of the State of California, including of course women (some of whom are pregnant), infants and children, the elderly, the sick, and

those with genetic polymorphisms or acquired differences which affect their susceptibility to carcinogens. In general it has been assumed that the upper-bound risk estimates obtained from the standard toxicodynamic models described below are sufficiently health-protective to cover the intrinsic variability of the adult human target population, in spite of the fact that these models do not explicitly address this type of variability, except in the few cases where an estimate is based on epidemiological data from a large and unselected study group (U.S. EPA, 2005a). However, various analyses (Drew et al., 1983; Barton et al., 2005; Appendix J) have suggested that this assumption is inadequate to cover the expected variability within a human population that includes infants and children. Accordingly both U.S. EPA (2005b) and this document now offer guidance on the use of age-specific adjustment factors to allow for the potentially greater sensitivity of infants and children to chemical carcinogenesis.

The ability to accommodate human variability with regard to the toxicokinetic factors affecting susceptibility to carcinogens varies with the level of detail used in the particular assessment. If the generic interspecies extrapolation approach based on body weight is used without any explicit toxicokinetic model, then the assumption is made, as in the case of toxicodynamic variability, that the overall health-protective assumptions made are sufficient to cover the toxicokinetic variability. On the other hand if explicit models such as those referenced in the following paragraph are used, this variability may be more explicitly accommodated by using parameter values which are taken as point estimates from measured distributions of population values, or by using Monte Carlo techniques to include those distributions in the model (Bois et al., 1996; OEHHA, 1992; 2001b).

Toxicokinetic Models

Considerable literature exists showing the importance of understanding the toxicokinetics of carcinogens in understanding their mechanism of action, sites of impact and dose-response relationships. U.S. EPA (2005) in Section 3.1 refers to the importance of identifying an appropriate dose metric for the dose-response analysis. Early cancer risk assessments typically used applied dose as the dose metric, which is adequate in simple cases provided appropriate correction factors are applied for interspecies extrapolation. However, it is often observed that the uptake, metabolism and elimination of the carcinogenic substance (and/or a procarcinogen and metabolites) is non-linear, especially at the higher doses employed in experimental animal studies (Hoel *et al*., 1983, Gaylor *et al*., 1994). Extrapolation to lower doses where such relationships tend to linearity (Hattis, 1990) is aided by the use of toxicokinetic models. These may be relatively simple compartment models, or sophisticated "physiologically based pharmacokinetic (PBPK) models" which to a greater or lesser degree model the actual biochemical and physiological events of toxicokinetic importance. Applications of both types of model may be found in various risk assessment documents prepared for the Toxic Air Contaminants program (and other OEHHA risk assessments). Since the details vary widely according to the nature of the chemical and the availability of appropriate kinetic data these general guidelines will defer to those examples rather than attempt a fuller exposition here. Further analysis of the use of toxicokinetic modeling in extrapolation from animals to humans, and in accounting for interindividual variability among adult humans, infants and children is presented in the Air Toxics Hot Spots *Technical Support Document for the Derivation of Noncancer Reference Exposure Levels* (OEHHA, 2008). Although this refers to the use of toxicokinetic modeling in non-cancer risk assessment, the primary considerations are similar for cancer risk assessment.

Toxicodynamic Models

An early use of mechanistic analysis to support risk assessment was the development of the Armitage-Doll multistage model of dose-response for carcinogenesis. The multistage model was initially developed on theoretical grounds, and by examination of epidemiological and animal data on time to tumor incidence. Subsequent discovery of the molecular biology of proto-oncogenes has provided a basis for explaining the model in terms of actual biological events and systems (Barrett and Wiseman, 1987). This model was developed by Crump and others into the "linearized multistage model", which has been extensively used for carcinogen risk assessment. It leads to a number of partially verifiable predictions, including linearity of the dose-response relationship at low doses, which is observed for many genotoxic carcinogens. It also predicts the form of the dose-response relationship at higher doses, which generally follow a polynomial form (subject to sampling and background corrections) except where other identifiable factors such as pharmacokinetics intervene.

It has been argued that the simple linearized form of the multistage model has limitations as a description of carcinogenic mechanisms, which detract from its usefulness and generality. Cell proliferation is known to be important in the progression of cancer. It may actually be the primary mechanism of action for a few carcinogens, as opposed to the direct modification of DNA by the carcinogen or a metabolite which is assumed to cause the mutational event at each stage in the original multistage description. A cell proliferation model has been developed (Moolgavkar and Knudson, 1981), which retains the concept of an initiating mutational event (in most cases caused by interaction of the chemical with DNA, although it could also be a spontaneous mutation) as in the original multistage model, but also considers proliferation, death or terminal differentiation of both normal and initiated cells. This model is thought to better describe the biological events in carcinogenesis. However, it has not been used extensively in risk assessment because it requires many parameters that are difficult to define and measure (such as proliferation and death rates for various classes of cell). If these cannot be accurately determined, the model has too many free parameters and is not helpful in defining extrapolated values for risk assessment purposes. This highlights a general problem in using mechanistic models in carcinogen risk assessment, which is that the carcinogenesis data themselves are generally insufficient to define fully the dose response curve shape at low doses or provide much mechanistic information. The analysis is therefore supplemented with policy-based assumptions (such as the expectation of linearity at low doses) and, wherever possible, additional experimental measurements relating to the mechanism of action, in order to make meaningful prediction of risk from environmental exposures to humans.

Because of the difficulties in validating simplified mechanistic models such as the basic multistage model, and the additional difficulty of parameter estimation with more complex mechanistic models, the new U.S. EPA guidelines (U.S. EPA, 2005a) and some recent California risk assessments have chosen instead to use a less overtly mechanistic approach. This approach combines benchmark dose methodology (described below) with an explicit choice of the method for low-dose extrapolation, either assuming low-dose linearity or, for certain carcinogens where data indicate that this is appropriate, a "margin of exposure" or safety/uncertainty factor based approach. This benchmark method is now normally recommended for carcinogen dose response analysis, and the results generally differ little from those derived by the linearized multistage model. Although the linearized multistage method is no longer recommended as the default approach for cancer potency estimation it remains a plausible alternative in many cases, and still

has useful applications, such as for time-to-tumor analyses for which benchmark methods are not yet widely available. Additionally, a considerable number of existing cancer potencies in Appendices A and B, and used in the Air Toxics Hot Spots program were derived by this method. Many of these would not be significantly different if calculated by the benchmark approach, and are unlikely to be replaced soon by newly calculated values. The linearized multistage method will therefore also be briefly described here.

Benchmark Dose Methodologies

The use of benchmark dose methodology has been explored by various investigators [including Gaylor et al. (1998); van Landingham et al. (2001) and Crump (1984, 1995, 2002)] as a tool for dose response extrapolation. This has been recommended in regulatory guidelines for both carcinogenic (U.S. EPA, 2005a) and non-carcinogenic (U.S. EPA, 1995) endpoints. The basic approach is to fit an arbitrary function to the observed incidence data, and to select a "point of departure" (POD) (benchmark dose) *within the range of the observed data.* From this a low dose risk estimate or assumed safe level may be obtained by extrapolation, using an assumed function (usually linear) or by application of uncertainty factors. The critical issue here is that no assumptions are made about the nature of the underlying process in fitting the data. The assumptions about the shape of the dose response curve (linear, threshold, etc.) are explicitly confined to the second step of the estimation process, and are chosen on the basis of policy, mechanistic evidence or other supporting considerations. The benchmark chosen is a point at the low end of the observable dose-response curve. Usually a dose at which the incidence of the tumor is 10% is chosen for animal studies, although lower effect levels may be appropriate for large epidemiological data sets. Because real experimental data include variability in the response of individual subjects, and measurement errors, likelihood methodology is applied in fitting the data. A lower confidence bound (usually 95%) of the effective dose (LED_{10}), rather than its maximum likelihood estimate (MLE), is used as the point of departure. This properly reflects the uncertainty in the estimate, taking a cautious interpretation of highly variable or error-prone data. It also reflects the instability of MLE values from complex curve-fitting routines, which has been recognized as a problem also with the linearized multistage model.

For cancer dose-response estimation using the benchmark dose method, either animal bioassay data or epidemiological data provide a suitable basis. In the absence of a pharmacokinetic model (which could provide tissue-specific dose metrics), the potency would ordinarily be based on the time-weighted average exposure during the exposure or dosing period. The model used to fit the data can be chosen from a range of available alternative quantal models, depending on which provides the best fit to the data in the observable range. In practice, the multistage polynomial fit developed for the linearized multistage model works well for most tumor data sets. Here it is being used merely as a mathematical curve-fitting tool, where the model well fits the data set, without making assumptions about its validity as a biological model of carcinogenesis.

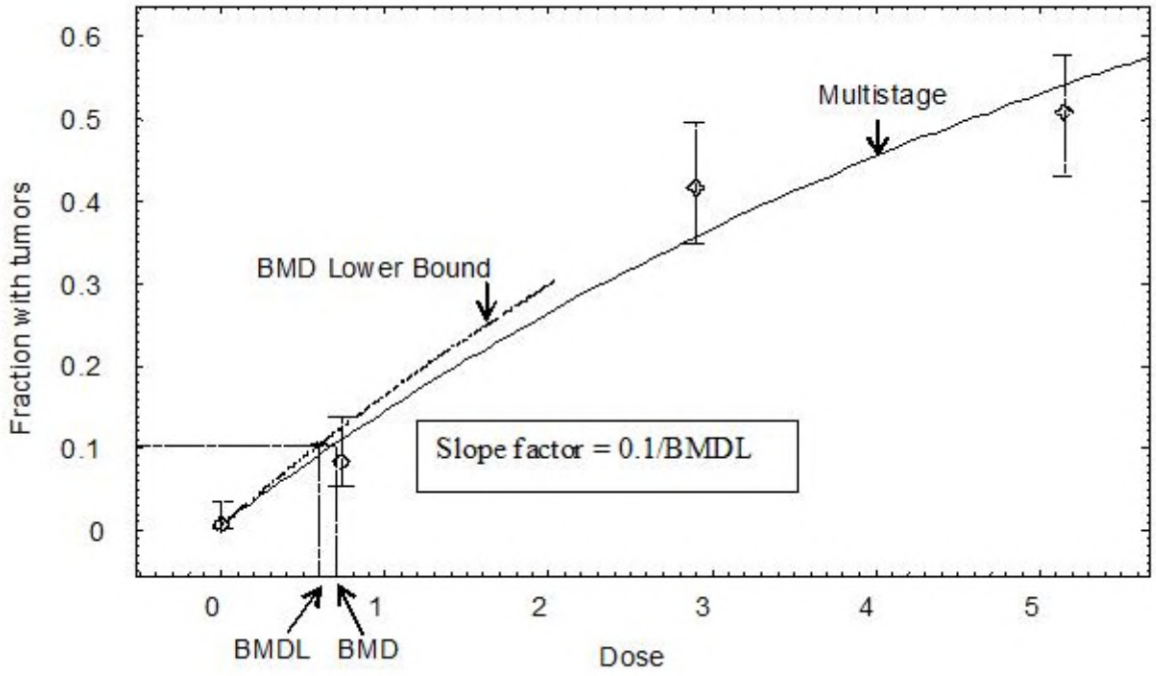
Suitable polynomial fits and estimates of the benchmark may be obtained using U.S. EPA's BMDS software. The benchmark often used is the 95% lower confidence bound on the dose producing 10% tumor incidence. However, if data are available which include a significant dose-response at less than 10% tumor incidence, then that lower benchmark should be used (*e.g.,* LED_{05} or LED_{01}). Other software such as Tox_Risk, which was used for the linearized multistage model, has been

used successfully, although the earlier GLOBAL program and its relatives are less suitable as curve-fitting tools for benchmark dose analysis.

Since it is usually assumed in cancer risk estimation that the low-dose response relationship is linear, risk estimates and a potency value (slope factor) may be obtained by linear extrapolation from an appropriate benchmark dose. The potency is the slope of that line ($0.1/LED_{10}$). The low dose linearity assumption is a general default for any carcinogen, and it is unlikely to be altered for genotoxic carcinogens.

A calculation using the benchmark dose approach (using a polynomial model with exponents restricted to zero or positive values), and linear extrapolation from the LED_{10} to obtain a potency estimate is shown in Figure 1 (the figure was generated by the U.S. EPA's BMDS program). This is based on tumor incidence data from an actual experiment with vinyl bromide in rats (Benya *et al*., 1982), with metabolized dose calculated by means of a pharmacokinetic model (Salmon *et al.,* 1992). The value of q_1* obtained by this calculation would then be corrected for the duration of the experiment if it had lasted for less than the standard rat lifetime, and for bodyweight and route-specific pharmacokinetic factors as described below. This is in addition to the correction for exposure duration that would be necessary if the study had not lasted for 105 weeks, and the interspecies correction, both of which are described below.

Figure 1. Benchmark dose calculation for tumor data in rats exposed to vinyl bromide



From Salmon *et al*. (1992), based on data from Benya *et al*. (1982)

Linearized Multistage Model

Quantal Analyses

A "multistage" polynomial (U.S. EPA, 1986, 2005a; Anderson *et al.*, 1983), based on the mechanistic insights of the original Armitage and Doll model of cancer induction and progression, has been used extensively by U.S. EPA, OEHHA and other risk assessors to model the dose response for lifetime risk of cancer. It usually is used for analysis of animal bioassay data, although related approaches have occasionally been used with epidemiological data. In mathematical terms, the probability of dying with a tumor (P) induced by an average daily dose (d) is:

$$P(d) = 1 - \exp[-(q_0 + q_1 d + q_2 d^2 + \ldots + q_i d^i)]$$

with constraints

$$q_i \geq 0 \text{ for all } i.$$

Equivalently, $$A(d) = 1 - \exp\left[- (q_1 d + q_2 d^2 + \cdots + q_k d^k)\right],$$

where $$A(d) = \frac{P(d) - P(0)}{1 - P(0)}$$ is the extra risk over background at dose d.

The q_i model parameters are constants that can be estimated by fitting the polynomial to the data from the bioassay, *i.e.* the number of tumor bearing animals (as a fraction of the total at risk) at each dose level, including the controls. The fit is optimized using likelihood methodology, assuming that the deviations from expected values follow a χ^2 distribution, with the number of degrees of freedom (and hence the maximum number of terms allowed in the polynomial) determined by the number of points in the data set. All the coefficients of the terms are constrained to be zero or positive, so the curve is required to be straight or upward curving, with no maxima, minima or other points of inflection. In addition to the maximum likelihood estimates of the parameters, the upper 95% confidence limits on these parameters are calculated.

The parameter q_0 represents the background lifetime incidence of the tumor. The 95% upper confidence limit of the slope factor q_1 (q_1^*), is termed the cancer potency. The maximum likelihood estimate (MLE) of q_1 is not usually regarded as a reliable estimate for several reasons. First, it fails to reflect the uncertainty and variability in the data which affect the value of the estimate. This is an important issue for protection of public health, which is emphasized by current regulatory guidelines. Secondly, due to the variable order of the polynomial and the effect of some terms being zero as opposed to having a small but finite value, the MLE is unstable, and may show large and unpredictable changes in response to very slight changes in the input data. It may also erratically have a zero value, even when the data imply a significant positive dose-response relationship. The MLE is not a measure of central tendency for this estimate distribution (which is always asymmetrical and often multi-peaked). For small doses, the cancer potency is the ratio of excess lifetime cancer risk to the average daily dose received. Details of the estimation procedure are given in Crump (1981) and Crump, Guess, and Deal (1977). Several software programs are available to perform the necessary calculations, including U.S. EPA's BMDS, Tox_Risk and the earlier GLOBAL programs by Crump and colleagues, and Mstage, written by Crouch (1987).

When dose is expressed in units of mg/kg-d, the potency is given in units of $(\text{mg/kg-d})^{-1}$. Likewise, when the model input is in units of concentration ($\mu g/m^3$, ppb), the potency is given in units of $\mu g/m^3)^{-1}$ pr $(\text{ppb})^{-1}$. As in the case of potencies obtained by the benchmark approach, the experiment-based potency value needs to be corrected for less-than lifetime or intermittent exposure, and extrapolated from the test species to humans. Risk calculations using potency value estimated using the linearized multistage model predict the cancer risk at low doses only, with the higher order terms of the fitted polynomial being ignored since their contribution is negligible at low doses.

Selection of Site and Tumor Type

In developing cancer potency estimates from animal data, standard practice has been to use dose-response data for the most sensitive tumor site as the basis of the estimate (CDHS, 1985). Where tumors of more than one histological type (*e.g.,* adenomas and carcinomas) are observed at a single

site, the combined incidence, *i.e.* proportion of animals affected with at least one tumor of any of the relevant types, is used for dose-response assessment. The same rules for combining tumor types are generally applied in determining statistical significance for carcinogen identification (IARC, 2006). Tumor types considered to represent different stages of progression following initiation of a common original normal cell type are combined, whereas tumor types having different cellular origins are generally not combined by this procedure. Other considerations that may influence choice of site for dose response estimation include the quality of the data (especially, the statistical impact of a high or variable rate of a particular tumor type and site in control animals), and biological relevance to humans. However, it is an important principle that, just as for the hazard identification phase, concordance of site or tumor type between animal models and human health effects may occur but is not assumed or required.

Carcinogens Inducing Tumors at Multiple Sites

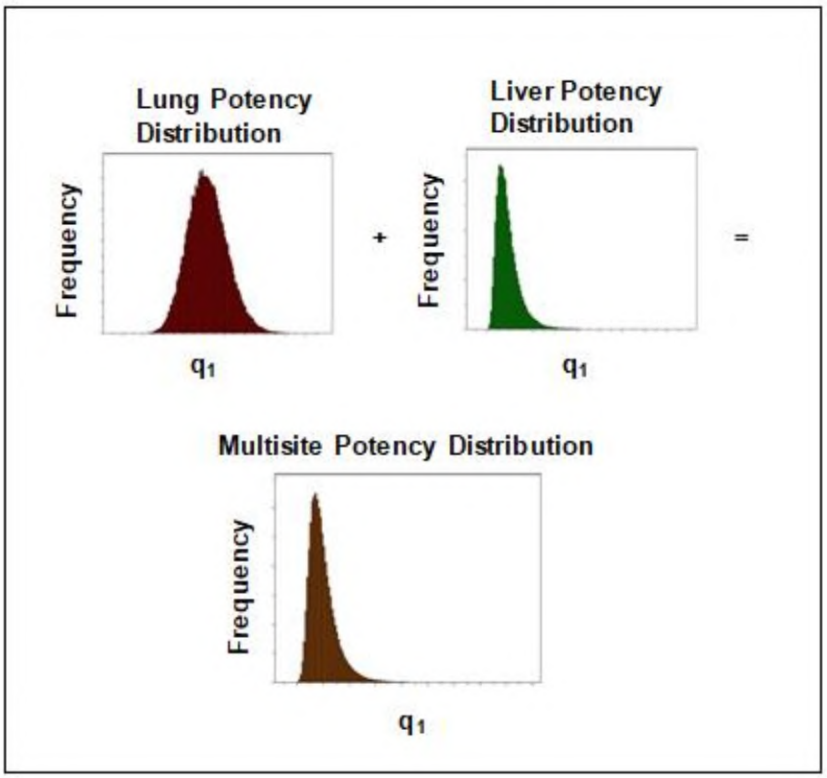
For most carcinogens, the selection of the most sensitive site in the animal studies is recognized as providing a risk estimate which is appropriate to protect human health. However, for chemicals that induce tumors at multiple sites, the single-site approach may underestimate the true carcinogenic potential. For example, the overall assessment of cancer risk from cigarette smoking (U.S. DHHS, 1982) or ionizing radiation (NRC, 1990) is not based on risk at one site, such as lung cancer. Instead, total cancer risk is estimated from all the sites at which agent-induced tumors are observed (lung, bladder, leukemia, etc), combined.

For carcinogens that induce tumors at multiple sites and/or with different cell types in a particular species and sex, OEHHA derives the animal cancer potency by probabilistically summing the potencies from the different sites and/or cell types. Using the combined potency distribution takes into account the multisite tumorigenicity and provides a basis for estimating the cumulative risk of all treatment-related tumors.

The linear term (q_1) of either the multistage model or the multistage-in-dose, Weibull-in-time model is first estimated based on the dose-response data for each of the treatment-related tumor sites. Statistical distributions, rather than point estimates, are generated at each site by tracing the profile likelihood of the linear term (q_1) (Zeise et al., 1991). The distributions of q_1 for each of the treatment-related sites are then statistically summed using a Monte Carlo approach and assuming independence (Figure 2). The sum is created by adding the linear term for each tumor site, according to its distribution, through random sampling. The upper 95 percent confidence limit on the summed distribution is taken as the multisite animal cancer potency estimate (McDonald et al., 2003, McDonald and Komulainen, 2005).

OEHHA has applied this approach in several recent dose-response analyses, including that for naphthalene presented in Appendix B of this document.

Figure 2. Addition of potency distributions for multi-site cancer potency derivations.



Early-Lifestage Cancer Potency Adjustments

In recent years, there have been growing concerns regarding the exposure of children to environmental chemicals, including the possibility that they may be more susceptible than adults to injury caused by those chemicals. The California Legislature passed the Children's Environmental Health Protection Act (Senate Bill 25, Escutia; Chapter 731, Statutes of 1999; "SB 25") to help address these concerns. Under SB25, OEHHA is mandated to consider infants and children specifically, where data permit, in evaluating the health effects of Toxic Air Contaminants (TACs).

The development of cancer is one of the adverse health effects that may occur in children as a result of exposure to environmental chemicals. The document "Prioritization of Toxic Air Contaminants under the Children's Environmental Health Protection Act" (OEHHA, 2001a) noted that risks of cancer from exposures to carcinogens occurring from conception through puberty can be different than those from exposures occurring in adulthood. Exposure to a carcinogen early in life may result in a greater lifetime risk of cancer for several reasons:

1. Cancer is a multistage process and the occurrence of the first stages in childhood increases the chance that the entire process will be completed, and a cancer produced, within an individual's lifetime.
2. Tissues undergoing rapid growth and development may be especially vulnerable to carcinogenic agents. During periods of increased cell proliferation there is rapid turnover of DNA, and more opportunity for misrepair of damage (*e.g.*, DNA breaks, crosslinks, adducts) or alterations to result in permanent changes to the DNA (*e.g.*, mutations, altered DNA methylation) that may ultimately lead to cancer.
3. During early development, a greater proportion of the body's cells are relatively undifferentiated stem cells, and as such represent a large target population of somatic cells capable of passing along permanent changes to the DNA during future cell divisions.
4. There may be greater sensitivity to hormonal carcinogens early in life since the development of many organ systems is under hormonal control (*e.g.*, male and female reproductive systems, thyroid control of CNS development).
5. Other factors that may play a role in increased cancer risk from exposures during critical developmental periods include differences in immunological activity, intestinal absorption, biliary and kidney excretion, blood and fat distribution, and expression of enzyme systems that activate or detoxify carcinogens.

Data in humans and animals for a variety of carcinogens suggest that exposures to such carcinogens early in life may result in a greater lifetime risk of cancer compared to exposures later in life. Examples of this effect in humans are carcinogenicity due to ionizing radiation, diethylstilbestrol (DES), chemotherapeutic agents, and tobacco smoke.
Ionizing radiation exposure carries an increased risk of cancer when exposures occur early in life compared to adult exposures for a number of tumor types. Children exposed to ionizing radiation (diagnostic X-rays) *in utero* demonstrate a larger excess of leukemia cases than children exposed to ionizing radiation postnatally (NRC, 1990). Exposure to radioisotopes (^{131}I, ^{137}Cs, ^{134}Cs, ^{90}Sr) as a consequence of the 1986 Chernobyl nuclear accident resulted in an elevated thyroid cancer

incidence in children but not adults (Moysich, 2002). Treatment of children for Hodgkin's lymphoma with both chemotherapeutic agents and irradiation has been shown to increase the risk of secondary tumors (Swerdlow et al., 2000; Franklin et al., 2006). Age at irradiation in Hodgkin's disease patients treated with radiotherapy strongly influenced the risk of developing breast cancer. The relative risk (RR) of developing breast cancer was 136 for women treated before 15 years of age, 19 for women 15-24 years of age, and 7 for those 24-29 years of age. In women above 30 years of age, the risk was not increased (Hancock *et al*., 1993).

DES was administered to pregnant women in the 1940s-1960s for the purpose of preventing pregnancy loss. In 1970, Herbst and Scully described 7 cases of vaginal adenocarcinoma (6 cases of the clear-cell type) in women aged 15-22 years. This type of cancer is extremely rare in that age range. A follow-up epidemiological study included an additional case, and noted the fact that the mothers of 7 of the 8 patients had been treated with DES during their pregnancy (Herbst *et al*., 1971). Reports by other investigators confirmed the association between maternal use of DES during pregnancy and the development of vaginal adenocarcinoma in their female offspring (Preston-Martin, 1989). It was observed that *in utero* DES exposure resulted in female genital tract morphological changes which correlated with both dose and duration of exposure, and those changes were not related to the maternal conditions which were the reason for the DES administration. Additionally, the risk of occurrence of those morphological changes declined with increasing gestational age at first exposure (O'Brien *et al*., 1979; Preston-Martin, 1989). In contrast, vaginal adenocarcinoma incidence did not increase in the exposed mothers themselves, indicating an increased early-life susceptibility to the carcinogenic effects of DES.

There is evidence in the epidemiological literature indicating that exposure to tobacco smoke during puberty may increase risk of breast cancer later in life, particularly among women who are NAT2 slow deacetylators (Marcus *et al*., 2000; Morabia *et al*., 2000; Lash and Aschengrau, 1999). Wiencke *et al*. (1999) report that early age at initiation of smoking is associated with a higher level of DNA adducts in lung tissue of former-smokers with lung cancer.

It has also been observed by Smith *et al*. (2006) that human *in utero* or early childhood exposure to arsenic in drinking water results in significantly increased lung cancer incidences during adult life.

Data from animal studies provide additional examples of increased sensitivity to early life (typically postnatal and juvenile) exposures. These effects span a range of target tissues, including the liver (vinyl chloride, safrole), brain (methylnitrosourea), reproductive tract (DES, tamoxifen), and lung (urethane) (OEHHA, 2001a).

In the following sections we summarize two efforts to evaluate quantitatively the effect of lifestage at exposure on carcinogenic response in experimental animal studies. The first section provides a description of OEHHA's analysis of data on the effect of age at exposure on carcinogenic potency. (Details of this analysis are in Appendix J.) The second section describes U.S. EPA's work in this area. (We also provide the published paper in Appendix I that presents the U.S. EPA analyses.) Both analyses used extant data available in the published literature. U.S. EPA used their analysis to modify the procedures they have used to estimate cancer risk by weighting risk by specific factors for childhood exposures. The weighting factors are a policy choice supported by U.S. EPA's data analysis. The results of OEHHA's analysis, summarized below and described in detail

in Appendix J, support the decision to modify policy to weight risk when exposure occurs during childhood.

OEHHA Analysis of the Effect of Age at Exposure on Cancer Potency

The analysis of animal cancer studies which include early life exposure by the Reproductive and Cancer Hazard Assessment Branch (RCHAB) of OEHHA also supports the application of lifestage-specific cancer potency factor adjustments. This analysis is provided in detail as Appendix J of this document.

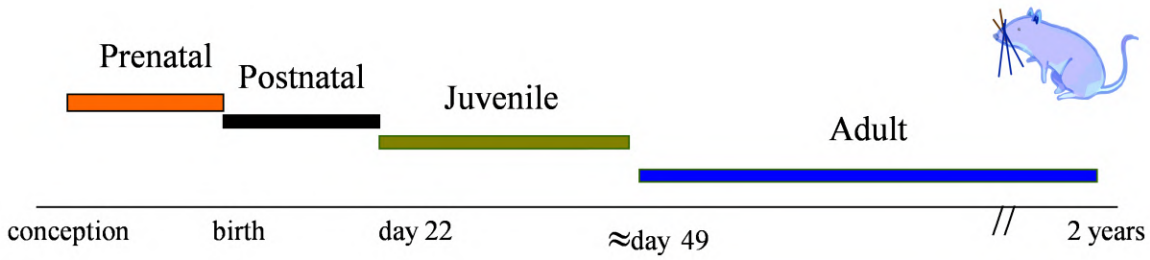
Early-in-life susceptibility to carcinogens has long been recognized by the scientific community and clinicians as a public health concern. Numerous scientific publications and symposia have addressed this issue over the years and the scientific literature contains a number of human clinical findings and epidemiological studies of early life cancer susceptibility. While there are many indications of increased human cancer susceptibility in early life, the magnitude of the impact has been difficult to gauge. Until recently risk assessment procedures have not in general addressed the issue. As described in the next section, in 2005 the U.S. EPA adopted an approach to weight carcinogens by age at exposure if they act via a mutagenic mode of action. The California legislature in 2000 directed OEHHA to assess methodologies used in addressing early-in-life risk, compile animal data to evaluate those methods, and develop methods to adequately address carcinogenic exposures to the fetus, infants, and children (Children's Environmental Health Initiative [AB 2872, Shelly]; California Health and Safety Code [HSC] section 901 [a] through [e]).

OEHHA assessed cancer risk assessment methodologies, and found that the existing risk assessment approaches did not adequately address the possibility that risk from early-in-life and adult exposures may differ. OEHHA further concluded that there was a need to address early-in-life cancer risk, and undertook studies to develop methods for doing so. Age-related cancer susceptibility data were identified from published animal cancer bioassays in which these issues were addressed. Two types of studies with early-in-life exposures were compiled. The first type are "multi-lifestage exposure studies." These studies have at least two groups exposed during different lifestages: One dose group is exposed to a chemical only during one of the following lifestages (Figure 3):

- prenatal (from conception to birth),
- postnatal (from birth to weaning),
- juvenile (from weaning to sexual maturity).

The second dose group is exposed for some period of time at an older age, preferably during the adult lifestage, that is, after sexual maturity. This group served as the reference group. In some cases where there was no adult exposure group, animals exposed as juveniles served as the reference group. Multi-lifestage exposure studies are available for many chemicals, enabling the exploration of patterns in early-life susceptibility across chemicals.

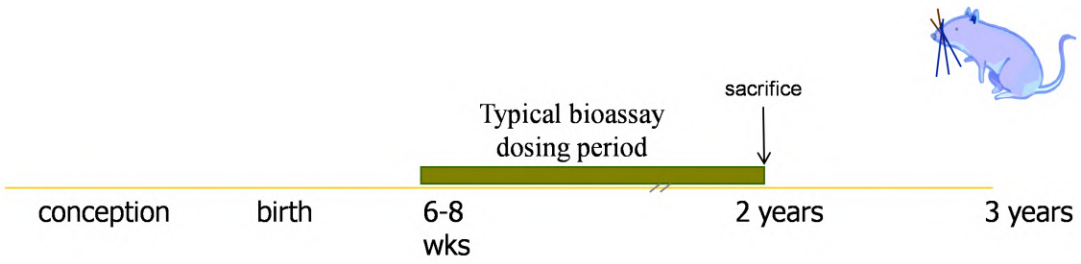
Figure 3. Definition of Rodent Lifestage Adopted in the OEHHA Analyses



OEHHA also conducted "chemical-specific case studies" of early-life sensitivity for two carcinogens, ethyl-N-nitrosoamine (DEN) and N-ethyl-N-nitrosourea (ENU) that combine data from a number of studies. These "chemical-specific case studies" were conducted to explore the feasibility of analyzing chemical-specific data on age susceptibility from single-lifestage exposure experiments. For these chemicals, OEHHA compiled from the literature a second type of study, "single-lifestage exposure experiments." In these experiments dose groups were exposed only during a particular lifestage and, unlike the "multi-lifestage exposure studies," there was no requirement that the same study also include groups exposed during a different lifestage. Thus, single-lifestage exposure experiments were identified as being either prenatal, postnatal, juvenile, or adult exposure studies. For each of the two chemicals, there were many prenatal studies conducted that were compiled, analyzed, and grouped together. Postnatal studies from different publications were similarly compiled, analyzed and grouped together, as were juvenile studies. Adult studies were not available for either DEN or ENU, thus for both chemicals juvenile exposure studies served as the referent for prenatal studies, and for postnatal studies.

Typical cancer bioassays such as those conducted in rats and mice by NTP involve exposing animals starting at six to eight weeks of age, which is the time at which these animals reach sexual maturity (late teenagers relative to humans). The experiments are run for two years, ending when the animal is in late middle age. Thus, early and very late life exposures are not included in the typical rodent bioassay (see Figure 4). If the NTP bioassay is used as a basis for estimating cancer potency, the potency and resulting risk estimates may be too low. Thus OEHHA focused on finding studies that evaluated early in life exposures.

Figure 4. Dosing Period for Typical Rodent Bioassays.



Since bioassays examining the effect of age at exposure on carcinogenesis were conducted by various investigators for different purposes, there is a great deal of variation across studies in terms of dose selection, duration of exposure, number of animals, and length of study duration. To be included in the compilation of studies with early life exposure, a study or an experimental group in a study had to meet minimum requirements.

The criteria for study inclusion are as follows:

- Treated groups were exposed to a single chemical carcinogen or a single carcinogenic chemical mixture.
- Study groups were not compromised by severe treatment-related non-cancer toxicity.
- Overall the duration of exposure period plus observation period exceeded 40 weeks, unless animals died of tumor.
- For included dose groups, the study must report age at dosing, age at sacrifice, and site-specific tumor incidence.
- Each lifestage exposure treatment group has an appropriate concurrent control group, or, for rare tumors only, an appropriate historical control.
- The studies were on mammals.
- Each treatment and control group consists of at least ten animals, unless the conduct and design of the study was well done in all other aspects (*e.g.*, the length of the study was sufficiently long to observe treatment-related tumors) and tumor incidence was high in treated groups and very low in controls.
- Site specific tumor data were reported, not only total number of tumor bearing animals.
- The test compound was administered in the diet, water, via gavage, or by intraperitoneal (i.p.), intravenous (i.v.), or subcutaneous (s.c.) injection. For dermal and subcutaneous injection studies, distal tumor findings are utilized (for dermal, other than skin tumors; for injection, non-injection site tumors).

- While studies designed to histopathologically examine tumors at multiple sites were preferred, studies that examined only a select set of organ/tissue sites were not excluded if the sites examined were known with confidence to be the only target tissues for the chemical and lifestage in question in that particular strain of animal.

Different approaches were taken to identify animal cancer studies that included groups of animals exposed during early life stages. First, MEDLINE and TOXLINE (National Library of Medicine) databases were searched using combinations of various key words for cancer (*e.g.*, tumor(s), neoplasm(s), cancer, neoplasia, cancerous, neoplasms-chemically induced) and for early-life exposure (*e.g.*, age, age-at-exposure, development (al), prenatal, *in utero*, gestation (al), postnatal, neonatal, juvenile, weaning, weanling, adolescent, adolescence, young). Second, the extensive compilation of bioassays in the *Survey of Compounds which have been Tested for Carcinogenic Activity*, was reviewed. This survey, formerly maintained by the National Cancer Institute as Public Health Service Publication Number 149, or PHS 149, is now available from a private source electronically as CancerChem, 2000. Third, from bibliographies from relevant published papers additional studies were identified. Finally the Single Dose Database developed by Calabrese and Blain (1999) was obtained and utilized to identify additional publications that appeared to contain potentially useful data. All of these publications were evaluated to determine if the study dosed separate groups of animals early in life and at or near adulthood. A total of 145 publications, providing data on 84 chemicals, were identified as meeting the criteria for study inclusion. A subset of these met the criteria for inclusion in the multi-lifestage exposure analysis.

Finally, for the OEHHA multi-lifestage analyses, we define "experiment" as a study component consisting of a control group as well as a treated group(s) exposed during the same lifestage (*i.e.*, prenatal, postnatal, juvenile or adult), and using the same experimental protocol (*e.g.*, route of exposure, strain, species, laboratory). Thus, by our definition one publication may report multiple experiments.

In the OEHHA analysis, data from studies on 23 unique carcinogens, 20 of which are considered to act via primarily genotoxic modes of action, were analyzed. Of these 20 carcinogens, 15 are thought to require metabolic activation to the ultimate carcinogenic species (Table 1). Fourteen carcinogens, including one thought to act via primarily nongenotoxic modes of action, were included in the prenatal multi-lifestage exposure studies. Eighteen carcinogens, including two thought to act via primarily nongenotoxic modes of action, were included in the postnatal multi-lifestage exposure studies. Five carcinogens were included in the juvenile multi-lifestage exposure studies. The case study chemicals, DEN and ENU, are both genotoxic. ENU is a direct acting alkylating agent, while DEN requires metabolic activation.

Table 1. Carcinogens for which studies with multi-lifestage exposures in animal studies are available

Genotoxic carcinogens requiring metabolic activation
Benzidine Benzo[a]pyrene Dibutylnitrosamine Diethylnitrosamine (DEN) 7,12-Dimethylbenz[a]anthracene (DMBA) Dimethylnitrosamine (DMN) Di-n-propylnitrosamine (DPN) 1 -Ethyl-nitrosobiuret 2-Hydroxypropylnitrosamine 3-Hydroxyxanthine 3-Methylcholanthrene (3-MC) 4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) Safrole Urethane Vinyl chloride
Genotoxic carcinogens not requiring metabolic activation
Butylnitrosourea 1,2-Dimethylhydrazine Ethylnitrosourea (ENU) Methylnitrosourea (MNU) ß-Propiolactone
Nongenotoxic carcinogens
1,1-Bis(p-chlorophenol)-2,2,2-trichloroethane (DDT) Diethylstilbestrol (DES) 2,3,7,8-Tetrachlorodibenzodioxin (TCDD)

Cancer Potency Estimation

Statistical methods were developed and used to analyze the data and derive measures of early-life susceptibility. These are described in detail in Appendix J. In brief, a cancer potency (the slope of the dose response curve) was developed for each of the experiments selected using the linearized multistage model. This model was chosen because of widespread use in risk assessment, and its flexibility in being able to fit many different data sets needed to evaluate the effect of lifestage-at-exposure on cancer potency. The dose metric used for the potency analyses is cumulative dose normalized to body weight. The cancer potency is thus expressed as the increase in tumor probability with increasing cumulative dose in units of mg/kg body weight.

To take into account uncertainty in potency estimation, cancer potencies are depicted by a statistical distribution, rather than by a single, fixed value, using methods described in Appendix J. While these methods have typically been used to obtain and report the 95th percentile of the cancer slope parameter for cancer risk assessment purposes, here OEHHA utilized the full distribution of the cancer slope parameter to derive measures of early-life susceptibility to carcinogens. This was done to systematically take into account uncertainty in the analysis.

For experiments where treatment related tumors were observed at multiple sites or at the same site but arising from different cell types, slopes from these sites were statistically combined by summing across the potency distributions (assuming independence across the sites that were observed) to create an overall multisite cancer potency. It is not uncommon that a carcinogen causes more than one type of cancer or causes tumors at different sites depending on lifestage at exposure. For example, in humans tobacco smoke causes cancers of the lung, bladder, and certain other organs. This multi-site carcinogenicity is frequently observed in animal experiments as well. In order to account for this, all treatment-related tumors that were observed in a given lifestage were taken into account in estimating cancer potency from that particular experiment.

Addressing Early-Age Sensitivity in Estimating Cancer Risk: Age Sensitivity Factors

Inherent Sensitivity of Lifestages – Lifestage Potency Ratios

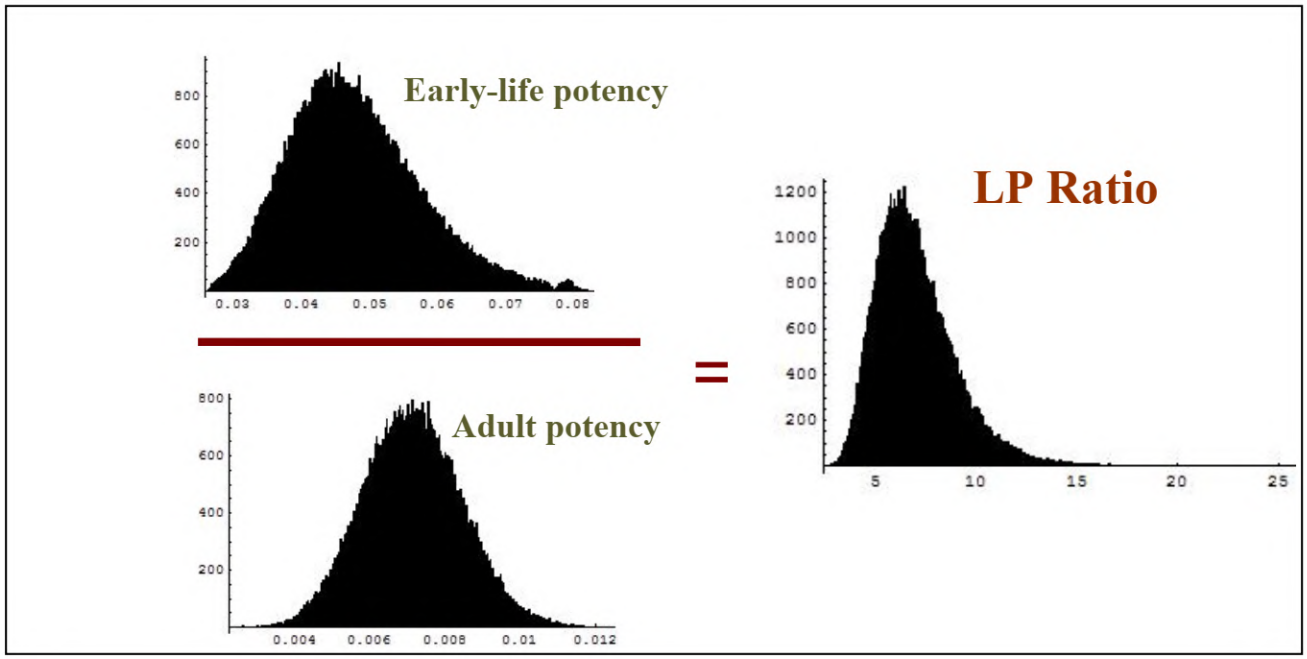
For this analysis, OEHHA calculates the ratio of cancer potency derived from an early lifestage exposure experiment(s) to that derived from an experiment(s) conducted in adult animals. OEHHA used the potency distributions for the individual lifestage exposures, rather than a point estimate, to derive the ratios. The lifestage cancer potency ratio is then described as a distribution and one can select specific percentiles from the distribution to better understand and bound the uncertainty (Figure 5). Of particular importance is the location of the ratio distribution in relation to the reference value of 1.0, which would mean no difference in risk from exposures at early versus adult lifestages. A lifestage cancer potency ratio distribution that primarily lies above the value of 1.0 indicates early life exposures to a carcinogen result in a stronger tumor response relative to adult exposure. Conversely, a lifestage cancer potency ratio distribution that mainly lies below the value of 1.0 indicates early life exposure to a carcinogen results in a weaker tumor response relative to adult exposure.

A lifestage potency (LP) ratio distribution was derived for each multi-lifestage study, resulting in 22 prenatal ratio distributions representing 14 unique carcinogens, 55 postnatal LP ratio distributions representing 18 unique carcinogens, and seven juvenile LP ratio distributions representing five unique carcinogens. The LP ratio distributions for a given early lifestage were combined into a single "LP ratio mixture distribution," in order to show the range of susceptibilities of that lifestage to the carcinogens studied.

LP ratio mixture distributions for a given early lifestage were developed by (1) obtaining a single LP ratio distribution for each chemical (when a chemical is represented by more than one study) and then (2) equally sampling across all chemicals. When a chemical is represented by more than one study, then the LP ratio distributions from all studies of that chemical were combined by equally sampling from each LP ratio distribution via Monte Carlo methods to obtain a single LP ratio distribution for that chemical. (Appendix J describes this in more detail, as well as a

sensitivity analysis that included two alternative sampling methods.) Once each chemical is represented by a single LP ratio distribution, then the LP ratio mixture distribution for each early lifestage (prenatal, postnatal, and juvenile) is obtained by equally sampling across all of the chemicals via Monte Carlo methods.

Figure 5. Lifestage Potency Ratio (LPR) distribution.

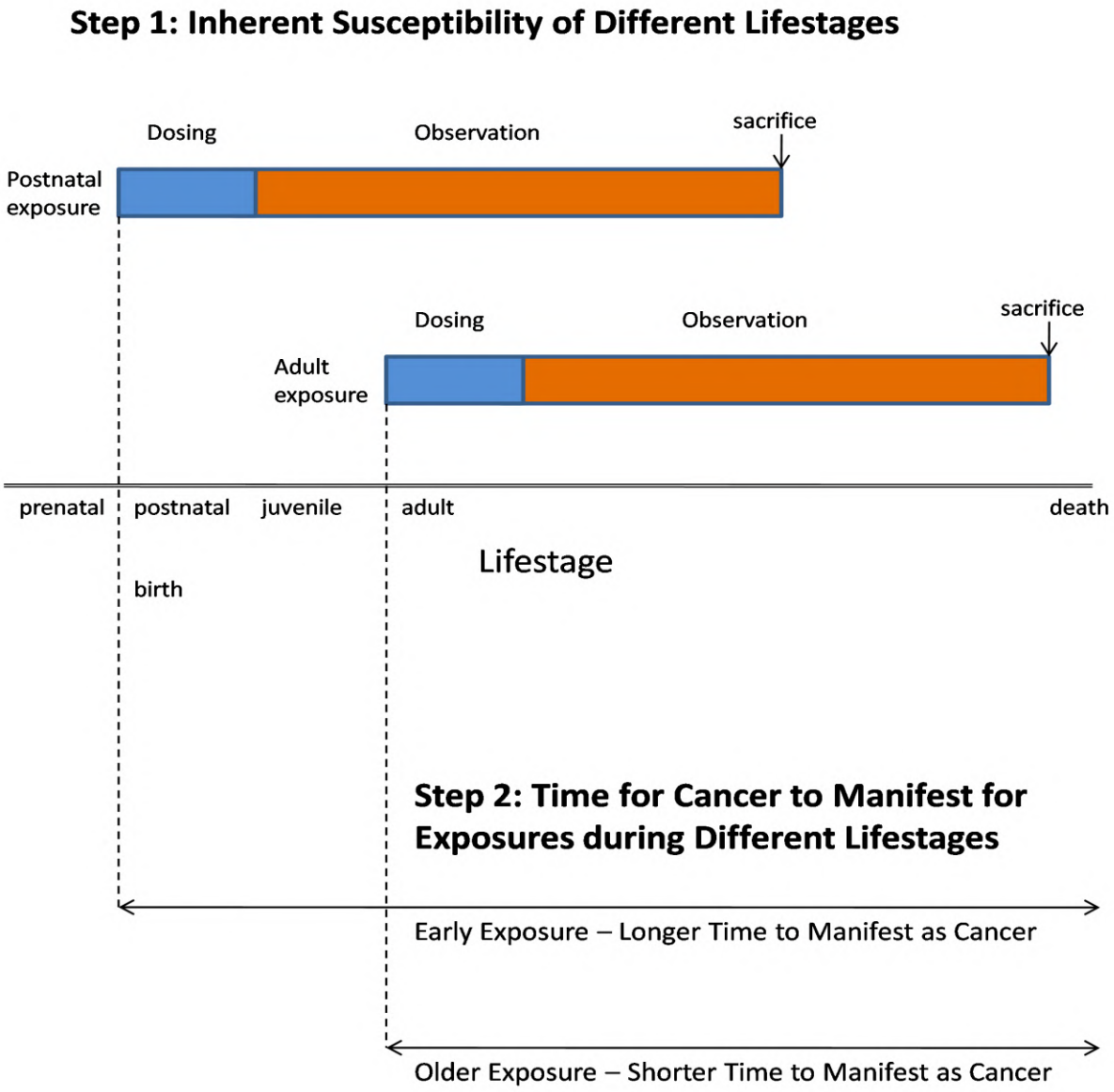


Effect of Longer Time Period for Cancer to Manifest

The LP ratios described above characterize the inherent susceptibility of early lifestages to carcinogen exposure, by comparing potencies for individuals followed for similar periods of time and similarly exposed, but exposed during different lifestages. Age-specific adjustments to the cancer potency must also take into account the longer period of time that carcinogen exposure to the young has to manifest as cancer. Empirical data from studies of both humans and animals demonstrate that, for many cancers, cancer risk increases with age, or time since first exposure. While some cancers have been seen to increase by as much as the sixth power of age, a general approach taken for example by the National Toxicology Program in analyzing tumor incidences in its chronic bioassays is to assume that cancer risk increases by the third power of age. Thus, consistent with the approach used by the NTP in analyzing rodent cancer bioassay data, the longer period of time that exposed young have to develop tumors is addressed by taking into account time-of-dosing. This was done by multiplying the LP ratio by a time-of-dosing factor, to yield an age sensitivity factor (ASF). Specifically, the prenatal LP ratio is multiplied by a factor of 3.0, the postnatal LP ratio is multiplied by a factor of 2.9, and the juvenile LP ratio is multiplied by 2.7. Thus, ASFs were developed for each experiment, by first calculating the LP ratio to address inherent susceptibility of early lifestages relative to adults, and then accounting for the effect of years available to manifest a tumor following carcinogen exposure. (see Figure 6). Note that we

are not using the term "sensitivity" in the immunologic sense (*e.g.*, sensitization), but rather are using the term more generically.

Figure 6. Issues addressed by the Age-Sensitivity Factor (ASF)



Application of this approach for risk associated with lifetime exposures would include an ASF of less than 1 for exposures during the latter part of adult life for carcinogens that act on early stages. Therefore, the addition of this adjustment to the younger lifestages but not to the later part of the adult period could overestimate the risk of whole-life exposures. On the other hand, the 70 year "lifetime" used in estimating lifetime cancer risk does not reflect the longer lifespan of the U.S. population. Further, as noted above, the animal bioassays on which potency was based typically exclude pre-weaning dosing and sacrifice animals during their late middle-age. Use of cancer potencies calculated from standard assays can therefore underestimate lifetime cancer risk. The ASF calculated for carcinogens includes both inherent sensitivity of developing animals and the available time since exposure to develop cancer.

Results of OEHHA Analysis

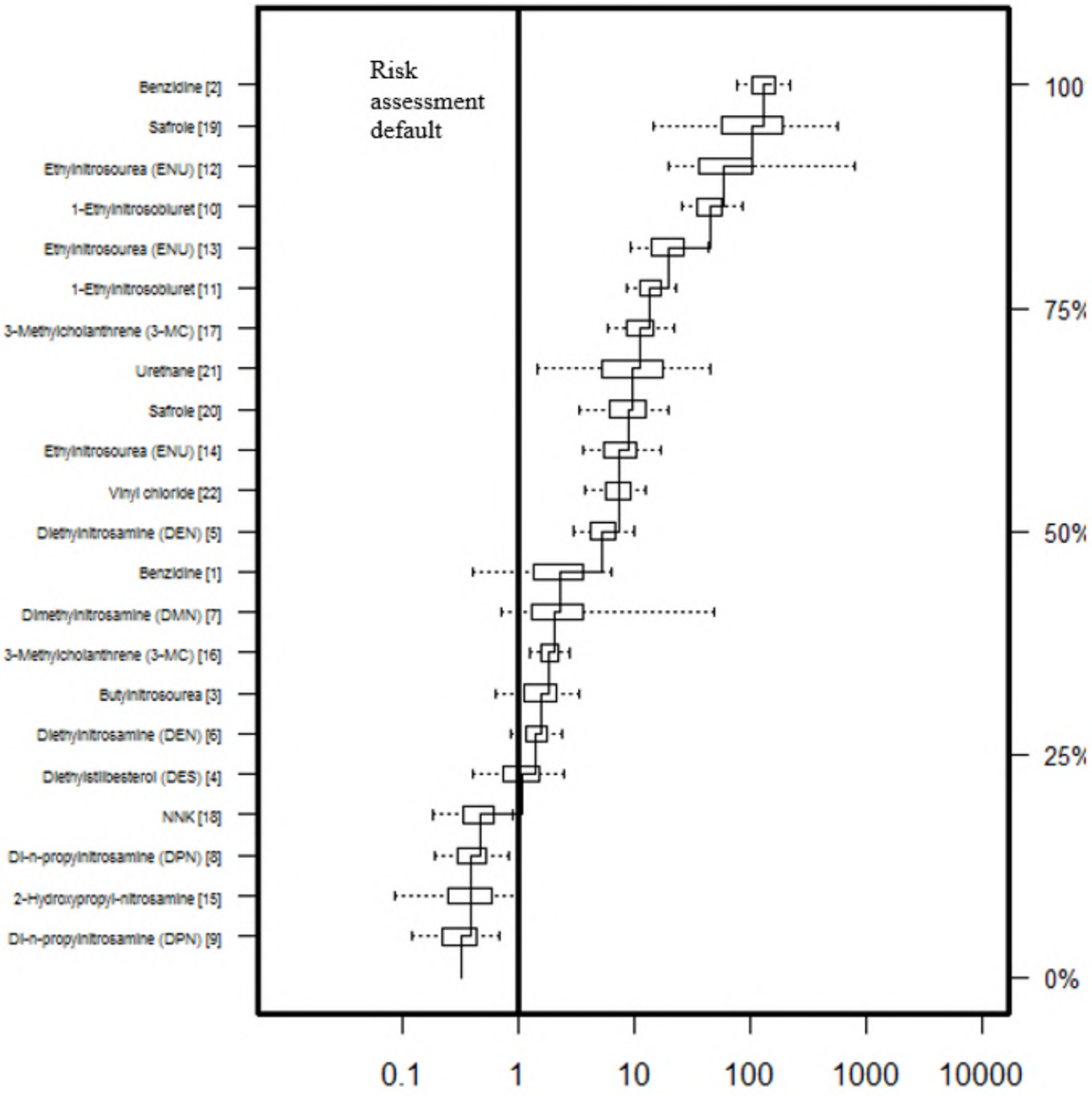
The analyses indicate that both the prenatal and postnatal lifestages can be, but are not always, much more susceptible to developing cancer than the adult lifestage. The analyses also indicated that the ASFs for these age windows vary by chemical, gender and species.

Regarding prenatal lifestage exposure, few cases were indicative of equal inherent adult and prenatal susceptibility, with an LP ratio of unity. The LP ratio distribution was roughly bimodal, with LP ratios for several studies significantly greater than unity and several others significantly less than unity. Figure 7 below shows the ASFs from each of the prenatal multi-lifestage exposure studies, displayed as a cumulative frequency profile. The median of the prenatal ASF mixture distribution was 2.9 (see also Table 6 in Appendix J),

The modality in the prenatal LP ratio distribution was reflected in the DEN and ENU case studies, with results for DEN suggesting inherently less sensitivity than older animals from exposure *in utero*, and for ENU just the opposite. For the DEN and ENU case studies, the referent groups were juvenile rather than adult animals, and the results may have underestimated the LP ratio and ASF, to the extent that some of the apparent sensitivity for DEN and ENU in the prenatal period carries through to the juvenile period. ENU is a direct acting carcinogen that does not require metabolic activation, whereas DEN can not be metabolized to any significant extent by fetal tissues until relatively late in gestation. This may explain the lower fetal susceptibility of DEN. However, prenatal metabolic status is not the sole determinant of prenatal susceptibility; *e.g.*, benzidine and safrole require metabolic activation and exhibit greater susceptibility from prenatal exposure.

The median of the postnatal ASF mixture distribution was 13.5 (see Table 7 in Appendix J). Figure 8 below shows the ASFs from each of the postnatal multi-lifestage exposure studies, displayed as a cumulative frequency profile. Thus, for the chemicals studied, there was generally greater susceptibility to carcinogens during the early postnatal compared to the adult period, particularly when the ASF accounts for the longer period cancer has to manifest when exposure occurs early in life. The DEN and ENU case studies also exhibited substantial extra susceptibility during the postnatal period. To summarize, for most of the carcinogens studied here, rodents are inherently more sensitive in the postnatal period, as indicated by Figure 8.

Figure 7. Prenatal ASF Cumulative Frequency Profile

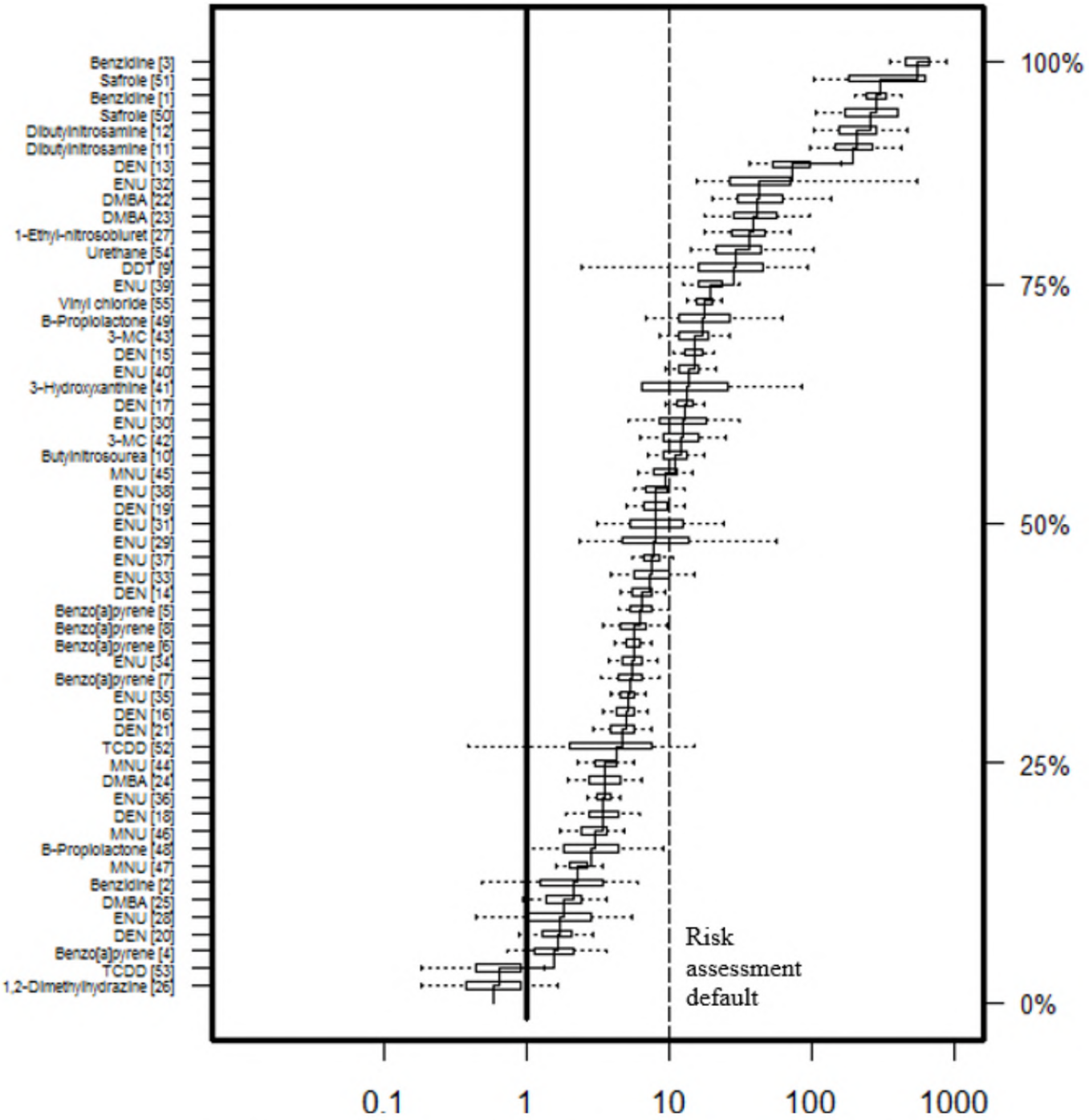


The median of the prenatal ASF mixture distribution was 2.9 (see also Table 6 in Appendix J). References are given in the legend on the next page

Figure 7 Legend (References as in Appendix J)

1. Vesselinovitch *et al.* (1979a), mouse, B6C3F_1, F, day -9 to 0
2. Ibid, M, day -9 to 0
3. Zeller *et al.* (1978), rat, Sprague Dawley, M/F day -2
4. Turusov *et al.* (1992), mouse, CBA, F, day -2
5. Mohr et al. (1975), hamster, Syrian Golden, day -15 to -1
6. Mohr *et al.* (1995), hamster, Syrian Golden, F, day -3
7. Althoff *et al.* (1977), hamster, Syrian Golden, M/F, day -9 to -3
8. Ibid, day -9 to -3
9. Althoff and Grandjean (1979), hamster, Syrian Golden, F, day -9 to -3
10. Druckrey and Landschutz (1971), rat, BD IX, M/F, day -10
11. Ibid, day -3
12. Naito *et al.* (1981), rat, Wistar, day -9
13. Ibid, day -9
14. Tomatis *et al.* (1977), rat, BDVi, F, day -5
15. Althoff and Grandjean (1979), hamster, Syrian Golden, M/F, day -9 to -3
16. Tomatis *et al.* (1971), mouse, CF-1, F day -4 to -1
17. Turusov *et a*l. (1973), mouse, CF-1, F, day -2
18. Anderson *et al.* (1989), mouse, C3H & B6C3 F_1,M/F day -8 to -4
19. Vesselnovitch *et al.* (1979a), mouse, B6C3 F_1, M, day -9 to -3
20. Vesselnovitch *et al.* (1979b), mouse, B6C3 F_1, F day -9 to -3
21. Choudari Kommineni *et al.* (1970), rat, MRC, M/F, day -4
22. Maltoni *et al.* (1981), rat, Sprague Dawley, M/F day -13 to -7

Figure 8. Postnatal ASF Cumulative Frequency Profile



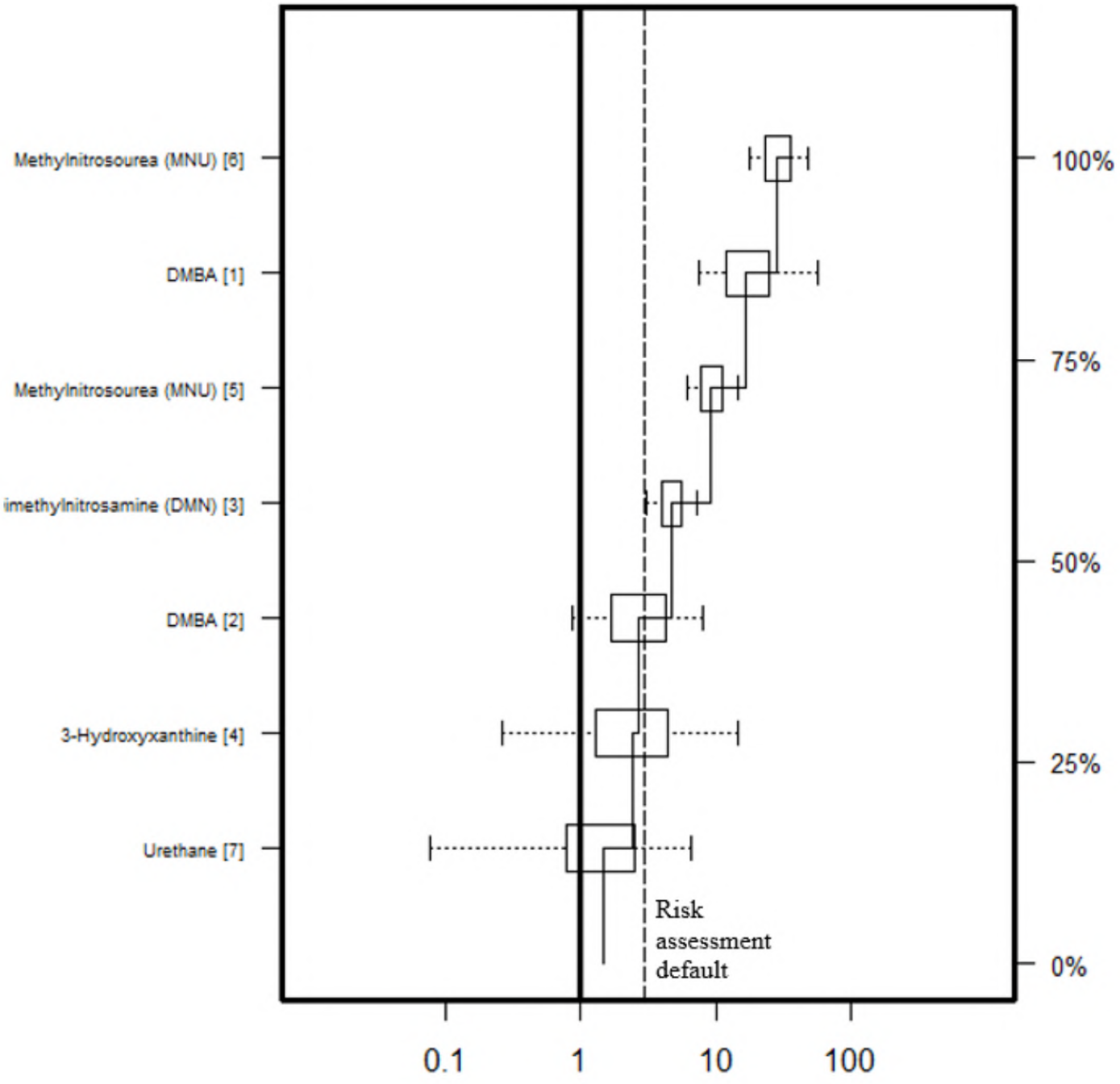
The median of the postnatal ASF mixture distribution is 13.5. The dotted line represents the default ASF for weighting risk for carcinogen exposures to humans between the third trimester and 2 years of age (see next section). References are given in the legend on the next page.

Figure 8 Legend (References as in Appendix J)

1 Vesselinovitch *et al.* (1975b), mouse, B6C3F$_1$, M, day 7-27
2 Vesselinovitch *et al.* (1979), mouse, B6C3F$_1$, F, day 1-21
3 Ibid, M, day 1-21
4 Truhaut *et al.* (1966), mouse, swiss, M/F, day 1
5 Vesselinovitch *et al.* (1975a), mouse, B6C3F$_1$, F, day 1
6 Ibid, M, day 1
7 Ibid, C3A F$_1$, F, day 1
8 Ibid, M, day 1
9 Vesselinovitch *et al.* (1979a), mouse, B6C3F$_1$, M, day 1-28
10 Zeller *et al.* (1978), rat, Sprague Dawley, M/F, day 2
11 Wood *et al.* (1970), mouse, IF x C57, F, day 1-15
12 Ibid, M, day 1-15
13 Rao and Vesselinovitch (1973), mouse, B6C3F$_1$, M, day 15
14 Vesselinovitch *et al.* (1984), mouse, B6C3F$_1$, F, day 1
15 Ibid, M, day 1
16 Ibid, F, day 15
17 Ibid, M, day 15
18 Ibid, C3A F$_1$, F, day 1
19 Ibid, M, day 1
20 Ibid, F, day 15
21 Ibid, M, day 15
22 Meranze *et al.* (1969), rat, Fels-Wistar, F, day 10
23 Ibid, M, day 10
24 Walters (1966), mouse, BALB/c, F, day 17
25 Ibid, M, day 17
26 Martin *et al.* (1974), rat, BDIX, M/F, day 10
27 Druckrey and Landschutz (1971), rat, BDIX, M/F, day 10
28 Naito *et al.* (1985), gerbil, mongolian, F, day 1
29 Ibid, M, day 1
30 Bosch (1977), rat, WAG, F, day 8
31 Ibid, M, day 8
32 Naito *et al.* (1981), rat, Wistar, F, day 7
33 Ibid, M, day 7
34 Vesselinovitch *et al.* (1974), mouse, B6C3F$_1$, F, day 1
35 Ibid, M, day 1
36 Ibid, F, day 15
37 Ibid, M, day 15
38 Ibid, C3A F$_1$, F, day 1
39 Ibid, M, day 1
40 Ibid, M, day 15
41 Anderson *et al.* (1978), rat, Wistar, F, day 9
42 Klein (1959), mouse, A/He, F, day 8-31
43 Ibid, M, day 8-31
44 Terracini and Testa (1970), mouse, B6C3F$_1$, F, day 1
45 Ibid, M, day 1
46 Terracini *et al.* (1976), mouse, C3Hf/Dp, F, day 1
47 Ibid, M, day 1
48 Chernozemski and Warwick (1970), mouse, B6A F$_1$, F, day 9
49 Ibid, M, day 9
50 Vesselinovitch *et al.* (1979a), mouse, B6C3F$_1$, M, day 1-21
51 Vesselinovitch *et al.* (1979b), mouse, B6C3F$_1$, M, day 1-21
52 Della Porta *et al.* (1987), mouse, B6C3F$_1$, F, day 10-45
53 Ibid, M, day 10-45
54 Choudari Kommineni *et al.* (1970), rat, MRC, M/F, day 1-17
55 Maltoni *et al.* (1981), rat, Sprague Dawley, M/F, day 1-35

There were only five chemicals and seven studies, two of which were not independent, available to examine susceptibility in the juvenile period. The juvenile LP ratios indicated significantly greater susceptibility in this period for three independent studies, with the remaining studies consistent with equal inherent susceptibility to adult animals (see Figure 16 in Appendix J). Figure 9 below shows the ASFs from each of the juvenile multi-lifestage exposure studies, displayed as a cumulative frequency profile. The median of the juvenile ASF mixture distribution was 4.5 (see Table 8 in Appendix J).

Figure 9. Juvenile ASF Cumulative Frequency Profile



The median of the juvenile ASF mixture distribution is 4.5. The dotted line represents the default value for weighting risk for carcinogen exposures between 2 and 15 years of age (see next section).

Figure 9 Legend (References as in Appendix J)

1. Meranze *et al.* (1969), rat, Fels-Wistar, F, day 45
2. Ibid, M, day 45
3. Noronha and Goodall (1984), rat, CRL/CDF, M, day 46
4. Anderson *et al.* (1978), rat, Wistar, F, day 28
5. Grubbs *et al.* (1983), rat, Sprague Dawley, F, day 50-57; adult comparison group dosed on days 80-87
6. Ibid, F, day 50-57; adult comparison group dosed on days 140-147
7. Choudari Kommineni *et al.* (1970), rat, MRC, M/F, day 28-43

The studies that comprise the set of multi-lifestage exposure studies available for these analyses were not homogeneous. That is, they do not represent observations from the same distribution. Sensitivity analyses were conducted to test the robustness of the findings to different procedures for analyzing data and combining results. Of the methods used to combine the LC ratio distributions for underlying studies within each lifestage, the method of equally weighting studies within a chemical appeared to best represent the available data.

In calculating the ASF, to take into account the longer period of time for early carcinogen exposures to result in tumors, the hazard function was assumed to increase with the third power of age. This assumption is standard and has been borne out by a number of observations (Bailer and Portier, 1988). If the true rate of increase with age is greater than that, then the use of these ASFs may result in underestimates of the true sensitivity of these early life stages.

As the multi-lifestage exposure and case studies show, there appears to be considerable variability in age-at-exposure related susceptibility across carcinogens. There is also variability in age-at-exposure related susceptibility among studies of the same carcinogen. The sources of variability evident in the analyzed studies include timing of exposure within a given age window, and gender, strain, and species differences in tumor response. The set of studies identified and analyzed was not sufficiently robust to fully describe the variability quantitatively. This variability raises concerns that selection of the median (the 50th percentile) estimates may considerably underestimate effects for certain agents or population groups. Relatively large variability in humans in response to carcinogens is expected to be common (Finkel, 1995). On the other hand, the numbers of carcinogens represented in the available data are limited and may not be representative of the population of carcinogens to which we are exposed (*e.g.*, greater than 500 on the Proposition 65 list alone). Thus, the size of the weighting factors used to weight risk by age at exposure is a policy decision.

Several of the carcinogens studied induced tumors at multiple sites in the same experiment, and at different sites, depending upon the lifestage during which exposure occurred. For these cases the combined multisite potency distribution referred to above was the basis for the lifestage comparison. This approach differs from other researchers investigating early vs. late in life differences who focused on tumor site-specific measures of carcinogenic activity (*e.g.*, Barton *et al.*, 2005; Hattis *et al.*, 2004, 2005). OEHHA believes that use of combined multisite potency distributions provides a more complete approach for considering age specific differences in carcinogenic activity. However, the observation that early life is generally a period of increased

susceptibility was similarly found using the tumor site-specific approach by these other researchers.

One limitation of the approach was the focus on lifestages, without attempting to describe changes in susceptibility that occur within a lifestage. Timing of carcinogen exposure within a given age window can affect the cancer outcome. For example, experiments with 1-ethyl-1-nitroso-biuret in prenatal and adult rats showed a three-fold difference in activity between groups exposed on prenatal day -10 versus prenatal day -3. In a second example, female rats exposed early in the adult period were more than three times as sensitive to the breast cancer effects of MNU as females exposed six weeks later. In general, the adult comparison groups in the multi-lifestage exposure studies were fairly young. The extent to which this may result in an overall bias of the results presented here is unclear. Also, for several cases, juvenile animals were used as the later life exposure group. In these cases the ASFs are likely underestimates of the relative sensitivity of the prenatal and postnatal lifestages, compared to that of the adult lifestage.

Excluded from the analysis were early in life studies in which the period of exposure for a specific exposure group crossed multiple lifestages. An example of results from studies of this type is provided by mouse studies for two non-genotoxic carcinogens, diphenylhydantoin (Chhabra *et al*., 1993a) and polybrominated biphenyls (PBBs) (Chhabra *et al*., 1993b), in which exposures began prior to conception, and continued throughout the prenatal, postnatal, and post-weaning period, up to the age of eight weeks. The data demonstrate an increased sensitivity of the early life period. Some studies that crossed multiple lifestages were included in the analyses of Barton *et al*. (2005) (Appendix I), which are consistent with the general conclusions discussed above.

Selection of Default Age-Sensitivity Factors (ASF)

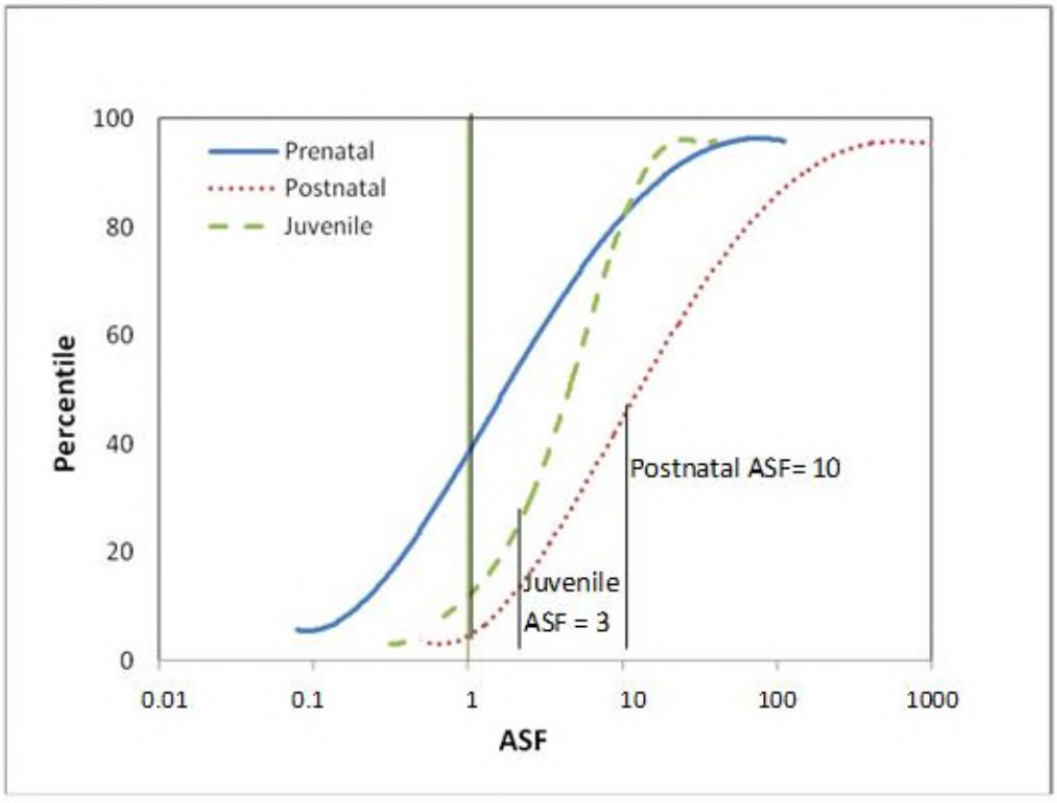
Selection of appropriate values to use to weight exposures that occur early in life using default ASFs for prenatal, postnatal and juvenile exposures is complicated by the limited database of chemicals and studies available for analysis, and the broad distribution of results for different chemicals as is shown in Figure 7, Figure 8, and Figure 9 (see also Appendix J). In view of the variability thus shown, and the considerable uncertainty in applying conclusions from this relatively small set of chemicals to the much larger number of chemicals of concern, it is probably unreasonable to specify a default ASF with greater than half-log precision (*i.e.* values of 1, 3, 10, 30 etc.). Further, rodents are born at a stage of maturity that approximates a third trimester human. Therefore, in the absence of chemical-specific data, OEHHA proposes to apply a default ASF of 10 for the third trimester to age 2 years, and a factor of 3 for ages 2 through 15 years to account for potential increased sensitivity to carcinogens during childhood. A factor of 10 falls just below the median estimate of the ASF for postnatal studies. This is also the value selected by U.S. EPA; while it is consistent with the OEHHA analysis, it may underestimate risk for some chemicals. The broad distribution of observed chemical-specific sensitivity ratios clearly indicates that there are some chemicals for which the sensitivity ratio is much larger than 10. Further research is needed to develop criteria for identifying these cases. Similarly, a factor of 3 for juvenile exposures is consistent with the range of estimates derived from the multi-lifestage exposure studies, and falls close to the median juvenile ASF estimate. It is acknowledged that there are few data available on which to base an estimate for the juvenile period. A factor of 3 adjusts for the longer time available for cancer to manifest, but may not fully account for some inherent differences in susceptibility to cancer, for example the observed susceptibility of breast tissue of

pubescent girls exposed to radiation. For specific carcinogens where data indicate enhanced sensitivity during lifestages other than the immediate postnatal and juvenile periods, or demonstrate ASFs different from the default ASFs, the chemical-specific data should be used in order to adequately protect public health.

The ASFs will be applied to all carcinogens, regardless of the theorized mode of action. While U.S. EPA currently intends to apply weighting factors only to those carcinogens with "a mutagenic mode of action" (U.S.EPA, 2005), OEHHA notes that there is evidence that early life is a susceptible time for carcinogens that are thought to act via non-mutagenic mode of action (DES is a prime example). Defining a mutagenic mode of action may be problematic if approached narrowly (ERG, 2008). Further, carcinogens may have multiple modes of action and one mode may predominate over other modes at different lifestages. The complexity of carcinogenesis argues against restricting the ASF to chemicals acting via a mutagenic mode of action.

Figure 10 provides a visual comparison of the ASF mixture distributions for the three early-life stages, prenatal, postnatal, and juvenile. In this figure, which is in log space, the policy choice of an ASF of 10 for exposures during the third trimester to age 2 years and 3 for the period of life from 2 to 15 years of age are indicated as vertical lines. It is apparent from this figure that weighting risk from exposures to carcinogens early in life is well-supported.

Figure 10. Prenatal, Postnatal, and Juvenile ASF Mixture Distributions and relation to default ASFs



OEHHA recognizes the limitations in the data and analyses presented, as discussed above. However, the analyses do provide some guidance on the extent to which risk may be over or underestimated by current approaches. While there is a great deal of variability across chemicals in the prenatal ASFs, the data indicate that the potency associated with prenatal carcinogen exposure is not zero. A factor of 3 is close to the median ASF, while a factor of 10 falls roughly at the 70th percentile of the prenatal ASF estimate. An ASF could be applied as a default when calculating lifetime cancer risk in humans arising from carcinogen exposures that occur *in utero*. In view of the considerable variability in the data for different carcinogens and the limited database available for analysis, OEHHA is not proposing the application of a specific factor to cancer potency estimates for prenatal exposures in the first and second trimesters as a default position in these Guidelines. However, given that the rodent is born at a stage of maturation similar to a third trimester fetus, it is reasonable to include the third trimester in the 10X potency weighting proposed up to age 2 years. The applicability of a cancer potency adjustment factor for first and second trimester prenatal exposure will be evaluated on a case-by-case basis, and may be used as evidence develops that supports such use. The consideration of prenatal exposures, including application of an appropriate susceptibility factor, would not make a large difference for risk estimates based on continuous lifetime exposures, due to the relatively short duration of gestation. However, risk estimates for short-term or intermittent exposures would be slightly increased by inclusion of the risks to the fetus during the prenatal period. Thus, risk may be underestimated when the first and second trimesters are excluded from the analysis.

Age Bins for Application of ASFs

The choice of human ages to which the ASFs apply is based on toxicodynamic and toxicokinetic considerations. Important toxicodynamic factors related to susceptibility to carcinogens include the rate of cellular proliferation and differentiation, which is quite high during organ maturation. In addition, toxicokinetic differences by age are important, due to impacts on detoxification and clearance of carcinogens (see following section). OEHHA's analysis of the influence of age-at-exposure on carcinogenesis broke the experimental rodent data into age bins that we termed "lifestages" including prenatal, "postnatal" (birth to weaning, about day 21) and "juvenile" (weaning to sexual maturation, or about day 22 to about day 49). Experiments were placed into the lifestage bins if exposure occurred at some time during the experimental rodent age bin.

There is no simple way to compare the rodent age groups used in the OEHHA analysis of available data to equivalent age groups in humans. Complicating factors include variations in organ system structural and functional maturation both within and between species. Further, the rodent age bins were chosen by gross indicators of development namely birth, weaning and sexual maturation, not on the basis of known susceptibility to carcinogenesis. Thus, critical factors relating to carcinogen susceptibility by age are the focus of the choice of human age bins to which the ASFs of 10 and 3 apply, rather than an attempt at exact correlation of rodent lifestage bin with human age.

The investigations used by OEHHA to evaluate the relationship between age at exposure and cancer potency were not conducted by standardized protocol. Further, the windows of susceptibility are quite varied by chemical and organ system, even within the lifestages defined in the OEHHA analysis. This complicates choosing a default ASF and the human age bin to which it applies. Examples from animal studies provided in Appendix J include the chemical diethylnitrosamine (DEN). The cancer potency varied over several orders of magnitude depending

on when during gestation and postnatal life the exposure occurred. A three-fold difference in potency between exposure on prenatal day -3 and prenatal day -10 is noted for 1-ethyl-1-nitrosobiuret in rats. There are also human examples of extensive variation of potency by age at exposure, including radiation, DES, and chemotherapeutic agents. The diversity of responses to different agents obviously underscores uncertainty in the choice of age bins to apply the default ASFs. However, the ASFs are a ***default*** to use when you have no chemical-specific data on influence of age-at-exposure on potency in order to protect public health. There will always be specific chemical examples where the ASF for either the third trimester-<2 yrs or 2-<16 yrs age bin is quite a bit larger or quite a bit smaller than the default.

In the following sections, we discuss our logic in proposing age bins of third trimester to age 2 years, and 2 to age <16 years to which the ASFs of 10 and 3 apply, respectively, and indicate the impact on risk estimates of these age bins.

Toxicokinetic Factors Relevant to Age Bins

Choice of the age-bins to which the default ASFs are applied is based on our understanding of the two primary drivers of age-related sensitivity to carcinogens, namely age-related toxicokinetic factors and toxicodynamic factors. In the case of toxicokinetics, the largest postnatal differences in xenobiotic metabolic capability occur between infants and adults. As noted in OEHHA (2001) and reviewed in detail elsewhere (*e.g.*, Cresteil et al., 1998; Ginsberg et al., 2004), hepatic drug metabolism by the cytochrome P-450 family of enzymes and the Phase II conjugating enzymes undergoes a maturation process during the first few years of life. The hepatic cytochrome P-450 enzymes exist in fetal isoforms at birth, and progressively change to adult isoforms at a relatively early stage of postnatal development. Thus, in humans the metabolic capability towards prototypical substrates develops over the first year of life towards adult levels. Similarly, the largest differences in metabolic capability of Phase II enzymes (conjugation of xenobiotic metabolites prior to excretion) tend to be between infants and adults. Other factors such as renal capability also are most different between neonates and adults. Thus, the first 2 years of life would encompass the increased sensitivity of early life stages due to toxicokinetic differences between early life and adulthood.

Ontogeny of Cytochrome P-450 Enzymes in Humans.

Cresteil (1998) describes three groups of neonatal cytochrome P-450: Cyp3A7 and Cyp4A1 present in fetal liver and active on endogenous substrates; an early neonatal group including Cyp2D6 and 2E1 which surge within hours of birth; and a later developing group, Cyp3A4, Cyp2Cs, and Cyp1A2. Total Cyp 3A protein, a major cytochrome P-450 enzyme responsible for biotransformation of many xenobiotics, is relatively constant in neonates and adults. However, Cyp3A7 is the primary fetal form (Hakkola et al., 1998), while Cyp3A4 is the primary adult hepatic form of the 3A series. At one month Cyp3A4 activity is about one-third of that in the adult liver (Lacroix et al., 1997; Hakkola et al., 1998). Allegaert *et al*. (2007) stated that Cyp3A4 (testosterone-6ß-hydroxylase) activity equaled or exceeded adult activity after 1 year of age. Cyp2E1, which metabolizes benzene, trichloroethylene and toluene, among others, increases gradually postnatally, reaching about one-third of adult levels by one year of age and attains adult levels by 10 years of age (Vieira et al., 1996; Cresteil, 1998). Cyp1A2, and Cyp2C9 and 2C19, the most abundant Cyp2 enzymes in adult human liver, appear in the weeks after birth, and reach

30% to 50% of adult levels at about 1 year of age (Treluyer et al., 1997; Hines and McCarver, 2002). Cyp1A1 is expressed in fetal liver where it can activate such xenobiotics as benzo[a]pyrene and aflatoxin B1 (Shimada et al., 1996), but is less important in adult liver (Hakkola et al., 1998).

Ontogeny of Cytochrome P-450 Enzymes in Rodents.

Hart et al. (2009) report developmental profiles of a number of cytochrome P-450 enzymes (measured as levels of mRNA transcripts of the specific genes) in mice. They identified three groups of isoforms. Group 1 (Cyp3A16 in both sexes; Cyp3A41b in males) appeared rapidly after birth but declined to essentially zero at 15-20 days, which is the period of weaning in mice. A second group (Cyp2E1, Cyp3A11 and Cyp4A10 in both sexes; Cyp3A41b in females) also increased rapidly after birth, but reached a stable maximal level by postnatal day 5. The third group (Cyp1A2, Cyp2A4, Cyp2B10, Cyp2C29, Cyp2D22, Cyp2F2, Cyp3A13 and Cyp3A25) were expressed only at low levels until days 10 to 15, but reached high stable levels by day 20.

ElBarbry et al. (2007) examined the developmental profiles of two toxicologically significant cytochrome P-450 enzymes, Cyp1A2 and Cyp2E1 in rats. mRNA transcripts of these genes were very low postnatally, but thereafter increased to reach a peak at or shortly after weaning (postnatal day 21 - 28 for rats). Immunoreactive Cyp1A2 and Cyp2E1 proteins were first detectable at postnatal day 3 and reached 50% of adult levels at weaning and adult levels at puberty. Differences in profiles between gene expression as mRNA and appearance of specific proteins as determined by immunoassay may reflect changes in the relative importance of transcription and translation control processes at various phases in development. Enzyme activities characteristic of Cyp1A2 and Cyp2E1 were found to parallel gene expression levels (ElBarbry et al., 2007) rather than immunodetectable protein levels, so there may also be issues of cross-reactivity between these two isoenzymes and others for which gene expression was not measured in these experiments.

In summary, the gene expression data in rats and mice show differences in details, but broadly resemble one another in that the main changes occur in the early postnatal period, with the major adjustments completed at or around the time of weaning, although the adult pattern may not be completely established until puberty. There do not appear to be substantive data for experimental species other than rats and mice, although the situation in humans appears similar in general outline and one may conclude that this pattern or some variant of it is characteristic of mammalian species in general.

Ontogeny of Phase II Enzymes

Phase II conjugating enzymes are generally less active in the neonate than the adult (Milsap and Jusko, 1994). Hence, there is concern that detoxification and elimination of chemicals is slower in infants. In humans, expression of some of the UGT enzymes matures to adult levels in two months after birth, although glucuronidation of some drugs by the UGT1A subfamily does not reach adult levels until puberty (Levy et al., 1975; Snodgrass, 1992; McCarver and Hines, 2002). Reduced glucuronidation in neonates slows the clearance of *N*-hydroxyarylamines, phenol, and benzene metabolites. Acetylation by the N-acetyltransferases and sulfation by sulfotransferases are generally somewhat comparable to adult levels, although it varies by tissue and by specific sulfotransferase (McCarver and Hines, 2002). Human glutathione sulfotransferase (GST) is present as a fetal isoform which decreases postnatally, while GST-alpha and GST-mu increase

over the first few years of life to adult levels (McCarver and Hines, 2002). Epoxide hydrolase, important in detoxifying reactive epoxide metabolites, is present in neonatal liver although at much reduced activity relative to adults (McCarver and Hines, 2002).

Clearances of Drugs in Infants and Children vs. Adults

Several investigators have evaluated age-related drug disposition (Renwick, 1998; Renwick et al., 2000; Ginsberg et al., 2002; Hattis et al., 2003). Renwick et al. (2000) noted higher internal doses in neonates and young infants versus adults for seven drugs that are substrates for glucuronidation, one with substrate specificity for CYP1A2, and four with substrate specificity for CYP3A4 metabolism. Ginsberg et al (2002) evaluated toxicokinetic information on 45 drugs in children and adults metabolized by different cytochrome P-450 pathways, by Phase II conjugations, or eliminated unchanged by the kidney. These authors noted half-lives 3-9-fold longer in infants than those in adults. It was also shown that the bulk of the elevated child/adult half-life ratios occurred primarily in the 0 to 6 month age range, and that for some compounds the clearance is actually higher in the 6 month to 2 year age grouping. In evaluating the interindividual variability by age, Hattis et al (2003) note that the largest interindividual variability occurs in the youngest children, apparently due to variability in development of critical metabolism and elimination pathways. Anderson and Holford (2008) noted that a comparison of three early-life drug clearance models (surface area, allometric ¾ power and per kilogram scaling) all demonstrated an increase in clearance over the first year of life due to the maturation of metabolic capacity.

Renal elimination depends on maturity of processes related to tubular reabsorption and secretion, and glomerular filtration rates. At birth, the glomerular filtration rate (GFR) is low (2-4 ml/min), increases in the first few days (8-20 ml/min) and slowly increases to adult values in 8-12 month old infants (Plunkett et al., 1992; Kearns et al, 2003).

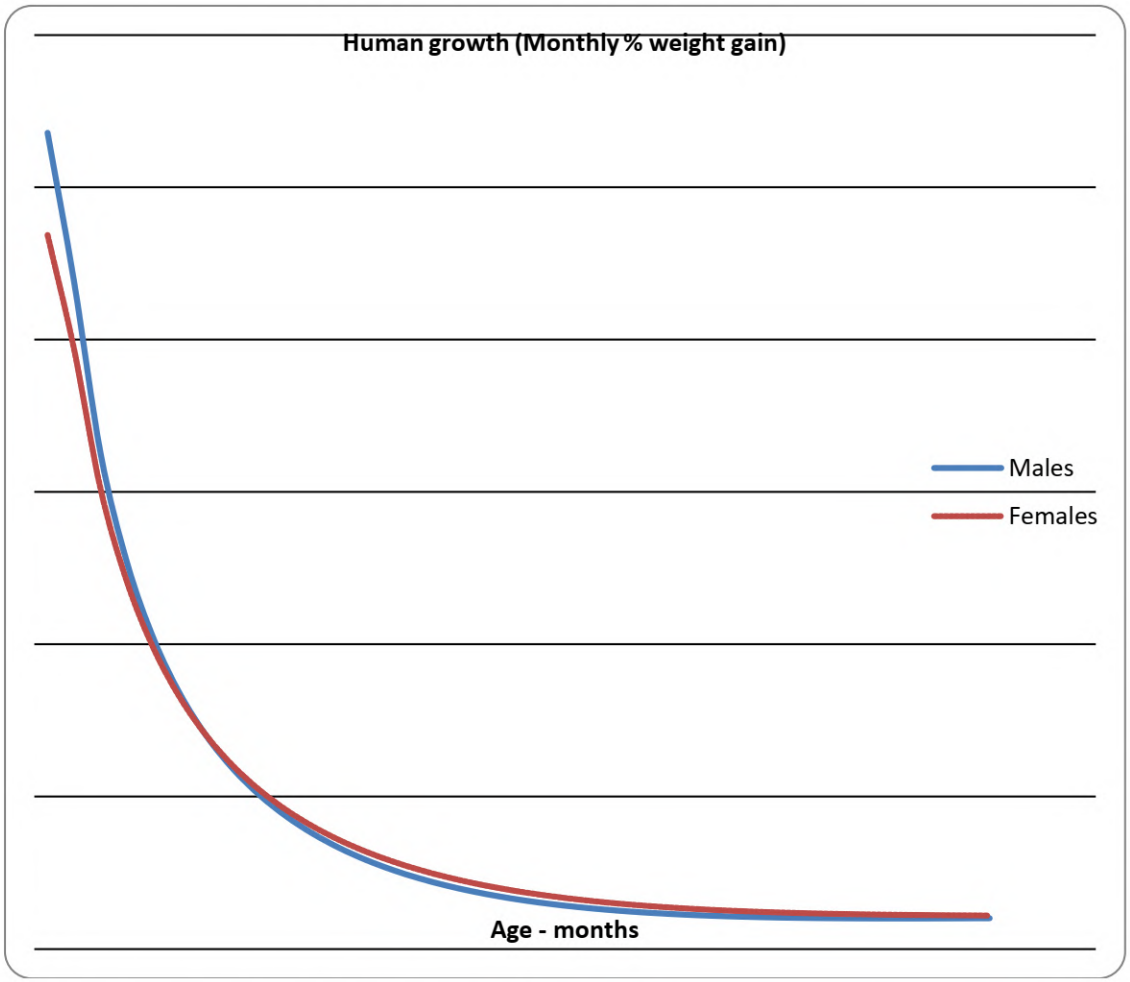
Newborn and young animals have less capacity to excrete chemicals into the bile than do adult animals. A number of chemicals are excreted more slowly via bile in neonates than adult rats, including ouabain, the glucuronide conjugate of sulfobromophthalein (Klaassen, 1973), and methyl mercury (Ballatori and Clarkson, 1982), resulting in a longer half-life in neonates.

Toxicodynamic Factors Relevant to Age Bins

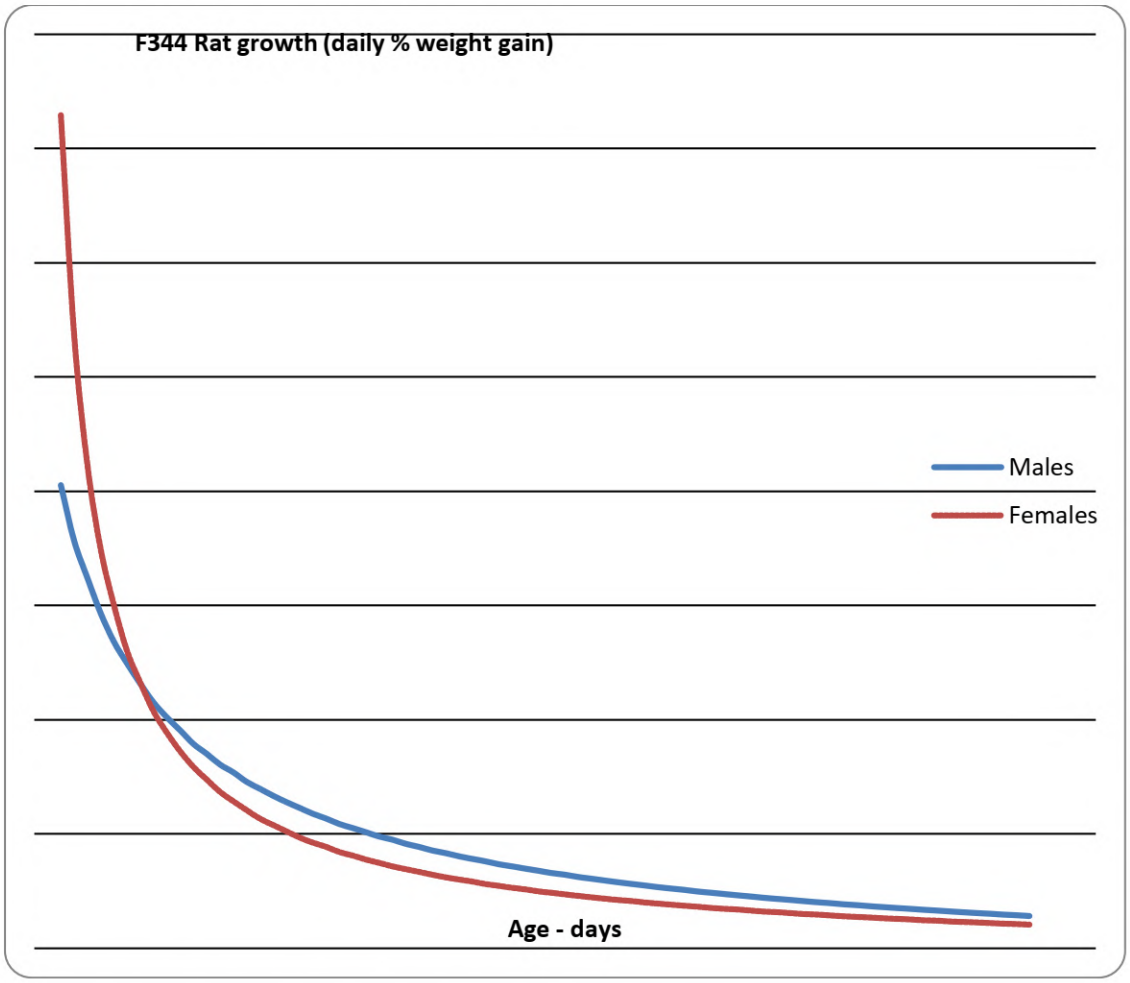
Important as the developmental changes in toxicokinetics are in determining sensitivity to carcinogens and other toxicants, it is likely that the toxicodynamic differences, *i.e.* intrinsic differences in susceptibility to carcinogenesis at the tissue or cellular level, are even more influential. Changes in cell division rates and differentiation, which are thought to be important toxicodynamic determinants of susceptibility to carcinogenesis, peak in the first 2 years of life for most major organ systems. Cell division continues to accommodate growth throughout childhood and adolescence, extending in some cases even into the young adult period in both humans and experimental animals. Adolescence is an important period for organ cell division and differentiation for the mammary gland and reproductive organs.

As noted above, one of the key factors influencing susceptibility to carcinogenesis is believed to be cell division rate, which acts both by forcing error-prone repair which fixes DNA damage as mutated gene sequences (McLean et al, 1982) and by promoting expansion of mutated clones

(Moolgavkar and Knudson, 1981). Actual cell division rates as a function of age are hard to determine for practical and (in the human case) ethical reasons. However, growth curves expressed as the proportional increment in body weight with time may be regarded as a reasonable although not perfect surrogate since for most tissues of the body cell size does not change markedly during growth. Both humans and rodents show remarkably high growth rates in infancy, which then drop steeply to a lower but still significant rate during childhood. A growth spurt at the beginning of adolescence is noticeable in its absolute magnitude, especially in males, but does not approach the proportional growth rate seen in infancy. The time intervals proposed to reflect the period of highest sensitivity to carcinogenesis (up to about 21 days in rodents, up to 24 months in humans) encompass the period of highest growth rate and thus it is assumed the highest cell division rates, as show in the following charts:



Data from CDC NHANES 2000:
http://www.cdc.gov/nchs/about/major/nhanes/growthcharts/datafiles.htm



Data from Tables A3 and A4 of Appendix J

Cell division rates in adult rodents and humans are harder to relate to growth curves since at least some tissues retain active cell division as part of their ongoing functionality and repair. In humans growth in body weight slows to essentially zero at the end of adolescence (and any later increments represent tissue specific changes such as increase in muscle or adipose tissue mass rather than overall growth). On the other hand, rodents continue to increase in body size (at a modest rate compared to that seen in earlier lifestages) throughout the adult period. However, it appears reasonable to conclude from the body weight data that an essentially adult pattern of overall cell division is established by the late adolescent period (age six weeks in rodents; 16 years in humans). However, increased cell division and cell differentiation are seen in the reproductive system and its accessories during puberty.

Organ Development

The age intervals chosen for the ASFs are generally supported by human organ system development data. Examples of supporting data are available for the lung, brain, immune system and liver. Zeltner and Burri (1987) stated that postnatal lung development consists of an alveolar stage, which lasts to about 1-1.5 years of age, and a stage of microvascular maturation, which exists from the first months after birth to the age of 2-3 years. Pinkerton and Joad (2006) describe

alveolar proliferation as occurring most prominently in the 0-2 year age range, with alveolar expansion continuing in the 2-8 year age range. Ballinoti et al. (2008) demonstrated that addition of alveoli rather than expansion is a major mode of lung growth in infants and toddlers by measuring a constant carbon monoxide diffusion capacity to lung volume from 3 through 23 months of age. Kajekar (2007) also considered the 0-2 age range to be the primary period of alveolar development, although there is continued cellular proliferation resulting in lung growth and expansion up to approximately 18 years of age.

Rice and Barone (2000) note that most of the cell proliferation phase of human radial glia and neuronal growth is finished by 2 years of age, based on evidence in Bayer et al. (1993). They note further that numerous studies have shown actively proliferating brain regions are more susceptible to anti-mitotic agents than the same structures after active proliferation ceases. Peak brain growth as a percentage of body weight occurs at birth and around post-natal day (PND) 7-8 in humans and rats, respectively (Watson *et al.*, 2006). De Graaf-Peters and Hadders-Algra (2006) reviewed the ontogeny of the human central nervous system and found that a large amount of axon and dendrite sprouting and synapse formation and the major part of telencephalic myelination take place during the first year after birth. While the brain continues to remodel itself throughout life, cellular proliferation in the whole brain peaks by about one year of age and is relatively complete by age 2. Development of the blood-brain barrier (BBB) appears to continue in humans until approximately 6 months of age. Rat BBB functionality is essentially complete by approximately two weeks after birth (Watson *et al.*, 2006).

The immune system development occurs in stages, primarily prenatally in primates and both pre- and post-natally in rodents (Dietert et al., 2000). Formation and expansion of hematopoetic stem cells is followed by expansion of lineage-specific stem cells, colonization of bone marrow and thymus, and maturation of cells to immunocompetence. In the primate, this is largely complete by 1 to 2 years of age (Holsapple et al., 2003), although establishment of immune memory develops throughout childhood and beyond. In the rodent, maturation to immunocompetence occurs postnatally from birth to about 30 days of age. In terms of carcinogenesis, perhaps one of the more important immune cells is the NK cell, thought to be responsible for immune surveillance and killing of circulating transformed cells. Based on immunohistochemistry, the principal cell lines including NK cells are present at gestation day 100 in the monkey and are at about 60% of adult values at birth (Holladay and Smialowicz, 2000).

As noted above, renal and hepatic clearance are both lower in humans at birth than in adults. Nephrogenesis is complete by 35 weeks gestation in humans and before birth in the mouse (but after birth in the rat). The ability to concentrate urine and the development of acid-base equilibrium appear in the first few months after birth (Zoetis and Hurtt, 2003). Renal clearance of drugs, a function of a number of processes in the kidney, appears to be comparable to adults within the first few months of life (Hattis et al., 2003; Ginsberg et al., 2002), while glomerular filtration, which rises rapidly over the first few postnatal months, is at adult values by two years of age (Zoetis and Hurtt, 2003). While complete anatomic maturity of the human liver is noted by 5 years of age (Walthall et al, 2005), liver function also appears to mature within the first year of life as seen by drug clearance studies cited above.

Critical Windows of Susceptibility to Carcinogens

It has been shown that there are critical windows during development both pre-and postnatally where enhanced susceptibility to carcinogenesis occurs (Anderson et al, 2000). Some of these observations relate to factors affecting the incidence of cancers in childhood, resulting from prenatal or preconception mutational events. For example, prenatal exposure to ionizing radiation and DES can result in leukemia and vaginal carcinoma, respectively, in childhood. Although obviously a source of great concern, these cancers appearing during childhood are relatively rare compared to cancers appearing later in life. Thus the concern in risk assessment for early in life exposures is to address the lifetime cancer incidence as a result of these exposures, including both cancers appearing during childhood and those appearing later.

OEHHA (see Appendix J) and other investigators (U.S. EPA, 2005; Barton et al, 2005; Hattis et al., 2004) have examined the available rodent data on sensitivity to carcinogenic exposures early in life. All these investigators found substantial increases in sensitivity to carcinogens in animal studies where exposures to young animals were compared to similar exposures to adults. Hattis et al. (2004) reported maximum likelihood estimates for the ratio of carcinogenic potency during the period from birth to weaning to the adult potency of between 8.7 and 10.5, whereas Barton et al (2005) reported a weighted geometric mean of 10.4 for the ratio of juvenile (less than 6-8 weeks) to adult potency in rodents. However, the number of experiments which provide information of this type, and the carcinogenic agents which have been studied, are relatively limited. Hattis examined several different datasets and study designs, but these covered only 13 different chemicals, while the mean value reported by Barton et al. was based on only six of the 18 chemicals which they examined. OEHHA's analysis included data in rodents on 23 chemicals, and found median potency ratios of 13.5 for the postnatal period (birth to day 22) and 4.5 for the juvenile period (postnatal days 22 to ~49) relative to adults (day ~49 to 2 years). These potency ratios include the adjustment for time to manifest tumor (*e.g.*, age to the power of three), unlike the earlier investigations. All these investigations identified variations in the observed lifetime potency ratio depending on the type of experimental design, the sex of the animals, the time of exposure and especially between chemicals. Nevertheless these analyses, although falling far short of a comprehensive evaluation of the age dependence of carcinogenic potency for all the chemicals of interest, do show a consistent overall trend of increasing potency for exposures early in life, especially soon after birth.

An evaluation of cancer induction by ionizing radiation also provides support for the concept of enhanced sensitivity to carcinogenesis at younger ages. Various studies of this phenomenon have been undertaken in animal models, but the important point for the present discussion is that epidemiological data exist which indicate age-dependent sensitivity in humans (U.S. EPA, 1994; 1999). The most extensive data set showing age-dependent effects is that for Japanese survivors of the atomic bomb explosions at Hiroshima and Nagasaki. Analysis of these data shows linear increases in tumor incidence at a number of sites with increasing radiation dose and younger age at exposure. There are other data suggesting humans are more susceptible to chemical carcinogens when exposure occurs in childhood. These data exist for tobacco smoke (Marcus et al., 2000; Wiencke et al., 1999) and chemotherapy and radiation (Mauch et al., 1996; Swerdlow et al., 2000; Franklin et al., 2006).

Proposed Age Bins for Application of Default Age Sensitivity Factors

In developing a default science-based risk assessment policy to address this general conclusion, one key variable to define is the age interval or intervals over which age-dependent sensitivity factors should be applied. Different investigators have considered different age ranges, but in general the more sensitive period has at least been defined as including the time from birth up to mid-adolescence when the major phases of growth and hormonal change are complete. It is also recognized that, apart from the dramatic prenatal developmental events, the earliest postnatal stages represent the greatest differences in physiology and biochemistry from the adult. This reflects the immaturity of many organ systems, extremely rapid growth, and the incomplete maturation of various metabolic capabilities. As noted earlier, the rodent age bins in OEHHA's analysis were based on gross developmental milestones (birth, weaning, sexual maturity). OEHHA's analysis of studies that included exposure sometime between birth and weaning indicated this period as having the highest sensitivity to carcinogenesis. The data for the later juvenile period (postnatal days 22 to ~ 49) are somewhat sparse, covering only three carcinogens and only one where there are corresponding data for both postnatal and juvenile lifestages. However, it appears based on the overall range of potency ratios observed for the juvenile period that sensitivity to many carcinogens is elevated in this period also, but to a lesser extent than during the first 22 days. [Hattis et al. (2005) and Barton et al. (2005) report analyses for exposures at any time during the juvenile period, i.e. up to 6-8 weeks, and do not separate by additional age bins].

Weaning is not such an obvious or consistently timed transition for humans, being subject to a wide range of cultural and economic variables. However, it is generally considered that the human infant period encompasses the first two years of life. This period includes the most rapid periods of cellular division and differentiation for the major organ systems (excluding the breast and reproductive organs). Although there is linear growth between 2 and 8 years of age, the organ development is largely although not entirely complete.

Thus, considering both the development of major organ systems and the associated differences in toxicodynamic and toxicokinetic factors, OEHHA initially proposed to apply the postnatal ASF derived from rodent studies (birth to 21 days) to the human age intervals of birth - < 2 years. Similarly, OEHHA chose to apply the "juvenile" ASF derived from rodent studies (22 - ~49 days) to the human ages 2 - < 16 years. This timetable was also selected by U.S. EPA (2005) in their supplemental guidance for assessing early-life susceptibility to carcinogens. They describe their choice of critical periods as follows:

> "The adjustments described below reflect the potential for early-life exposure to make a greater contribution to cancers appearing later in life. The 10-fold adjustment represents an approximation of the weighted geometric mean tumor incidence ratio from juvenile or adult exposures in the repeated dosing studies (see Table 8). This adjustment is applied for the first 2 years of life, when toxicokinetic and toxicodynamic differences between children and adults are greatest (Ginsberg et al., 2002; Renwick, 1998). Toxicokinetic differences from adults, which are greatest at birth, resolve by approximately 6 months to 1 year, while higher growth rates extend for longer periods. The 3-fold adjustment represents an intermediate level of adjustment that is applied after 2 years of age through <16 years of age. This upper age limit represents middle adolescence following the period of rapid developmental changes in puberty and the conclusion of growth in body height in

NHANES data (Hattis et al., 2005). Efforts to map the approximate start of mouse and rat bioassays (i.e., 60 days) to equivalent ages in humans ranged from 10.6 to 15.1 years (Hattis et al., 2005)."

There is general agreement that rodents are born at a maturational stage approximately equivalent to a third trimester human fetus. Thus, there is good rationale to include the third trimester of pregnancy in the age bin for application of the ASF of 10. Therefore, OEHHA is applying the ASF of 10 for exposures during the third trimester of pregnancy to age 2. The default ASF values used by OEHHA are summarized in Table 2.

While there is strong evidence that growth and therefore cell proliferation rates and cell differentiation are extremely high prior to age 2, and lower (although still elevated relative to the adult) thereafter, there is still residual uncertainty with respect to the cut point for application of the ASFs of 10 and 3. Thus, another possible approach would be to move the cut point for the application of the ASF of 10 to a later age to account for this uncertainty. We present the effect on risk estimates of varying cut points in Table 3 and Table 4.

Table 2. Default Age Sensitivity Factors to be used to estimate cancer risks to infants and children

R (third trimester to age 2yrs)	10
R (age 2 to age 16 yrs)	3
R (age 16 to 70 yrs)	1

Application of ASFs in Risk Assessment

The effect of using the proposed default ASFs in calculating cancer risk over a 70 year lifetime, and for a 9 year exposure common in the Hot Spots program risk assessments is demonstrated in Table 3 and Table 4 below. Ignoring for the moment the increased exposures to carcinogens that children experience, the effect of the weighting factors is to increase the lifetime cancer risk by about 2. For risks from shorter exposures, such as the commonly used 9 year exposure scenario, OEHHA proposes to evaluate risk from exposures starting at the third trimester in the surrounding general population. The weighting factors in this case increase the risk to a larger extent. Depending on the exposure scenario, the use of age-specific distributions for uptake rates for air, food and water would also increase the risk estimates significantly independent of any application of ASFs. This is because the uptake rates for all these media per unit of body weight are higher in children and, especially, infants.

Assessing risks to short-term exposures to carcinogens involves additional uncertainties. The cancer potency factors are generally based on long-term exposures. However, in reality, the local air districts in California are frequently assessing risk from short term activities related to construction, mitigation of contaminated soils, and so forth. OEHHA recommends that when assessing such shorter term projects, the districts assume a minimum of 2 years of exposure and apply the slope factors and the 10 fold ASF to such assessments. Exposure durations longer than 2 years would use the method for the remaining years as noted above.

Table 3. Example of default ASF use for a lifetime exposure (not adjusted for age-specific exposure)

Carcinogen Potency = 1 $(mg/kg\text{-}d)^{-1}$
Exposure = 0.0001 mg/kg-d
No consideration of differences of exposure

No adjustment: Lifetime Risk = potency × dose	Risk
70 year Lifetime risk = 1 × 0.0001	**1.0×10^{-4}**

With proposed default ASF of 10 for third trimester to age 2, and 3 for ages 2 to 16 years: LR = Σ (potency x dose x ASF x fraction of lifetime)	ASF	Duration	Risk
R (third trimester to age 2yrs)	10	2.25/70	0.321×10^{-4}
R (age 2 to age 16 yrs)	3	14/70	0.600×10^{-4}
R (age 16 to 70 yrs)	1	54/70	0.771×10^{-4}
70 year Lifetime Risk			**1.7×10^{-4}**

For comparison, if ASF of 10 were applied to age 5, and ASF of 3 for the ages 5 to 16 years: LR = Σ (potency x dose x ASF x fraction of lifetime)	ASF	Duration	Risk
R (birth to age 5)	10	5.25/70	0.750×10^{-4}
R (age 5 to 16 yrs)	3	11/70	0.471×10^{-4}
R (age 16 to 70 yrs)	1	54/70	0.771×10^{-4}
70 year Lifetime Risk			**2.0×10^{-4}**

Table 4. Example of default ASF use for a 9-year exposure

Carcinogen Potency = 1 $(mg/kg\text{-}d)^{-1}$
Exposure = 0.0001 mg/kg-d
No consideration of differences of exposure

No adjustment: Total Risk = potency × dose x fraction of lifetime		Duration	Risk
9-year Total Risk		9/70	**0.13×10^{-4}**
With default ASF of 10 for third trimester to age 2 and 3 thereafter: LR = Σ (potency x dose x ASF x fraction of lifetime)	ASF	Duration	Risk
R (third trimester to age 2yrs)	10	2.25/70	0.321×10^{-4}
R (age 2 to 9 yrs)	3	7/70	0.300×10^{-4}
9 year Total Risk			**0.62×10^{-4}**
For comparison, if ASF of 10 applied to age 5, and ASF of 3 thereafter: LR = Σ (potency x dose x ASF x fraction of lifetime)	ASF	Duration	Risk
R (birth to age 5 yrs)	10	5/70	0.750×10^{-4}
R (age 5 to 9 yrs)	3	4/70	0.171×10^{-4}
9 year Total Risk			**0.92×10^{-4}**

Special Consideration of Puberty

In addition to the general concerns over increased sensitivity to carcinogenesis during infancy and childhood, there are specific concerns for exposure during the period when hormonal and developmental changes associated with puberty are in process, especially for carcinogens with hormonal modes of action or with impacts on the reproductive system and its accessory organs. At puberty, there is increased development of breast and reproductive organs that clearly involves rapid cellular division and differentiation. Thus, for carcinogens that induce mammary and reproductive organ cancers, puberty represents a time of increased sensitivity. As noted in the section on Selection of Default Age-Sensitivity Factors (page 50), if the risk assessor is evaluating a chemical with the potential for more than usually enhanced potency during this period, such as those which induce mammary or reproductive organ tumors (*e.g.*, a polycyclic aromatic hydrocarbon), then the risk assessment may use a larger ASF to calculate risk from exposure during puberty. OEHHA may recommend chemical-specific ASFs for puberty to the local air quality management districts for use in the Air Toxics Hot Spots program.

U.S.EPA Analysis of the Effect of Age at Exposure on Cancer Potency

U.S. EPA addressed the potential for increased susceptibility to cancer caused by environmental chemicals when the exposure occurs during an early lifestage in "Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens" (U.S. EPA, 2005b) (referred to henceforth as the Supplemental Guidance). This document is intended to be a companion to the revised "Guidelines for Carcinogen Risk Assessment" (U.S. EPA, 2005a). We present a summary of their analysis, which supports the policy decision to weight cancer potency and therefore risk by age-at-exposure. As previously noted, there are several methodological differences between the U.S. EPA analysis and the OEHHA analysis. Of note, in the OEHHA analysis all treatment-related tumors that were observed in a given lifestage exposure experiment were taken into account in estimating cancer potency. Thus in comparing cancer potencies associated with early life vs. adult exposure, OEHHA compared the total cancer risk associated with exposure during a given lifestage, rather than comparing the risk for cancers at one single site in each lifestage, as the U.S. EPA did. In addition, the age groupings are somewhat different in the U.S. EPA analysis from those used by OEHHA in their analysis (described above). For example, prenatal (*in utero*) exposures were not part of the analysis performed by U.S. EPA, and that Agency's analyses did not distinguish between postnatal and juvenile exposures.

U.S. EPA oral exposure cancer risk methodology relies on estimation of the lifetime average daily dose, which can account for exposure factor differences between adults and children (*e.g.*, eating habits and body weight). However, early lifestage susceptibility differences have not been taken into consideration when cancer potency factors were calculated. The Supplemental Guidance document focused on studies that define the potential duration and degree of increased susceptibility that may arise from early-life exposures. An analysis of those studies including a detailed description of the procedures used was published in Barton *et al.* (2005) (included as Appendix I). The criteria used to decide if a study could be included in the quantitative analysis are as follows (excerpted from U.S. EPA, 2005b):

1. Exposure groups at different post-natal ages in the same study or same laboratory, if not concurrent (to control for a large number of potential cross-laboratory experimental variables including pathological examinations),
2. Same strain/species (to eliminate strain-specific responses confounding age-dependent responses),
3. Approximately the same dose within the limits of diets and drinking water intakes that obviously can vary with age (to eliminate dose-dependent responses confounding age-dependent responses),
4. Similar latency period following exposures of different ages (to control for confounding latency period for tumor expression with age-dependent responses), arising from sacrifice at >1 year for all groups exposed at different ages, where early-life exposure can occur up to about 7 weeks. Variations of around 10 to 20% in latency period are acceptable,
5. Postnatal exposure for juvenile rats and mice at ages younger than the standard 6 to 8 week start for bioassays; prenatal (*in utero*) exposures are not part of the current analysis. Studies that have postnatal exposure were included (without adjustment) even if they also involved prenatal exposure,

6. "Adult" rats and mice exposure beginning at approximately 6 to 8 weeks old or older, *i.e.* comparable to the age at initiation of a standard cancer bioassay (McConnell, 1992). Studies with animals only at young ages do not provide appropriate comparisons to evaluate age-dependency of response (*e.g.*, the many neonatal mouse cancer studies). Studies in other species were used as supporting evidence, because they are relatively rare and the determination of the appropriate comparison ages across species is not simple, and
7. Number of affected animals and total number of animals examined are available or reasonably reconstructed for control, young, and adult groups (i.e., studies reporting only percent response or not including a control group would be excluded unless a reasonable estimate of historical background for the strain was obtainable).

Cancer potencies were estimated from a one-hit model (a restricted form of the Weibull time-to-tumor model), which estimates cumulative incidence for tumor onset. U.S. EPA (2005b) compared the estimated ratio of the cancer potency from early-life exposure to the estimated cancer potency from adult exposure. The general form of the equation for the tumor incidence at a particular dose, [P(dose)] is:

$$P(dose) = 1-[1-P(0)]\exp(-\text{cancer potency}*\text{dose})$$

where P(0) is the incidence of the tumor in controls. The ratio of juvenile to adult cancer potencies at a single site were calculated by fitting this model to the data for each age group. The model fit depended upon the design of the experiment that generated the data. Studies evaluated by U.S. EPA had two basic design types: experiments in which animals were exposed either as juveniles or as adults (with either a single or multiple dose in each period), and experiments in which exposure began either in the juvenile or in the adult period, but once started, continued through life.

The model equations for the first study type are:

$$P_A = P_0 + (1-P_0)\,(1-e^{-m_A \delta_A})$$

$$P_J = P_0 + (1-P_0)\,(1-e^{-m_A e^{\lambda} \delta_J})$$

where A and J refer to the adult and juvenile period, respectively, λ is the natural logarithm of the juvenile:adult cancer potency ratio, P_0 is the fraction of control animals with the particular tumor type being modeled, P_x is the fraction of animals exposed in age period x with the tumor, m_A is the cancer potency, and δ_x is the duration or number of exposures during age period x.

The goal of the model is to determine λ, which is the logarithm of the estimated ratio of juvenile to adult cancer potencies. This serves as a measure of potential susceptibility for early-life exposure.

For the second study type, the model equations take into account that exposures that were initiated in the juvenile period continue through the adult period. The model equations for the fraction of animals exposed only as adults with tumors in this design are the same as in the first study type, but the fraction of animals whose first exposure occurred in the juvenile period is:

$$P_J = P_0 + (1-P_0)\,(1-e^{-m_A\, e^{\lambda\,(\delta_J - \delta_A)} - m_A\,\delta_A})$$

δ_J includes the duration of exposure during the juvenile period and the subsequent adult period.

Parameters in these models were estimated using Bayesian methods and all inferences about the ratios were based on the marginal posterior distribution of λ. A complete description of these procedures (including the potential effect of alternative Bayesian priors that were examined) was published in Barton *et al.* (2005) (Appendix I). This method produced a posterior mean ratio of the early-life to adult cancer potency, which is an estimate of the potential susceptibility of early-life exposure to carcinogens. Ratios of greater or less than one indicate greater or less susceptibility from early-life exposure, respectively.

U.S. EPA reviewed several hundred studies reporting information on 67 chemicals or complex mixtures that are carcinogenic via perinatal exposure. Eighteen chemicals were identified which had animal study designs involving early-life and adult exposures in the same experiment. Of those 18 chemicals, there were overlapping subsets of 11 chemicals involving repeated exposures during early postnatal and adult lifestages and 8 chemicals using acute exposures (usually single doses) at different ages. Those chemicals are listed in Table 5.

Table 5 Chemicals having animal cancer study data available with early-life and adult exposures in the same experiment.

Chemical	Study Type
Amitrole	repeat dosing
Benzidine	repeat dosing
Benzo[a]pyrene (BaP)	acute exposure
Dibenzanthracene (DBA)	acute exposure
Dichlorodiphenyltrichloroethane (DDT)	lifetime exposure, repeat dosing
Dieldrin	lifetime exposure, repeat dosing
Diethylnitrosamine (DEN)	acute exposure, lifetime exposure
Dimethylbenz[a]anthracene (DMBA)	acute exposure
Dimethylnitrosamine (DMN)	acute exposure
Diphenylhydantoin, 5,5-(DPH)	lifetime exposure, repeat dosing
Ethylnitrosourea (ENU)	acute exposure
Ethylene thiourea (ETU)	lifetime exposure, repeat dosing
3-Methylcholanthrene (3-MC)	repeat dosing
Methylnitrosourea (NMU)	acute exposure
Polybrominated biphenyls (PBBs)	lifetime exposure, repeat dosing
Safrole	lifetime exposure, repeat dosing
Urethane	acute exposure, lifetime exposure
Vinyl chloride (VC)	repeat dosing

U.S. EPA calculated the difference in susceptibility between early-life and adult exposure as the estimated ratio of cancer potency at specific sites from early-life exposure over the cancer potency from adult exposure for each of the studies that were determined qualitatively to have appropriate study designs and adequate data. The results were grouped into four categories: 1) mutagenic chemicals administered by a chronic dosing regimen to adults and repeated dosing in the early postnatal period (benzidine, diethylnitrosamine, 3-methylcholanthrene, safrole, urethane and vinyl chloride); 2) chemicals without positive mutagenicity data administered by a chronic dosing regimen to adults and repeated dosing in the early postnatal period (amitrole, dichlorodiphenyltrichloroethane (DDT), dieldrin, ethylene thiourea, diphenylhydantoin, polybrominated biphenyls); 3) mutagenic chemicals administered by an acute dosing regimen (benzo[*a*]pyrene, dibenzanthracene, diethylnitrosamine, dimethylbenzanthracene, dimethyl-nitrosamine, ethylnitrosourea, methylnitrosourea and urethane); 4) chemicals with or without positive mutagenicity data with chronic adult dosing and repeated early postnatal dosing.

The acute dosing animal cancer studies were considered qualitatively useful by U.S. EPA because they involve identical exposures with defined doses and time periods demonstrating that differential tumor incidences arise exclusively from age-dependent susceptibility. However, they

were not used to derive a quantitative cancer potency factor age adjustment, primarily because most of the studies used subcutaneous or intraperitoneal injection as a route of exposure. These methods have not been considered quantitatively relevant routes of environmental exposure for human cancer risk assessment by U.S. EPA, for reasons including the fact that these routes of exposure are expected to have a partial or complete absence of first pass metabolism which could affect potency estimates. Additionally, U.S. EPA decided that cancer potency estimates are usually derived from chronic exposures, and therefore, any adjustment to those potencies should be from similar exposures.

The repeated dosing studies with mutagenic chemicals using exposures during early postnatal and adult lifestages were used to develop a quantitative cancer potency factor age adjustment. Studies with repeated early postnatal exposure were included in the analysis even if they also involved earlier maternal and/or prenatal exposure, while studies addressing only prenatal exposure were not used in the analysis. The weighted geometric mean susceptibility ratio (juvenile to adult) for repeated and lifetime exposures in this case was 10.4 (range 0.12 – 111, 42% of ratios greater than 1).

USEPA suggests the use of age-dependent-adjustment factors (ADAF) for chemicals acting through a mutagenic mode of action., based on the results of the preceding analysis, which concluded that cancer risks generally are higher from early-life exposure than from similar exposure doses and durations later in life:

1. For exposures before 2 years of age (i.e., spanning a 2-year time interval from the first day of birth until a child's second birthday), a 10-fold ADAF.

2. For exposures between 2 and <16 years of age (i.e., spanning a 14-year time interval from a child's second birthday until their sixteenth birthday), a 3-fold ADAF.

3. For exposures after turning 16 years of age, no adjustment (ADAF=1).

The ADAF of 10 used for the 0 – 2 years of age range is approximately the weighted geometric mean cancer potency ratio from juvenile versus adult exposures in the repeated dosing studies. U.S. EPA considered this period to display the greatest toxicokinetic and toxicodynamic differences between children and adults. Data were not available to calculate a specific dose-response adjustment factor for the 2 to <16-year age range, so EPA selected an ADAF of 3 because it was half the logarithmic scale difference between the 10-fold adjustment for the first two years of life and no adjustment (*i.e.*, 1-fold) for adult exposure. The ADAF of 3 represents an intermediate level of adjustment applied after 2 years of age through <16 years of age. The upper age limit (16 years of age) reflects the end of puberty and the attainment of a final body height. U.S. EPA recognizes that the use of a weighted geometric mean of the available study data to develop an ADAF for cancer potencies may either overestimate or underestimate the actual early-life cancer potency for specific chemicals, and therefore emphasizes in the Supplemental Guidance that chemical-specific data should be used in preference to these default adjustment factors whenever such data are available.

U.S. EPA is recommending the ADAFs described above only for mutagenic carcinogens, because the data for non-mutagenic carcinogens were considered to be too limited and the modes of action

too diverse to use this as a category for which a general default adjustment factor approach can be applied. OEHHA considers this approach to be insufficiently health protective. There is no obvious reason to suppose that the toxicokinetics of non-mutagens would be systematically different from those of mutagens. It would also be inappropriate to assume by default that non-mutagenic carcinogens are assumed to need a toxicodynamic correction factor of 1. Most if not all of the factors that make individuals exposed to carcinogens during an early-lifestage potentially more susceptible than those individuals exposed during adulthood also apply to non-mutagenic carcinogen exposures (*e.g.*, rapid growth and development of target tissues, potentially greater sensitivity to hormonal carcinogens, differences in metabolism). It should also be noted that carcinogens that do not cause gene mutations may still be genotoxic by virtue of causing chromosomal damage. Additionally, many carcinogens do not have adequate data available for deciding on a specific mode of action, or do not necessarily have a single mode of action. For these reasons, OEHHA will apply the default cancer potency factor age adjustments described above to all carcinogens unless data are available which allow for the development of chemical-specific cancer potency factor age adjustments. In those cases, an agent-specific model of age dependence (based on observational or experimental data) might be used, or alternative (larger or smaller) adjustment factors and age ranges may be applied where understanding of the mechanism of action and target tissues makes this appropriate.

Other Source Documents for Cancer Risk Assessment Guidance

As noted previously, the cancer potencies and unit risks tabulated in this technical support document have been developed by various programs over a number of years. The methods used therefore necessarily varied according to the date of the assessment and the program responsible. The following section summarizes the sources and procedures most commonly applied, and their historical context where this is apposite.

United States Environmental Protection Agency (U.S. EPA)

The U.S. EPA was one of the first regulatory agencies to develop and apply cancer risk assessment methodology. Their guidance documents and technical publications have been influential for many programs, including the California Air Toxics (Toxic Air Contaminants and Hot Spots) programs.

Guidelines for Carcinogen Risk Assessment (U.S. EPA, 1986)

Prior to the more recent guidelines updating project which, after nearly ten years of internal and public review drafts culminated in the 2005 final revision (see below), U.S. EPA carcinogen risk assessment procedures were generally as described in Anderson *et al*. (1983) and "Guidelines for Carcinogen Risk Assessment" (U.S. EPA, 1986). These methods, which are outlined below, were used to calculate the Integrated Risk Information System (IRIS) cancer potency values, some of which are cited in this document. U.S. EPA has always indicated that cancer risk estimates based on adequate human epidemiologic data are preferred if available over estimates based on animal data. Although the newer guidelines offer alternative methods for dose-response analysis of animal bioassays, and updated consideration of specific topics such as lifestage-related differences in sensitivity, and mechanism of action for some types of carcinogen, the underlying principles and many of the specific procedures developed in these original guidelines are still applicable and in use.

U.S. EPA Calculation of Carcinogenic Potency Based on Animal Data

In extrapolating low-dose human cancer risk from animal carcinogenicity data, it is generally assumed that most agents that cause cancer also damage DNA, and that the quantal type of biological response characteristic of mutagenesis is associated with a linear non-threshold dose-response relationship. U.S. EPA stated that the risk assessments made with this model should be regarded as conservative, representing the most plausible upper limit for the risk. The mathematical expression used by U.S. EPA in the 1986 guidelines to describe the linear non-threshold dose-response relationship at low doses is the linearized multistage procedure developed by Crump (1980). This model is capable of fitting almost any monotonically increasing dose-response data, and incorporates a procedure for estimating the largest possible linear slope at low extrapolated doses that is consistent with the data at all experimental dose levels. A description of the linearized multistage procedure has been provided above (page 29). U.S. EPA used an updated version (GLOBAL86, Howe *et al*., 1986) of the computer program GLOBAL79 developed by Crump and Watson (1979) to calculate the point estimate and the 95% upper confidence limit of the extra risk $A(d)$.

U.S. EPA separated tumor incidence data according to organ sites or tumor types. The incidence of benign and malignant tumors was combined whenever scientifically defensible. U.S. EPA considered this incidence combination scientifically defensible unless the benign tumors are not considered to have the potential to progress to the associated malignancies of the same histogenic origin. The primary comparison in carcinogenicity evaluation is tumor response in dosed animals as compared to contemporary matched control animals. However, U.S. EPA stated that historical control data could be used along with concurrent control data in the evaluation of carcinogenic responses, and notes that for the evaluation of rare tumors, even small tumor responses may be significant compared to historical data. If several data sets (dose and tumor incidence) are available (different animal species, strains, sexes, exposure levels, exposure routes) for a particular chemical, the data set used in the model was the set where the incidence is statistically significantly higher than the control for at least one test dose level and/or where the tumor incidence rate shows a statistically significant trend with respect to dose level. The data set generating the highest lifetime cancer risk estimate (q_1^*) was chosen where appropriate. An example of an inappropriate data set would be a set which generates an artifactually high risk estimate because of a very small number of animals used. If there are 2 or more data sets of comparable size for a particular chemical that are identical with respect to species, strain, sex and tumor sites, the geometric mean of q_1^* estimated from each of those data sets was used for risk estimation. U.S. EPA assumed that mg/surface area/day is an equivalent dose between species. Surface area was further assumed to be proportional to the 2/3 power of the weight of the animal in question. Equivalent dose was therefore computed using the following relationship:

$$d = \frac{l_e * m}{L_e * W^{2/3}}$$

where L_e = experimental duration, l_e = exposure duration, m = average dose (mg/day) and W = average animal weight. Default average body weights for humans, rats and mice are 70, 0.35 and 0.03 kg, respectively.

Exposure data expressed as ppm in the diet were generally converted to mg/day using the relationship m = ppm * F * r, where ppm is parts per million of the chemical in the diet, F is the weight of the food consumed per day in kg, and r is the absorption fraction (assumed to be 1 in the absence of data indicating otherwise). The weight of food consumed, calories required, and animal surface area were generally all considered to be proportional to the 2/3 power of the animal weight, so:

$$m \propto \text{ppm} * W^{2/3} * r, \text{ or } \quad \frac{m}{r W^{2/3}} \propto \text{ppm}$$

The relationship could lead to the assumption that dietary ppm is an equivalent exposure between species. However, U.S. EPA did not believe that this assumption is justified, since the calories/kg food consumed by humans is significantly different from that consumed by laboratory animals (primarily due to differences in moisture content). An empirically derived food factor, $f = F/W$

was used, which is the fraction of a species' body weight consumed per day as food. U.S. EPA (1986) gave the *f* values for humans, rats and mice as 0.028, 0.05 and 0.13, respectively.

Dietary exposures expressed as concentrations in ppm were converted to mg/surface area using the following relationship:

$$\frac{m}{r * W^{2/3}} = \frac{\text{ppm} * F}{W^{2/3}} = \frac{\text{ppm} * f * W}{W^{2/3}} = \text{ppm} * f * W^{2/3}$$

Exposures expressed as mg/kg/day ($m/Wr = s$) were converted to mg/surface area using the relationship:

$$\frac{m}{rW^{2/3}} = s * W^{2/3}$$

The calculation of dose when exposure is via inhalation was performed for cases where 1) the chemical is either a completely water-soluble gas or aerosol and is absorbed proportionally to the amount of inspired air, or 2) where the chemical is a partly water-soluble gas which reaches an equilibrium between the inspired air and body compartments. After equilibrium is attained, the rate of absorption is proportional to metabolic rate, which is proportional to the rate of oxygen consumption, which is related to surface area.

Exposure expressed as mg/day to completely water-soluble gas or aerosols can be calculated using the expression $m = I * v * r$, where I is the inspiration rate/day in m^3, v is the concentration of the chemical in air (mg/m^3), and r is the absorption fraction (assumed to be the same for all species in the absence of data to the contrary; usually 1). For humans, the default inspiration rate of 20 m^3 has been adopted. Inspiration rates for 113 g rats and 25 g mice have been reported to be 105 and 34.5 liters/day, respectively. Surface area proportionality can be used to determine inspiration rate for rats and mice of other weights; for mice, $I = 0.0345\ (W / 0.025)^{2/3}$ m^3/day; for rats, $I = 0.105\ (W / 0.113)^{2/3}$ m^3/day. The empirical factors for air intake/kg/day (i) for humans, rats and mice are 0.29, 0.64 and 1.3, respectively. Equivalent exposures in mg/surface area can be calculated using the relationship:

$$\frac{m}{W^{2/3}} = \frac{Ivr}{W^{2/3}} = \frac{iWvr}{W^{2/3}} = iW^{1/3}vr$$

Exposure expressed as mg/day to partly water-soluble gases is proportional to surface area and to the solubility of the gas in body fluids (expressed as an absorption coefficient r for that gas). Equivalent exposures in mg/surface area can be calculated using the relationships $m = kW^{2/3} * v * r$, and $d = m/W^{2/3} = kvr$. The further assumption is made that in the case of route-to-route extrapolations (*e.g.*, where animal exposure is via the oral route, and human exposure is via inhalation, or vice versa), unless pharmacokinetic data to the contrary exist, absorption is equal by either exposure route.

Adjustments were made for experimental exposure durations shorter than the lifetime of the test animal; the slope q_1^* was increased by the factor $(L/L_e)^3$, where L is the normal lifespan of the experimental animal and L_e is the duration of the experiment. This assumed that if the average dose d is continued, the age-specific rate of cancer will continue to increase as a constant function of the background rate. Since age-specific rates for humans increase by at least the 2nd power of the age, and often by a considerably higher power (Doll, 1971), there is an expectation that the cumulative tumor rate, and therefore q_1^*, will increase by at least the 3rd power of age. If the slope q_1^* is calculated at age L_e, it would be expected that if the experiment was continued for the full lifespan L at the same average dose, the slope q_1^* would have been increased by at least $(L/L_e)^3$.

U.S. EPA Calculation of Carcinogenic Potency Based on Human Data

U.S. EPA stated that existing human epidemiologic studies with sufficiently valid exposure characterization are always used in evaluating the cancer potency of a chemical. If they showed a carcinogenic effect, the data were analyzed to provide an estimate of the linear dependence of cancer rates on lifetime cancer dose (equivalent to the factor q_1^*). If no carcinogenic effect was demonstrated and carcinogenicity had been demonstrated in animals, then it was assumed that a risk does exist, but it is smaller than could have been observed in the epidemiologic study. An upper limit of cancer incidence was calculated assuming that the true incidence is just below the level of detection in the cohort studied, which is largely determined by the cohort size. Whenever possible, human data are used in preference to animal data. In human epidemiologic studies, the response is measured as the relative risk of the exposed cohort of individuals compared to the control group. The excess risk ($R(X)$ - 1, where $R(X)$ is relative risk) was assumed to be proportional to the lifetime average exposure X, and to be the same for all ages. The carcinogenic potency is then equal to $[R(X) - 1]/X$ multiplied by the lifetime risk at that site in the general population. According to this original procedure, the confidence limit for the excess risk was not usually calculated. This decision was ascribed to the difficulty in accounting for inherent uncertainty in the exposure and cancer response data. More recent assessments have taken the opposite view and attempted to calculate and characterize this uncertainty by determining confidence limits, *inter alia*.

Guidelines for Carcinogen Risk Assessment (U.S. EPA, 2005a)

U.S. EPA revised its "Guidelines for Carcinogen Risk Assessment" (referred to henceforth as the "U.S. EPA Guidelines") in 2005. Compared to the 1986 version of this document, more emphasis is placed on establishing a "mode of action" (MOA). The following excerpt provides a definition of this term:

> "The term "mode of action" is defined as a sequence of key events and processes, starting with interaction of an agent with a cell, proceeding through operational and anatomical changes, and resulting in cancer formation. A "key event" is an empirically observable precursor step that is itself a necessary element of the mode of action or is a biologically based marker for such an element. Mode of action is contrasted with "mechanism of action," which implies a more detailed understanding and description of events, often at the molecular level, than is meant by mode of action".

Cancer risk assessments performed under the prior U.S. EPA Guidelines sometimes included a MOA description. However, the 1986 U.S. EPA Guidelines did not explicitly mandate the development of a MOA description in cancer risk assessments.

The MOA information is then used to govern how a cancer risk assessment shall proceed. Tumor incidence data sets arising from a MOA judged to be not relevant to humans are not used to extrapolate a cancer potency factor. If an MOA cannot be determined or is determined to have a low-dose linear dose-response and a nonmutagenic MOA, then a linear extrapolation method is used to develop a cancer potency factor. The same linear extrapolation is used for all lifestages, unless chemical specific information on lifestage or population sensitivity is available. Carcinogens that act via an MOA judged to have a nonlinear low-dose dose response are modeled using MOA data, or the RfD/RfC risk assessment method is used as a default. Adjustments for susceptible lifestages or populations are to be performed as part of the risk assessment process.

If a carcinogen is deemed to act via a mutagenic MOA, then the data from the MOA analysis is evaluated to determine if chemical-specific differences between adults and juveniles exist and can be used to develop a chemical-specific risk estimate incorporating lifestage susceptibility. If this cannot be done, then early-life susceptibility is assumed, and age-dependent adjustment factors (ADAFs) are applied as appropriate to develop risk estimates. In cases where it is not possible to develop a toxicokinetic model to perform cross-species scaling of animal tumor data sets which arise from oral exposures, the U.S. EPA Guidelines state that administered doses should be scaled from animals to humans on the basis of equivalence of $mg/kg^{3/4}$-d (milligrams of the agent normalized by the 3/4 power of body weight per day). This is a departure from the 1986 U.S. EPA guidelines, which used a 2/3 power of body weight normalization factor. Other adjustments for dose timing, duration and route are generally assumed to be handled in similar fashion to that described for the 1986 guidelines, although of course updated parameter values would be used where available.

The 2005 U.S. EPA Guidelines also use benchmark dose methodology (described above, page 27) to develop a "point-of departure" (POD) from tumor incidence data. For linear extrapolation, the POD is used to calculate a cancer potency factor, and for nonlinear extrapolation the POD is used in the calculation of a reference dose (RfD) or reference concentration (RfC).

It should be noted that none of the cancer potency factors listed in this document were obtained from U.S. EPA risk assessments performed under the 2005 U.S. EPA Guidelines. All U.S. EPA IRIS cancer potency values contained in this document were obtained from risk assessments using the 1986 U.S. EPA Guidelines.

Office of Environmental Health Hazard Assessment (OEHHA), California Environmental Protection Agency

The cancer risk assessment procedures originally used by the Office of Environmental Health Hazard Assessment (OEHHA) are outlined in "Guidelines for Chemical Carcinogen Risk Assessments and their Scientific Rationale" (referred to below as the Guidelines) (CDHS, 1985). These procedures were generally used in generating Toxic Air Contaminant (TAC) cancer potency values, standard Proposition 65 cancer potency values and Public Health Goal (PHG) cancer

potency values. Expedited Proposition 65 cancer potency values depart somewhat from those procedures and are discussed separately below.

OEHHA cancer risk assessment methodology as described by CDHS (1985) generally resembled that used at that time by U.S. EPA (Anderson *et al*., 1983; U.S. EPA, 1986). OEHHA risk assessment practice similarly reflects the evolution of the technical methodology (*e.g.*, as described in U.S. EPA, 2005a) since the original guidelines were published. The basic principles and procedures described below are still considered applicable. More recent additions to OEHHA cancer risk assessment methods such as the use of benchmark dose methodologies and early-lifestage cancer potency adjustments are discussed above. The Guidelines state that both animal and human data, when available, should be part of the dose-response assessment.

OEHHA Calculation of Carcinogenic Potency Based on Animal Data

The procedures used to extrapolate low-dose human cancer risk from animal carcinogenicity data assumed that a carcinogenic change induced in a cell is transmitted to successive generations of cell descendants, and that the initial change in the cell is an alteration (*e.g.*, mutation, rearrangement, etc.) in the cellular DNA. Non-threshold models are used to extrapolate to low-dose human cancer risk from animal carcinogenicity data.

Several models were proposed for extrapolating low-dose human cancer risk from animal carcinogenicity data in the original Guidelines. These models include the Mantel-Bryan method (log-probit model), the one-hit model, the linearized multistage procedure, the gamma multihit model, and a number of time-to-tumor models. The Guidelines stated that time-to-tumor models (i.e., a Weibull-in-time model) should be used for low-dose extrapolation in all cases where supporting data are available, particularly when survival is poor due to competing toxicity. However, the Guidelines also noted the difficulty of determining the actual response times in an experiment. Internal tumors are generally difficult to detect in live animals and their presence is usually detected only at necropsy. Additionally, use of these models often requires making the determination of whether a tumor was the cause of death, or was found only coincidentally at necropsy when death was due to other causes. Further, competing causes of death, such as chemical toxicity, may decrease the observed time-to-tumor for nonlethal cancers by allowing earlier necropsy of animals in higher dose groups. The linearized multistage (LMS) procedure was noted as being an appropriate method for dose extrapolation in most cases, with the primary exception being a situation in which sufficient empirical data are available to indicate a dose-response curve of a "quasi-threshold" type (*e.g.*, flat for two or three dose levels, then curving sharply upwards). In this case, the LMS procedure may underestimate the number of stages and overestimate the low-dose risks. In this case, the gamma multihit model was suggested as being a potential alternative. The Mantel-Bryan model was described as having little biological basis as applied to carcinogenesis, and being likely to underestimate risks at low doses. The Guidelines stated that this model should not be used for low dose extrapolation. More recent practice has departed from these original guidelines in some respects, for instance by experimenting with cell-proliferation based models in a few cases. However, the LMS model remained the preferred extrapolation model for most purposes. Some of the difficulties in achieving a satisfactory fit to tumor incidence data were found to be alleviated by application of toxicokinetic models and use of an internal rather than applied dose metric with the LMS model. This has resulted in the alternative models originally advocated (Gamma multihit, Mantel-Bryan) being mostly

abandoned. As noted above (Dose-Response Assessment, page 23), the use of allegedly biologically based statistical models such as LMS has fallen from favor in recent years, and benchmark dose methodology has become the preferred method for extrapolating cancer potency values from animal cancer incidence data. However, it should also be noted that results generated by the LMS model and benchmark dose methodology from the same data set are often quite similar.

The 1985 Guidelines stated that both animal and human data, when available, should be part of the dose-response assessment. Although preference was given to human data when these were of adequate quality, animal studies may provide important supporting evidence. Low-dose extrapolation of human cancer risk from animal carcinogenicity data was generally based on the most sensitive site, species and study demonstrating carcinogenicity of a particular chemical, unless other evidence indicates that the data set in question is not appropriate for use. Where both benign and malignant tumors are induced at the same site and the benign tumors are considered to have the potential to progress to malignant tumors, the incidence data for both types of tumors could be combined to form the basis for risk assessment. Pharmacokinetic data on chemical metabolism, effective dose at target site, or species differences between laboratory test animals and humans were considered in dose-response assessments when available. In performing exposure scaling from animals to humans, the "surface area" correction (correcting by the 2/3 power of body weight) was used unless specific data indicate that this should not be done. The Guidelines assumed that in the absence of evidence to the contrary, chemicals that cause cancer after exposure by ingestion will also cause cancer after exposure by inhalation, and vice versa. These original proposals have continued in use with little change except that currently, TAC and PHG cancer potency factor calculations use a 3/4 power of body weight correction for interspecies scaling, in line with current U.S. EPA practice. The standard Proposition 65 cancer potency factor calculations still use a 2/3 power correction because the cancer potency calculation method is specified in regulation (California Health and Safety Code 25249.5 *et seq*.).

Cancer unit risk factors [in units of $(\mu g/m^3)^{-1}$] have been calculated from cancer potency factors [in units of $(mg/kg\text{-}day)^{-1}$] using the following relationship:

$$UR = \frac{CPF * 20\ m^3}{70\ kg\ *\ CV}$$

where UR is the cancer unit risk, CPF is the cancer potency factor, 70 kg is the reference human body weight, 20 m^3 is the reference human inspiration rate/day, and CV is the conversion factor from mg to µg (= 1000). The cancer unit risk describes the excess cancer risk associated with an inhalation exposure to a concentration of 1 $\mu g/m^3$ of a given chemical; the cancer potency factor describes the excess cancer risk associated with exposure to 1 mg of a given chemical per kilogram of body weight.

It should be noted that although this default method is still used in deriving published cancer unit risk values, for site-specific risk assessments age-appropriate distributions and percentile values are used in the current version of the Hot Spots exposure assessment document. Where exposure to children occurs (as it does in most exposures to the general population surrounding a source

site) it is also necessary to apply the age-specific adjustment factors for the appropriate durations in accordance with the guidance offered above (Page 30 *et seq.*).

OEHHA Calculation of Carcinogenic Potency Based on Human Data

Human epidemiologic studies with adequate exposure characterization are used to evaluate the cancer potency of a chemical. If they show a carcinogenic effect, the data are analyzed to provide an estimate of the linear dependence of cancer rates on lifetime cancer dose. The 1985 Guidelines stated that with continuous exposure, age-specific incidence continues to increase as a power function (*e.g.*, t^3 or t^4) of the elapsed time since initial exposure. Lifetime risks can be estimated by applying such a power function to the observed data and extrapolating beyond the actual followup period. OEHHA has generally undertaken the calculation of study power and confidence bounds on the potency estimate as important tools to establish the credibility of the estimate obtained and in comparing this with other estimates (from other human studies or from animal data). Due to the diversity in quality and type of epidemiological data, the specific approaches used in OEHHA risk assessments based on human epidemiologic studies vary on a case by case basis rather than following explicit general guidelines. Examples of the methods used can be observed in the Toxic Air Contaminant documents (these documents are listed in Appendix D: the methods used are described in the compound summaries provided in Appendix B).

Expedited Proposition 65 Cancer Risk Assessment Methodology

Expedited cancer potency values developed for several agents listed as carcinogens under Proposition 65 (California Health and Safety Code 25249.5 *et seq*.) were derived from selected animal carcinogenicity data sets of the Carcinogenic Potency Database (CPDB) of Gold *et al.* (1984, 1986, 1987, 1989, 1990, 1997) using default procedures specified in the administrative regulations for Proposition 65 (Title 22 California Code of Regulations [CCR] 12703). OEHHA hazard assessments usually describe all relevant data on the carcinogenicity (including dose-response characteristics) of the chemical under examination, followed by an evaluation of any pharmacokinetic and mechanistic (*e.g.*, genotoxicity) data. An evaluation of the data set for the chemical may indicate that adjustments in target dose estimates or use of a dose response model different from the default are appropriate. The procedure used to derive expedited Proposition 65 cancer potency values differs from the usual methodology in two ways. First, it relies on cancer dose response data evaluated and extracted from the original literature by Gold *et al.* Second, the choice of a linearized multistage procedure for generating cancer potency values is automatic, and pharmacokinetic adjustments are not performed. The methods used to develop expedited cancer potency values incorporate the following assumptions:

1. The dose response relationship for carcinogenic effects in the most sensitive species tested is representative of that in humans.
2. Observed experimental results can be extrapolated across species by use of the interspecies factor based on "surface area scaling."
3. The dose to the tissue giving rise to a tumor is assumed to be proportional to the administered dose.
4. The linearized multistage polynomial procedure can be used to extrapolate potency outside the range of experimental observations to yield estimates of "low" dose potency.

5. Cancer risk increases with the third power of age.

The Carcinogenic Potency Database of Gold *et al.* (1984, 1986, 1987, 1989, 1990) contains the results of more than 4000 chronic laboratory animal experiments on 1050 chemicals by combining published literature with the results of Federal chemical testing programs (Technical Reports from the Carcinogenesis Bioassay Program of the National Cancer Institute (NCI)/National Toxicology Program (NTP) published prior to June 1987). The published literature was searched (Gold *et al*., 1984) through the period December 1986 for carcinogenicity bioassays; the search included the Public Health Service publication "Survey of Compounds Which Have Been Tested for Carcinogenic Activity" (1948-1973 and 1978), monographs on chemical carcinogens prepared by the International Agency for Research on Cancer (IARC) and Current Contents. Also searched were Carcinogenesis Abstracts and the following journals: British Journal of Cancer, Cancer Letters, Cancer Research, Carcinogenesis, Chemosphere, Environmental Health Perspectives, European Journal of Cancer, Food and Chemical Toxicology, Gann, International Journal of Cancer, Journal of Cancer Research and Clinical Oncology (formerly Zeitschrift fur Krebsforschung und Klinische Onkologie), Journal of Environmental Pathology and Toxicology, Journal of Toxicology and Environmental Health, Journal of the National Cancer Institute, and Toxicology and Applied Pharmacology. Studies were included in the database if they met the following conditions:

1. The test animals were mammals.
2. Chemical exposure was started early in life (100 days of age or less for hamsters, mice and rats).
3. Route of administration was via the diet, drinking water, gavage, inhalation, intravenous injection or intraperitoneal injection.
4. The test chemical was administered alone (not in combination with other chemicals).
5. Chemical exposure was chronic (*i.e.* duration of exposure was at least one-fourth the standard lifespan for that species), with not more than 7 days between exposures.
6. The experiment duration was at least half the standard lifespan for the species used.
7. The study design included a control group and at least 5 animals/exposure group.
8. No surgical interventions were performed.
9. Pathology data were reported for the number of animals with tumors (not total number of tumors).
10. All results reported were original data (not analysis of data reported by other authors).

Included in their data set tabulations are estimates of average doses used in the bioassay, resulting tumor incidences for each of the dose levels employed for sites where significant responses were observed, dosing period, length of study and histopathology. Average daily dose levels were calculated assuming 100% absorption. Dose calculations follow procedures similar to those of Cal/EPA and U.S. EPA; details on methods used and standard values for animal lifespans, body weights, and diet, water and air intake are listed in Gold *et al.* (1984). OEHHA (1992) reviewed the quality assurance, literature review, and control procedures used in compiling the data and found them to be sufficient for use in an expedited procedure. Cancer potency estimates were

derived by applying the mathematical approach described in the section below to dose response data in the Gold *et al.* database.

The following criteria were used for data selection:

1. Data sets with statistically significant increases in cancer incidence with dose ($p \leq 0.05$) were used. (If the authors of the bioassay report considered a statistically significant result to be unrelated to the exposure to the carcinogen, the associated data set was not used.)
2. Data sets were not selected if the endpoint was specified as "all tumor-bearing animals" or results were from a combination of unrelated tissues and tumors.
3. When several studies were available, and one study stood out as being of higher quality due to numbers of dose groups, magnitude of the dose applied, duration of study, or other factors, the higher quality study was chosen as the basis for potency calculation if study results were consistent with those of the other bioassays listed.
4. When there were multiple studies of similar quality in the sensitive species, the geometric mean of potencies derived from these studies was taken. If the same experimentalists tested two sexes of the same species/strain under the same laboratory conditions, and no other adequate studies were available for that species, the data set for the more sensitive sex was selected.
5. Potency was derived from data sets that tabulate malignant tumors, combined malignant and benign tumors, or tumors that would have likely progressed to malignancy.

Cancer potency was defined as the slope of the dose response curve at low doses. Following the default approach, this slope was estimated from the dose response data collected at high doses and assumed to hold at very low doses. The Crump linearized multistage polynomial (Crump *et al.*, 1977) was fit to animal bioassay data:

$$\text{Probability of cancer} = 1 - \exp[-(q_0 + q_1 d + q_2 d^2 + ...)]$$

Cancer potency was estimated from the upper 95% confidence bound on the linear coefficient q_1, which is termed q_1^*.

For a given chemical, the model was fit to a number of data sets. As discussed in the section above, the default was to select the data for the most sensitive target organ in the most sensitive species and sex, unless data indicated that this was inappropriate. Deviations from this default occur, for example, when there are several bioassays or large differences exist between potency values calculated from available data sets.

Carcinogenicity bioassays using mice and/or rats will often use an exposure duration of approximately two years. For standard risk assessments, this is the assumed lifespan for these species. Animals in experiments of shorter duration are at a lower risk of developing tumors than those in the standard bioassay; thus potency is underestimated unless an adjustment for experimental duration is made. In estimating potency, short duration of an experiment was taken into account by multiplying q_1^* by a correction factor equal to the cube of the ratio of the assumed standard lifespan of the animal to the duration of the experiment (T_e). This assumes that the cancer hazard would have increased with the third power of the age of the animals had they lived longer:

$$q_{animal} = q_1^* * (104 \text{ weeks}/T_e)^3$$

In some cases excess mortality may occur during a bioassay, and the number of initial animals subject to late occurring tumors may be significantly reduced. In such situations, the above described procedure can, at times, significantly underestimate potency. A time-dependent model fit to individual animal data (i.e., the data set with the tumor status and time of death for each animal under study) may provide better potency estimates. When Gold *et al.* indicated that survival was poor for a selected data set, a time-dependent analysis was attempted if the required data were available in the Tox Risk (Crump *et al.*, 1991) data base. The Weibull multistage model (Weibull-in-time; multistage-in-dose) was fit to the individual animal data.

To estimate human cancer potency, q_{animal} values derived from bioassay data were multiplied by an interspecies scaling factor (K; the ratio of human body weight (bw_h) to test animal body weight (bw_a), taken to the 1/3 power (Anderson *et al.*, 1983)):

$$K = (bw_h/bw_a)^{1/3}$$

Thus, cancer potency = $q_{human} = K * q_{animal}$

Chemical-specific Descriptions of Cancer Potency Value Derivations

Unit Risk and potency values for chemicals whose cancer potency values were obtained from Toxic Air Contaminant documents, standard or expedited Proposition 65 documents, U.S. EPA's Integrated Risk Information System (IRIS) documents and Health Effects Assessment Summary Table (HEAST) entries, or from other documents prepared by OEHHA's Air Toxicology and Epidemiology Branch or Pesticide and Environmental Toxicology Branch are presented in Appendix A. Information summaries for these chemicals are presented in Appendix B.

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Exhibit H

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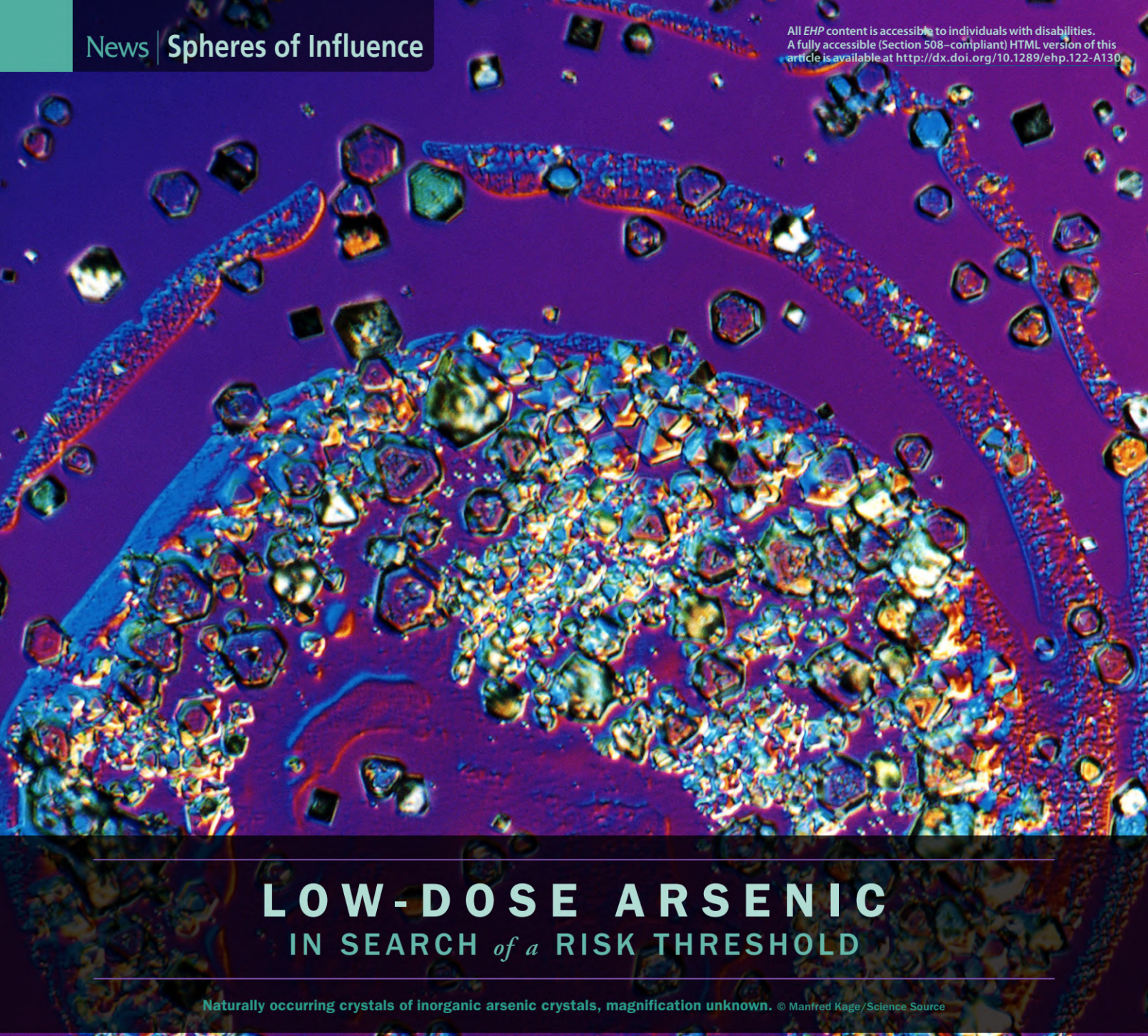

LOW-DOSE ARSENIC
IN SEARCH *of a* RISK THRESHOLD

Naturally occurring crystals of inorganic arsenic crystals, magnification unknown. © Manfred Kage/Science Source

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Scientists long ago linked high levels of arsenic in groundwater to cancer and other environmental illnesses, particularly in Taiwan, Bangladesh, and South America, where the contamination can often reach extraordinarily high levels of 1,000 ppb or more. Now concerns are shifting to the health effects of much lower doses such as those that many Americans live with every day.

Margaret Karagas, who directs the Children's Environmental Health and Disease Prevention Research Center at Dartmouth College, says researchers increasingly believe that arsenic risks are more widespread than previously recognized, particularly during vulnerable periods such as pregnancy and childhood. Protecting against low-level exposure is challenging, however, given that arsenic is a natural element in the Earth's crust and ubiquitous throughout the environment.

Moreover, the evidence for low-dose effects is controversial. One view holds that arsenic has a dose threshold below which exposures aren't harmful. But controversial studies in the peer-reviewed literature increasingly suggest this threshold may not exist, so that any exposure—no matter how small—could boost risks for diabetes, heart disease, immunological problems, and cancer.[1,2,3,4,5,6]

The disagreement is a problem for regulators who face mounting pressure to set or reduce standards for arsenic. The U.S. Environmental Protection Agency (EPA) is grappling with a revised estimate of arsenic carcinogenicity that, if enacted, would result in unattainable clean-up standards, according to Susan Griffin, a senior toxicologist with the EPA's Region 8 office in Denver, Colorado. The U.S. Food and Drug Administration (FDA) is also under pressure to regulate arsenic in foods, especially rice, which readily absorbs the metal as it grows, making it a top source of dietary exposure.

The focus on rice comes on the heels of a new "action level" of 10 ppb for arsenic in apple juice that was proposed by the FDA in July 2013.[7] This new value, which tightens the agency's previous "level of concern" of 23 ppb (and which has yet to be formally adopted), was motivated in part by mounting publicity over low doses of arsenic in the diet, including media-directed efforts by the public-interest group Consumers Union (CU) to raise awareness on the issue. Growing public scrutiny has put a spotlight on the complex question of how very low arsenic exposures may affect human health.

A Historical View

That arsenic can be lethal has been known since antiquity. But lethal doses of arsenic are difficult to quantify, and they depend on solubility, valence states, and other factors. The Agency for Toxic Substances and Disease Registry suggests that the minimal lethal exposure in humans ranges from 1 to 3 ppm, with death resulting from cardiovascular collapse and hypovolemic shock.[8]

Researchers didn't perceive arsenic as an environmental health threat until studies in Taiwan, and later in Chile, linked levels in groundwater with skin cancers such as squamous cell carcinoma (which is rarely fatal) and a condition called black foot disease (which affects blood vessels, leading to gangrene). Villagers were exposed to the arsenic beginning in the early twentieth century after artesian wells were drilled throughout southwestern Taiwan to avoid saltwater intrusion from shallower wells.[9] The U.S. Public Health Service aimed to protect against the arsenic-related skin problems seen in Taiwan when it set a 50-ppb standard for arsenic in drinking water in 1942, which was then adopted by the EPA in 1975.[10]

The levels deemed "low" in early environmental health research on arsenic were much higher than what's considered low today. Studies from Taiwan up to the 1980s described groundwater levels of up to 300 ppb as low, of up to 600 ppb as moderate, and values beyond that as high.[10,11] These delineations were based on a view that consuming arsenic in groundwater, while harmful, wasn't fatal in the long run.

Two pivotal studies led researchers to reconsider that point. Chien-Jen Chen, who was then a teaching assistant at the National Taiwan University College of Medicine, and colleagues showed that arsenic could, in fact, boost risks for fatal malignancies at groundwater concentrations far less than 600 ppb. Published in 1985, the first study reported statistically significant associations between chronic exposure to artesian well water in Southwestern Taiwan and elevated mortality from cancers of the lung, bladder, and other internal organs.[12,13] And in their follow-up study, Chen and colleagues reported that this relationship was dose-dependent—i.e., that cancer rates grew with higher arsenic exposure—and that mortality rates were especially high in areas where blackfoot disease also was endemic.[11]

Joseph Graziano, a professor of environmental health sciences and pharmacology at Columbia University, says Chen's data had far-reaching consequences that scientists are still grappling with today. Without evidence to the contrary, the EPA defaulted to what is still a standard regulatory assumption: namely that any exposure to a carcinogen, no matter how small, increases cancer risk to some degree. Therefore, the National Research Council (NRC) now describes arsenic levels beyond 150 ppb as high, between 150 ppb and 50 ppb as moderate, and below 50 ppb as low.[14]

But linear assumptions drive considerable risk even at low exposures. Extrapolating from high-dose human data, the NRC predicted in 1999 that the 50-ppb water standard could induce cancer in as many as 1 in 100 people.[15]

By that time, the EPA had already been engaged in technical review on arsenic for years. The agency ultimately evaluated more than 300 studies and drew on expert opinions from the NRC, the National Drinking Water Council, and its own Science Advisory Board (SAB) before it finally dropped the standard from 50 to 10 ppb in 2001[16]—a level the NRC estimated might lead to a cancer risk of approximately 1 in 300 for people exposed over a lifetime.[17] According to Craig Steinmaus, an associate adjunct professor in epidemiology at the University of California, Berkeley, School of Public Health, the EPA by necessity had to factor cost and technical feasibility as well as health into the 10-ppb drinking water standard.

Debating the Standard

The EPA's risk assumptions on arsenic were criticized by researchers who felt it was inappropriate to extrapolate low-dose effects from the high-dose Taiwanese studies. Samuel Cohen, a professor of pathology and microbiology at the University of Nebraska Medical Center, has long maintained that arsenic has a dose threshold below which exposures are not harmful. According to Cohen's own research with rodents (in addition to *in vitro* and *in vivo* studies by other researchers), arsenic is carcinogenic only at doses high enough to induce cytotoxicity followed by regenerative cell proliferation. If prolonged, he says, that mechanism can spawn tumors in the bladder, lungs, and skin.

But Cohen insists this whole process depends on the generation of reactive arsenic metabolites that, in turn, interact with sulfhydryl groups in critical cell proteins. And at minimal doses (below 10 ppb in drinking water given to experimental animals or 100 ppb in well water consumed by humans, he says), arsenic exposure doesn't generate enough reactive metabolites to induce tumor growth, suggesting that arsenic has a dose threshold. Moreover, Cohen claims that only direct reactions with DNA produce linear, nonthreshold dose responses for cancer, but according to the evidence, he says, inorganic arsenic is not DNA-reactive.[18]

"A linear dose–response line goes against what we know about arsenic's basic biology," Cohen says. "What we show in the lab shows there must be a threshold phenomenon."

Other scientists disagree. Steinmaus, for instance, counters that rodents may not be good models for human arsenic metabolism given that "they don't get cancer at doses that clearly cause cancer in humans." He says, "You need to interpret those data cautiously."

Moreover, high-dose human data from Taiwan are valuable because they remove some of the uncertainty associated with

Arsenic in U.S. Private Wells

Despite the 10-ppb upper limit on inorganic arsenic in municipal water, neither the EPA nor state governments regulate arsenic in private wells. However, a 2001 EPA study found that 13 million U.S. residents get their drinking water from private wells that exceed the federal arsenic standard.[35,36,37] Similarly, in 2009 the U.S. Geological Survey (USGS) tested 1,774 private wells nationwide and found that 6.8% of them exceeded the EPA standard (these are the most recent national data available on arsenic in private wells).[38]

According to Leslie DeSimone, a water quality specialist with the USGS, 90% of the exceedances were below 50 ppb, but measured concentrations ranged as high as 242 ppb, with the highest levels detected in the West, Midwest, parts of Texas, and New England. During a survey of Maine wells conducted in the mid to late 2000s, USGS scientists measured a concentration of 3,100 ppb in the coastal town of Danforth.[39] Maine resides within a belt of arsenic-laden bedrock that extends north from New York.

Bill Wilber, chief of the USGS National Water Quality Assessment Program, says in some cases simply drilling a well introduces oxygen and other elements that alter the chemistry of the underlying geology, liberating arsenic from bedrock and allowing it to seep into the water column. "So you can find a big exceedance in one well and not in another that's just fifty feet away," Wilber says.

According to Andy Smith, state toxicologist with the Maine Division of Environmental Health, the cost of a home-based system to remove arsenic from well water ranges from $300 for a point-of-use system (i.e., at the faucet) to as much as $9,000 for point-of-entry systems that treat water for the whole household. Federal or state assistance to purchase these systems generally isn't available, Smith says.

exposure, Steinmaus claims. Villagers in Taiwan often spend much of their lives in one general location, so the arsenic measured in local well water likely reflects their actual long-term intake. By contrast, populations in the United States and other developed countries with lower arsenic levels in groundwater are more mobile, leading to a strong likelihood of exposure misclassification. This statistical bias occurs when individual subjects in epidemiology studies are classified as having consumed more—or less—of a substance over a given duration than they actually ingested, making it difficult to accurately estimate disease associations.

Thus, the EPA SAB concluded in 2010 that—given the size and stability of the population, as well as the inclusion of long-term exposure patterns—the Taiwanese data were "still the most appropriate source for estimating bladder and lung cancer risk to humans."[10] But the SAB also stated that published studies from countries with low levels of arsenic in drinking water (which the SAB defined as up to 160 ppb) should be critically evaluated.[10]

Evidence for Low-Dose Impacts

Low-dose studies are now ongoing in a number of countries, including various locations throughout the United States. For instance, in 2013 Ana Navas-Acien, an associate professor of environmental sciences and epidemiology at the Johns Hopkins Bloomberg School of Public Health, published results from a prospective study showing that urinary arsenic concentrations reflecting low and moderate drinking water exposures were associated with lung, prostate, and pancreatic cancer,[5] as well as with cardiovascular disease,[2] among Native Americans living in Arizona, Oklahoma, and the Dakotas.

Navas-Acien's team measured arsenic in urine samples that had been collected and frozen between 1989 and 1991. The cohort of nearly 4,000 individuals had originally been assembled for the Strong Heart Study (SHS), an evaluation of cardiovascular health in Native Americans launched by the National Heart, Lung and Blood Institute in 1988. According to Navas-Acien, Native Americans included in the SHS tend to be more geographically stable than the general U.S. population, limiting the potential for exposure misclassification.[5] "They get the same exposure to arsenic year after year that they got at birth," she explains.

By matching local well water data collected by the EPA and urinary arsenic measures from the SHS samples with information from death certificates up through 2008, Navas-Acien could study the relationship between arsenic exposure and cancer mortality. Her team's results suggested that arsenic had a linear dose response with lung cancer in particular, although Navas-Acien points out that confidence intervals were wide at doses below 5 ppb in well water, indicating uncertainty at the lowest exposure levels.

A similar linear response was also estimated for prostate and pancreatic cancer, but with even wider confidence intervals at the lowest doses. However, the excess relative risks estimated for prostate and pancreatic cancer in Navas-Acien's study are much greater than they are for lung cancer; this is inconsistent with findings from other areas such as Taiwan, and therefore raises questions among some researchers about the validity of the findings. Navas-Acien's team didn't evaluate bladder cancer or skin cancer because of the small number of cases.

In a separate study of the same SHS cohort, Navas-Acien reported an association between low-dose arsenic exposures and higher rates of cardiovascular disease.[2] That study is one of the first prospective cohort studies to evaluate arsenic-related cardiovascular risk, including both incidence and mortality, in a population from the United States.

These findings add to a wealth of data emerging from what could be the largest evaluation of arsenic toxicity yet undertaken: the Health Effects of Arsenic Longitudinal Study (HEALS), which launched in Bangladesh in 2000.[19] Coordinated by Graziano and Habibul Ahsan, a professor of epidemiology, medicine, and human genetics at the University of Chicago, HEALS has over time assembled a cohort of tens of thousands of individuals living in the district of Araihazar, where arsenic levels measured in well water have ranged from nondetectible to more than 900 ppb.

The HEALS team first reported an association between arsenic and high blood pressure in 2007 at well water concentrations of 10–40 ppb. Since then, HEALS has yielded dozens of papers associating arsenic at levels below 50 ppb with health conditions including heart disease, hematuria (blood in the urine), and impaired lung function.[20,21,22] Studies also showed that increased total urinary arsenic was associated with skin lesions such as melanosis and keratosis, which are known precursors to skin cancer.[23,24] "HEALS is an ongoing effort, and we are expanding the design and questions that we can answer with longer follow-up," Ahsan says.

The Regulatory Landscape

Confronted with mounting evidence of arsenic's low-dose effects, its commercial uses are being phased out. Of particular concern are uses in agriculture, which can result in potentially significant human exposures. According to a November 2013 NRC report, foods dominate human arsenic exposures when the levels in drinking water drop below 50 ppb (drinking water drives the exposures when its arsenic content exceeds that amount).[14]

In some cases, agricultural soils are naturally high in arsenic, but arsenical herbicides also can leave residues that accumulate in crops. Most of these herbicides have now been phased out (with some exceptions made for turfgrass and cotton),[25,26] but what remains in soil from past applications has been especially problematic in apple orchards, where these herbicides were routinely used, and in rice grown on old cotton fields that were treated with the chemicals.

Arsenical feed additives used to promote growth and prevent disease in poultry and swine may also be problematic for human consumers. However, these additives are also being phased out. Production of the feed additive roxarsone ceased voluntarily in 2011 after the FDA detected inorganic arsenic in the livers of chickens that ate it.[27] The manufacturers of roxarsone and two other arsenical feed additives have requested that the FDA withdraw approval of these products.[28] The agency is currently considering a request to ban a fourth additive, nitarsone.[28]

Now the FDA is weighing how to impose standards for arsenic in foods. The proposed standard of 10 ppb in apple juice was a first step in this direction, but advocates with CU say the agency should go further by imposing a 120-ppb standard for inorganic arsenic in rice.[29] In November 2012 CU published the results of a study showing that 223 samples of rice and rice-based products sold in the United States contained inorganic arsenic at concentrations ranging from 29.4 to 210 ppb.[30] In addition, Dartmouth investigators reported that brown rice syrup, a sweetener, might expose consumers to "significant concentrations" of inorganic arsenic.[31] (Arsenic tends to accumulate in the aleurone layer of the rice grain, which gives brown rice its color. This layer is removed to produce white rice.[31])

The FDA followed up with its own report on 1,300 samples of rice and rice products, which found that concentrations of inorganic arsenic ranged from an average 0.1 µg per serving in infant formula to an average 7.2 µg per serving in brown rice.[32] For perspective, Aaron Barchowsky, a professor of environmental and occupational health at the University of Pittsburgh School of Public Health, says that daily consumption of 3 liters of water at the 10-ppb standard amounts to a 30-µg dose of inorganic arsenic.

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In a 6 September 2013 statement, the FDA said the amount of detectable arsenic in the sampled rice and rice products was too low to cause "any immediate or short-term adverse health effects."[33] FDA spokesperson Shelly Burgess says the statement referred to short-term effects only, and not skin, bladder, or lung cancer.

But Michael Crupain, director of *Consumer Reports*' Food Safety and Sustainability Center, insists that chronic low-level exposures over time are still a concern, especially for infants fed formula made with brown rice syrup, which had the highest levels detected in CU's survey. The FDA is now performing a draft risk assessment for arsenic in rice, which agency officials say could guide further actions.

Also on the regulatory front, the EPA is grappling with its numerical estimate of arsenic's cancer potency. This value, known as a cancer slope factor (CSF), guides important regulatory policies, including clean-up standards at contaminated waste sites. Set in 1998, the original CSF for arsenic was based on nonmelanoma skin cancers observed in the early Taiwanese studies.

In 2010 the EPA proposed a revised CSF as part of an arsenic reassessment under the agency's Integrated Risk Information System (IRIS).[10] The proposed CSF, which was based on newer reports of associations with more dangerous lung and bladder cancers, was 17 times greater than the older value. But that new value was protested by industry and other affected stakeholders, even some of the agency's own scientists. Griffin, of EPA Region 8, says that with the revised CSF, arsenic clean-up levels would drop 100-fold, which is below natural background levels of arsenic in western states.

The proposal was subsequently dropped by the EPA, and under a congressional mandate the agency is now revising its arsenic reassessment with a focus on both cancer and noncancer end points. On 7 November 2013 the NRC presented a report that the EPA will use for guidance in drafting a new IRIS document.[14] Graziano, who chairs the NRC committee, says the EPA will submit the revised document by 2015. And at that point, he says, NRC scientists will review it to ensure that dose–response relationships between inorganic arsenic and its effects are "appropriately estimated and characterized."

Continued Debate

Meanwhile the debate over low-dose health risks from arsenic will likely continue on two fronts: how to apply mechanistic findings from animal and *in vitro* research to human responses, and how to address fundamental uncertainties in the human data.

A key question is whether the recent epidemiological literature supports estimates of cancer risk predicted from linear dose–response models. Dozens of studies over the last 15 years have investigated human cancer risk from arsenic exposure at sites around the world. According to a 2011 review published by Herman Gibb, president of environmental consulting firm Tetra Tech Sciences, these studies provide conflicting evidence, in part because the sample sizes needed to quantify risks at drinking water doses less than 100 ppb are larger than what's ordinarily achievable.[34]

Steinmaus argues that the high-dose epidemiology data may ultimately be most suitable for risk assessment, "but when you extrapolate down from those doses, the risks are huge." He adds, "This raises the question of whether linear extrapolations are suitable, and herein lies the big controversy."

Charles W. Schmidt, MS, an award-winning science writer from Portland, ME, has written for *Discover Magazine*, *Science*, and *Nature Medicine*.

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Exhibit I

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Arsenic and cancer: evidence and mechanisms

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Abstract

Arsenic is a potent carcinogen and poses a significant health concern worldwide. Exposure occurs through ingestion of drinking water and contaminated foods and through inhalation due to pollution. Epidemiological evidence shows arsenic induces cancers of the skin, lung, liver, and bladder among other tissues. While studies in animal and cell culture models support arsenic as a carcinogen, the mechanisms of arsenic carcinogenesis are not fully understood. Arsenic carcinogenesis is a complex process due its ability to be metabolized and because of the many cellular pathways it targets in the cell. Arsenic metabolism and the multiple forms of arsenic play distinct roles in its toxicity and contribute differently to carcinogenic endpoints, and thus must be considered. Arsenic generates reactive oxygen species increasing oxidative stress and damaging DNA and other macromolecules. Concurrently, arsenic inhibits DNA repair, modifies epigenetic regulation of gene expression, and targets protein function due its ability to replace zinc in select proteins. While these mechanisms contribute to arsenic carcinogenesis, there remain significant gaps in understanding the complex nature of arsenic cancers. In the future improving models available for arsenic cancer research and the use of arsenic induced human tumors will bridge some of these gaps in understanding arsenic driven cancers.

Keywords

arsenic; cancer; carcinogenesis; DNA damage; mechanism

INTRODUCTION

Over millennia, humans have harnessed the unique properties of arsenic for medicinal, agricultural, commercial, and decorative purposes. At the same time, humans have been subject to the stealthy toxicity of arsenic as an odorless and tasteless, intentional or unintentional, poison. Our complicated relationship with arsenic continues to this day.

Therapeutic uses of arsenic have been documented for thousands of years in traditional Chinese medicine and early western medicine. Two forms of arsenic were included in the

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Shennong Materia Medica in 200 BCE and Hippocrates is believed to use arsenic pastes to treat skin disorders (Au, 2011; Hughes et al., 2011; Paul et al., 2022; Chen & Costa, 2021). In 1786 Thomas Fowler reported on the medicinal effects of his arsenic solution for a broad range of infectious diseases and skin and blood disorders, in addition to other health conditions. The noted antimicrobial properties of arsenic led to the development of Salvarsan in the early 1900s as an effective treatment of syphilis garnering a Nobel prize for Paul Ehrlich in 1908. In the past, various forms of arsenic, including those used in traditional Chinese medicine and Fowler's solution, were employed as cancer therapeutics especially for cancers of the blood and skin (Au, 2011; Hughes et al., 2011; Paul et al., 2022; Chen & Costa, 2021). The FDA approved arsenic trioxide as a chemotherapeutic for leukemia in 2000 bringing an ancient drug into the modern era.

Other arsenic compounds have been beneficial as rodenticides, pesticides for agricultural crops and wood preservatives (Hughes et al., 2011; Bencko and Foong, 2017). Arsenic-based pigments were used in paints, fabrics and wallpapers based on a coveted emerald green color (Hughes et al., 2011). However, the medicinal and non-medicinal uses of arsenic revealed human toxicities based on unintended exposures. Widespread use of lead arsenate as a pesticide in apple and cherry orchards ultimately led to an official ban in the United States in 1988 (Hughes et al., 2011). The lasting legacy of this use is evident in millions of acres of land contaminated with lead arsenate. Chromated copper arsenate continues to be used as a wood preservative for non-residential purposes and organic arsenicals remain in restricted use as broad-spectrum herbicides. The potential for further contamination of soils and water by inorganic and organic arsenic compounds is under periodic review by the US Environmental Protection Agency (EPA).

Arsenic toxicity has been exploited for political gains through strategic poisonings leading to the often quoted statement labeling arsenic as the "king of poisons and poison of kings". Modern toxicological focus largely centers on the human health consequences of medicinal, occupational and environmental exposures to arsenic. Studies on health effects of human exposures through natural or anthropogenic arsenic contamination in soils and water led to adoption of drinking water standards worldwide currently at 10 ppb. Despite efforts to limit arsenic exposures, it is estimated that 200 million people or more are exposed to toxic levels of arsenic worldwide (Costa 2021). This chapter will focus on arsenic carcinogenicity and cover human population evidence for arsenic as a carcinogen, mechanisms of arsenic carcinogenicity, the carcinogenic potential of different forms of arsenic and conclude with a brief discussion of areas for future research.

SECTION 1: HUMAN STUDIES

Arsenic is a worldwide health concern due to prevalence in the environment and established human toxicity (Podgorski, 2020; Agency for Toxic Substances and Disease Registry (ATSDR), 2007; ATSDR, 2016; Naujokas et al., 2013). Arsenic is present in rocks, soil and water, and background environmental levels may be increased by mining, burning of fossil fuels, and application of agricultural pesticides and herbicides (Gundert-Remy et al., 2015). In recognition of its toxic potential, arsenic is at the top of the ASTDR Priority List (https://www.atsdr.cdc.gov/spl/index.html). Occupational exposures are limited by the US

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Occupational Safety and Health Administration to 10 μg/m^3, and recommended drinking water exposure limits of 10 μg/L (10 ppb) have been established by the EPA and the World Health Organization (WHO) (WHO, 2011; EPA, 2014).

The majority of human population studies focus on chronic arsenic ingestion through drinking water as the predominant exposure route (Andrew et al., 2003; Banerjee et al., 2007; Podgorski, 2020, ATSDR, 2007, ATSDR, 2016; WHO, 2011). Many parts of the world have high levels of arsenic in groundwater and aquifers with populations that use these water sources for household needs. One arsenic prediction model based on household groundwater-usage statistics estimates that between 94 and 220 million people may be exposed to high arsenic concentrations (Podgorski, 2020). Indeed, many seminal health studies have focused on populations in areas of the world with high levels of arsenic in water sources including, but not limited to, Bangladesh, India, Taiwan and Chile (ATSDR, 2007; ATSDR, 2016; Banerjee et al., 2017; Farzan et al., 2021; Moore et al., 2002). Some studies have established the relationship between arsenic levels in water and arsenic in biological specimens such as urine, hair and nails (Mahata et al., 2003; Maki-Paakkanen et al., 1998; Ruíz-Vera et al., 2019).

More recently, greater attention has been paid to food as a source of arsenic exposure (Oberoi 2014; Gundert-Remy 2015; Arslan et al., 2017; Wong et al., 2022). Food crops may contain elevated arsenic levels through irrigation with arsenic-containing water, cultivation in arsenic contaminated fields, or use of agricultural products containing arsenic (Gundert-Remy et al., 2015; Wong et al., 2022). Rice has become a notable concern due to arsenic's uptake and accumulation in this plant compared to other common grains such as wheat (Karagas et al., 2019). There is evidence of greater urinary arsenic in individuals reporting higher rice consumption compared to those with low rice consumption even in areas of low arsenic drinking water exposure (Gossai et al., 2017).

The relationships between arsenic exposure and cancer are clear. Cancer is one of the health effects of concern; arsenic is classified as a Class I human carcinogen by the International Agency for Research on Cancer (IARC) with strong experimental and human population evidence to support arsenic carcinogenicity (IARC, 2004; Moore et al., 2002; Srinivas et al., 2019; Tam et al., 2020). The strongest evidence for organ-specific arsenic carcinogenicity is in skin, lung, bladder and kidney with evidence for arsenic contributions to other cancers (WHO, ATSDR, 2007, ATSDR, 2016; Palma-Lara et al., 2020) (Figure 1).

Skin Cancer

Various non-cancerous skin lesions are associated with long term exposure to inorganic arsenic including changes in pigmentation, plantar-palmar hyperkeratinization and hyperkeratotic warts and corns (ASTDR, 2007; Hunt et al., 2014). These skin changes are most common in areas with high arsenic levels in drinking water and are viewed as sensitive indicators of chronic arsenic exposure (ASTDR, 2007; Hunt et al., 2014; Cheng et al., 2016). Skin lesions and cancer appear to be more prevalent at exposures to drinking water levels in excess of 50 μg/L and evidence linking arsenic to skin cancer is less conclusive at lower arsenic levels (Boffetta et al., 2020, Lamm et al., 2021; Karagas et al., 2015). Recent

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findings suggest that ingestion of arsenic containing foods in the diet such as rice may also contribute to skin cancer risk (Karagas et al., 2019; Gossai et al., 2017).

The most common tumors associated with arsenic exposure are keratinocytic tumors including squamous cell carcinomas, which may develop from hyperkeratotic warts or corns, and basal cell carcinomas (ASTDR, 2007; Karagas et al., 2015; Palma-Lara et al., 2020). There is less consistent evidence for arsenic-associated melanoma although it has been reported in Bangladesh (Choudhury et al., 2018), but not in the United States (Langston et al., 2022; Bedaiwi et al., 2021; Yager et al., 2016) or there are too few studies to draw firm conclusions (Matthews et al., 2019).

Lung Cancer

Epidemiological evidence indicates increased incidence of lung cancer in workers exposed to arsenic in the copper mining and smelting industry and ingestion through contaminated water (ASTDR 2007; Smith et al., 2012; Steinmaus et al., 2014; Palma-Lara et al., 2020). Studies conducted in Chilean cohorts born during periods of low versus high arsenic exposure from water reveal increased incidence of several cancers, including lung cancer, associated with the high exposure period (ASTDR, 2010; Smith et al., 2006). Similarly, mitigation efforts to decrease arsenic ingestion from contaminated water in Taiwan led to reduction in lung cancer rates (Su et al., 2011). No associations were identified for lung cancer and arsenic in soil in Taiwan despite reported associations between lung cancer and other metals in the same soils (Huang et al., 2013). These findings and others support the conclusion that lung cancer is increased upon chronic exposure to arsenic in drinking water (ASTDR, 2007; Kuo et al., 2017a; Su et al., 2011; Chen et al., 2010; Heck et al., 2009). There is evidence for dose dependence (Chen et al., 2010); however, the associations are less strong at low arsenic exposures (Shao et al., 2021; Tsuij et al., 2019)

The most common type of lung cancer associated with arsenic exposure is squamous cell carcinoma (Kuo et al., 2017; Heck et al., 2009; Taeger et al., 2009). The correlation between arsenic and squamous cell carcinoma was more pronounced at higher exposure levels; adenocarcinoma and small cell carcinoma of the lung were not associated with arsenic level in the drinking water in a Taiwan population (Kuo et al., 2017) although other investigators reported increased adenocarcinoma and small cell carcinomas of the lung with arsenic exposure (Chen et al., 2010; Guo et al., 2004). A study of former German uranium miners exposed to arsenic found that the arsenic-related type of lung cancer differed in miners based on evidence of silicosis. Arsenic was associated with increased squamous cell carcinoma in miners without silicosis. In contrast non-small cell lung cancer was related to arsenic exposure in miners with silicosis (Taeger et al., 2009) suggesting that other underlying factors may influence the specific lung cancer arising because of arsenic exposure.

Bladder Cancer

Population studies identify a clear relationship between elevated arsenic levels in drinking water and bladder cancer (IARC, 2004; ASTDR, 2007; Smith et al., 2012; Krajewski et al., 2021). A recent study found evidence for oxidative DNA damage in residents exposed to arsenic from artesian well-water in Taiwan and concluded that arsenic exposure and

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DNA damage predicted the risk of bladder cancer (Tsai et al., 2021). In the US, arsenic concentrations in drinking water were positively associated with bladder cancer in both men and women (Mendez et al., 2017; Baris et al., 2016) and a spatial cluster analysis of bladder cancer mortality identified significant hot spots. Further study concluded that there was a significant association between bladder cancer mortality and arsenic intake from well water (Amin et al., 2019; Baris et al., 2016). Notably, well water is not subject to federal regulation and may exceed the EPA recommended maximum contaminant level. As with other arsenic-associated cancers, there is not uniform agreement on risks linked to lower exposures (Kayajanian, 2003) although a meta-analysis suggested that exposure to 10 μg/L of arsenic in drinking water may double the risk of bladder cancer (Saint-Jacques et al., 2014). Arsenic ingestion through food is also considered a potentially important source of exposure that may contribute to bladder and other cancers (Gundert-Remy et al., 2015; Oberoi et al., 2014; Karagas et al., 2019).

There are several studies that indicate arsenic exposure may influence bladder cancer progression and clinical outcomes. Comparisons of clinicopathological characteristics in bladder cancer patients from an arsenic contaminated region versus two reference areas found significantly greater proportions of locally advanced and high-grade tumors in the arsenic-exposed patients (Fernandez et al., 2020). Patients from areas of high arsenic exposure in Taiwan versus low arsenic exposure found worse prognosis in the patients from areas of high arsenic and this was most pronounced in the disease-free survival of early-stage disease (Chang et al., 2021). Similar findings were reported for patients in West Bengal, India where measured arsenic accumulation in bladder tumor tissue was associated with advanced tumors, poor prognosis and disease recurrence after treatment (Ghosh et al., 2021). These observations may be related to distinct mechanisms of arsenic carcinogenesis (Zhou et al., 2021; Palma-Lara et al., 2020) as described in Section 2.

Additional Cancers and Cancer Risk Due to Prenatal and Early Life Exposure

Although the evidence for arsenic-associated cancers is strongest for skin, lung and bladder tumors, there are other cancers that are linked to arsenic exposure. There is significant evidence for arsenic induced kidney cancer (Smith et al., 2012; Krajewski et al., 2021; Saint-Jacques et al., 2014; Ferreccio et al., 2013a; Naujokas et al., 2013; Palma-Lara et al., 2020; Chen and Costa, 2021) and liver cancer (Naujokas et al., 2013; Palma-Lara et al., 2020; Chen & Costa, 2021; ASTDR, 2010). There is more limited evidence for increased gastrointestinal tract (Krajewski et al., 2021; ASTDR, 2010), laryngeal (Smith et al., 2012), prostate (Lamm et al., 2021) and breast cancer (Moslehi et al., 2020) risk with elevated arsenic exposure (Abuawad et al., 2021). In the case of breast cancer, it appears that genetic factors may play an important modifying role in arsenic-associated risk (Moslehi et al., 2020).

Gestational and early life exposure to arsenic is associated with a variety of long-term health effects including increased risk of cancer in humans (Smeester and Fry, 2018; Martinez and Lam, 2021). Studies conducted in Northern Chile provide strong evidence for the cancer consequences of prenatal and early life arsenic exposures. In 1958, the levels of arsenic in drinking water increased nearly 10-fold to 870 ppb and remediation efforts in the 1970s

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reduced arsenic in drinking water to near pre-1958 levels. This led to human cohorts with different levels and timing of arsenic exposure (Smith et al., 2012). Increased mortality rates were observed for bladder, laryngeal, lung, kidney, liver and other cancers (Smith et al., 2012; Ferreccio et al., 2013b; Steinmaus et al., 2014). Long latency patterns of 25 years or more after early life exposure have been reported for liver, kidney and bladder cancers, often accompanied by evidence for higher incidence and cancer mortality in children and young adults (Yuan et al., 2010; Marshall et al., 2007; Liaw et al., 2008). These findings point to arsenic cancer risks that can persist decades after exposure in early life stages. Given evidence from experimental animal models that prenatal arsenic exposure elevates cancer development (Martinez and Lam, 2021; Waalkes et al., 2007), arsenic exposures across the entire lifespan are a concern.

Modifying Factors of Arsenic Carcinogenesis

Arsenic is one of a limited number of metals or metalloids that is metabolized to methylated forms (Roy et al., 2020). Biotransformation of inorganic arsenic to mono and dimethyl forms (MMA and DMA, respectively) occurs through the enzyme arsenic methyltransferase (AS3MT) and arsenic is excreted as a mixture of inorganic and methylated forms (Roy et al., 2020, see also Section 3). Population studies suggest that the different forms of arsenic are not equivalent in carcinogenic potential. Studies of the proportion of inorganic and methylated arsenic species found that individuals with high urinary inorganic percent or low DMA present were more likely to develop bladder cancer (Chung et al., 2013) and a meta-analysis found that bladder and lung cancer were increased significantly with increasing MMA percent in the urine (Melak et al., 2014). Positive associations between percent urinary MMA and cancers of the breast and skin in addition to lung and bladder also have been reported (Abuawad 2021; Gamboa-Loira et al., 2017; Huang et al., 2018). There is increasing evidence that polymorphisms and expression levels of AS3MT may lead to differences in arsenic metabolism (Delgado et al., 2021) and are important factors in arsenic-related cancer risk and outcomes (Song et al., 2020; Huang et al., 2018; Lin et al., 2018; De la Rosa et al., 2017).

Co-exposures of arsenic and DNA damaging agents can amplify carcinogenesis with the greatest evidence in human populations for skin, lung and bladder cancers. The risk of arsenic-associated skin lesions that can be precursors to cancer was greater with sun exposure (Chen et al., 2006). Furthermore, arsenic exposure and smoking increase risk of lung and bladder cancers with evidence for significant arsenic dose effect (Tsuda et al., 1995; Karagas et al., 2004; Chen et al., 2010; Chen et al., 2004; Koutros et al., 2018; Ferreccio et al., 2013b). These population-based findings are consistent with experimental findings of arsenic co-carcinogenesis (Zhou et al., 2021). Cumulatively, the evidence derived from studies of human populations exposed to arsenic indicate that arsenic is a human carcinogen both as a single agent and the carcinogenic effects can be modified by multiple factors including genetic polymorphisms and toxic co-exposures.

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SECTION 2: MECHANISMS OF ARSENIC CARCINOGENESIS

The diverse range of cellular effects of arsenic exposure create a complex landscape for studying arsenic carcinogenesis. Many processes affected by arsenic exposure are interconnected further complicating our understanding of arsenic's effects. This section will discuss key mechanisms of arsenic carcinogenesis focusing on oxidative stress, the role of DNA damage and repair in genotoxicity, epigenetic changes, and how arsenic interacts with proteins to affect major pathways of carcinogenesis.

Oxidative Stress

Oxidative stress is a cornerstone of arsenic toxicity and carcinogenesis. It plays a role in DNA damage, repair inhibition and cellular mechanisms related to cell stress and cell death. Arsenic induces elevated levels of reactive oxygen species (ROS) and reactive nitrogen species (RNS) that are damaging to macromolecules in the cell including DNA and protein (Ding et al., 2005; Wang et al., 2013) (Figure 2). Oxidative stress due to arsenic exposure is initiated by intracellular metabolism of arsenic, which involves glutathione (GSH) as a necessary mediator. GSH depletion during arsenic metabolism may result in reduced ability to ameliorate damaging ROS, both endogenous and those produced by the direct effects of arsenic in the cell. Arsenic metabolism also produces additional reactive intermediates. For example, the dimethylarsenic peroxyl radical, which is formed in the metabolism of dimethylarsenic acid, a methylated form of inorganic arsenic, further requires antioxidant remediation, and this intermediate has been shown to induce DNA damage (Flora et al., 2007; Yamanaka, 1994; Yamanaka et al., 1995). Specific forms of arsenic and their effects on oxidative stress are discussed in Section 3.

In general, reactive species arise due to the reduction of molecular oxygen to form superoxide radical anions ($O_2^{\cdot -}$), hydrogen peroxide (H_2O_2), hydroxyl radicals (•OH), hydroperoxyl radicals (HOO•), singlet oxygen (O_2), and peroxyl radicals (ROO•) (Wiseman and Halliwell, 1996). Arsenic facilitates the formation of these species by targeting several different processes. The role of arsenic in production of ROS is observed in the mitochondria where it causes dysregulation of the electron transport chain (Hosseini et al., 2013). Arsenic inhibits succinate dehydrogenase activity responsible and altering the balance of oxidative phosphorylation and O_2 production which perpetuates formation of additional ROS while also altering mitochondrial membrane potential (Hosseini et al., 2013; Yen et al., 2012). Mitochondria also contain elevated levels of sulfhydryl containing enzymes due to their redox-prominent role making many enzymes in the mitochondria molecular targets of arsenic exposure (Netto et al., 2002). Arsenic induced ROS also leads to formation of oxidative DNA damage, which can be measured as 8-hydroxy-2'-deoxyguanosine (8-OHdG) (Chayapong et al., 2017; Ding et al., 2005; Kessel et al., 2002). NADPH oxidase (NOX), which is activated by arsenic and stimulates increased generation of ROS, is one mechanism of increase DNA damage through oxidative stress (Cooper et al., 2022).

Arsenic causes various forms of cellular damage, which enhances the formation of radicals in the cell, adding to oxidative stress. For example, arsenic exposure leads to the formation of oxidized lipids, which can be used as a biomarker for arsenic-induced oxidative

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stress. Lipid peroxidation contributes to protein damage and compromised mitochondrial permeability forming a cycle of increased damage to macromolecules and ROS (Li et al., 2020; Mahajan et al., 2018; Nutt et al., 2005).

Arsenic generates RNS including nitric oxide (NO•), which further interacts with another product of arsenic exposure, $O_2^{\cdot -}$, to produce peroxynitrite ($ONOO^-$), which can affect DNA and proteins (Pace et al., 2017). $ONOO^-$ induces the nitration of tyrosine in proteins potentially altering their function. $ONOO^-$ also can cause S-nitrosation of cysteine residues in proteins, which was demonstrated in a study on the DNA repair protein, PARP-1 and was inhibited by the production of ROS and RNS after exposure to arsenic (Zhou et al., 2019). Additionally, $ONOO^-$ interacts with guanine forming 8-nitroguanine, which is used as a biomarker for RNS production (Kawanishi and Hiraku, 2006). Levels of arsenic exposure have been correlated with increased levels of 8-nitroguanine in epidemiology studies (Navasumrit et al., 2019; Phookphen et al., 2017). Arsenic-induced ROS and RNS increase oxidative stress leading to direct and indirect damage to DNA, proteins, and signaling pathways involved in maintaining genomic integrity. These effects are further discussed in the following sections.

Genotoxicity

Arsenic carcinogenesis is a complex process. However, the current body of research suggests genotoxicity arising as damage to genetic information is a key driver of arsenic-induced cancers and is a result of combined induction of DNA damage, inhibited DNA repair, and aberrant cell division. Genotoxicity begins with damage to genetic material. There is sufficient data showing arsenic exposure results in various forms of DNA damage including DNA double- and single-strand breaks and other lesions such as 8-nitroguanine and 8-OHdG as discussed above (Ding et al., 2005; Dong and Luo, 1993; Dutta et al., 2015; Okayasu et al., 2003). However, arsenic does not directly interact with DNA to cause damage, and there is a lack of strong evidence of arsenic forming adducts with DNA. Instead, studies show arsenic induced oxidative stress is responsible for the majority of DNA damage after arsenic exposure (Kumar et al., 2016). Studies show RNS and ROS inhibitors and pre-treatment with antioxidants attenuate DNA damage after arsenic exposure suggesting oxidative stress is a major contributor in arsenic-induced DNA damage (Ding et al., 2005; Lynn et al., 1998; Nesnow et al., 2002). This effect was also observed in arsenic-exposed human populations (Biswas et al., 2010) and animal studies (Balakumar et al., 2012; Kadirvel et al., 2007)

DNA double strand breaks are a particularly lethal form of DNA damage and if left unrepaired result in cell death. Arsenic-induced DNA double strand breaks have been identified in a number of studies (Guillamet et al., 2004; Mouron et al., 2006; Okayasu et al., 2003; Xie et al., 2014). If mis-repaired, these DNA double strand breaks in sites of key tumor suppressor genes may lead to changes to the genetic material and carcinogenesis. This result is also true of single-strand breaks and the formation of intra-DNA adducts and crosslinks with proteins and other cellular molecules (Bau et al., 2002; Dong et al., 1993; Mouron et al., 2001; Wang et al., 2001). DNA adducts and DNA-protein adducts may also contribute to the formation of DNA double strand breaks if mis-repaired (Bau et al., 2002, Wang et al., 2001). Several studies show arsenic exposure results in crosslinking of

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proteins, including DNA repair proteins, with DNA potentially inhibiting repair processes and contributing to genomic instability (Garman et al., 1997; Gebel et al., 1998; Mustra et al., 2007). In another study arsenic-induced DNA-protein crosslinks were observed with gross chromosomal changes including sister chromatid exchanges, a hallmark of genomic instability (Mouron et al., 2005).

Genomic instability is a common driver of cancers and is associated with exposure to many metals including arsenic (Mitkovska et al., 2020; Wu et al., 2019; Wise and Wise, 2012). DNA damage and dysregulation of cell division induced by arsenic ultimately leads to gross changes to genetic material including formation of micronuclei (Basu et al., 2004; Navasumrit et al., 2019), both numerical and structural chromosome instability (States, 2015), and microsatellite instability (Wu et al., 2017). Numerical chromosome instability associated with arsenic exposure has been observed in both human populations (Dulout et al., 1996), cell culture models (Eguchi et al., 1997; Salazar et al., 2010; Sciandrello et al., 2002), and animal studies (Kashiwada et al., 1998). Numerical chromosome instability can arise due to uncoupling mechanisms involved in cell division, such as changes in mitotic checkpoints and centrosome dysregulation, and is considered a driving force of carcinogenesis (Sansregret and Swanton, 2017). Arsenic induces prolonged mitotic arrest resulting in aneuploidy (Eguchi et al., 1997; Yih et al., 1997). Other studies have shown arsenic disrupts centrosome function (States et al., 2002; Suzuki et al., 2009), which can be carried down through cell populations even after removal of arsenic suggesting these changes may be permanent and heritable (Sciandrello et al., 2002). Another endpoint of altered cell division is the formation of micronuclei, which form as a result of lagging chromosomes and chromosome fragments, and these events have been observed in arsenic-exposed cells (Moore et al., 1996), workers (Lewińska et al., 2007; Vuyyuri et al., 2006), and in populations exposed to arsenic in drinking water (Tian et al., 2001; Warner et al., 1994).

Structural chromosomal changes including chromatid exchanges, ring structures, and dicentric chromosomes have been identified in arsenic-exposed human populations (Banerjee et al., 2007; Ghosh et al., 2006; Mahata et al., 2003). Other studies have identified chromatid gaps associated with arsenic exposure and urine levels (Maki-Paakkanen et al., 1998). Importantly for carcinogenesis, increases in chromosomal aberrations have been associated with arsenic-induced cancers and pre-cancerous lesions. For example, chromosome aberrations were found in patients with arsenic-induced Bowen's disease (Ghosh et al., 2007), arsenic-induced stomach cancer (Boffetta et al., 2007), and were higher in bladder cancer patients with arsenic exposure than those without (Moore et al., 2002).

Telomere maintenance and stability is closely tied to maintaining genomic stability. Several recent studies in an arsenic exposed human population found exposure was associated with altered telomere length, which is also attributed to enhanced chromosomal instability and cancer (Chatterjee et al., 2018; Villarreal et al., 2019). Guanine bases are a target of arsenic-induced oxidative damage. Thus, telomeres, rich in guanine, are a target of arsenic exposure. For example, Coluzzie et al., 2014 showed telomeric changes, included enriched DNA damage and shortening, occurred because of arsenic-induced oxidative stress. These telomeric changes may contribute to compromised protection provided by telomeres in

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maintaining chromosomal integrity. Other studies have identified arsenic-induced oxidative stress as a source of telomere attrition and structural chromosome instability arising as end-to-end fusions, and these effects were reduced by the addition of antioxidants (Liu et al., 2003). Epidemiology studies have confirmed arsenic exposure is associated with decreased telomere length and increased risk of skin carcinomas (Farzan et al., 2021; Grau-Perez et al., 2019; Srinivas et al., 2019) while other studies have shown the opposite (Gao et al., 2015).

The literature supports genomic instability represented as structural and numerical chromosome instability and alterations to chromosome maintenance (telomeres) as a prominent mechanism of arsenic-induced carcinogenesis. While these changes are evident the mechanisms of how they arise are important in understanding arsenic carcinogenesis. Changes in cell division were discussed above in association with numerical chromosome instability. However, structural chromosome instability is most associated with DNA damage (discussed above) and failure of robust DNA repair pathways as discussed below.

DNA repair

Arsenic induces a variety of DNA lesions, each with distinct repair pathways (Figure 3). Inhibited DNA repair after arsenic exposure is considered a driving mechanism of genomic instability and arsenic-induced cancers and research in this area has uncovered detailed cellular mechanisms of arsenic carcinogenesis. Mechanistic studies show arsenic affects critical repair factors in pathways of DNA repair including excision repair pathways, nucleotide excision repair (NER), base excision repair (BER) and strand break repair pathways, homologous recombination (HR), and non-homologous end joining (NHEJ).

Excision repair mechanisms are used to remove oxidative damage to nucleotides. Non-bulky damage to DNA bases, such as arsenic-induced 8-oxoguanine and apurinic and apyrimidinic sites, are repaired by BER. BER has been shown to be essential in repairing oxidative damage after arsenic exposure (Lai et al., 2011). Meanwhile BER genes were found to have decreased expression in HaCaT cells exposed to arsenic exposure (Ding et al., 2021). Specifically, human 8-oxoguanine DNA glycosylase I (Ebert et al., 2011), DNA polymerase β, and APE1 (Sykora and Snow, 2008) were found to have suppressed or altered expression and activity in human lung cells after arsenic exposure contributing to repressed BER function.

NER is responsible for repairing bulky type DNA lesions and is particularly important when considering arsenic as a co-carcinogen. NER repairs bulky lesions such as cyclobutane DNA photoproducts induced by ultraviolet radiation (UVR) and DNA adducts as a result of polyaromatic hydrocarbon (PAH) exposure. Arsenic alters NER through several mechanism. Individuals exposed to arsenic in drinking water were found to have decreased expression of DNA repair genes across in cell culture and human populations (Andrew et al., 2003; Andrew et al., 2006). Studies focused on NER after arsenic exposure have identified specific protein targets of arsenic including XPC, XPA, and ERCC1 (Holcomb et al., 2017; Huestis et al., 2016; Muenyi et al., 2011; Nollen et al., 2009; Zhou et al., 2014). Other mechanisms of arsenic-inhibited NER include inhibited protein function. Arsenic inhibits the activity of DNA ligase III and DNA ligase I (Hu et al., 1998). Extensive studies have also found zinc finger proteins in the NER pathway, including XPA are targeted by arsenic exposure altering

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their function and are further discussed in Section 3 below (Huestis et al., 2016; Zhou et al., 2014). In addition to direct protein effects, polymorphisms in NER genes were found to be associated with non-melanoma skin cancer and arsenic exposure (Applebaum et al., 2007).

If NER or BER fail to repair DNA damage, double strand breaks can arise. These breaks are repaired by NHEJ or HR as a final attempt to repair the damage and maintain genomic integrity. However, studies show that both NHEJ and HR are impaired by arsenic exposure. Notably Morales et al., 2016 found arsenic shifted repair to the more error-prone alt-NHEJ pathway from the high-fidelity HR repair pathway potentially resulting in mis-repaired DNA double strand breaks and increased genomic instability. Arsenic has been shown to affect HR repair by altering recruitment of HR repair factors including BRCA1 and RAD51 (Zhang et al., 2014). Arsenic increased sumoylation of Mus18, an endonuclease involved in cyclobutane pyrimidine dimers (CPDs) and 6,4'PP HR repair, resulting in compromised DNA damage response (Hu et al., 2017). PARP-1 may play a role in double strand break repair due to changes to PARylation and therefore recruitment of DNA double strand break repair factors. PARP-1 also plays a role in BER, NHEJ, single strand break repair, and as a zinc finger protein has been shown to be a primary target of arsenic exposure, which will be discussed in Section 3.

Epigenetic changes

While studies have identified DNA repair deficiency as a mechanism of arsenic carcinogenesis, epigenetic regulation contributes to changes in DNA repair after arsenic exposure. Decreased gene expression is an established effect of arsenic exposure and studies show arsenic alters DNA methylation patterns across the genome with some sex differences (Bailey et al., 2013; Broberg et al., 2014; Nohara et al., 2011). Increased methylation of promotors involved in DNA repair has been associated with modified expression after arsenic exposure and was observed across different repair pathways. For example, BRCA1, ERCC2, MLH1, and OGG1 all had increased promoter methylation after arsenic exposure often associated with decreased expression (Hossain et al., 2012; Paul et al., 2014; Selmin et al., 2019; Wang et al., 2021). These studies support the finding that DNA methylation is associated with persistent genomic instability (Mauro et al., 2015). Confirming the importance of these finding are studies showing altered methylation patterns in populations exposed to arsenic (Bhattacharjee et al., 2018; Intarasunanont et al., 2012).

DNA methylation may be affected by the metabolism of arsenic, which involved methylation steps. Long term arsenic exposure has been associated with DNA hypomethylation as a result of depleted S-adenosylmethionine (SAM) (Reichard et al., 2007). While the mechanisms are not fully understood, SAM depletion results in decreased DNA methyltransferase activity, which may contribute to this effect (Du et al., 2018). Depletion of SAM and methylation activity may also affect histone methylation.

Posttranslational histone modifications, including methylation and acetylation, play an important role in gene expression. Arsenic has been shown to affect each of these posttranslational modifications creating a complicated landscape for understanding how they alter gene expression and accessibility and recruitment of DNA repair factors to sites of DNA damage. One study found the altered balance of H3K9me2, H3K36me3

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and H4K20me2 after arsenic exposure may lead to decreased repair ability at sites of DNA damage (Li et al., 2016). Directly related to expression of DNA repair genes, arsenic increased H3K9me2 was found to reduced expression of genes involved in BER (Ding et al., 2021). Other studies show global histone methylation patterns after arsenic exposure are a contributing factor in malignant transformation (Ge et al., 2018) and cell transformation (Qiu et al., 2021). Zhang et al., 2020 found histone demethylase JDHM2A is responsible for regulating H3K9 dimethylation after arsenic exposure as a potential mechanism.

Arsenic altered levels of histone acetylases may also contribute to changes in gene expression, especially of DNA repair genes. H3K18ac was downregulated after arsenic exposure and this effect was notable in the promoter regions of NER protein genes (Zhang et al., 2020). Arsenic may also inhibit accessibility to repair sites of DNA damage through decreased histone acetylation. For example, arsenic decreased global H4K16Ac, notable for its role in relaxing chromatin, with concentration and time (Jo et al., 2009). Mechanisms of altered histone acetylation, including the effect of arsenic on histone acetyltransferases following arsenic exposure has been linked to zinc finger protein interactions (Tam et al., 2017).

Epigenetic alteration of gene expression is also affected by arsenic-induced changes in microRNAs, which have been linked to inhibited DNA repair, increased sensitivity to oxidative stress, and cellular transformation, and have been proposed to be used as biomarkers of arsenic exposure (Sturchio et al., 2014). Various cohorts of arsenic exposed people around the world have been evaluated for changes in microRNA expression to understand which microRNAs may be playing a role in disease progression (Al-Eryani et al., 2018a; Banerjee et al., 2019; Beck et al., 2018; Ruiz-Vera et al., 2019). Specific microRNAs have been linked with arsenic-induced skin lesions and cancers. For example, Banerjee et al., 2017 found miR-21 contributes to skin lesion and cancer in chronically exposed individuals.

Cell culture studies have looked closely at the role of specific microRNAs altered by arsenic exposure in targeted pathways of cancers. A study of prolonged exposure to arsenic used HaCaT cells as a model for skin cancer and identified dynamic changes in microRNA expression at different stages of exposure and transformation (Banerjee et al., 2022). Looking at specific microRNAs, Gonzalez et al., 2015 found arsenic upregulated miR-21, miR-200a, and miR-141 expression, and determined a likely association with pathways of melanoma progression. Another cell culture study found miR-200b was associated with malignant transformation of bronchial epithelial cells (Wang et al., 2011). These studies have investigated associations between microRNAs and cellular transformation and carcinogenesis. Others have focused on earlier processes in arsenic carcinogenesis. For example, arsenic altered microRNAs were implicated in targeting specific pathways such as the TP53 pathway, implicated to have early effects contributing to carcinogenesis (Al-Eryani et al., 2018b). An *in vivo* study in rats found arsenic-responsive microRNAs are likely involved in pathways of oxidative stress, specifically related to genes that regulate GSH levels (Ren et al., 2015).

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MicroRNA studies in human populations and in experimental models have been used to understand how they may affect DNA repair. For example, Wei et al., 2018 found miR-145 was upregulated in individuals exposed to toxic levels of arsenic, and this effect was replicated in a cell culture model where it was found to target expression of ERCC2, potentially having a negative impact on DNA repair. From these studies it is likely microRNAs play a role in pathways of arsenic-induced carcinogenesis and modulating expression DNA repair genes.

Protein Effects

Arsenic-dependent changes to protein expression were discussed above. However, arsenic also affects protein directly. Recent studies have focused on how arsenic affects protein folding signaling pathways and protein function. For example, arsenic induced endoplasmic reticulum protein folding stress, which contributed to autophagy defects but not oxidative stress suggesting this effect is independent of ROS (Dodson et al., 2018). Endoplasmic reticulum protein folding effects have been observed in other arsenic studies as well and is associated with autophagy (Wadgaonkar and Chen, 2021).

While arsenic-altered protein expression and processing contribute to carcinogenic mechanisms, studies show arsenic can interact with zinc finger proteins causing inhibited function, and as briefly mentioned in Section 1, has a significant effect on zinc finger protein interactions. Zinc finger proteins are highly sensitive to oxidation due to thiol groups that play a central role in their function (Krishna et al., 2003). This structure is protected and maintained by a zinc ion, which coordinates a combination of 4 cysteine and histidine residues within the zinc finger domain. Zinc fingers can be found in several arrangements of cysteine and histidine including C2H2, C3H1, C4 and more complex structures like C4C4 ring domains (Klug et al., 2010; Razin et al., 2012). These structures are largely responsible for protein binding nucleic acids and with other proteins (Eom et al., 2016; Fu and Blackshear, 2017).

The mechanisms of arsenic disruption of zinc finger proteins involves the direct displacement of zinc by arsenic within the zinc finger domain. However, different forms of arsenic bind the specific zinc finger orientations depending on the ratio of cysteine and histidine. In general, arsenic has a lower binding affinity for protein with one or two cysteines compared to those with three or four (Asmuss et al., 2000; Kitchin and Wallace, 2006a; Kitchen and Wallace, 2006b). However, while arsenite and arsenic trioxide show a preference to bind to C3H1 and C4 zing finger domains methylated arsenic can bind to all three C2H2, C3H1, and C4 types (Zhou et al., 2014). Details of specific forms of arsenic in carcinogenic mechanisms is discussed in Section 3. Arsenic is similar enough to zinc to competitively displace it from the zinc finger, but in doing so induces a conformational shift within the domain altering how the protein functions (Quintal et al., 2011). The selectivity of different forms of arsenic to bind zinc finger domains with specific combinations of cysteine and histidine also suggests binding selectivity and may impact specific carcinogenic mechanisms differently.

Arsenic displacement of zinc has significant implications for protein in many cell regulatory pathways affecting DNA repair and gene expression (Huestis et al., 2016; Zhou et al.,

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2020a). Many studies have focused on the impact of arsenic on zinc finger proteins involved in DNA repair (Cooper et al., 2014; Ding et al., 2017; Tam et al., 2020; Zhou et al., 2011; Zhou et al., 2015). After DNA damage, repair proteins must form complexes around the damage site, which requires binding to the damaged DNA. DNA-binding proteins use zinc fingers for this purpose, and therefore if disrupted, can destabilize DNA repair complexes at sites of damage and inhibit repair. The DNA repair protein PARP-1 is a C3H1 zinc finger DNA binding protein shown to be a sensitive target of arsenic exposure inhibiting its function (Ding et al., 2009; Walter et al., 2007). This disruption interferes with DNA binding and recruitment of other DNA repair factors involved in different pathways of repair including NER and BER (Chaudhuri et al., 2017). Arsenic was also found to bind and displace zinc in XPA, a critical DNA repair factor in NER (Huestis et al., 2016).

Arsenic may impact DNA repair by modulating access to sites of DNA damage. Zhang et al., 2014 found arsenic was able to bind to RNF20 and RNF40 RING finger domains causing a conformational shift in these proteins. The RNF20 and RNF40 RING fingers are responsible for the monoubiquitinating histone H2B and promoting access of DNA double strand break repair factors to sights of DNA damage (Zhang et al., 2014). Indeed, Recruitment of DNA repair factors including the HR repair protein, RAD51, to sites of double strand breaks was impaired after arsenic exposure. Similarly, arsenic was found to bind the FANCL E3 ubiquitin ligase and RING finger protein, altering recruitment of DNA repair factors to sites of DNA interstrand crosslinks (Jiang et al., 2017). These studies demonstrate arsenic can impact the function of different types of zinc finger proteins. Additionally, this interference affects different mechanisms of DNA damage repair and recruitment highlighting the dynamic and vast effect arsenic can have on cellular processes.

Signaling Pathways

Altered signaling after arsenic exposure contributes to checkpoint control, DNA repair response, and cell survival changes linking them together. Many pathways altered by arsenic exposure are interconnected and likely affect multiple mechanisms of arsenic carcinogenesis. One study using arsenic as a case study predicted top pathways associated with arsenic exposure include stress response, apoptosis, cell cycle, and protein signaling pathways such as MAPK, Jak-STAT, and p53 (Davis et al., 2008). MAPK signaling disruption has been observed in cell culture studies to increase cell invasiveness (Tingting et al., 2010). Predictions on arsenic's effect in signaling pathways including JNK, EGFR, AKT, PI3L, mTOR, and Nrf2-Keap1 have been extensively validated in other studies as well (Chen et al., 2013; Kang and Lee, 2008; Fu et al., 2021; Wang et al., 2017). These pathways are interconnected but are largely related to cell survival and escape from cell death and transformation.

The EGFR pathway has been closely linked with alterations of DNA repair and cell proliferation after arsenic exposure. Tong et al., 2015 found DNA mismatch repair was inhibited after arsenic exposure by promoting EGFR expression. Another study found EGFR and HB-EGF were activated in arsenic-transformed cells to promote cell proliferation (Wang et al., 2020). Recently a study in lung epithelial cells found EGFR expression was enhanced

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after acute and chronic arsenic exposure, but the mechanism responsible for these changes was different depending on the exposure time (Kim et al., 2020).

The balance of cell survival and cell death pathways are shifted after arsenic exposure (Dreval et al., 2018; Watcharasit et al., 2012). The Nrf2-Keap1 signaling pathway is a cellular mechanism implicated in promoting cell survival and when dysregulated is considered to have cancer-promoting functions. Specifically, constitutively active Nrf2 leads to a variety of downstream implications including altered expression of growth factors, antioxidant proteins, transcription factors, and protein processing due to its activity in binding antioxidant response elements (AREs) in the promoter of genes (Hayes et al., 2010). Studies show arsenic constitutively activates Nrf2 is closely tied to the alteration of the autophagy pathway (Lau et al., 2013; Zhou et al., 2020b). Indeed, studies show arsenic increases autophagy activity (Bolt et al., 2010; Pucer et al., 2010).

Many studies have investigated the PI3K AKT, and mTOR pathways in arsenic cellular transformation and malignancy (Chen and Costa, 2018). When these pathways are unregulated normal cell growth becomes aberrant. Chronic arsenic exposure alters the PI3K/AKT pathway and is associated with anchorage-independent growth and cell migration (Carpenter and Jiang, 2013). Other studies have found autophagy dysfunction is tied to PI3K and mTOR signaling (Liang et al., 2020). Evidence shows in arsenic-transformed cells the AKT pathway is implicated in enhancing invasiveness (Wang et al., 2012) while being regulated upstream by JNK to promote alterations in phosphorylation of proteins involved in altering expression of tumor suppressors and oncogenes (Chen et al., 2013).

SECTION 3: CHEMICAL FORMS OF ARSENIC AND CARCINOGENESIS

Inorganic and Organic Arsenic Forms, Exposure, and Metabolism

Arsenic exists in several different oxidation states and various chemical forms (Carlin at al., 2016; Bolt and Henglestler, 2018). There are two major oxidation states of arsenicals, trivalent and pentavalent. Both oxidation states exist naturally (Carlin at al., 2016; Zhu et al., 2014). Arsenic occurs naturally in many minerals, usually in combination with sulfur and metals. Humans can be exposed to arsenic through different forms and oxidation states, and metabolism of arsenic also converts one form or oxidation state to another (Watanabe and Hirano, 2013). Each form/oxidation state may have different exposure routes, organ/tissue distribution, toxicity, and carcinogenic effects (Watanabe and Hirano, 2013; Sattar et al., 2016). There are two major forms of arsenicals, inorganic and organic. Inorganic arsenicals are the major form of arsenic exposure, occupationally and environmentally. Organic arsenicals are mainly acknowledged as metabolites of arsenic, specifically, in methylated forms (Negro Silva et al., 2017; Cohen et al. 2006).

Trivalent arsenicals are found in the form of sodium/potassium arsenite and arsenic trioxide (Dopp et al., 2005). Pentavalent arsenicals are mainly found as sodium arsenate. The environmental existence of inorganic arsenicals is in two major phases, solid and a liquid. Inorganic arsenicals in ground water can be found in both trivalent and pentavalent forms (Zheng et al., 2017). The trivalent and pentavalent forms mainly exist in oxic and anoxic

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waters, respectively, due to their chemical properties. Drinking water is a major source of environmental exposure of inorganic arsenicals (Carlin at al., 2016; Zhu et al., 2014; Mantha et al., 2017). As mentioned in Section 1 arsenicals may also be accumulated in plants through irrigation (Zhu et al., 2014; Mantha et al., 2017; Dominguez-Gonzales et al., 2020), such as rice and vegetables, which also serve as a significant source of inorganic arsenic exposures. Trivalent and pentavalent arsenicals also exist in soil which leads to inhalation exposure from dust (Liu et al., 2016, Alamdar et al., 2016). Occupational exposure of arsenic can occur in facilities that manufacture pesticides, herbicides, and other agricultural products (Baker et al., 2018). Mine smelters and woodworking facilities are also major sources of occupational inorganic arsenic exposures.

Organic arsenicals are not commonly found naturally in the environment. Organic arsenicals include arsanilic acid, arsenosugars, and methylated arsenicals. Methylated arsenicals are produced as a consequence of inorganic arsenic biotransformation in various organisms. Humans may be exposed to methylated arsenicals from ingestion of seafood and meat (Yoshinaga and Narukawa, 2021; Naess et al., 2020).

Trivalent arsenic uptake into eukaryotes is mediated mainly by proteins in the aquaporin superfamily (AQPs) (Agre et al., 2002). Mammalian AQPs were first identified to transport trivalent arsenic in rat and mice as AQP9 and AQP7, respectively (Liu et al., 2002). Meanwhile, trivalent arsenic has also been shown to be taken up by glucose transporters such as GLUT1 (Liu et al., 2006) and hexose permeases (Liu et al., 2004). Both aquaglyceroporins and glucose permeases are bidirectional routes of trivalent arsenic into and out of cells.

Organic arsenic forms contribute to arsenic toxicity mainly through metabolic pathways. The metabolism of arsenic after absorption consists of two major types of reactions; oxidative methylation and reduction (Li et al., 2017; Hughes et al., 2011) (Figure 4). First, arsenite is oxidatively methylated into monomethylarsonic acid (MMA^{V}). MMA^{V} is thus reduced into monomethylarsonous acid (MMA^{III}). Second, MMA^{III} is oxidatively methylated into dimethylarsonic acid (DMA^{V}), then reduced into dimethylarsonous acid (DMA^{III}). The metabolism of arsenic plays a critical role in toxicity and carcinogenesis. The exact mechanisms of action of different arsenic forms is still unclear, but various hypotheses have been proposed.

Under drinking water exposure, an animal study of organ distribution of arsenicals suggested that kidney, lung and liver contain highest levels of arsenic (Li et al., 2013). In lung, the major form is DMA^{III} at almost all time points (Kenyon et al., 2005). At early stages of exposure, liver and kidney contain all forms of arsenicals, such as MMA^{III}, MMA^{V}, DMA^{III}, DMA^{V}, and inorganic arsenic. At later stages, both liver and kidney show an increase in the percentage of DMA^{III} in arsenicals (Kenyon et al., 2005). In contrast, blood and brain contains the lowest level of all arsenic forms compared to other organs across all time points. Inorganic and organic arsenicals were also reported to be strongly accumulated in reproductive organs (Pant et al., 2004).

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The subcellular distribution of arsenicals largely depends on the cell type. According to the characteristics of arsenic metabolism, there are two different types of cells, methylating (such as hepatocytes) and non-methylating (such as urothelial cells) (Dopp et al., 2010). The membrane permeability and the efficacy of arsenic uptake depend upon both the arsenic species and the cell type (Dopp et al., 2005). Uptake rates of MMA^{III} and DMA^{III} were highest and exceeded those of their pentavalent counterparts by several orders of magnitude. Non-methylating cells accumulate higher amounts of arsenic within the cell than the methylating cells, and cellular uptake and efflux seem to be faster in methylating cells. Elevated concentrations of arsenic are present in the ribosomal fraction of non-methylating cells and in nucleic and mitochondrial fractions of methylating cells. However, cytotoxic and genotoxic effects are more pronounced in methylating cells (Dopp et al. 2008), which also suggests that methylated forms of arsenic may have greater cytotoxic effects than inorganic arsenic forms.

Carcinogenesis of Arsenic Forms

Arsenic exposure is mainly in the form of trivalent inorganic arsenic through gastrointestinal absorption. Different forms and oxidation state of arsenicals play various roles in carcinogenesis (Wadgaonkar and Chen, 2021). Some research indicates that organic arsenic forms such as MMA and DMA are most relevant to skin and bladder cancers (Gamboa-Loira et al., 2017). MMA and DMA are both positively related to almost all types of cancers (Gamboa-Loira et al., 2017; Di Giovanni et al., 2020; Kuo et al., 2017; Jomova et al., 2011). However, DMA level was found to be negatively correlated to lung cancer only (Gamboa-Loira et al., 2017).

MMA^{III} induces malignant transformation in a human bladder urothelial cell line (Bredfeldt et al., 2006), and this kind of transformation is irreversible (Wnek et al., 2010). Acute and chronic MMA^{III} exposure induces MAPK and COX-2, which may be a mechanism of bladder carcinogenesis (Eblin et al., 2007). Also, MMA^{III} alters histone modification patterns in human bladder cells (Ge et al., 2018). There are still gaps in research progress on organic arsenic forms and liver and lung cancers.

The molecular mechanisms of arsenic induction of various cancers can be summarized into two major categories: a) the trivalent arsenicals activate or inhibit signaling proteins or alter protein structure by reacting with proteinaceous thiol groups and b) inorganic or organic arsenicals activate ROS signaling or ROS-related signaling pathways. Carcinogenesis of inorganic arsenicals is related to both mechanisms. However, organic arsenicals are predominantly reported to correspond to ROS-dependent mechanisms at present (Huang et al., 2017). Current literature suggests that both inorganic and organic arsenicals contribute to arsenic carcinogenesis. It remains to be determined which specific form of arsenic is the most carcinogenic, although the answer may likely depend on the chemical properties of arsenical and the target organ.

Forms of Arsenic and Reactive Oxygen Species

Almost all forms and oxidation states of arsenicals can induce ROS and relevant signaling pathways (Lee et al., 2016). For example, for arsenic trioxide, superoxide induction occurs

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through HO-1, hydrogen peroxide and also RNS such as nitric oxide and peroxynitrite (Zhou et al., 2019; Chen et al., 2008; Gurr et al., 2003). In murine embryonic maxillary mesenchymal cells, pentavalent arsenic leads to oxidative injury initiating cell death cascade, triggering cytotoxicity, mitochondrial dysfunction, and activation of caspase-9 (Singh et al., 2010). Specifically, the antioxidant N-acetylcysteine attenuates the effect of pentavalent arsenic, suggesting that ROS production may contribute to the mechanism of pentavalent arsenic cytotoxicity.

In human bladder urothelial cells, MMA^{III} is known to produce ROS (Wnek et al., 2011). In smooth muscle cells, MMA^{III} has been reported as a mitochondria toxicant that elevates ROS through mitochondrial and non-mitochondrial pathways (Pace et al., 2016). In rat liver cells, MMA^{III} has the highest potential of ROS generation, followed by DMA^{III}, then arsenic trioxide (Naranmandura et al., 2011). In human bladder urothelial cells, MMA^{III} was also observed to generate higher ROS than the same concentration of arsenic trioxide (Eblin et al., 2006). In human myeloid leukemic HL-60 cells, MMA^{III} and DMA^{III} cause apoptosis through inhibition to mitochondrial membrane potential and oxidative stress (Rehman et al., 2014). Caspase-9 and caspase-3 were significantly activated by MMA^{III} and DMA^{III} exposure. Similarly, antioxidant N-acetylcysteine is also able to reverse these effects (Rehman et al., 2014).

In HepG2 cells, MMA^{V}, DMA^{V}, or trimethylarsine (TMA^{V}) significantly induced CYP1A1 and NQO1 through an Hsp90 pathway (Anwar-Mohamed et al., 2014). ROS production by MMA^{V} exposure is also significantly higher than arsenic trioxide. Overall, MMA^{V} and DMA^{V} have moderate effect when compared to MMA^{III} and DMA^{III}, but the effects become stronger in a reductive environment, for example when there is a low ROS/GSH ratio (Sakurai et al., 2005).

In total, inorganic and organic arsenicals both contribute to ROS generation and ROS-dependent signaling pathways. However, there are still debates on which arsenic form generates higher ROS *in vivo*. It is still largely unclear whether metabolism of arsenic could enhance or reduce the strength of ROS effect. In addition, there is still limited knowledge on the differences of ROS type generated from different arsenicals, which should be of importance to ROS-related mechanisms.

Forms of Arsenic and DNA Damage/Repair

As mentioned in Section 2, trivalent arsenic inhibits DNA repair through direct interaction with zinc finger DNA repair proteins such as PARP-1 and XPA. For pentavalent arsenicals, there is no evidence currently demonstrating direct interaction with zinc fingers. However, pentavalent arsenicals are able to generate ROS which are not only able to induce DNA damage but also impair DNA repair pathways (Flora, 2011; Schwerdtle et al., 2003). Therefore, in contrast to trivalent arsenicals, which inhibit DNA repair through both direct and ROS pathways, pentavalent arsenicals inhibit DNA repair only through ROS-dependent signaling pathways.

In natural killer cells, at low concentration, MMA^{III} induces oxidative stress, DNA damage, and inhibits cell growth. DNA damage positively correlates with oxidative stress, indicating

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that at environmentally relevant concentrations, MMA^{III} has a genotoxic effect (Xu and Wang, 2018). In human bladder urothelial cells, low-level chronic exposure to MMA^{III} elevates DNA damage, which remains at a high level after removal of MMA^{III}, and elevated levels of ROS also play a role in MMA^{III} induced-DNA damage (Wnek et al., 2009). While pentavalent arsenicals only act through ROS-dependent pathways, MMA^{III} has two potential interdependent mechanisms for human bladder urothelial cell transformation; elevated levels of MMA^{III}-induced DNA damage through the production of ROS and the direct MMA^{III}-induced inhibition of PARP-1 (Wnek et al., 2011), which has been confirmed *in vitro* (Zhou et al., 2014).

In T cells, MMA^{III} induces strong genotoxicity in the early developing T cells in the thymus. In terms of MMA^{III} induced genotoxicity and apoptosis, double negative ($CD4^{-}$ $CD8^{-}$) T cells were much more sensitive than double positive cells (Xu et al., 2017). ROS-dependent mechanisms are particularly important. For example, superoxide is involved either directly or indirectly in producing DNA damage in cells exposed to trivalent methylated arsenicals. DMA^{III} and MMA^{III} produced significantly more DNA damage in the homozygous knockout mouse splenocytes than in the splenocytes from the wild-type or heterozygous mice (Tennant and Kligerman, 2011).

Overall, the DNA damage effect and DNA repair inhibition capabilities of various arsenic forms and oxidative states largely depend on the tissue or cell type. Intriguingly, in bladder or human urothelial cells, DMA^{III} and MMA^{III} are the most hazardous arsenicals when considering cytotoxicity and genotoxicity (Bailey et al., 2012; Wang et al., 2007). However, in lung and skin cells, trivalent arsenicals show higher potency for DNA damage (Bolt and Hengstler, 2018; Sattar et al., 2016). This may be because of a difference in metabolism or cellular arsenic uptake.

Conclusion

There is extensive and strong epidemiological evidence that links arsenic exposure with increased risk of developing various types of cancer. Arsenic is ranked number one by the Agency for Toxic Substances and Disease Registry (ATSDR) on their priority list of substances that are determined to pose the most significant potential threat to human health. The most effective and efficient strategy to decrease arsenic-induced cancer risk is to reduce arsenic exposure. Based on convincing research findings, in 2001, U.S. EPA adopted a new standard for arsenic in drinking water of 0.01 mg/l or 10 parts per billion (ppb), replacing the old standard of 50 ppb. The same standard has since been used by most countries around the world. However, it is estimated that over 200 million people world-wide remain exposed to arsenic above this level (Li and Costa 2022).

Over the last several decades, extensive research has been carried out to investigate and identify various molecular and cellular changes caused by arsenic that are associated with known carcinogenic processes. Despite tremendous progress to date, we still do not fully understand exactly how arsenic causes cancer development, and what are the key cancer-driving events that play critical roles in arsenic-induced cancer. One of the significant barriers in research is the lack of relevant and appropriate animal models that mimic the

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development of arsenic-induced cancer in humans, probably due to differences in genetics and arsenic metabolism between rodents and humans. Recent development in humanized mice could potentially provide an important tool to help resolve these critical questions (Koller et al., 2020).

Another major issue is that while current research has identified many individual molecular targets of arsenic involved in carcinogenic processes, it is difficult to assess which of these altered processes are predominantly responsible for arsenic-induced cancer in humans. The recent advances in whole genome sequencing and the associated informatics technology could help identify, using unbiased approaches, target molecules and processes that drive the mutation and tumorigenesis at the whole genome level.

Abbreviations

8-OHdG	8-hydroxy-2'-deoxyguanosine
AQP	aquaporin
AS3MT	arsenic methyltransferase
ATSDR	Agency for Toxic Substances and Disease Registry
BER	base excision repair
CPD	cyclobutene pyrimidine dimer
DMA	Dimethylated arsenic
DMA^{III}	dimethylarsonous acid
DMA^{V}	dimethylarsonic acid
EPA	US Environmental Protection Agency
GSH	glutathione
HR	homologous recombination
IARC	International Agency for Research on Cancer
MMA	Monomethylated arsenic
MMA^{III}	monomethylarsonous acid
MMA^{V}	monomethylarsonic acid
NER	nucleotide excision repair
NHEJ	non-homologous end joining
NOX	NADPH oxidase
PAH	polyaromatic hydrocarbons

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RNS	Reactive nitrogen species
ROS	Reactive oxygen species
TMA(V)	trimethylarsine
UVR	ultraviolet radiation
WHO	World Health Organization

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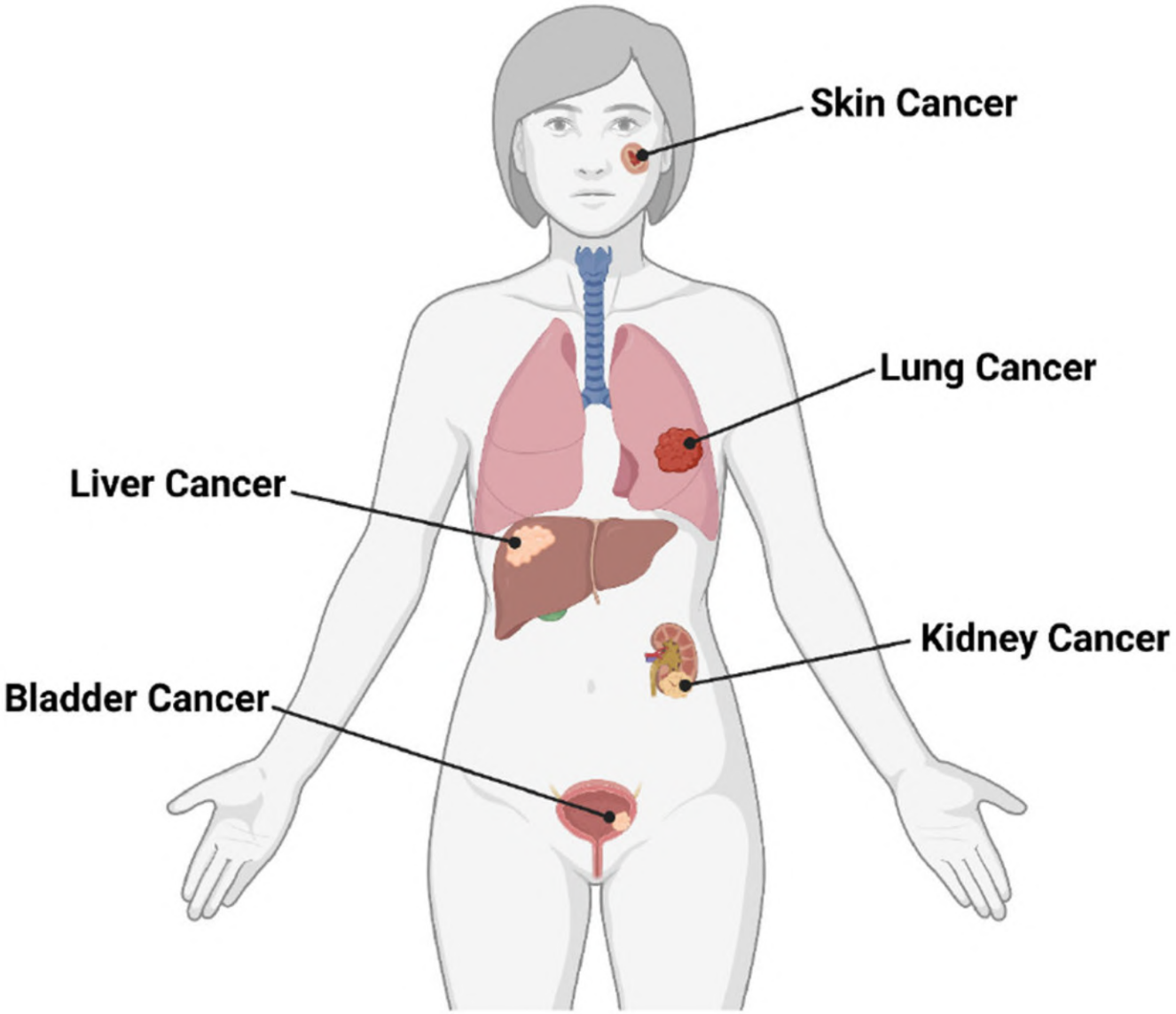

Figure 1.

Cancers associated with arsenic exposure. Epidemiology studies support the association of arsenic exposure through drinking water with increased risk of developing skin, lung, bladder, kidney, and liver cancers.

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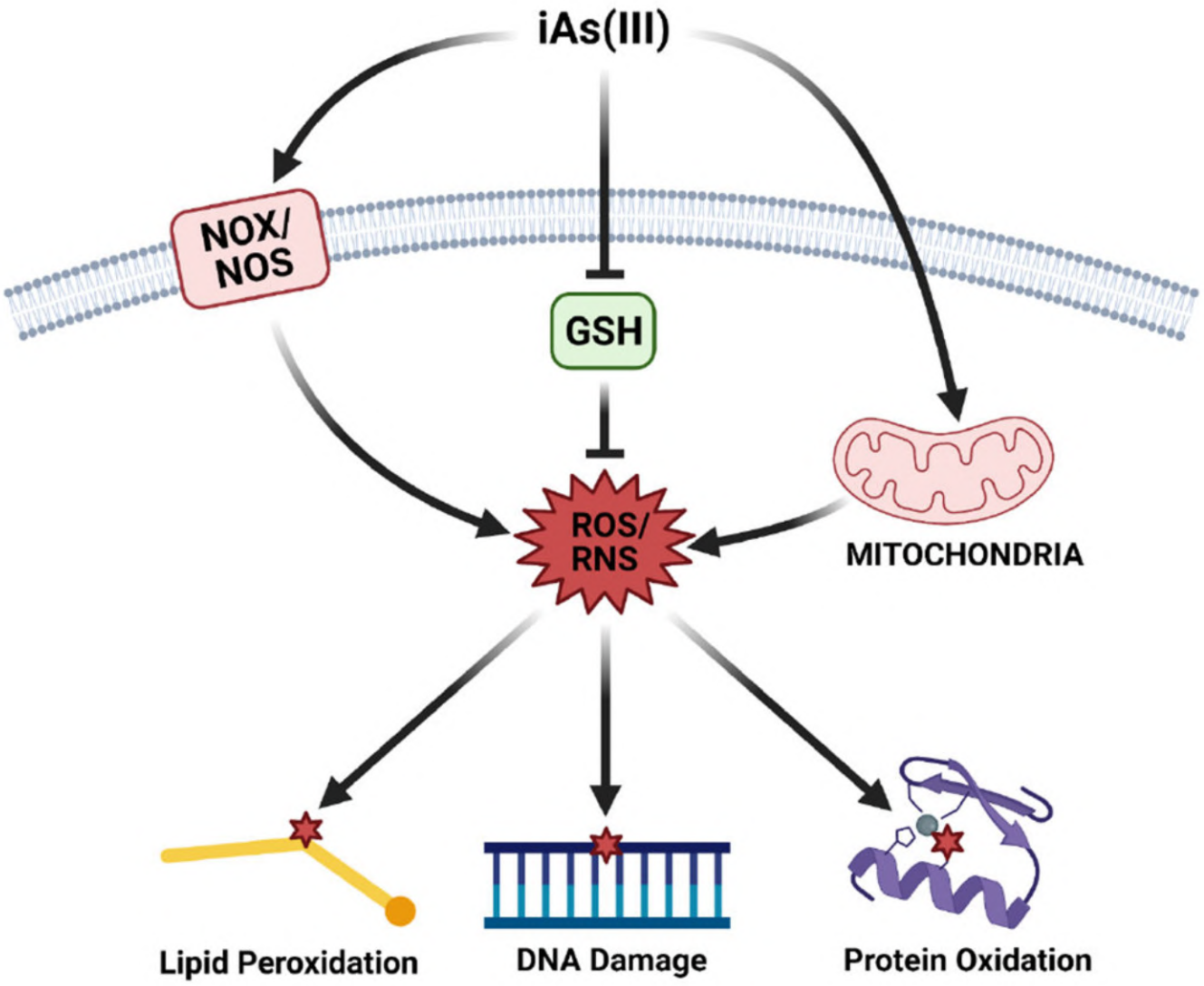

Figure 2. Mechanism of arsenic-induced ROS and oxidative damage to macromolecules.

Arsenic exposure stimulates the production of ROS and RNS through mechanisms such as the dysregulation of the electron transport chain and stimulation of enzymes such as NADPH oxidase and nitric oxide synthase. The depletion of GSH through the metabolism of arsenic further promotes redox imbalance. Consequently, macromolecules such as DNA, protein, and lipids are damaged by arsenic-induced ROS and RNS.

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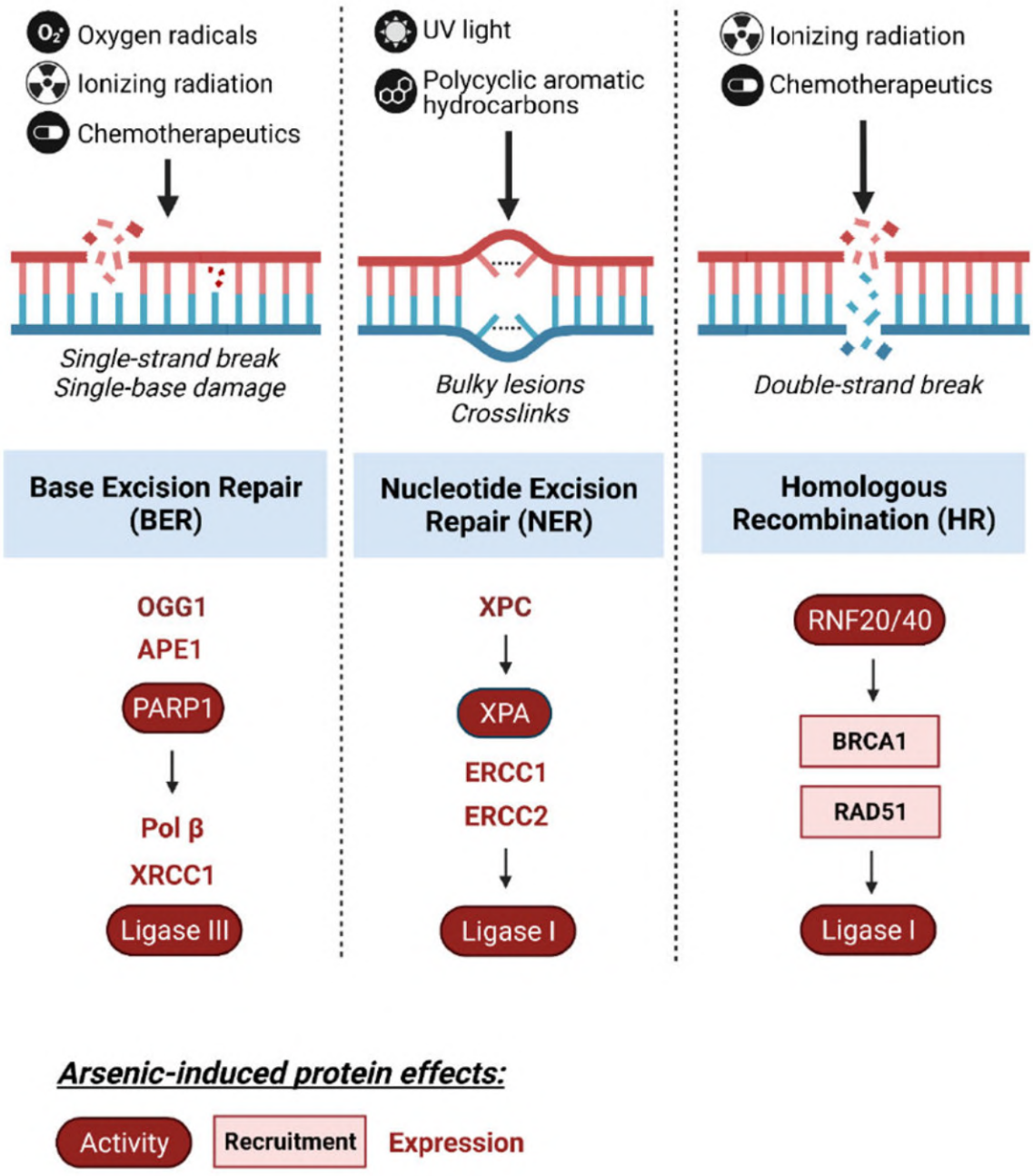

Figure 3. Arsenic inhibits DNA repair.

Exposure to DNA damaging agents such as ROS, UV light, and ionizing radiation can generate single-base damage, bulky lesions, and double-strand breaks, respectively. These types of damage are remediated by repair pathways which contain critical DNA repair proteins that facilitate the recruitment of repair proteins, removal of damage, and the synthesis and sealing of undamaged DNA. Arsenic alters the function of key DNA repair proteins through several means: zinc finger domain inhibition leading to loss of activity,

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disruption in recruitment to DNA damage, and the suppression of expression by altering transcription and protein turnover.

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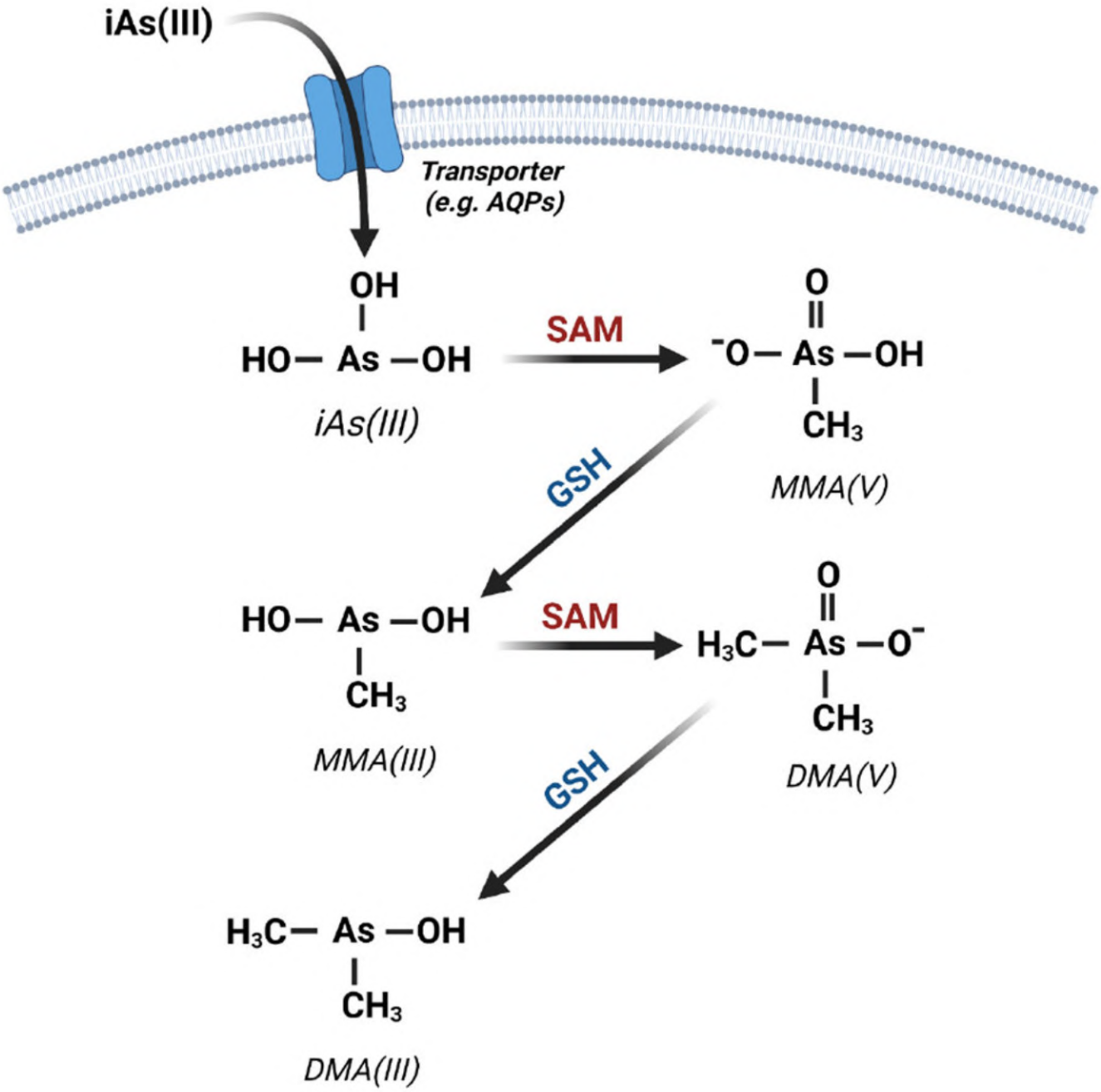

Figure 4.

The metabolism of arsenic. The uptake of trivalent arsenic into eukaryotes is mediated through several transporters such as AQPs. Trivalent arsenic is metabolized by successive oxidative methylation and reduction reactions. First, iAs(III) is oxidatively methylated into MMA(V) by S-adenosyl methionine (SAM), then reduced into MMA(III) by GSH. Second, MMA(III) is oxidatively methylated into DMA(V), then reduced into DMA(III)

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Exhibit J

A Section 508–conformant HTML version of this article is available at http://dx.doi.org/10.1289/ehp.1510144.

Estimating Children's Soil/Dust Ingestion Rates through Retrospective Analyses of Blood Lead Biomonitoring from the Bunker Hill Superfund Site in Idaho

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Background: Soil/dust ingestion rates are important variables in assessing children's health risks in contaminated environments. Current estimates are based largely on soil tracer methodology, which is limited by analytical uncertainty, small sample size, and short study duration.

Objectives: The objective was to estimate site-specific soil/dust ingestion rates through reevaluation of the lead absorption dose–response relationship using new bioavailability data from the Bunker Hill Mining and Metallurgical Complex Superfund Site (BHSS) in Idaho, USA.

Methods: The U.S. Environmental Protection Agency (EPA) *in vitro* bioavailability methodology was applied to archived BHSS soil and dust samples. Using age-specific biokinetic slope factors, we related bioavailable lead from these sources to children's blood lead levels (BLLs) monitored during cleanup from 1988 through 2002. Quantitative regression analyses and exposure assessment guidance were used to develop candidate soil/dust source partition scenarios estimating lead intake, allowing estimation of age-specific soil/dust ingestion rates. These ingestion rate and bioavailability estimates were simultaneously applied to the U.S. EPA Integrated Exposure Uptake Biokinetic Model for Lead in Children to determine those combinations best approximating observed BLLs.

Results: Absolute soil and house dust bioavailability averaged 33% (SD ± 4%) and 28% (SD ± 6%), respectively. Estimated BHSS age-specific soil/dust ingestion rates are 86–94 mg/day for 6-month- to 2-year-old children and 51–67 mg/day for 2- to 9-year-old children.

Conclusions: Soil/dust ingestion rate estimates for 1- to 9-year-old children at the BHSS are lower than those commonly used in human health risk assessment. A substantial component of children's exposure comes from sources beyond the immediate home environment.

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Introduction

Ingestion Rate Background

Consumption of fine soil and dust particulates, especially by young children, is the dominant route of exposure for lead and other contaminants (Laidlaw et al. 2014; Landrigan et al. 1975; Lanphear et al. 1998, 2003). Childhood soil and dust ingestion occurs via multiple pathways, including hand-to-mouth transfer, mouthing of objects, and contaminated food. These pathways are dependent on individual behaviors, exposure time, and environmental conditions (Zahran et al. 2013a). Accurate estimates of the soil and household dust ingestion rate (IR) pathway are needed to assess children's exposures and health risks associated with trace metals and persistent organic chemical residues in the home or play environment, and to make informed cleanup decisions.

Early estimates of soil/dust IRs in children were based on studies of trace elements in soil and feces, yielding uncertain estimates due to analytical uncertainty, limited sample size, and short study duration (Batelle 2005; Doyle et al. 2010; Sedman and Mahmood 1994; Stanek et al. 2012; U.S. EPA 2011, 2012). Currently, national U.S. Environmental Protection Agency (EPA) central tendency soil/dust IRs of 60 mg/day (children 6 weeks to < 12 months of age) and 100 mg/day (children 1 to < 6 years of age) are based on these tracer studies (U.S. EPA 2011). More recent studies have used dermal transfer to estimate soil and dust IRs. Ozkaynak et al. (2011) modeled the frequency of hand and object mouthing in children 3 years to < 6 years of age, resulting in a mean total soil/dust IR of 68 mg/day (95th percentile: 224 mg/day). Similarly, Wilson et al. (2013) used a mechanistic model including parameters for particle loading on skin, transfer to hands, hand surface area, mouthing surface area, hand-to-mouth frequency, saliva dissolution, and exposure time, to estimate an average combined soil/dust IR of 61 mg/day for children 7 months to 4 years of age. Meta-analysis of four major studies using stochastic modeling of the most reliable tracers resulted in an average soil ingestion estimate of 26 mg/day (95th percentile: 79 mg/day) for children 1–8 years of age (Stanek et al. 2012). Findings from large-scale reviews and integration of data from tracer, mechanistic, validation modeling/measurement, and empirical relation (biomonitoring/environmental concentration) studies suggest that mean IRs in children are < 100 mg/day and may be as low as 40–80 mg/day (Bierkens et al. 2011; Moya and Phillips 2014).

Soil/dust IR and bioavailability are sensitive parameters in the U.S. EPA Integrated Exposure Uptake Biokinetic (IEUBK) Model for Lead in Children. The IEUBK model currently uses default IRs ranging from 85 to 135 mg/day for 6-month- to 6-year-old children and 30% absolute bioavailability for ingested soil and indoor dust (U.S. EPA 2013). The first use of the IEUBK model to develop site-specific cleanup levels was at the Bunker Hill Mining and Metallurgical Complex Superfund Site (BHSS) in northern Idaho (CH2M Hill 1991; TerraGraphics 1990; U.S. EPA and IDHW 1991, 1992). The dose–response relationship observed between soil, dust, and blood lead levels (BLLs) was consistently lower at the BHSS than IEUBK model predictions using the default parameters (TerraGraphics 1990; von Lindern et al. 2003b). This was nominally attributed to lower soil/dust bioavailability (18%), although it was acknowledged that the reduced

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I.v.L., S.S., and C.B. are employees of TerraGraphics Environmental Engineering, Inc., which is a consultant to the Idaho Department of Environmental Quality, and held two contracts at the time of this project for scientific and engineering support services for the Bunker Hill Superfund Site. TerraGraphics was also a consultant to U.S. EPA to conduct analyses for this research project. I.v.L. served on the U.S. Clean Air Science Advisory Committee for the Integrated Science Assessment for Lead in the Ambient Air and the Review of the Air Quality Criteria Document for Lead. C.B. and I.v.L. are also employed by TerraGraphics International Foundation, a nonprofit organization. The other authors declare they have no actual or potential competing financial interests.

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dose response was likely a combination of lower bioavailability and IRs (von Lindern et al. 2003b).

BHSS Background

In 1974, soon after the lead smelter operators bypassed emission controls destroyed by a baghouse fire, > 95% of children 1–9 years of age living within 3 mi of the smelter had BLLs exceeding 40 µg/dL (Yankel et al. 1977). Lead health interventions have been ongoing since that time. The smelter closed in 1981 and remediation began in 1986, representing one of the world's largest, most comprehensive, and well-documented lead health response cleanups (U.S. EPA 2005, 2010; von Lindern et al. 2003a, 2003b). From 1988 through 2002, soil from > 3,500 properties within the 21-mi^2 area surrounding the smelter was removed and replaced with up to 1 ft of clean fill averaging ≤ 50 mg/kg. Hundreds of families with children received lead health education and in-home follow-up investigations through a local Lead Health Intervention Program (LHIP). The LHIP tested children's BLLs, achieving participation rates > 50% among 0- to 9-year-old children for 15 consecutive years through door-to-door recruitment and incentive payments. Annual blood lead survey results were used to prioritize soil cleanup until the Remedial Action Objective (RAO) of < 5% of children with BLLs ≥ 10 µg/dL was achieved. From 1988 through 2002, homes of young children (0–6 years), pregnant women, and older children with BLLs ≥ 10 µg/dL were remediated first, regardless of location within the site. Beginning in 1994, all soils in contiguous neighborhoods with lead levels ≥ 1,000 mg/kg were removed and replaced, regardless of BLLs. This cleanup prioritization coupled with families moving within the affected communities resulted in a dynamic, complex combination of soil/dust exposures affecting individual children.

Blood lead data, collected during the seasonal peak in late summer, were matched to dust lead concentrations (from samples collected from household vacuum cleaners) and soil lead data to monitor the relationship between children's BLLs and environmental exposures to ensure cleanup was effective. Four variables were used to quantify soil and dust exposures throughout the cleanup: house dust, yard soil, neighborhood soil, and community soil lead concentrations. The neighborhood soil variable is the mean of all yard soils within a specific radius of the home, excluding the home's yard soil lead concentration. This was calculated for 200-ft, 500-ft, and 1,000-ft radii. The community soil variable is the mean of all yard soils within the community, excluding the home and neighborhood radius soil lead concentrations. The prioritized cleanup rapidly reduced the number of children residing in homes with soil lead concentrations ≥ 1,000 mg/kg and markedly decreased yard soil exposures for those families. Neighborhood soil lead concentrations progressively declined until the block-by-block cleanup strategy was implemented in 1994, and then decreased faster as contiguous neighborhoods were remediated. Community soil lead mean concentrations declined steadily until 2002 when yard soil replacement was mostly complete. House dust lead exposures (dust lead concentrations from homes of children with BLL measurements) decreased following the yard, neighborhood, community, and industrial complex cleanups but lagged the community soil means by a decade or more (von Lindern et al. 2003a).

By 2002, children's mean BLLs decreased to 2.2 µg/dL. In 2013, the health district conducted the first comprehensive blood lead survey since 2002, recruiting an estimated 50% of children 6 months to 9 years of age living within the 21-mi^2 area using incentive payments and door-to-door solicitation. The geometric mean BLL among 1- to 5-year-old children tested was 2.2 µg/dL (SD ± 1.8) compared with the most recent U.S. mean of 1.3 µg/dL (CDC 2013), with 2 of 276 children having levels ≥ 10 µg/dL, indicating that the cleanup continues to meet the RAO of 95% of children < 10 µg/dL (TerraGraphics 2015). Over the 15 years of active cleanup (1988–2002), education, and intervention, the LHIP amassed approximately 5,400 blood lead observations (referred to as the parent database) from nearly 2,340 individuals, yielding 2,176 records of blood/soil/dust lead concentrations (TerraGraphics 2004; von Lindern et al. 2003b, 2003a).

Subsequent to the cleanup at the BHSS, the U.S. EPA adopted an *in vitro* methodology to estimate site-specific bioavailability of lead in soil and dust (U.S. EPA 2012). This methodology was applied to a subset of archived soil and dust samples from the BHSS, and results were applied to the parent database. The objective of this study was to estimate age-specific soil/dust IRs through reanalysis of the dose–response relationship using new soil and house dust lead bioavailability data. In light of uncertainties and limitations of fecal tracer soil ingestion studies, these site-specific estimates likely have broader application to the IEUBK model and to human health risk assessment.

Methods

Blood lead samples collected from children participating in the LHIP were obtained through written informed consent from parents as well as child assent. The annual LHIP surveys are public health actions undertaken by state and local health authorities. TerraGraphics secured approval from the University of Idaho's Institutional Review Board for this project. No additional survey data or samples were collected from human subjects for this analysis.

Sample Analyses

In total, 271 samples (193 house dust samples, 73 yard soil samples, and 5 quality control samples) sieved to 80 mesh (or < 0.177 mm) were analyzed for total lead (Method 6010B) and *in vitro* bioaccessibility (TerraGraphics 2012; U.S. EPA 2007, 2012). U.S. EPA's *in vitro* assay measures the solubility, or bioaccessibility, of lead in soil and dust samples to estimate (*in vivo*) bioavailability. The 80 mesh sieve for both soil and dust was initiated at the BHSS in 1974 and focuses analyses on particle sizes more likely to adhere to hands and other surfaces and be ingested by children (Panhandle District Health Department et al. 1986; Ruby and Lowney 2012). Archived soil and dust samples collected between 1986 and 2002 were retrieved from storage. Those with intact seals, legible identification numbers, and sufficient mass for analysis were then checked to ensure that blood lead data and information on child age and sex, home location, and property remediation status were available. A temporal and geographic subset of samples meeting these criteria was randomly selected and analyzed at the laboratory. Reanalyzed soil and dust lead concentrations were compared to historical values using linear regression. *In vitro* bioaccessibility results were converted to *in vivo* relative bioavailability and absolute bioavailability (ABS) following U.S. EPA methods using comparison to a lead acetate reference (0.5) following Equation 1 (U.S. EPA 2007, 2009, 2012):

$$\mathrm{ABS} = (0.878 \times \mathrm{IVBA} - 0.028) \times 0.5, \quad [1]$$

where IVBA = *in vitro* bioaccessibility.

Community mean ABS values for unremediated yard soils and house dust, and site-wide ABS means for postremediation soils were integrated into the parent database. Annual site-wide ABS means were calculated using a weighted average of bioavailable lead (product of concentration and bioavailability) from remediated and unremediated yards.

Quantitative Analyses

Soil and dust partitions, age-specific IRs, and lead uptake from sources other than soil and dust were determined through structural equations modeling (SEM). SEM is a statistical multivariate methodology appropriate for pathways analysis, defined as a network of linear relations between variables. SEM was applied by von Lindern et al. (2003b) to reflect the exposure pathways of yard, community, and neighborhood soils (Ullman and Bentlar 2003). The 2003 SEM was

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repeated using absorbed and bioavailable lead (instead of blood and total soil and dust lead levels), using SAS® software version 8 (SAS Institute Inc.). Several combinations of variables, including neighborhood soil means using radii of 200 ft, 500 ft, and 1,000 ft and age- and year-specific soil and dust categorical variables (i.e., grouped by both age and calendar year), were alternatively added, and model fit was evaluated by five criteria: *a*) convergence, *b*) chi-square probability test ($p > 0.05$), *c*) goodness of fit index (GFI) (> 0.90), *d*) parameters with significant t-statistics ($p < 0.05$), and *e*) parameter performance in subsequent IEUBK model analyses, described below (Carey 1998; SAS Institute Inc. 2008; Suhr 2006; Wothke 2010). Both the chi-square and GFI measure the difference between the expected and observed covariance matrices. Higher chi-square probability indicates better fit. The GFI ranges from 0 to 1.0, with higher values indicating better fit (Jöreskog and Sörbom 1988; SAS Institute Inc. 2008). SEM equations were solved using mean values for the independent variables and model parameters to estimate: *a*) soil and dust lead pathway parameters, *b*) neighborhood and community soil effects on lead uptake, *c*) age-specific and temporal effects in lead intake and uptake, and *d*) source partition scenarios for use in subsequent IEUBK modeling.

Ingestion Rate Estimates

Total lead uptake (µg/day) was calculated by dividing the measured BLLs (µg/dL) by the age-specific biokinetic slope factors, referred to as CR^{-1} (day/dL), used in the original IEUBK model (Harley and Kneip 1985; Jacobs Engineering et al. 1989; Kneip et al. 1983; TerraGraphics 1990, 2012; U.S. EPA 1994). Total lead uptake was partitioned into components used in the IEUBK model: air, diet, water, and soil/dust. Lead uptake from soil and dust was estimated by partitioned dust, yard soil, neighborhood soil (used only in the SEM), and community soil subcomponents by subtracting air, dietary, and drinking-water uptakes estimated from the IEUBK model default values (U.S. EPA 2001), as shown in Equation 2:

$$\begin{aligned} UP_{sd} &= [(C_d \times IR_d \times ABS_d) \\ &\quad + (C_{ys} \times IR_{ys} \times ABS_{ys}) \\ &\quad + (C_{cs} \times IR_{cs} \times ABS_{cs}) \\ &\quad + (C_{ns} \times IR_{ns} \times ABS_{ns})] \\ &= UP_{tot} - [UP_{air} + UP_{diet} + UP_{water}], \end{aligned} \quad [2]$$

where UP = lead uptake (µg/day); C = concentration (mg/kg); IR = ingestion rate (mg/day); ABS = absolute bioavailability (unitless); and (subscripts): *sd* = combined soil/dust sources; *d* = house dust; *ys* = yard soil; *cs* = community soil; *ns* = neighborhood soil (SEM); *tot* = total sources; *air* = airborne source; *diet* = dietary source; *water* = water source.

Equation 2 can be rearranged to calculate total soil/dust IRs [IR_{sd} (mg/day) is the sum of IR_d, IR_{ys}, IR_{cs}, and IR_{ns}] by assigning partition coefficients, i.e., fractional contributions to total soil/dust ingestion by each source, as follows in Equation 3:

$$\begin{aligned} IR_{sd} = 1{,}000 \times \{UP_{sd}/[&(C_d \times PT_d \times ABS_d) \\ &+ (C_{ys} \times PT_{ys} \times ABS_{ys}) \\ &+ (C_{cs} \times PT_{cs} \times ABS_{cs}) \\ &+ (C_{ns} \times PT_{ns} \times ABS_{ns})]\}, \end{aligned} \quad [3]$$

where PT = partition coefficient.

Partition coefficients used in these analyses included the IEUBK model default, those originally developed to support BHSS cleanup criteria, and values derived from SEM. Partition coefficients, resulting age-specific soil/dust IRs (using Equation 3), and bioavailability were input to the IEUBK model batch-mode analyses (IEUBKwin v1.1 build 11) to compare predicted and observed BLLs. The combined IR and partition scenarios showing best-predicted BLLs were evaluated by linear regression and sums of squared error (SSE). The slope nearest to 1.0 coupled with the highest r^2, highest F-statistic, and lowest sum of squared residuals from linear regression, as well as the SSE (squared difference between observed and predicted geometric mean BLLs), were used to determine the scenario(s) that best represent observed BLLs. The age-specific soil and dust IR estimates were then determined based on these scenario(s).

Results

Sample Analysis

The selected subset of historical data was considered generally representative of the parent database (e.g., lead concentration and child's age) (Table 1). The reanalyzed soil and dust lead concentrations were not significantly different

Table 1. Comparison of the parent BHSS database with the subset of records selected for reanalysis (historical data).

	Parent data set						Selected subset					
City	Minimum	Maximum	Average	SD	Geometric mean	Geometric SD	Minimum	Maximum	Average	SD	Geometric mean	Geometric SD
Kellogg	Parent data set $n = 3{,}054$						Selected subset $n = 118$					
Age (years)	0	9	5.1	2.7	—	—	1	9	5.5	2.6	—	—
Blood lead (µg/dL)	1	54	6.4	4.7	5.1	2.0	2	41	7.6	5.7	6.3	1.8
Soil lead (mg/kg)	100	13,400	954	1,625	274	4.4	100	6,930	1,407	1,849	435	5.2
Dust lead (mg/kg)	32	52,700	1,213	2,839	733	2.4	88	5,530	1,373	1,093	985	2.3
Page	Parent data set $n = 161$						Selected subset $n = 15$					
Age (years)	0	9	5.1	2.6	—	—	1	9	4.3	2.8	—	—
Blood lead (µg/dL)	1	26	7.0	4.7	5.7	1.9	3	12	5.6	2.4	5.2	1.5
Soil lead (mg/kg)	53	3,480	557	668	287	3.2	100	1,670	541	420	387	2.5
Dust lead (mg/kg)	69	2,070	678	496	478	2.6	86	1,680	706	567	467	2.9
Pinehurst	Parent data set $n = 1{,}369$						Selected subset $n = 117$					
Age (years)	0	9	5.1	2.6	—	—	1	9	5.2	2.4	—	—
Blood lead (µg/dL)	1	26	4.6	3.1	3.8	1.9	1	17	4.3	2.6	3.7	1.7
Soil lead (mg/kg)	31	3,060	438	424	312	2.3	37	1,700	469	356	369	2.0
Dust lead (mg/kg)	22	15,000	639	1,053	417	2.4	45	15,000	625	1,427	383	2.3
Smelterville	Parent data set $n = 642$						Selected subset $n = 57$					
Age (years)	0	9	4.9	2.7	—	—	1	9	4.5	2.6	—	—
Blood lead (µg/dL)	1	55	7.0	5.4	5.6	2.0	2	30	7.5	4.9	6.4	1.7
Soil lead (mg/kg)	100	10,700	953	1,921	245	4.3	100	8,170	1,037	1,821	242	4.8
Dust lead (mg/kg)	54	11,300	1,127	1,257	757	2.5	393	4,210	1,387	807	1,190	1.8
Wardner	Parent data set $n = 173$						Selected subset $n = 5$					
Age (years)	0	9	5.2	2.7	—	—	1	8	4.8	3.1	—	—
Blood lead (µg/dL)	1	20	6.6	3.8	5.5	1.9	2	8	4.6	2.2	4.2	1.6
Soil lead (mg/kg)	100	34,800	759	2,925	224	3.5	100	13,200	3,104	5,705	484	9.6
Dust lead (mg/kg)	130	6,000	1,005	1,112	700	2.3	307	2,220	1,147	697	959	2.1

from historical results (r^2 = 0.99, p < 0.01, n = 73; and r^2 = 0.91, p < 0.01, n = 193, respectively), indicating that samples were not compromised during storage. The reanalyzed sample results are summarized in Table 2. Mean soil bioavailability ranged from 30% to 39% by community, averaging 33% (SD ± 4%); dust bioavailability ranged from 27% to 30%, averaging 28% (SD ± 6%). Three "clean" soil samples were obtained in 2011 from borrow piles used to replace contaminated property soils. No clean yard soil samples were previously collected and archived. Consequently, these three samples represent postremediation replacement clean soils, and bioavailability results averaged 15% (SD ± 0.6%; data not shown). Linear regression relating soil and dust bioavailability to lead concentration showed a weak relationship (r^2 = 0.15, p = 0.0006 and r^2 = 0.045, p = 0.0028, respectively).

SEM Analyses

Several plausible SEM combinations met the model acceptance criteria. In each accepted model, bioavailable lead in dust and soils from the home yard, neighborhood, and community were all significant independent predictors of total blood lead uptake. Based on experience with the BHSS cleanup and development of the parent database, numerous combinations of spatial, temporal, and age-specific variable constructs and database time periods were explored (data not shown). Of the three neighborhood radii, 500 ft showed the best fit by combined chi-square test and parameter t-values. Age-specific coefficients for dust concentration among the youngest children (6 to < 24 months old) were significant (p < 0.01), implying different IRs, with a significant intercept representing uptake from other sources. Coefficients for age-specific and year-specific soil concentration variables were not significant (p > 0.05). The SEM with temporal variables showed marginally significant (p = 0.05) positive dust coefficients for 6- to 23-month-old children in 1994–1998, suggesting higher dust IRs during those years.

Source partitions using three SEM combinations were evaluated in subsequent IEUBK model analyses: Model 1 (1989–2002 database) included a term allowing calculation of year-specific IRs, and model 2 (1989–1998 database) and model 3 (1989–2002 database) assumed constant source contributions and IRs throughout each respective time period (Tables 3 and 4). Soil/dust IRs and source partitions were estimated by substitution of mean soil and dust lead concentrations in the model equations.

Model 2, shown in Equations 4 and 5 (chi-square test: p = 0.7416, n = 1,571; Table 3), was selected based on performance in subsequent IEUBK modeling:

$$\ln(UP_{tot}) = [0.1466 \times \ln(C_d \times ABS_d)] + [0.0516 \times \ln(C_{ys} \times ABS_{ys})] + [0.0440 \times \ln(C_d \times ABS_d \times \text{age0–1})] + [0.0613 \times \ln(C_d \times ABS_d \times \text{age1–2})] + [0.0661 \times \ln(C_{ns} \times ABS_{cs})] + [0.0954 \times \ln(C_{cs} \times ABS_{cs})] + 0.7666 \quad [4]$$

Table 2. Community averages of reanalyzed archived soil and house dust samples.

	Soil			Dust		
City	n	Soil lead (mg/kg) (mean ± SD)	Soil ABS (%) (mean ± SD)	n	Dust lead (mean ± SD) (mg/kg)	Dust ABS (%) (mean ± SD)
Kellogg	24	2,656 ± 1,624	34 ± 3	66	1,179 ± 934	28 ± 6
Page	7	778 ± 417	33 ± 4	12	753 ± 529	27 ± 5
Pinehurst	33	569 ± 463	32 ± 4	75	762 ± 2,131	28 ± 6
Smelterville	8	4,136 ± 2,192	39 ± 2	36	1,239 ± 550	30 ± 4
Wardner	1	2,030	30	4	892 ± 415	27 ± 5
Overall	73	1,686 ± 1,748	33 ± 4	193	996 ± 1,472	28 ± 6

ABS, absolute bioavailability.

Table 3. Structural equations modeling (SEM) results.

	Model 1 (1989–2002)			Model 2 (1989–1998)			Model 3 (1989–2002)		
Variables	Slope coefficient	t-Value[a]	Standardized coefficient	Slope coefficient	t-Value[a]	Standardized coefficient	Slope coefficient	t-Value[a]	Standardized coefficient
UP_{tot} (Equation 4)									
ln(UP_d)	0.1347	8.43	0.2575	0.1466	7.95	0.2762	0.1360	8.50	0.2598
ln(DUSTage0–1)	0.0450	2.80	0.0132	0.0440	2.24	0.0116	0.0450	2.79	0.0132
ln(DUSTage1–2)	0.0501	4.06	0.0273	0.0613	6.23	0.0333	0.0667	7.45	0.0363
ln(DUST1994–1998)	0.0336	1.95	0.0128	—	—	—	—	—	—
ln(UP_{ys})	0.0611	6.09	0.1027	0.0516	4.82	0.0866	0.0601	5.99	0.1010
ln(UP_{ns})	0.0647	3.30	0.1364	0.0661	2.41	0.1396	0.0636	3.24	0.1341
ln(UP_{cs})	0.1594	6.03	0.3439	0.0954	2.75	0.2050	0.1571	5.94	0.3389
Intercept	0.3639	3.34	0.1316	0.7666	5.55	0.2670	0.3820	3.52	0.1382
Error	—	—	0.2098	—	—	0.2021	—	—	0.2100
Bioavailable dust lead (Equation 5)									
ln(UP_{ys})	0.1039	7.57	0.0914	0.1054	7.31	0.0938	0.1039	7.57	0.0914
ln(UP_{ns})	0.0751	2.77	0.0828	0.1126	3.01	0.1262	0.0751	2.77	0.0828
ln(UP_{cs})	0.3350	9.35	0.3782	0.2582	5.50	0.2944	0.3350	9.35	0.3782
Intercept	2.3390	16.52	0.4418	2.5994	14.67	0.4804	2.3339	16.52	0.4418
Error	—	—	0.1523	—	—	0.1468	—	—	0.1523
Baseline bioavailable lead (µg/dL)	1.4			2.2			1.5		
Baseline bioavailable dust lead (mg/kg)	37.0			48.1			36.9		
n		2,034			1,571			2,034	
Goodness of fit index		0.9995			0.9999			0.9998	
χ^2		4.7284			0.598			1.5347	
Degrees of freedom		3			2			2	
Pr > χ^2		0.1928			0.7416			0.4642	
r^2 Total uptake		0.9560			0.9591			0.9559	
r^2 Bioavailable dust lead		0.9768			0.9785			0.9768	

Abbreviations: χ^2, chi-square; cs, community soil; d, dust; DUSTage0–1, bioavailable dust lead if the child was 6–11 months; DUSTage1–2, bioavailable dust lead if the child was 12–23 months; DUST1994–1998, bioavailable dust lead if the year was 1994, 1995, 1996, 1997, or 1998. ln, natural log; ns, neighborhood soil; Pr, probability; r^2, r-squared; tot, total; UP, uptake; ys, yard soil.
[a]t-Values ≥ 1.96 are equivalent to p-values < 0.05.

$$\ln(C_d \times ABS_d) = [0.1054 \times \ln(C_{ys} \times ABS_{ys})] + [0.1126 \times \ln(C_{ns} \times ABC_{cs})] + [0.2582 \times \ln(C_{cs} \times ABS_{cs})] + 2.5994, \quad [5]$$

where ln = natural log; C_{ns} = neighborhood soil arithmetic mean using 500-ft radius (mg/kg); age0–1 = 1 for 6–11 months, otherwise 0; age1–2 = 1 for 12–23 months, otherwise 0; ABS_{cs} applies to both C_{ns} and C_{cs} values.

The SEM standardized regression coefficients (Table 3) yielded partition coefficients of 50% house dust/25% yard soil/10% arithmetic mean neighborhood soil/15% arithmetic mean community soil (50/25/10/15) (Table 4) used in subsequent calculation of age-specific IRs.

Ingestion Rate Estimates

Figure 1 summarizes arithmetic and geometric mean soil/dust IRs calculated for four source partition scenarios: *a*) the IEUBK model default 55% dust/45% yard soil (55/45), *b*) the original BHSS model applying 40% dust/30% yard soil/30% geometric mean community soil (40/30/30G) (Panhandle District Health Department 1986), *c*) the same partition using arithmetic average community soil (40/30/30A), and *d*) the SEM (50/25/10/15). Calculated IRs were observed in three general ranges. The highest IR estimates were arithmetic means for the 55/45 partition and are near the IEUBK model recommended values (also shown in Figure 1). Mid- and low-range IR estimates are approximately one-third and one-half lower, respectively [corresponding numeric data with 95% confidence interval (CI) and percentiles are provided in Table S1].

IEUBK Model Results

The four IR and partition scenarios with the best agreement are from the mid-range IRs shown in Figure 1 (i.e., 40/30/30G-geometric mean IR (geoIR), 55/45-geoIR, 50/25/10/15-arithmetic mean IR (aveIR), 40/30/30A-aveIR; the high- and low-range IRs, respectively, over- and underpredicted observed BLLs (data not shown). Figure 2 shows the results of the SSE and linear regression analyses for annual observed and predicted geometric mean BLLs for the four scenarios with the best agreement. Observed geometric mean BLLs ranged from > 8 µg/dL in the late 1980s to near 2 µg/dL in 2002, and observed geometric standard deviations (GSDs) ranged from 1.52 to 2.12 (n = 2,176). GSDs calculated from the IEUBK batch runs for these four scenarios ranged from 1.42 to 2.10, with medians around 1.7 (see Table S2), consistent with the IEUBK model default GSD of 1.6.

Each of the four scenarios represents a plausible source partition and estimated lead intake scenario, produces similar IR estimates (Table 5), and shows temporal variability in the SSE, with the largest SSEs in 1988 (see Table S3). The scenarios with the smallest total SSE for 1989–2002 were 40/30/30G-geoIR, 55/45-geoIR, and 50/25/10/15-aveIR. The 40/30/30A-geoIR was similar to the 50/25/10/15-aveIR and had the next smallest SSE for those same years. Although all four scenarios showed temporal variation in predicting observed BLLs, the 50/25/10/15-aveIR had the lowest SSEs in the early and later years of the cleanup (1989–1990 and 1996–2002, respectively), whereas the 40/30/30G-geoIR had the lowest SSE in the middle years of the cleanup (1991–1995). Additionally, linear regression indicated that the 50/25/10/15-aveIR and the 40/30/30A-aveIR scenarios were best-fit models due to a slope coefficient nearest 1.0, in combination with highest r^2, largest F-statistic, and smallest sum of squared residuals (see

Table 4. Structural equations modeling (SEM) results for soil/dust contributions (%).

Variables	Model 1 (1989–2002) 0–2 years	Model 1 (1989–2002) 2–9 years	Model 1 (1989–2002) Value[a]	Model 2 (1989–1998) 0–2 years	Model 2 (1989–1998) 2–9 years	Model 2 (1989–1998) Value[a]	Model 3 (1989–2002) 0–2 years	Model 3 (1989–2002) 2–9 years	Model 3 (1989–2002) Value[a]
Contribution of dust/soil ingestion									
House dust	40	37	40	48	45	50	41	38	40
Yard	30	30	30	28	30	25	30	31	30
Neighborhood	11	11	10	9	10	10	11	11	10
Community	19	23	20	15	15	15	18	20	20
Contribution to lead in blood									
House dust			17			22			16
Yard			35			34			33
Neighborhood			14			15			14
Community			34			29			37

[a]Values are rounded to total 100%.

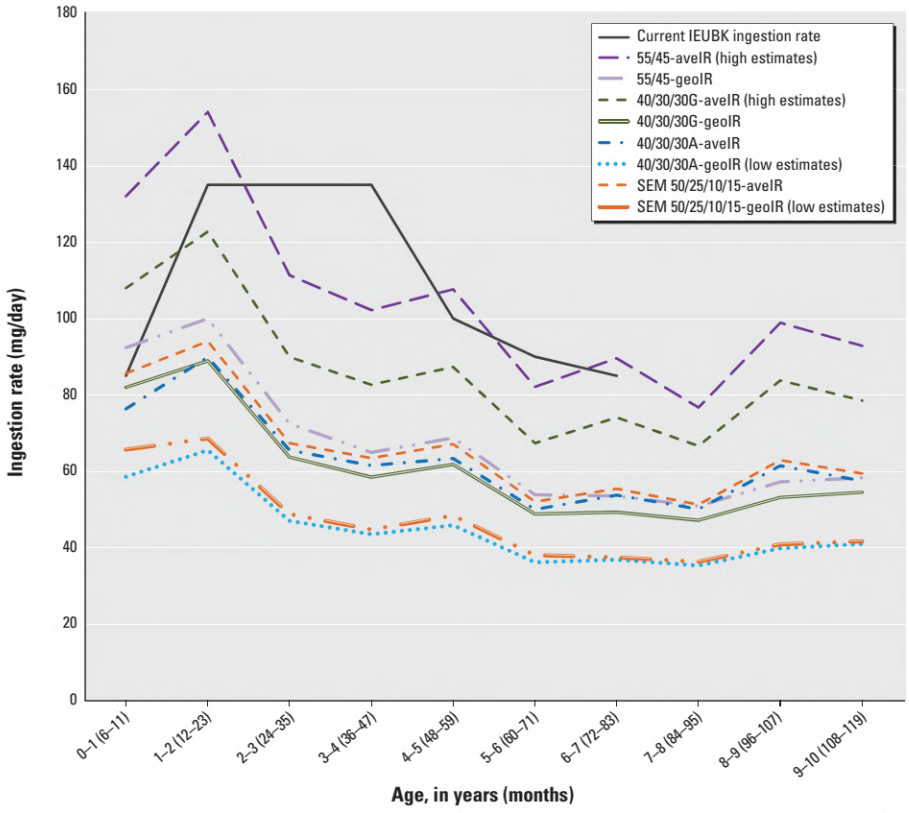

Figure 1. Arithmetic and geometric mean age-specific soil/dust ingestion rates (IRs) for four soil/dust partition scenarios. Included are current Integrated Exposure Uptake Biokinetic (IEUBK) model IRs and calculated age-specific mean soil/dust IRs for the four partition scenarios. For each age (6 months–9 years), arithmetic mean IRs (aveIR) and geometric mean IRs (geoIR) are shown. 55/45 is the partition of dust/yard soil, 40/30/30 is the partition of dust/yard/community soil, and SEM 50/25/10/15 is the partition of dust/yard/neighborhood/community soil. Corresponding numeric data, with 95% CI and percentile distributions for each model and age, are provided in Table S1.

Table S4). The age-specific IRs and 95% CIs for the 50/25/10/15-aveIR scenario are shown in Figure 3 because this scenario had the lowest SSEs in multiple years and was one of the best-fit linear regressions. Figure 3 also shows age-specific IRs recommended by U.S. EPA risk assessment guidance (U.S. EPA 1994, 2011).

Discussion

At the BHSS, children's soil/dust exposures have been investigated since the 1970s, and the IEUBK model has been used to evaluate the dose–response relationship since 1986. Use of the IEUBK model default IRs, bioavailability and soil/dust partition failed to account for soil sources beyond the immediate home yard and consistently overpredicted observed BLLs. In 1990, the BHSS cleanup criteria were developed using the 40/30/30G partition accounting for community soils and reduced soil/dust lead uptake (compared with the IEUBK model default). The overprediction of BLLs using default IEUBK model values was resolved by lowering soil and dust lead bioavailability, although it could have been explained by several combinations of reduced IRs or bioavailability. However at the time, it was not possible to determine which was predominant. In this study, we used a newly available laboratory method to estimate soil and house dust ABS. The soil and house dust bioavailability results of 33% and 28%, respectively, are similar to the recommended 30% IEUBK model default values and those found in other BHSS studies (Maddaloni et al. 1998). These findings suggest that IRs, not ABS, should be reduced by about 40% from the IEUBK default values to best represent the dose–response relationship observed at the BHSS.

In this study, the more rigorous SEM pathways analyses resulted in several plausible models, all suggesting that community and neighborhood soil sources, in addition to the yard soil source, are independent contributors to total lead uptake and bioavailable lead in house dust. Others have recently confirmed the importance of soil beyond the immediate home yard (Laidlaw et al. 2014; Zahran et al. 2013a, 2013b). The 50/25/10/15-aveIRs were derived from the only partition including neighborhood soils and exhibited the lowest SSEs in multiple years. These IRs were calculated using arithmetic-mean neighborhood and community soil exposures. The central tendency statistic that better approximates geographic area exposures has been the subject of debate and remains unresolved; the arithmetic mean represents an aggregate biased by high or low concentrations, and the geometric mean is the most likely concentration in the prescribed area. Two of the four select models employed arithmetic means, one used the geometric mean, and the IEUBK model default scenario uses individual observations and assumes the effect of soils beyond the home yard is included in house dust. However, all four models produced similar IRs with the average nearly identical to the 50/25/10/15-aveIRs, indicating the source partition is critical in describing lead intake.

Age-specific and temporal effects, also examined with SEM, suggested children 6–23 months of age exhibited greater lead intake rates from house dust than older children, consistent with the study by Wilson et al. (2013). Additionally, SEM analyses including year-specific variables suggested dust intake rates for younger children may have been lower early in the cleanup (1989–1993) and higher during the middle years of the cleanup (1994–1998). However, only age- and year-specific intake rates of interior dust were statistically significant predictors (Table 3); consequently, age- and year-specific IRs for soil intake (yard, neighborhood, or community) were not included in our final model (data not shown). Several factors may have caused temporal variations in IRs, or partition coefficients. Aggressive LHIP education and intervention programs may have resulted in a temporary reduction in soil/dust intake by children. Alternatively, elevated dust loadings caused by flooding and

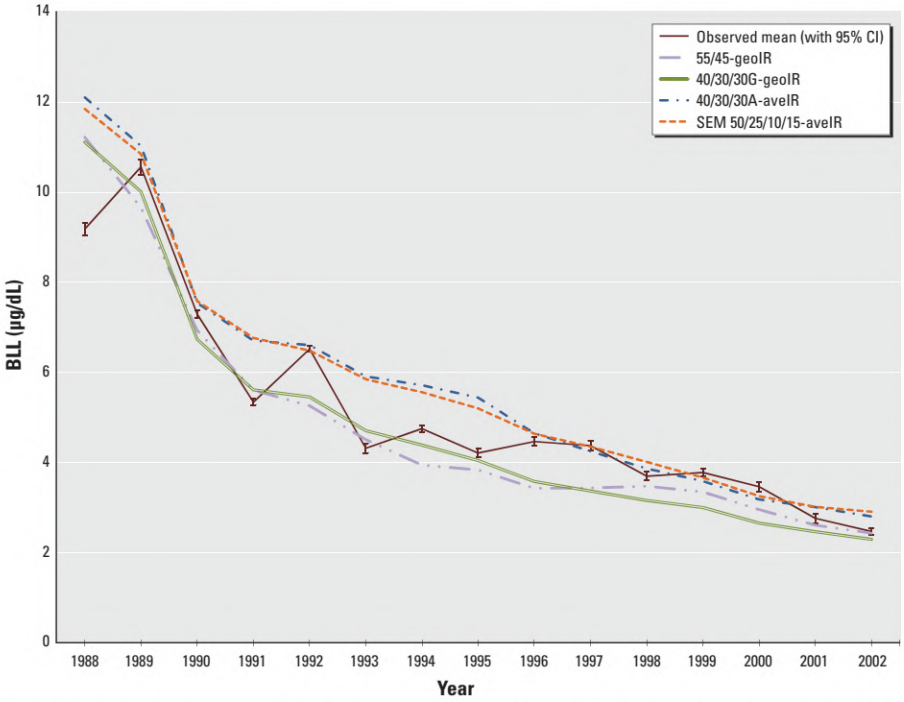

Figure 2. Observed and predicted geometric mean blood lead levels (BLLs) by year for four scenarios that best predict observed BLLs. Predicted geometric mean BLLs for the four scenarios are compared with observed BLLs from 1988 through 2002. Observed BLLs include error bars for the 95% confidence interval (CI). Abbreviations: aveIR, arithmetic mean ingestion rate; geoIR, geometric mean ingestion rate. 55/45 is the partition of dust/yard soil, 40/30/30 is the partition of dust/yard/community soil, and SEM 50/25/10/15 is the partition of dust/yard/neighborhood/community soil. Corresponding numeric data, with 95% CI and percentile distributions for each model and age, are provided in Table S1.

Table 5. Mean age-specific soil/dust ingestion rates (mg/day) for four scenarios that best predict observed blood lead levels.

Age[a] (years)	55/45[b]-geoIR	40/30/30G[c]-geoIR	40/30/30A[c]-aveIR	50/25/10/15[d]-aveIR	Average all models
0–1	92	82	76	86	84
1–2	100	89	90	94	93
2–3	72	64	66	67	67
3–4	65	58	62	63	62
4–5	69	62	63	67	65
5–6	54	49	50	52	51
6–7	54	49	54	55	53
7–8	51	47	50	51	50
8–9	57	53	61	63	59
9–10	58	54	57	59	57

Abbreviations: aveIR, arithmetic mean ingestion rate; geoIR, geometric mean ingestion rate.
[a]0–1 = 6–11 months, 1–2 = 12–23 months, 2–3 = 24–35 months, etc. [b]Dust/yard soil. [c]Dust/yard/community soil; G = geometric mean; A = arithmetic mean. [d]Dust/yard/neighborhood/community soil.

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construction activities may have exacerbated ingestion in the middle years of the cleanup. However, SEM and IEUBK model sensitivity analyses investigating alternate time period (years) variable constructs suggested that variation in calculated IRs may be an artifact of the source partitions, nature of the data, or progression of the cleanup. At the beginning of the cleanup, there was little difference between community soil and neighborhood soil concentrations. As area-wide cleanups predominated, these variable concentrations diverged between 1994 and 1998 and returned to similar concentrations by 2000 (TerraGraphics 2004). The 50/25/10/15 SEM is the only partition scenario that captures spatial differentiation in soil outside the home yard through the neighborhood soil variable. It is also possible that various periods of the cleanup exhibited different partition ratios from landscape changes or LHIP activities.

The truncated 1989–1998 database was used to derive the select SEM partition because from 1999 forward, the yard, neighborhood, and community soil variables were dominated by remediated homes. Lead concentrations were not measured in remediated yards. Instead, a nominal value of 100 mg/kg was assigned to represent the maximum allowable recontamination level. Replacement soils, and presumably yard soil concentrations immediately following remediation, averaged ≤ 50 mg/kg (LFR Inc. 2008; McCulley, Frick & Gilman Inc. 1997). Consequently, remediated soil lead concentrations were likely biased high and reflected less variation in the final years of the cleanup. Including 1999–2002 in the SEM analyses could bias the standardized coefficients for soil lead parameters used to estimate source effects.

Additionally, SEM coefficients were based on 1,571 of 4,019 observations in the 1989–1998 database. Most missing variable measurements for the SEM subset were house dust lead levels, implying the home lacked a vacuum cleaner, and were associated with likely dustier homes and higher BLLs (TerraGraphics 2004; U.S. EPA 2000; von Lindern et al. 2003a, 2003b). As a result of the missing house dust levels, mean values for key variables in the SEM subset differ from those in the parent database; particularly, mean absorbed lead was about 11% greater for children with no dust lead observation. Because total absorbed lead was allocated to source variables, higher absorbed blood lead implies potentially higher soil/dust IRs, absorption rates, or dust lead concentrations, or a combination thereof among these underrepresented children. The LHIP provides free loaner high-efficiency particulate arresting vacuum cleaners to residents to address this need.

This study is part of larger cleanup and public health response. It was not a designed experiment. The LHIP paid participants a modest fee for blood and house dust samples specifically to identify and provide follow-up services to children at risk. Factors such as self-selection, repeat blood leads, uncontrolled vacuum dust samples, lack of a home vacuum cleaner, intervention responses, other lead sources, community awareness, and assumed clean soil values could bias the IRs higher or lower. Many of these factors were discussed in detail by von Lindern et al. (2003b).

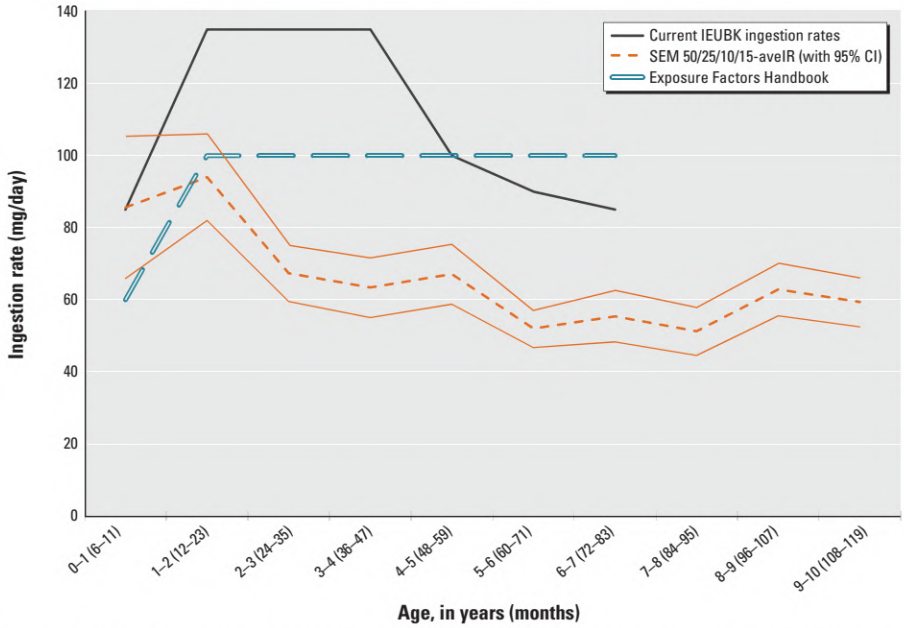

Figure 3. Mean age-specific ingestion rates (IRs) with 95% confidence intervals (CI) for the structural equations modeling (SEM) partition scenario. SEM 50/25/10/15 partition scenario (of dust/yard/neighborhood/community soil) with arithmetic mean IRs (aveIR) for ages 6 months–9 years, including 95% CI, are compared with current Integrated Exposure Uptake Biokinetic (IEUBK) model IRs and *Exposure Factors Handbook* IRs (ages 6 months–6 years only) (U.S. EPA 1994, 2011).

Conclusions

The addition of *in vitro* soil and house dust bioavailability estimates to the BHSS lead health database facilitated analysis of absorbed and bioavailable soil/dust lead, which improves understanding of the dose–response relationship and supports improved estimates of total soil/dust IRs. Bioavailability was substantially underestimated in the original BHSS risk assessment. The IEUBK model, using default bioavailability and default soil/dust IRs, consistently overpredicted BLLs collected from > 50% of resident children, and this was likely attributable to overestimating IRs. Although remediation activities were based on an inaccurate combination of IRs and bioavailability estimates, remediation was nonetheless effective in achieving the objective of < 5% of children with BLLs ≥ 10 µg/dL.

Soil and dust IRs at the BHSS from 1988 through 2002 averaged 66 mg/day (95% CI: 57, 75 mg/day) for children 6 months–9 years of age, and peaked at 94 mg/day (95% CI: 82, 106 mg/day) at age 12–23 months. The estimated IRs were lower than both IEUBK default and the U.S. EPA *Exposure Factors Handbook* recommended values for all ages except the youngest age group (< 12 months) (U.S. EPA 2001, 2011). The average IRs are 40% less than IEUBK default recommendations and 30% lower than estimates in the *Exposure Factors Handbook* (shown in Figure 3), and are consistent with recent studies and reviews suggesting values < 100 mg/day (Bierkens et al. 2011; Moya and Phillips 2014; Ozkaynak et al. 2011; Wilson et al. 2013).

Soil/dust IRs are among the most sensitive variables in the IEUBK and other risk assessment models used at hazardous waste sites (Griffin et al. 1999; TRW Lead Committee 2014). Accurately estimating lead intake requires simultaneously quantifying both soil/dust IRs and the soil/dust source partition. Inclusion of neighborhood and community soil exposures is essential to estimating soil/dust lead intake. These findings suggest that approximately half of the lead intake is from house dust and half is from soil, equally attributed to the immediate home yard and surrounding neighborhood/community. Additionally, the importance of soil outside the home environment varies with distance, not property boundaries, and intake estimates should account for soil sources in the immediate neighborhood and greater community.

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Exhibit K

ESTIMATION OF AGE-SPECIFIC SOIL AND DUST INGESTION RATES FOR U.S. CHILDREN: UPDATE TO THE DEFAULT VALUES FOR THE INTEGRATED EXPOSURE UPTAKE BIOKINETIC MODEL FOR LEAD IN U.S. CHILDREN

OVERVIEW

Since 1994, the Office of Land and Emergency Management (OLEM), formerly known as the Office of Solid Waste and Emergency Response (OSWER), has recommended the Integrated Exposure Uptake Biokinetic Model for Lead in Children (IEUBK model) as a risk assessment tool to support environmental cleanup decisions at current or future anticipated residential sites (U.S. EPA, 1994a, b). The IEUBK model predicts blood lead levels (PbB) in young children (birth to 7 years of age) exposed to lead from several sources and routes. The IEUBK model uses more than 100 input parameters that are initially set to default values. Of these, there are 46 parameters that may be input, or modified, by the user; the remainder are internal variables that are unavailable for modification (U.S. EPA, 1994a).

The IEUBK model uses empirical data from numerous studies of lead uptake and biokinetics, contact and intake rates of children with contaminated media, and data on the presence and behavior of environmental lead to predict a plausible distribution centered on the geometric mean (GM) of PbB for a hypothetical child or population of children (U.S. EPA, 2020).[1] The relative variability of PbB concentrations around the GM is defined as the geometric standard deviation (GSD). The GSD encompasses biological and behavioral differences, measurement variability from repeat sampling, variability as a result of sample locations and analytical variability.[2] From the distribution, the IEUBK model estimates the risk (*i.e.*, probability) that a child's or a population of children's PbB concentration will not exceed a certain PbB concentration (U.S. EPA, 1998, 1994a; White et al., 1998).

Ingestion of fine soil and dust particulates, especially by young children, is the dominant route of exposure for lead. (Laidlaw et al., 2014; Landrigan et al., 1975; Lanphear et al., 1998, 2003). Childhood soil and dust ingestion occurs via multiple pathways, including hand-to-mouth transfer, mouthing of objects, and contaminated food. The rate at which soil and dust is ingested are dependent on a child's age, individual behaviors, exposure time, total dust and soil accessible and environmental conditions (Zahran et al., 2013a,b). Age-specific estimates of the soil and dust ingestion rate pathway are needed to assess children's exposures in the home or play environment, and to make informed cleanup decisions.

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[1] The GM represents the central tendency estimate (*e.g.*, mean, 50th percentile) of PbB concentration of children from a hypothetical population (Hogan et al., 1998). If an arithmetic mean (or average) is used, the model provides a central point estimate for risk of an elevated PbB level. By definition a central tendency estimate is equally likely to over- or under-estimate the lead-intake at a contaminated site. Upper confidence limits (UCLs) can be used in the IEUBK model; however, the IEUBK model results could be interpreted as a more conservative estimate of the risk of an elevated PbB level. See U.S. EPA (1994a) for further information.

[2] The IEUBK model uses a log-normal probability distribution to characterize this variability (U.S. EPA, 1994a). The biokinetic component of the IEUBK model output provides a central estimate of blood lead concentration along with the distribution of possible blood lead concentrations in a population of similarly exposed children. In the IEUBK model, the GSD encompasses biological and behavioral differences, measurement variability from repeat sampling, variability as a result of sample locations, and analytical variability. The GSD is **not** intended to reflect variability in blood lead concentrations where different individuals are exposed to substantially **different** media concentrations of lead. The recommended default value for GSD (1.6) was derived from empirical studies with young children where both blood and environmental lead concentrations were measured (White et al., 1998).

The soil and dust ingestion rate is one of the most influential variables in the IEUBK model for lead in children (U.S. EPA, 1994a).

Early estimates of soil and dust ingestion rate in children were based on studies of trace elements in soil and feces (Battelle, 2005; Doyle et al., 2010; Sedman and Mahmood, 1994; U.S. EPA, 2011, 2012). The default values for the *Age-Dependent Soil and Dust Ingestion Rate* variable in the IEUBK model (v. 1.1, build 11) represent age-specific central tendency estimates for lead intake from soil and dust for children (6 to 84 months of age). The default values (v.1.1, build 11) are based on these tracer studies from a literature review and analysis performed during a review of the National Ambient Air Quality Standards (NAAQS) for lead (U.S. EPA, 1989, pp. A-16). The default soil and dust ingestion rate values are based on a study of soil ingestion in children (Sedman et al., 1989). This study utilized trace elements to quantify soil ingestion rates. The initial calibration of the IEUBK model employed these default values, and the results of a validation study performed in the early 1990s showed reasonably close agreement between model estimates using these intake values and empirical blood lead measurements (Hogan et al., 1998). The study that formed the basis for the existing default values did not, however, account for several factors that should be considered when designing a soil dust ingestion study (e.g., sieve to the currently recommended size fraction[3], sample household dust, soil outside of individual yards or the bioavailability of the lead in ingested soil or dust).

The purpose of this document is to provide the technical basis for an analysis of the currently available published literature to support an updated *Age-Dependent Soil and Dust Ingestion Rate (IRsd)* variable in the IEUBK model (Table 1). The updated age-specific soil and dust ingestion rate estimates for the *Age-Dependent Soil and Dust Ingestion Rate* variable in the IEUBK are based on soil and dust ingestion rates from scenario 3 of von Lindern et al. (2016). As described below in the Technical Analysis Section, this study was selected because it was determined that the approach employed by the authors provides the best central tendency estimate of age-specific soil and dust ingestion rates for use in the IEUBK to support risk assessments conducted under CERCLA or RCRA corrective action authority. The soil-dust ingestion rates from Scenario 3 results in soil-dust ingestion rates that are supported by other independent analyses that use dermal transfer to estimate soil and dust ingestion rate, specifically the modeled estimates from Ozkaynak et al. (2011) and Wilson et al. (2013) (see Table 2).

Soil/dust ingestion studies reviewed for this effort are not intended to specifically represent soil-dust ingestion for children who engage in pica behavior. The intake estimates for soil pica behavior would be greater than intake estimates for incidental ingestion of soil-dust, but reliable data for pica ingestion rates or frequency are not available[4].
The intended audience for this document is human health risk assessors familiar with using the IEUBK model in support of CERCLA and RCRA corrective action risk assessments. For further background information on both this variable and the use of the IEUBK model in Superfund lead risk assessment, refer to U.S. EPA (1994a) or the Technical Review Workgroup for Lead (TRW) website (https://www.epa.gov/superfund/lead-superfund-sites-guidance).

[3] Particle size should be similar to the fraction that adheres to skin to reflect the particles that are incidentally ingested during hand-to-mouth activity.
[4] See Chapter 5 of US EPA Exposure Factors Handbook for more information on pica.

Table 1. Recommended revision to default age-specific soil/ dust ingestion rates (mg/day) in the IEUBK model

Source	Age Category (months)							Basis for Age-Specific Value
	0<12	12<24	24<36	36<48	48<60	60<72	72<84	
IEUBK Model Default[a]	85	135	135	135	100	90	85	Methodology U.S. EPA, 1989 Data Source Sedman et al., 1989
Revised Soil/Dust Ingestion Rate	86	94	67	63	67	52	55	Methodology von Lindern et al., 2016 Ozkaynak et al., 2011 Wilson et al., 2013 Data Source von Lindern et al., 2016

[a]IEUBK model v. 1.1, build 11.

INTRODUCTION

The IEUBK model predicts PbB in young children (birth to 7 years of age) exposed to lead from several sources of exposure and routes. The IEUBK model uses more than 100 input parameters that are initially set to default values. Of these, there are 46 parameters that may be input, or modified, by the user; the remainder are locked (U.S. EPA, 1994a). Default values represent national averages or other central tendency values derived from empirical data in the open literature. Default values include a) lead concentrations in exposure media (*e.g.*, diet representative of national food sources); b) contact and intake rates (*e.g.*, soil/dust ingestion); and c) exposure durations (White et al., 1998). The representativeness of IEUBK model output is wholly dependent on the representativeness of the data (often assessed in terms of completeness, comparability, precision, and accuracy [U.S. EPA, 1994a]).

Representative site-specific data are essential for developing a risk assessment (as well as cleanup goals) that reflect the current or potential future conditions. The most common type of site-specific data is media-specific lead concentration information (air, water, soil, dust). Until recently, an inexpensive, validated method to estimate bioavailability of lead in soil or dust was not available. Receptor data (*e.g.*, age, body weight, breathing rate, or soil ingestion rate) does not typically vary from site to site.

To promote defensible and reproducible risk assessments and cleanup plans, while maintaining flexibility needed to respond to different site conditions, U.S. EPA recommends the Data Quality Objectives process (U.S. EPA, 2006). Data Quality Objectives provide a structured approach to collecting environmental data that will be sufficient to support decision-making (http://www.epa.gov/QUALITY/dqos.html).

TECHNICAL ANALYSIS

The initial default IEUBK total soil and dust ingestion rates were used in the development of the NAAQS (U.S. EPA, 1989). Rather than adding new data, many of the published studies since the initial default values were adopted in 1994 were reanalyzed data from previous studies. Moreover, the TRW identified a number of limitations of the re-analyses of the data that were published after 1994. For example, Stanek and Calabrese (2000) included estimates of daily soil ingestion that were significantly negative, biased by large negative values in the data. The decision to include the negative values and their consequent impact on the results was never addressed by the authors (Stifelman 2006). We have identified several newer and relevant studies on soil/dust ingestion from seven sources: Arnot et al., 2010; Bierkens and Cornelis, 2006; Jang et al., 2014; Ozkaynak et al., 2011; Stanek et al., 2012a,b; von Lindern et al., 2016; Wilson et al., 2013.

To evaluate these studies, the TRW Lead Committee used a data quality objective (DQO) approach (see Attachment 1). This approach (working through the first four steps of the DQO process) allowed the Committee to focus on identifying studies that provided information that would support a revision of the default age-specific soil-dust ingestion rates for use in the IEUBK model for assessing lead exposure at CERCLA and RCRA corrective action sites. Table 2 provides a summary of these literature sources.

The following studies were evaluated to support a revision to the soil and dust ingestion rate default parameter in the IEUBK. Arnot et al. (2010) described the Farfel Exposure Model (FHX) employed by Health Canada, which uses a soil/dust ingestion rate of 65 mg/day for children age 5-11 years, and 100 mg/day for toddlers (age 6-60 months). Bierkens and Cornelis (2006) derived a range of soil/dust ingestion values (23.2 to 116 mg/day assuming an 8-hour waking and outdoor period [alternate values for 12-hour waking and outdoor period shown in Table 2]) based on probabilistic modeling of other mouthing frequency and hand loading publications. A 4-day fecal study of Korean children age 0 to 84 months, using the limiting tracer method, calculated an arithmetic mean soil/dust ingestion rate of 118 mg/day and a geometric mean of 29.3 mg/day (Jang et al., 2014; tracer-specific data not provided in study). Ozkaynak et al. (2011) estimated a mean soil/dust ingestion rate for children 3 to 6 years of age (as compared to the age range of the IEUBK model which is children <72 months old) using stochastic human exposure and dose simulation (SHEDS) modeling, using activity diaries to estimate hand-to-mouth, and object-to-mouth contact rates. Stanek et al. (2012a,b) conducted a meta-analysis of their earlier four mass balance studies using stochastic modeling of the most reliable tracers of children from Amherst, Massachusetts; Anaconda, Montana; and Washington State. Soil pica data were excluded from their analysis. Soil/dust ingestion rates for children in specific age classes are shown in Table 2; an overall mean soil/dust ingestion rate of 25.5 mg/day (95th percentile 79.4 mg/day) was estimated. Similar to Ozkaynak et al. (2011), Wilson et al. (2013) calculated soil and dust ingestion rates using a mechanistic model including parameters for particle loading on skin, transfer to hands, hand surface area, mouthing surface area, hand-to-mouth frequency, saliva dissolution, and exposure time using deterministic and probabilistic methods. Results, which are dependent on exposure time, were calculated separately for soil and dust, then summed for a daily soil/dust ingestion rate.

In addition, the information available on soil and dust ingestion rate values in EPA's Exposure Factors Handbook (U.S. EPA, 2017) was also considered as part of this effort but was not included in the peer review of this document (which preceded the release of the Exposure Factors Handbook update). The difference between the soil and dust ingestion rate values in the

Exposure Factors Handbook (U.S. EPA, 2017) and those proposed herein was addressed by the Office of Research and Development evaluation of the IEUBK model. (U.S. EPA, 2020).

The study by von Lindern et al. (2016) satisfies many of the evaluation criteria described in the TRW Lead Committee's DQOs (see Attachment 1). The authors of that study used environmental information collected at the Bunker Hill Mining and Metallurgical Complex Superfund Site (BHSS) site in Idaho to compare archived soil and dust samples from the BHSS to children's blood lead levels monitored from 1989 through 2002 to calculate soil/dust ingestion rates using the IEUBK model. Over 15 years of active cleanup, the Lead Health Intervention Program amassed approximately 5,400 blood lead observations (referred to as the parent database) from nearly 2,340 children (ages 0–9 and with a >50% participation rate) and yielding 2,176 records of blood/soil/dust lead concentrations. The study by von Lindern et al. (2016) used measured peak blood leads, community soil, neighborhood soil, yard soil concentration, house dust concentration and bioavailability information with IEUBK model defaults for Air, Water, and Diet to estimate soil-dust ingestion rates (IRs_D) under different Structural Equations Modeling (SEM) scenarios.

In the Bunker Hill study, four variables were used to quantify soil and dust exposures: house dust, yard soil, neighborhood soil (the mean of all yard soils within 200, 500, and 1000 feet of the home, excluding the home's yard), and community soil (the mean of all yard soils within the community, excluding the home's yard and neighborhood). The 271 samples (193 house dust samples, 73 yard soil samples and 5 quality control samples) were sieved to 80 mesh (to account for the particle size that would likely adhere to a child's hands) and analyzed for total lead and bioavailability.

The default assumption for the IEUBK model is that the source of soil ingested is 55% dust and 45% yard soil (U.S. EPA, 1994b). Structural Equations Modeling (SEM) was used to evaluate three different scenarios of yard soil to dust, neighborhood soil, and community soil:

1. 55% house dust/45% yard soil (as currently in the IEUBK model),
2. 40% house dust/30% yard soil/30% community soil, (alternatively using arithmetic or geometric means for community soil) and
3. 50% house dust/25% yard soil/10% neighborhood soil/15% community soil (alternatively using arithmetic or geometric means for neighborhood and community soil).

Table 2. Data summary of average soil/dust ingestion rates in children from selected studies.

Source	Soil/Dust Ingestion Rate (mg/day)	Age Range	n	Summary of Evaluation
IEUBK Model Default Values[a]	85-135	Children 0-84 months (yearly values)	77	Existing IEUBK model soil-dust ingestion rates Based on technical analysis to support the NAAQS for Lead (U.S. EPA, 1989).
Arnot et al., 2010	100	Children 6 60 months (age range)	n/a[b]	Is not considered a support document for revising the soil/dust ingestion rate because these are assumed input parameters for an exposure model using exposure factors for the general population of Canada. They are based on Health Canada 1998, which is based on Binder et al., (1986), Clausing et al. (1987), Calabrese et al. (1989), and Van Wijnen et al. (1990). Farfel Exposure Model (FHX) and Health Canada. 1998.[b]
	65	Children age 5 to 144 months (age range)		
Bierkens and Cornelis, 2006[c]	23.2-116	Children 12-84 months (age range) 8-hr awake and outdoors	5,000 (model runs)	Supportive study based on the limited number of observations.. Ranges of ingestion rates derived from probabilistic modeling of data from other publications reporting mouthing frequency and hand loading (Holmes et al., 1999; AuYeung et al., 2003; and U.S. EPA exposure factors, 2017).
	34.8-174	Children 12-84 months (age range) 12-hr awake and outdoors		
Ozkaynak et al., 2011	68	Children 36-72 months (age range) Mean value	1,000 (model runs)	Supportive study based on lack of new observation data. The estimates are based on modeling using SHEDS and hand-to-mouth and object-to-mouth contacts.
Jang et al., 2014	118	Children 0-96 months Arithmetic mean	58 samples	New tracer data based on Korean children. Estimates based on aluminum. The publication lacked details of the study. Only feces and soil-dust collected. 5 children were used as control group to compensate for exposure from other sources.
	29.3	Children 0-96 months Geometric mean	58 samples	

Source	Soil/Dust Ingestion Rate (mg/day)	Age Range	n	Summary of Evaluation
Stanek et al., 2012a,b	3.8	Children 12 to 36 months old	39 samples	Meta-analysis of four existing mass balance studies. The reanalysis of existing data is not a direct measurement and is not considered a candidate for supporting a revised default age-specific soil-dust ingestion rate
	20.6	Children 24 to 36 months old	55 samples	
	32.2	Children 36 to 60 months old	47 samples	
	40.9	Children 48 to 108 months old	75 samples	
U.S EPA Exposure Factors Handbook (2017)	40 - 90	Children < 6 months, 6 months to < 1, 1 to <2 years, 2 to <6 years, 1 to <6 years , 6 to < 12 years	241 in key tracer studies, 2,599 biokinetic modeling studies, modeled estimates of 1,000 simulated individuals and 200,000 trials.	The overall rating was low based on criteria of Soundness, Applicability and Utility, Clarity and Completeness, Variability and Uncertainty, and Evaluation and Review.
von Lindern et al., 2016	52-94[d]	Children 12 to 72 months old (yearly values)	985[f] (measured PbB and environmental values used for model runs)	Reanalysis of archived soil and dust data from Bunker Hill Superfund Site, available information includes bioavailability data, particle size and children's blood lead levels monitored (in some cases longitudinal data) from 1988-2002. Evaluated various combinations of dust, yard soil, neighborhood soil, and community soil. Accurately predicted peak annual blood lead from children representing greater than 50% of all resident children for 15 consecutive years.
Wilson et al., 2013	61	Toddlers 7 to 60 months	200,000 (model runs)	The study is considered a supportive study due to new modeled data. This study models soil/dust ingestion rates in Canada using hand-to-mouth transfer.
	55	Children 60 to 144 months		

[a]IEUBK model v. 1.1, build 11.
[b]Health Canada values based on data from Binder et al., 1986; Clausing et al., 1987; Calabrese et al., 1989; and Van Wijnen et al., 1990.
[c]Study reports values in units of mg/hr. The range (2.9-14.5 mg/hour) was converted to mg/d assuming both an 8-hour and a 12-hour waking and outdoor period.
[d]Results of Structural Equations Modeling (SEM) assuming 50% dust, 25% yard soil, 10% neighborhood soil, and 15% community soil.
[e] von Lindern et al. (2016) employed a hybrid approach that measured peak blood leads, particle size, community soil concentration, neighborhood soil concentration, yard soil concentration, as well as house dust concentration, and used IEUBK Modeled defaults for Air, Water, and Diet to estimate IRs under different SEM scenarios to select the model which best fit the empirical distribution of blood leads, representative of over 50% of the community for 15 consecutive years.
[f] 985 is the sum of 12-72 month old children in the 50/25/10/15 partition from Table S-1 of Supplemental Material to von Lindern et al. (2016).

The authors selected the model that provided the best fit to the empirical distribution of blood leads, which represented over 50% of the community for 15 consecutive years. Though ingestion rates for all three scenarios were similar, scenario 3 above had the lowest sum of squared error (SSE) in the statistical evaluation[5]. For this scenario, the authors derived age-specific, arithmetic mean soil/dust ingestion rates ranging from 52 to 94 mg/day for children age 1 to 6 years, with 95% confidence intervals ranging from 47 to 106 mg/day (Table 3). The other two scenarios were less acceptable because they did not fit the data as well.

Table 3. Soil/dust ingestion rates for the 50% house dust/25% yard soil/10% neighborhood soil/15% community soil scenario for the 12-71 month age range that is used in the IEUBK model (von Lindern et al., 2016).

Age[a]	n	AvgIR (95% CI)[b]	Percentiles						
			5	10	25	50	75	90	95
0-12	54	86 (66, 105)	17	27	38	72	94	165	221
13-24	174	94 (82, 106)	16	22	42	69	123	188	250
25-36	202	67 (59, 75)	10	19	28	53	82	140	178
37-48	209	63 (55, 72)	10	14	26	47	76	130	156
49-60	192	67 (59, 75)	11	15	32	53	86	122	182
61-72	208	52 (47, 57)	10	12	23	41	74	102	126
73-84	218	55 (48,62)	7	11	21	41	68	116	171

[a] Months
[b] AvgIR (95% CI) = arithmetic mean ingestion rate (95% confidence intervals)

After evaluating the available literature using the DQOs (see Attachment 1), the TRW Lead Committee recommends the age-specific soil-dust ingestion rates from scenario 3 of von Lindern et al. (2016) as the basis for revising the default age-specific soil-dust ingestion rates in the IEUBK model for CERCLA and RCRA corrective action risk assessments. As described above, this study was selected because it was determined that the approach employed by the authors most closely fits the DQOs established by the TRW Lead Committee for this effort; the study by von Lindern et al. (2016) provides the best estimate of age-specific soil and dust ingestion rates for use in the IEUBK model at CERCLA and RCRA 5,400 blood lead observations from nearly 2,340 individuals, yielding 2,176 records of blood/soil/dust lead concentrations over a 15 year timeframe with a >50% participation rate. In total, 271 samples (193 house dust samples, 73 yard soil samples and 5 quality control samples) sieved to 80 mesh (the particle size that adheres to a child's hand and most likely to be ingested by children) were analyzed for total lead and *in vitro* bioaccessibility. Community mean absolute bioavailability values (ABS) for unremediated yards soils and house dust, and site-wide ABS means for post-remediation soils were integrated into the database. Annual site-wide ABS means were calculated using a weighted average of bioavailable lead from remediated and unremediated yards. Aggressive LHIP education and intervention programs may have resulted in a temporary reduction in soil-dust intake rates by children, although this conclusion is not supported by multiple systematic reviews (Nussbaumer-Streit, Yeoh *et al.* 2016). Alternatively, elevated dust loadings caused by flooding and construction activities may have exacerbated soil-dust ingestion rates in the middle years of the BHSS cleanup. However, SEM and IEUBK model sensitivity analysis suggested that variation in calculated ingestion rates may be an artifact of the source partitions, nature of the data, or progression of the cleanup. The data collected at the BHSS best represents conditions at most CERCLA and RCRA corrective action sites during the Remedial

[5] Sum of Squared Error (SSE) is a statistical measure of the discrepancy between empirical values and the estimation model results. Lower SSE means better model prediction

Investigation and Feasibility Study phase of the remedial process. The soil-dust ingestion rates from Scenario 3 of von Lindern et al. (2016) results in soil-dust ingestion rates for the IEUBK model that are supported by other independent analyses, specifically the modeled estimates from Ozkaynak et al. (2011) and Wilson et al. (2013) (see Table 2).

UNCERTAINTY

Several studies published since 1994 were not applicable to this variable; for example, they contained only adult data, evaluated sediment ingestion rates rather than soil ingestion rates, or were review papers summarizing or reanalyzing other studies. Among recent publications that provide new data for young children (see Table 2), the TRW Lead Committee considered the study by von Lindern et al. (2016) to provide the relevant age-specific estimates of soil-dust ingestion rates for young children because it satisfied the most evaluation criteria (see Attachment 1) compared with the other studies. The TRW Lead Committee acknowledges that the data used by von Lindern et al. (2016) are site-specific and consideration was given to whether the Bunker Hill site was representative of other hazardous waste sites in the US. The data collected for that study were from an area of known lead contamination and could represent higher levels of lead than found in some areas. Also, as these data were collected from a site where EPA and other authorities were actively engaged in public outreach to reduce exposure, the soil-dust ingestion rates could be lower than in communities lacking public education efforts to limit exposure to soil and dust and thus may not necessarily be appropriate as an estimate for the general population, although the effectiveness of education has not been demonstrated in any of the Cochrane systematic reviews (Nussbaumer-Streit et al., 2016). Alternatively, elevated dust loadings caused by flooding and construction activities may have exacerbated soil-dust ingestion rates in the middle years of the BHSS cleanup. However, SEM and IEUBK model sensitivity analysis suggested that variation in calculated ingestion rates may be an artifact of the source partitions, nature of the data, or progression of the cleanup. The TRW Lead Committee notes that these conditions would likely occur at any CERCLA or RCRA corrective action site where USEPA was engaged in a risk assessment and therefore this limitation may be considered a strength (in that the data are possibly a better fit for the intended purpose than soil-dust ingestion rates collected from a naïve population would be). Furthermore, the information from this study is supported by two independent studies (Ozkaynak et al., 2011; Wilson et al., 2013). Thus, in the absence of other high-quality information the estimates from von Lindern et al. (2016) shown in table 3 are likely to be most representative of soil dust ingestion rates for young children at CERCLA and RCRA corrective action sites. The TRW Lead Committee did not, as part of this review process, define study acceptance criteria (aside from using the DQOs to guide the evaluation), conduct a systematic review, or conduct quality assurance activities on the published data to identify anomalies such as incorrect units, duplicate samples, etc. Consideration of additional studies published in the future could inform further refinement of age-specific soil and dust ingestion rates.

RECOMMENDATIONS FOR THE IEUBK MODEL

Results from several new studies provide information on average soil dust ingestion rates from children 0-84 months old. In general, these studies support an average combined soil/dust ingestion rate from 50 to 100 mg/day for children younger than 84 months old that could be applied to children residing near a CERCLA or RCRA corrective action site. For example, the two supporting studies Ozkaynak et al. (2011) and Wilson et al. (2013) result in values of 68 mg/day and 55-61 mg/day, respectively. These values are consistent with the recommended age-specific soil-dust ingestion rates for some of the similar age groupings from von Lindern et al.

(2016). The age-specific soil/dust ingestion recommended as the default soil/dust ingestion rates in the IEUBK model are shown in Table 4.

Table 4. Recommended change to soil/dust ingestion rates for use in the IEUBK model.

Age (years)	Age-specific, Average Soil/Dust Ingestion Rate (mg/day)	Basis for Age-Specific Value
0-1	86	Age-specific arithmetic mean ingestion rates based on the best fit model from von Lindern et al., 2016 and supported by modeled estimates from Ozkaynak et al., 2011; Wilson et al., 2013
1-2	94	
2-3	67	
3-4	63	
4-5	67	
5-6	52	
6-7	55	

Based on the evaluation described in this document and many factors specific to CERCLA and RCRA corrective action sites, these soil-dust ingestion rates are appropriate for assessing exposure at contaminated areas where the IEUBK model is frequently used. The TRW Lead Committee recommends updating the default *Age-Dependent Soil and Dust Ingestion Rate* variable in the IEUBK model to the age-specific average soil/dust ingestion rates based on von Lindern et al. (2016) (Table 3). These default values are considered appropriate for all applications of the IEUBK model where current and future residential scenarios are being assessed for CERCLA and RCRA corrective action risk assessment. The updated age-specific soil-dust ingestion rates are incorporated into the IEUBK model as shown in Figure 1.

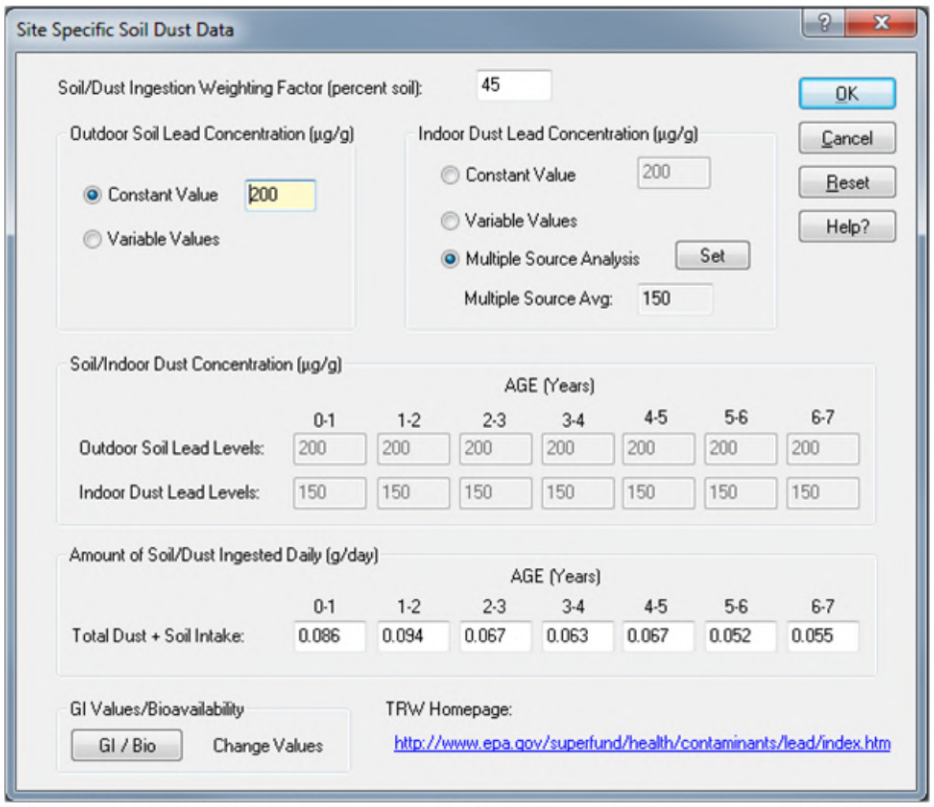

Figure 1. IEUBK Model Site Specific Soil Dust Data Entry Window with the Updated Soil/Dust Ingestion Rates.

IMPACT ON THE IEUBK MODEL PREDICTIONS

Using current IEUBK model (v.2) defaults for all parameters while implementing the proposed soil-dust rates will increase the preliminary remediation goal (PRG). Table 5 presents the updated estimates as well as the estimates from the previous analyses.

The PRGs in Table 5 are used to illustrate the impact when developing a screening level for lead in soil. As examples, the PRGs corresponding to PbBs of 10 µg/dL and 5 µg/dL are presented for illustrative purposes.

Table 5. Effects of changing the Soil-Dust Ingestion Rate (mg/day) in the IEUBK model

Study	Age Range	IRsd	P10 PRG[†]	P5 PRG[‡]
IEUBK Model (v1.1 build 11) default values	0-1 yr 1-2 yrs 2-3 yrs 3-4 yrs 4-5 yrs 5-6 yrs 6-7 yrs	85 mg/d 135 mg/d 135 mg/d 135 mg/d 100 mg/d 90 mg/d 85 mg/d	418 ppm	153 ppm
Proposed Update (based on von Lindern et al.	0-1 yr 1-2 yrs 2-3 yrs	86 mg/d 94 mg/d 67 mg/d	605 ppm	200 ppm

Study	Age Range	IRsd	P10 PRG[†]	P5 PRG[‡]
[2016]) using IEUBK v.2 default values	3-4 yrs 4-5 yrs 5-6 yrs 6-7 yrs	63 mg/d 67 mg/d 52 mg/d 55 mg/d		

[†] P10 PRG is the preliminary remediation goal for soil lead based on no more than 5% probability of exceeding a blood lead concentration of 10 µg/dL using IEUBK (v1.1. build 11) with default values for the 0-84 month age range.

[‡] P5 PRG is the preliminary remediation goal for soil lead based on no more than 5% probability of exceeding a blood lead concentration of 5 µg/dL using IEUBK (v1.1. build 11) with default values for the 0-84 month age range.

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ATTACHMENT 1. DATA QUALITY OBJECTIVES FOR THE SOIL-DUST INGESTION RATE LITERATURE EVALUATION

1. State the Problem
   - a. Current IEUBK Model soil-dust ingestion rates do not reflect recent studies, which have addressed many of the problems of previous studies
     - i. Age-specific rates
     - ii. Dust rates
     - iii. Confidence limits
     - iv. Analytical uncertainty
       1. CV
       2. Negative values
     - v. Study duration
       1. 5-20 days
     - vi. Untested tracer bioavailability assumptions
     - vii. Biomarkers
     - viii. Sampling uncertainty
       1. Particle size
       2. Dust
       3. Exposure area
     - ix. Number of subjects
     - x. Transparency
       1. Stanek & Calabrese Data was not shared, despite requests & assurances
     - xi. Consistency with other studies
       1. Multiple analyses of single datasets produce multiple estimates
     - xii. Potential Conflict (or appearance) of interest
       1. PRP funding

2. Identify the Decisions
   - a. IEUBK default
     - i. Age-specific values
     - ii. CTE values

3. Identify Inputs to the Decision
   - a. Literature search
   - b. Evaluation criteria
   - c. Peer review

4. Define the Study Boundaries
   - a. Timing
   - b. Schedule
   - c. Review process
   - d. Impacts to programs & agencies

FMI see https://www.epa.gov/fedfac/guidance-systematic-planning-using-data-quality-objectives-process

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Exhibit L

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October 6, 2021

Kelli Wetzel
Permit Writer, Air Quality Division
Idaho Department of Environmental Quality
1410 North Hilton
Boise, ID 83706

Subject: **Facility ID No. 085-00011, Perpetua Resources Idaho, Inc., Stibnite Gold Project –TAP Addendum Report**

Dear **Ms. Wetzel**:

Perpetual Resources, Inc. is providing the enclosed TAP Addendum report (Addendum) for the Stibnite Gold Project. The Addendum contains the hazardous air pollutant (HAP) and toxic air pollutant (TAP) emissions calculations provided in the PTC application and as requested by IDEQ, supplements that information to support IDEQ's responses to comments.

If you have any questions regarding this submittal, please contact me at 208-901-3053 or alan.haslam@perpetua.us.

Thank you for reviewing this information.

Sincerely,
Perpetua Resources

Alan Haslam
Vice President – Permitting

Enclosure: TAP Addendum Report

AIR SCIENCES INC.

DENVER • PORTLAND • LOS ANGELES

Stibnite Gold Project Permit to Construct Application

TAP Addendum

Prepared For:
PERPETUA RESOURCES IDAHO, INC.

PROJECT NO. 335-21-404
OCTOBER 5, 2021

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1.0 INTRODUCTION

On September 10, 2020 and February 18, 2021, the Idaho Department of Environmental Quality (IDEQ) provided notices for public comment on the Perpetua Resources Idaho, Inc. (hereafter referred to as Perpetua Resources) Stibnite Gold Project (SGP) complete application materials (Application), draft permit to construct (Draft PTC), and statement of basis (SOB). The public comments received included requests for additional information regarding hazardous air pollutant (HAP) and toxic air pollutant (TAP) emission estimates and modeling.

The purpose of this TAP Addendum (Addendum) is to provide that additional information to support IDEQ's responses to comments. The information provided in this Addendum confirms the following determinations made by Perpetua Resources and IDEQ at the time of the public notices:

1. The SGP is an area source for HAP emissions.

2. The SGP complies with the Idaho TAP provisions (IDAPA 58.01.01.210).

3. The SGP complies with the Idaho mercury rule (IDAPA 58.01.01.215).

This Addendum supplements information in the complete Application and supports those determinations highlighted during the public comment. Section 2.0 provides a description of the HAP/TAP emission calculations and source status. Section 3.0 provides a TAP emissions evaluation and modeling analysis, including TAP emission sources covered by IDAPA 58.01.01.210.20. Section 4.0 compares arsenic modeling analyses for actual and potential arsenic emissions. Section 5.0 provides a discussion of the emission reductions that demonstrate compliance with carcinogenic TAPs. Section 6.0 provides a Toxic Air Pollutant Reasonably Available Control Technology (T-RACT) analysis. Section 7.0 provides proposed permit conditions for demonstrating compliance with carcinogenic TAPs, and Section 8.0 provides a discussion of mercury emissions, including mercury emission sources covered by IDAPA 58.01.01.215.01.

IDAPA 58.01.01.210 and 215 reduce the information required from a PTC applicant and streamline the PTC review required by IDEQ in those circumstances where the HAP/TAP emissions are covered or addressed by federal regulations (IDAPA 58.01.01.210) or the mercury emissions are below a specific exemption threshold (IDAPA 58.01.01.215). Perpetua Resources referenced these rules in the Application and relied on these provisions to present a complete HAP/TAP emissions inventory that aligned with these rules. To support IDEQ's responses to public comments, IDEQ requested that Perpetua Resources expand its HAP/TAP analyses beyond the requirements of these rules and reconfirm compliance with TAP thresholds. This additional work reconfirms IDEQ's earlier findings that the SGP is an area source, and the proposed HAP/TAP emissions comply with IDAPA 58.01.01.210 and 215.

2.0 HAP/TAP EMISSIONS

During the two IDEQ public comment periods, IDEQ received comments regarding the following:

1. SGP source status for HAPs
2. Metal HAP/TAP emissions from fugitive dust
3. Metal HAP/TAP emissions from the autoclave and lime kiln processes
4. Fugitive emissions of hydrogen cyanide (HCN)

To support IDEQ's responses to comments and confirm the SGP area source status, the potential-to-emit (PTE)[1] HAP/TAP emission inventory in Appendix A of this Addendum contains emission calculations for all HAPs and TAPs emitted from all the SGP processes, including:

- Metals from mining fugitive dust emissions
- Metals from ore processing, ore concentration and refining, and lime, aggregate, and concrete production
- Antimony (Sb) emissions from the Sb drying and bagging circuit
- Sulfuric acid (H_2SO_4) and hydrogen sulfide (H_2S) from the autoclave, and hydrochloric acid (HCl) emissions and lime kiln
- Evaporative HCN from cyanide leaching and the tailings storage facility
- Various HAPs/TAPs from fuel storage and combustion
- Carbon disulfide emissions from the use of xanthate
- Evaporative mercury from mining surfaces

This HAP/TAP emission inventory was conducted for all 14 modeling scenarios evaluated in the Application. The emissions provided in Appendix A reflect the highest emissions scenario (HAP/TAP Emission Calculations – Scenario W3, 180,000 T/day).[2]

---

[1] PTE in this Addendum refers to the potential emissions after applying all proposed *air pollution control equipment and restrictions on hours of operation or on the type or amount of material combusted, stored or processed* per IDAPA 58.01.01.006.88 (i.e., PTE is the proposed permitted emissions).

[2] HAP/TAP Emission Calculations – Scenario W3, 180,000 T/day: HAP/TAP emissions based on the potential mining production rate of 180,000 tons per day (T/day) and the highest emissions scenario (Modeling Scenario W3).

2.1 Description of HAP Source Status

2.1.1 Controlled HAP Emissions

The controlled HAP emissions (PTE) from the SGP are below the major source thresholds; therefore, the SOB classified the SGP as an area source for HAP emissions. This is consistent with EPA's determination that all U.S. gold mine ore processing and production facilities are area sources.[3] The emissions inventory provided in Appendix A shows the total HAP emissions are 3.67 tons per year (ton/yr) for a single HAP and 12.56 ton/yr for all the HAPs combined for the highest emissions scenario (Modeling Scenario W3). The major source levels are 10 ton/yr for a single HAP and/or 25 ton/yr for all the HAPs combined.

2.1.2 Uncontrolled HAP Emissions

Uncontrolled HAP emissions are estimated to exceed 25 ton/yr, combined; therefore, to support the area source designation, Perpetua Resources committed to operational limitations and emission controls in the Application that achieve area source status.

2.2 Description of HAP/TAP Emission Calculations

This section provides a brief description of the methods used to calculate the HAP/TAP emissions provided in Appendix A. The references used for the HAP/TAP calculations were presented in the Application. Any new references are provided in this section.

2.2.1 Metal Emissions from Mining Fugitive Dust

The metal HAP/TAP emissions from fugitive dust generated by mining activities (drilling, blasting, excavating, hauling, etc.) were calculated by multiplying the HAP/TAP-specific median metal concentration in the ore[4] by the activity-specific total particulate matter (PM) emissions. The median metal concentrations were derived from over 55,000 core samples taken primarily from the more mineralized zones of the SGP pits (i.e., in and around gold ore deposits).

This emissions inventory does not reflect any of the emission reductions described in Section 5.0 for carcinogenic TAP compliance.

[3] *EPA recently gathered data and evaluated emissions of other HAP, including cyanide and non-mercury metals. The data indicate that the gold mining processing and production category consists of only area sources (i.e., facilities that emit less than ten tons per year of any one HAP and less than 25 tons per year of any combination of HAP)* (EPA 2010).

[4] Iron (Fe) and selenium (Se) were not included in the Application because the concentrations of these metals were similar to typical crustal abundance levels. In response to comments on HAPs/TAPs emissions, the concentrations of these metals (18,200 ppm of Fe and 0.4 ppm of Se) are provided (Midas Gold 2020).

2.2.2 Metal Emissions from Ore Processing and Lime/Aggregate Production

2.2.2.1 Crushing, Screening, and Material Handling

The metal HAP/TAP emissions generated by process and production sources (the crushing, screening, and handling of ore, limestone, lime, and aggregate) were calculated by multiplying the PM emissions from these sources by the median concentration of metals in the ore, limestone, lime, or aggregate. The ore median metal concentrations are discussed in Section 2.2.1. The limestone, lime, and aggregate metal concentrations are provided in Table 1.

The limestone metal concentrations were measured from core hole samples through the middle marble formation in the proposed limestone quarry's footprint. These rock samples were specifically analyzed to assess the formation as a viable limestone source. As a conservative estimate, the limestone metal profile was also used for aggregate production.

Table 1. Metal TAP Concentrations for Limestone and Lime

CAS	TAP Name	Concentration (ppm) [1]
7440-38-2	Arsenic	23
7440-41-7	Beryllium	0.8
7440-43-9	Cadmium	0.25
7440-48-4	Cobalt	4
7440-47-3	Chromium	15
7439-97-6	Mercury	0.02
7439-96-5	Manganese	236.5
7440-02-0	Nickel	5
7439-92-1	Lead	3
7440-36-0	Antimony	2.5
7723-14-0	Phosphorus	130
7440-22-4	Silver	0
7429-90-5	Aluminum	22,600
7440-39-3	Barium	145
1317-65-3	Calcium Carbonate [2]	274,500
1305-78-8	Calcium Oxide [3]	740,000
7440-50-8	Copper	5
7439-89-6	Iron	10,350
7439-98-7	Molybdenum	0.5
7440-28-0	Thallium	5
7440-61-1	Uranium	5

CAS	TAP Name	Concentration (ppm) [1]
7440-62-2	Vanadium	15.5
7440-33-7	Tungsten	5
7440-66-6	Zinc	18

[1] Median of 98 samples of the SGP limestone material (M3 2018).
[2] Calcium carbonate ($CaCO_3$) is used for limestone processing.
[3] Calcium oxide (CaO) is used for lime processing. 40% to 74% CaO (NLA 2007).

2.2.2.2 Lime Kiln

The non-mercury metal HAP/TAP emissions from the lime kiln were calculated by multiplying the PM emissions by the median concentration of metals in the limestone shown in Table 1. The mercury emissions from the lime kiln were conservatively estimated by assuming all mercury in the limestone feed is volatilized and emitted.

2.2.2.3 Autoclave

Mercury emissions from the SGP autoclave were based on the SysCAD modeling of the SGP autoclave performed by Perpetua Resources' engineering contractor: M3 Engineering. This modeling predicted 0.0105 grams per second of mercury emissions exiting the autoclave mercury control system, which is comprised of a venturi scrubber, a vent gas cleaning tower, a vent gas steam condensation tower, and one or more sulfur-impregnated activated carbon filters.

The non-mercury metal HAP/TAP emissions from the autoclave mercury control system are expected to be less than the mercury emissions because non-mercury HAP/TAP emissions are only particulates and more easily controlled by the emissions control system. Mercury emissions move through the control system as both particulate and gas. For this review, the non-mercury HAP/TAP emissions were conservatively assumed to be equal to the mercury emissions.

2.2.2.4 EW Cells, Pregnant Solution Tank, Retort, Furnace, and Carbon Kiln

Mercury emissions from the SGP electrowinning (EW) cells, pregnant solution tank, mercury retort, induction melting furnace, and carbon regeneration kiln were calculated based on stack test data from similar sources utilizing similar mercury control systems at Nevada gold mines.

The non-mercury metal HAP/TAP emissions exiting these mercury control systems are expected to be less than the mercury emissions because non-mercury HAP/TAP emissions are only particulates and more easily controlled by the emissions control system. Mercury emissions move through the control system as both particulate and gas. For this review, the non-mercury HAP/TAP emissions were conservatively assumed to be equal to the respective mercury emissions.

2.2.2.5 Antimony Dryer and Dry Bagging

The Sb circuit proposed in the Application was replaced with a new dewatering/packaging circuit. The new circuit eliminates the potential for metal emissions from dust and mercury evaporation emissions from concentrate heating. Instead, the Sb concentrate will be dewatered using a filter press and then bagged as a wet (damp) product. There are no HAP/TAP emissions associated with this new circuit.

2.2.3 Metal Emissions from Concrete Production

The metal HAP/TAP emissions from concrete production were calculated using EPA emission factors from AP-42 Section 11.12, Concrete Batching. This section provides controlled emission factors for cement silo filling and central mix batching. There are no emission factors for cement silo unloading. Therefore, the cement silo filling factors were used for cement silo unloading as a conservative estimate.

Chromium (VI) percentages of the total chromium were provided by IDEQ for cement silo filling and central mix batching. These percentages were used to calculate chromium (VI) emissions from cement silo filling and unloading and central mix batching.

There are no HAP/TAP emission factors for the dust generated from aggregate handling in the concrete production process. As a conservative estimate, the limestone metals profile provided in Table 1 of Section 2.2.2.1 was used to estimate the HAP/TAP emissions from aggregate handling.

2.2.4 H_2SO_4 and H_2S Emissions from the Autoclave

H_2SO_4 and H_2S emissions from the SGP autoclave were calculated based on source test data from similar autoclaves at gold mines in Nevada.

2.2.5 HCl Emissions from the Lime Kiln

The HCl emissions from the lime kiln were calculated using the HCl emission factor obtained from EPA's EPCRA Section 313 Guidance for Reporting Hydrochloric Acid (EPA 1999b).

2.2.6 HCN Emissions from Cyanide Leaching and Tailings Storage Facility

The evaporative HCN emissions from cyanide leaching and the tailings storage facility were calculated using the flux methodology developed by EPA and the Nevada Mining Association as part of the 40 CFR 63 rule-making process. The methodology is based on empirical measurements at several gold mines in Nevada taken under the direction of EPA. Numerous gold mines in several states have used this method since its development in 2010.

2.2.7 HAP/TAP Emissions from Fuel Storage and Fuel Combustion

HAP/TAP emissions from fuel combustion (propane and diesel) were calculated using fuel combustion rates and the applicable EPA AP-42 emission factors.

HAP/TAP emissions from fuel storage (gasoline) were calculated from the tank volatile organic compound (VOC) emissions multiplied by the weight percentages of HAP/TAP in the fuel. The percentages were obtained from EPA's EPCRA Section 313 Industry Guidance Metal Mining Facilities, Table 3-8 for gasoline (EPA 1999a).

2.2.8 Carbon Disulfide Emissions from Xanthate

Carbon disulfide (CS_2) emissions from potassium amyl xanthate (PAX) use were calculated based on the decomposition of xanthate to CS_2 gas. The decomposition rate was determined from published experimental data.

2.2.9 Evaporative Mercury Emissions from Mining Surfaces

Mercury can evaporate from rock surfaces in pits, tailings facilities, development rock storage facilities, and stockpiles. The rate of mercury evaporation (or flux) is a function of the mercury concentration in the material. Mercury flux rates and concentration measurements taken at a gold mine in Nevada were adjusted for the SGP mercury concentrations to estimate mercury flux emissions from the SGP pits, tailings facility, development rock storage facilities, and ore stockpiles.

3.0 TAP ANALYSIS

A complete inventory of the PTE TAP emissions is provided in Appendix A, as discussed in Section 2.0. Appendix A also identifies the applicability of IDAPA 58.01.01.210.20. According to IDAPA 58.01.01.210.20, no further demonstration of compliance with the TAP provisions is required to obtain a PTC for new source emissions, such as the SGP, from:

a. The equipment or activities covered by a New Source Performance Standards (NSPS) or National Emissions Standards for Hazardous Air Pollutants (NESHAP); or

b. The source category of equipment or activities addressed by a NSPS or NESHAP even if the specific equipment or activity is not subject to compliance requirements under the federal rule.

After applying IDAPA 58.01.01.210.20 as described in Section 3.1, the remaining TAP emissions are subject to further compliance demonstration and are compared to the screening emission levels (EL) described in Section 3.3. TAP emissions that below the screening EL, require no further demonstration of compliance with the TAP provisions. TAP emissions above the screening EL require modeling, as described in Section 3.4. To identify the TAPs subject to review, Section 3.2 provides a comparison of the metals analyzed in the SGP ore, development rock, and limestone to the TAPs listed in IDAPA 58.01.01.585 and IDAPA 58.01.01.586.

3.1 Equipment or Activities Covered or Addressed by NESHAP or NSPS

In accordance with IDAPA 58.01.01.210.20, the equipment and activities at the SGP that are either covered or addressed by NESHAP or NSPS are discussed in the following subsections. TAPs emitted from these sources that are also HAPs require no further evaluation to demonstrate compliance with the TAP provisions. TAP emissions from these sources that are not HAPs require additional review to demonstrate compliance with the TAP provisions.

3.1.1 NESHAP Subpart ZZZZ

40 CFR 63, Subpart ZZZZ, NESHAP for Stationary Reciprocating Internal Combustion Engines covers HAP emissions from the SGP emergency generators and fire pump (Source ID No. EDG1, EDG2, EDG3, and EDFP). IDAPA 58.01.01.210.20(a) applies to Source ID No. EDG1, EDG2, EDG3, and EDFP.

3.1.2 NESHAP Subpart AAAAA

40 CFR 63, Subpart AAAAA, NESHAP for Lime Manufacturing Plants addresses HAP emissions from the SGP lime manufacturing sources (Source ID No. LS12, LK, LS-L/U, LCR, and LKC).[5] IDAPA 58.01.01.210.20(b) applies to Source ID No. LS12, LK, LS-L/U, LCR, and LKC.

3.1.3 NESHAP Subpart CCCCCC

40 CFR 63, Subpart CCCCCC, NESHAP for Source Category: Gasoline Dispensing Facilities covers the SGP gasoline storage tanks (Source ID No. TG1 and TG2). IDAPA 58.01.01.210.20(a) applies to Source ID No. TG1 and TG2.

3.1.4 NESHAP Subpart EEEEEEE

40 CFR 63, Subpart EEEEEEE, NESHAP: Gold Mine Ore Processing and Production Area Source Category covers HAP emissions from the SGP autoclave (Source ID No. AC) and the EW cells, pregnant solution tank, mercury retort, induction melting furnace, and carbon regeneration kiln (Source ID No. EW, MR, MF, and CKD). IDAPA 58.01.01.210.20(a) applies to Source ID No. AC, EW, MR, MF, and CKD.

The NESHAP source category addresses HAP emissions from mining activities, specifically fugitive dust-generating activities (drilling, blasting, excavating, hauling, etc.), explosives use and storage (Source ID No. PS), cyanide leaching (Source ID No. CIP Leach 1-4, CIL 1-6, CIP 1-6, and CN Detox 1-2), tailings storage, ore processing (Source ID No. OC1-13), ore processing heating (Source ID No. ACB, CKB, PV, and HS), and the ore processing reagent use of PAX and sodium cyanide (NaCN). The NESHAP source category is defined as "*Gold Ore Mining ..., NAICS code 212221, Establishments primarily engaged in developing the mine site, mining, and/or beneficiating (i.e., preparing) ores valued chiefly for their gold content. Establishments primarily engaged in transformation of the gold into bullion or doré bar in combination with mining activities are included in this industry*" (EPA 2011b). EPA's rule-making docket (Docket ID EPA-HQ-OAR-2010-0239) provides documents evaluating HAP metal emissions from mining fugitive dust, HCN emissions from cyanide leaching, and downwind HCN ambient concentrations.[6]

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[5] NESHAP Subpart AAAAA defines the affected source as follows: *each lime kiln and its associated cooler, each individual PSH [processed stone handling] system. The individual types of emission units in a PSH system are conveying system transfer points, bulk loading or unloading systems, screening operations, bucket elevators, and belt conveyors-if they follow the processed stone storage bin or storage pile in the sequence of PSH operations. The materials processing operations (MPO) associated with lime products (such as quicklime and hydrated lime), lime kiln dust handling, quarry or mining operations, limestone sizing operations, and fuels are not subject to today's final NESHAP. Processed stone handling operations are further distinguished in the final NESHAP as follows: (1) whether their emissions are vented through a stack, (2) whether their emissions are fugitive emissions, (3) whether their emissions are vented through a stack with some fugitive emissions from the partial enclosure, and/or (4) whether the source is enclosed in a building* (69 Fed. Reg. 394, 397 (January 5, 2004)).

[6] EPA-HQ-OAR-2010-0239-0132, *Profile of the Metal Mining Industry;* EPA-HQ-OAR-2010-0239-0157, *Recommended Methodology for Quantification of Fugitive Dust Metals Emissions from Mining Activities for Title V Applicability;* EPA-HQ-OAR-2010-0239-0102, *QAPP Comprehensive Air Emissions Testing for Hydrogen Cyanide;* EPA-HQ-OAR-2010-0239-0134, -0135 -0136 -0137 -0161 -0162 -0378, *Meteorological and Hydrogen Cyanide (HCN) Fence Line Monitoring* reports.

In response to public comments, this Addendum applies IDAPA 58.01.01.210.20(a) to those sources of HAP emissions at the SGP that are covered by Subpart EEEEEEE. This Addendum provides further evaluation of the sources of HAP emissions that are addressed by the NESHAP per IDAPA 58.01.01.210.20(b) – the mining emissions.[7]

3.1.5 NSPS Subpart LL

40 CFR 60, Subpart LL, Standards of Performance for Metallic Mineral Processing Plant covers the SGP ore processing (Source ID No. OC1-13). IDAPA 58.01.01.210.20(a) applies to Source ID No. OC1-13.

3.1.6 NSPS Subpart OOO

40 CFR 60, Subpart OOO, Standards of Performance for Nonmetallic Mineral Processing Plants covers the SGP limestone processing sources (Source ID LS1-11 and LSBM), aggregate production (Source ID No. PCSP1 and PCSP2), and aggregate handling in the concrete production process (Source ID No. CA-L/U). IDAPA 58.01.01.210.20(a) applies to Source ID No. LS1-11, LSBM, PCSP1, PCSP2, CA-L/U.

3.2 Metals Review for TAP Provisions Applicability

Table 2 provides a comparison of the metals analyzed in the SGP ore, development rock, and limestone to the TAPs listed in IDAPA 58.01.01.585 and IDAPA 58.01.01.586.

Table 2. Metals Comparison to IDAPA 58.01.01.585-586 TAPs

Metal			TAP		
CAS	**Name**	**HAP?**	**CAS**	**Name**	**Is the Metal a TAP?**
7440-57-5	Gold	No	7440-57-5	Not listed	No
7440-22-4	Silver	No	7440-22-4	Silver - Including metal soluble compounds, as Ag	Yes, same CAS Yes, similar form No
7429-90-5	Aluminum	No	7429-90-5	Aluminum, including: Metal & Oxide Pyro powders Soluble salts	Yes, same CAS Yes, similar form No No
7440-36-0	Antimony	Yes	7440-36-0	Antimony & compounds, as Sb (handling & use)	Yes, same CAS
7440-38-2	Arsenic	Yes	7440-38-2	Arsenic compounds	Yes, same CAS
7440-39-3	Barium	No	7440-39-3	Barium, soluble compounds, as Ba	Yes, same CAS
7440-41-7	Beryllium	Yes	7440-41-7	Beryllium & compounds	Yes, same CAS

[7] A demonstration of compliance that applied IDAPA 58.01.01.210.20(a) and (b) to the sources of HAP emissions covered and addressed by the NESHAP is presented in the SOB (February 18, 2021).

Metal			TAP		
CAS	**Name**	**HAP?**	**CAS**	**Name**	**Is the Metal a TAP?**
7440-69-9	Bismuth	No	1304-82-1	Bismuth telluride undoped Bismuth telluride if selenium doped	No, Bi compounds are expected to be bismuthinite ($Bi2S_3$) and bismite (Bi_2O_3) [1]
7440-43-9	Cadmium	Yes	7440-43-9	Cadmium and compounds	Yes, same CAS
7440-70-2	Calcium	No	1317-65-3 156-62-7 1305-62-0 1305-78-8 1344-95-2 13397-24-5	Calcium carbonate Calcium cyanamide Calcium hydroxide Calcium oxide Calcium silicate (synthetic) Calcium sulfate	Yes [2] No, different CAS No, different CAS Yes [2] No, different CAS No, different CAS
7440-47-3	Chromium	Yes	7440-47-3 7440-47-3 16065-83-1 18540-29-9	Chromium metal, including: Chromium (II) compounds, as Cr Chromium (III) compounds, as Cr Chromium (VI) & compounds, as Cr+6	Yes, same CAS Yes, same CAS No, different CAS No, different CAS
7440-48-4	Cobalt	Yes	10210-68-1 16842-03-8 7440-48-4	Cobalt carbonyl, as Co Cobalt hydro carbonyl, as Co Cobalt metal, dust, and fume	No, different CAS No, different CAS Yes, same CAS
7440-50-8	Copper	No	7440-50-8	Copper: Fume Dusts & mists, as Cu	Yes, same CAS No Yes, similar form
7440-55-3	Gallium	No		Not listed	No
7439-89-6	Iron	No	1309-37-1 13463-40-6 7439-89-6	Iron oxide fume (Fe2O3), as Fe Iron pentacarbonyl, as Fe Iron salts, soluble, as Fe	No, different CAS No, different CAS Yes, same CAS
7439-91-0	Lanthanum	No		Not listed	No
7440-09-7	Potassium	No	1310-58-3	Potassium hydroxide	No, different CAS
7439-92-1	Lead	Yes		Not listed	No, criteria pollutant
7439-95-4	Magnesium	No	1309-48-4	Magnesium oxide fume	No, different CAS
7439-96-5	Manganese	Yes	7439-96-5	Manganese, as Mn, including: Dust & compounds Fume	Yes, same CAS Yes, similar form No
7439-97-6	Mercury	Yes		Not listed	No, regulated by mercury rules
7439-98-7	Molybdenum	No	7439-98-7	Molybdenum, as Mo, including: Soluble compounds Insoluble compounds	Yes, same CAS No Yes, similar form
7440-02-0	Nickel	Yes	7440-02-0 12035-72-2 7440-02-0	Nickel Nickel Subsulfide Nickel Refinery Dust	No, see Ni refinery dust No, different CAS Yes, same CAS and form

Metal			TAP		
CAS	**Name**	**HAP?**	**CAS**	**Name**	**Is the Metal a TAP?**
7723-14-0	Phosphorus	Yes	7723-14-0	Phosphorus	Yes, same CAS
			10025-87-3	Phosphorus oxychloride	No, different CAS
			10026-13-8	Phosphorus penta-chloride	No, different CAS
			1313-80-3	Phosphorus penta-sulfide	No, different CAS
			1314-56-3	Phosphorus pentoxide (ID)	No, different CAS
			7719-12-2	Phosphorus trichloride	No, different CAS
7782-49-2	Selenium	Yes	7782-49-2	Selenium and compounds, as Se	Yes, same CAS
7440-23-5	Sodium	No	26628-22-8	Sodium azide (CL)	No, different CAS
			7631-90-5	Sodium bisulfite	No, different CAS
			136-78-7	Sodium 2,4-dichloro-phenoxyethyl sulfate; see Sesone	No, different CAS
			62-74-8	Sodium fluoroacetate	No, different CAS
			1310-73-2	Sodium hydroxide	No, different CAS
			7681-57-4	Sodium metabisulfite	No, different CAS
7440-20-2	Scandium	No		Not listed	No
7440-24-6	Strontium	No		Not listed	No
7440-28-0	Thallium	No	7440-28-0	Thallium, soluble compounds, as Tl	Yes, same CAS
7440-29-1	Thorium	No		Not listed	No
7440-32-6	Titanium	No		Not listed	No
7440-33-7	Tungsten	No	7440-33-7	Tungsten, including: Insoluble compounds Soluble compounds	Yes, same CAS Yes, similar form No
7440-61-1	Uranium	No	7440-61-1	Uranium (natural) soluble & insoluble compounds, as U	Yes, same CAS
7440-62-2	Vanadium	No	1314-62-1	Vanadium, as V_2O_5 Respirable dust & fume	No, different CAS [3]
			12604-58-9	Ferrovanadium dust	No, different CAS
7440-66-6	Zinc	No	7440-66-6	Zinc metal (ID)	Yes, same CAS
			7646-85-7	Zinc chloride fume	No, different CAS
			1314-13-2	Zinc oxide fume	No, different CAS
			1314-13-2	Zinc oxide dust	No, different CAS

[1] Over 95% of the samples were at or below the detection limit for Bismuth of 2 ppm. Limited sampling for tellurium indicates 90% of the samples are below 0.5 ppm. Mineralogical studies have not identified telluride minerals as a significant phase in the deposits. Based on these low levels and deposit mineralogy, no significant bismuth telluride is expected to be found in the ore body or development rock.

[2] Although the CAS numbers do not match, the calcium in the ore, limestone, and aggregate is expected to be in the form of calcium carbonate ($CaCO_3$). For lime, the calcium will be in the form of calcium oxide (CaO).

[3] The principal vanadium mineral in Idaho shale-hosted vanadium deposits is metahewettite ($CaV_6O_{162} \bullet H2O$) (USGS n.d.). Although not a TAP, vanadium in the ore, limestone, and aggregate is conservatively assumed to be V_2O_5 for the purpose of the TAP evaluation included in this HAP/TAP Addendum.

3.3 Screening Level Analysis of TAP Emissions

As discussed in Section 2.0, the highest TAP emissions scenario is Model Scenario W3, that estimates emissions from a potential throughput of 180,000 T/day. Table A in Appendix A

provides a summary of the TAP emissions for Model Scenario W3, identifies whether the sources are covered or addressed by IDAPA 58.01.01.210.20(a) or (b) (Section 3.1), and notes the TAP screening EL. TAPs that exceed the screening EL are highlighted in Table A. These TAPs require further demonstrations of compliance with the applicable ambient air concentration (AAC) and are listed in Table 3 below.

Table 3. TAPs Exceeding the Screening Emission Level

CAS	TAP Name	Carcinogenic	SGP PTE (lb/hr) [1]	Screening EL (lb/hr)
7429-90-5	Aluminum	No	58.50	0.667
7440-38-2	Arsenic	Yes	0.544	0.0000015
7440-39-3	Barium	No	0.659	0.033
7440-41-7	Beryllium	Yes	0.00261	0.000028
7440-43-9	Cadmium	Yes	0.000435	0.0000037
1317-65-3	Calcium Carbonate	No	13.65	0.667
1305-78-8	Calcium Oxide	No	0.696	0.133
592-01-8	Cyanide	No	0.453	0.333
50-00-0	Formaldehyde	Yes	0.00189	0.00051
7439-89-6	Iron	No	15.04	0.067
7439-96-5	Manganese	No	0.244	0.067
7440-02-0	Nickel	Yes	0.00169	0.000027
7723-14-0	Phosphorus	No	0.530	0.007
7664-93-9	Sulfuric Acid	No	2.03	0.067
7440-28-0	Thallium	No	0.00867	0.007
7440-62-2	Vanadium	No	0.0237	0.003

[1] Model Scenario W3, 180,000 T/day Emissions

3.4 Modeling of TAP Emissions

To maintain consistency with the National Ambient Air Quality Standards (NAAQS) compliance analyses reviewed by IDEQ, the TAP modeling was performed using the same IDEQ-approved datasets and model versions described in the SOB from February 18, 2021. TAP modeling was conducted for the 14 modeling scenarios consistent with the NAAQS analyses. Scenario W5 was eliminated from the arsenic modeling, as discussed in Section 3.4.5.

3.4.1 Meteorological Data and Deposition

The meteorological dataset used for the TAP modeling was processed using EPA's Qian and Venkatram (Q&V) meteorological processing method. This method, which does not use the BULKRN keyword, is approved by EPA as a default method.

As discussed in the PTC application, EPA evaluated the performance of the model with the Q&V processed meteorological dataset as part of its model approval determination. This evaluation quantified the bias between the modeled concentrations and the actual observed concentrations. The results of EPA's evaluation showed a conservative bias of the model to overpredict concentrations by a factor of 1.41 to 3.21 (Air Sciences 2020, A-8 of Attachment A). Therefore, the meteorological dataset used in the TAP modeling is expected to predict conservatively high concentrations.

The particulate deposition parameters used in the NAAQS compliance analysis were derived for PM_{10} and $PM_{2.5}$. See Tables 24 and 25 in the SOB from February 18, 2021. Dust-related metal TAP emissions include total particulates (all size fractions of PM up to PM_{30}). Therefore, the deposition parameters for PM were calculated using the same methodology and EPA references used for PM_{10} and $PM_{2.5}$ in the NAAQS compliance analysis. The PM deposition parameters are provided in Table 4.

Table 4. PM Deposition Parameters by Source Category

Source Category	Parameter	PM				
		Bin 1	Bin 2	Bin 3	Bin 4	Bin5
Haul Roads	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.02	0.23	0.75	--	--
	Mass Mean Diameter (µm)	2.50	10.00	30.00	--	--
	Density (g/cm³) (DR average of YP, HF, WE)	2.46	2.46	2.46	--	--
Material Handling (Ore, DR, Limestone)	Bin Upper Diameter (µm)	2.50	5.00	10.00	30.00	--
	Mass Fraction	0.07	0.20	0.20	0.53	--
	Mass Mean Diameter (µm)	2.50	5.00	10.00	30.00	--
	Density (g/cm³) (Ore)	Pit-specific, see Table 5				
	Density (g/cm³) (DR)	Pit-specific, see Table 5				
	Density (g/cm³) (Limestone)	1.09	1.09	1.09	1.09	--
Baghouses	Bin Upper Diameter (µm)	2.50	6.00	10.00	30.00	--
	Mass Fraction	0.25	0.45	0.20	0.10	--
	Mass Mean Diameter (µm)	2.50	6.00	10.00	30.00	--
	Density (g/cm³) (Ore)	Pit-specific, see Table 5				
Diesel Engines	Bin Upper Diameter (µm)	1.00	2.50	6.00	10.00	30.00
	Mass Fraction	0.82	0.08	0.03	0.03	0.04
	Mass Mean Diameter (µm)	1.00	2.50	6.00	10.00	30.00
	Density (g/cm³) (Diesel Combustion)	1.00	1.00	1.00	1.00	1.00
Heaters and Boilers	Bin Upper Diameter (µm)	1.00	2.50	6.00	10.00	30.00
	Mass Fraction	0.23	0.22	0.25	0.09	0.21
	Mass Mean Diameter (µm)	1.00	2.50	6.00	10.00	30.00
	Density (g/cm³) (Propane Combustion)	1.24	1.24	1.24	1.24	1.24
	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--

Source Category	Parameter	PM				
		Bin 1	Bin 2	Bin 3	Bin 4	Bin5
Lime Loading and Unloading (Quick, Pebble)	Mass Fraction	0.05	0.29	0.66	--	--
	Mass Mean Diameter	2.50	10.00	30.00	--	--
	Density (g/cm^3) (Quick)	0.44	0.44	0.44	--	--
	Density (g/cm^3) (Pebble)	0.96	0.96	0.96	--	--
Lime Unloading (Quick, Pebble)	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.09	0.49	0.42	--	--
	Mass Mean Diameter (µm)	2.50	10.00	30.00	--	--
	Density (g/cm^3) (Quick)	0.44	0.44	0.44	--	--
	Density (g/cm^3) (Pebble)	0.96	0.96	0.96	--	--
Cement and Aggregate Loading and Unloading	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.05	0.29	0.66	--	--
	Mass Mean Diameter (µm)	2.50	10.00	30.00	--	--
	Density (g/cm^3) (Cement)	1.44	1.44	1.44	--	--
	Density (g/cm^3) (Aggregate)	1.28	1.28	1.28	--	--
Prill Loading and Unloading	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.05	0.30	0.65	--	--
	Mass Mean Diameter (µm)	2.50	10.00	30.00	--	--
	Density (g/cm^3) (Prill)	0.84	0.84	0.84	--	--
Refining Processes	Bin Upper Diameter (µm)	1.00	2.50	6.00	10.00	30.00
	Mass Fraction	0.72	0.10	0.07	0.03	0.08
	Mass Mean Diameter (µm)	1.00	2.50	6.00	10.00	30.00
	Density (g/cm^3) (Diesel Combustion)	1.00	1.00	1.00	1.00	1.00
Portable Crushing and Screening Plant	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.05	0.32	0.63	--	--
	Mass Mean Diameter (µm)	2.50	10.00	30.00	--	--
	Density (g/cm^3) (DR average of YP, HF, WE)	2.46	2.46	2.46	--	--
Lime Kiln and Ball Mill	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--
	Mass Fraction (Kiln)	0.27	0.28	0.45	--	--
	Mass Fraction (Ball Mill)	0.30	0.54	0.16	--	--
	Mass Mean Diameter (µm)	2.50	10.00	30.00	--	--
	Density (g/cm^3)	1.09	1.09	1.09	--	--
Blasting and Drilling	Bin Upper Diameter (µm)	2.50	10.00	30.00	--	--
	Mass Fraction	0.03	0.49	0.48	--	--
	Mass Mean Diameter (µm)	2.50	10.00	30.00	--	--
	Density (g/cm^3) (Ore or DR)	Pit-specific, see Table 5				
Dozing	Bin Upper Diameter (µm)	2.50	10.00	15.00	30.00	--
	Mass Fraction	0.11	0.08	0.06	0.75	--
	Mass Mean Diameter (µm)	2.50	10.00	15.00	30.00	--
	Density (g/cm^3) (Waste)	Pit-specific, see Table 5				

Table 5. Pit-Specific Ore and DR Densities for Deposition

Pit	Material	Density (g/cm^3)
YP	Ore	2.59
BT	Ore	2.00
HF	Ore	2.59
WE	Ore	2.68
YP	DR	2.48
BT	DR	2.00
HF	DR	2.34
WE	DR	2.57
Average (YP, HF, WE)	DR	2.46

3.4.2 Modeling for Non-Carcinogenic TAPs

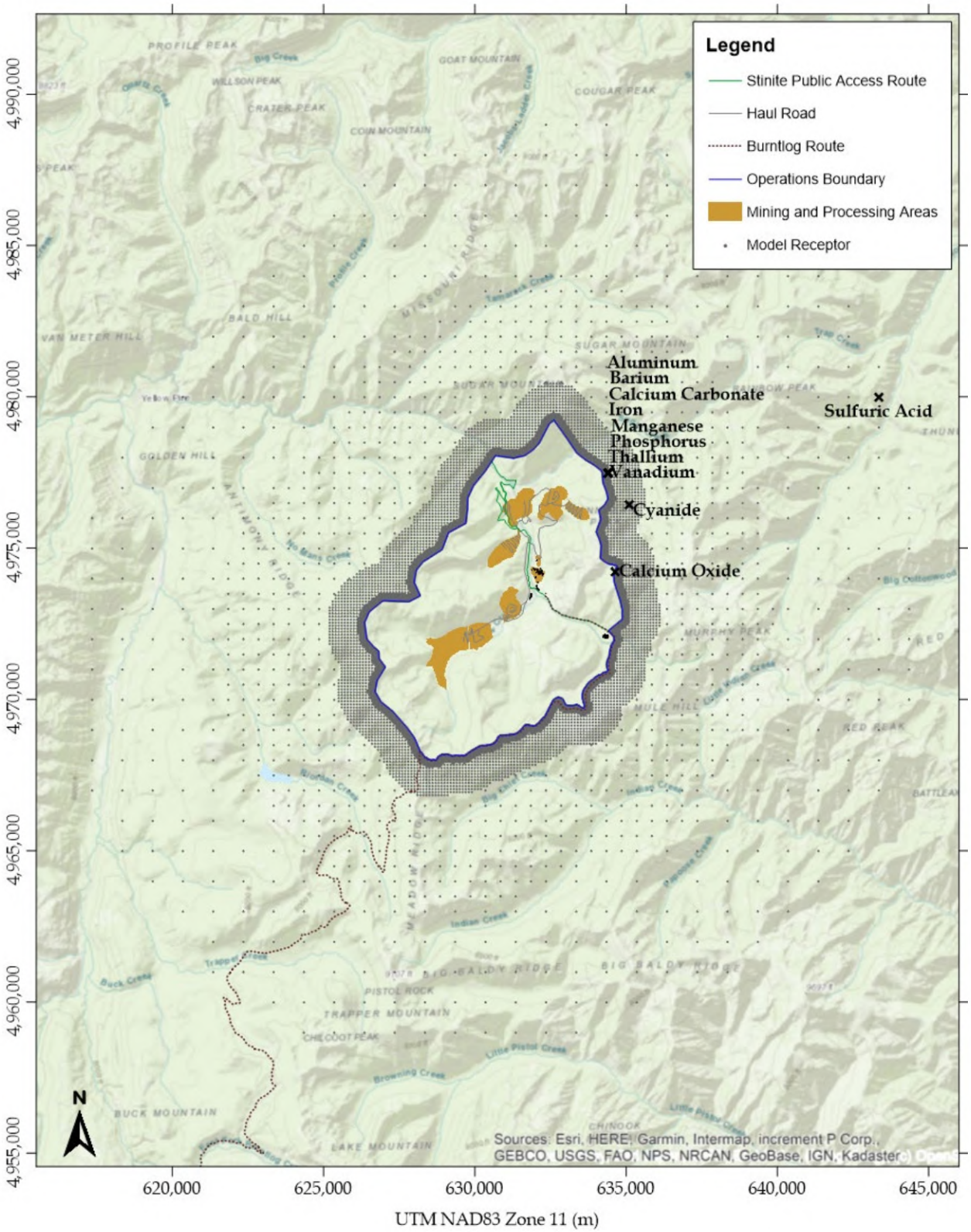
The non-carcinogenic TAPs subject to the AACs per IDAPA 58.01.01.585 were modeled at the emission levels shown in Table 3 above. The maximum 24-hour modeled concentration for each of the 14 modeling scenarios demonstrates compliance with the applicable AAC, as summarized in Table 6.

Table 6. Compliance Demonstration for Non-Carcinogenic TAPs

CAS	TAP Name	Highest Model Scenario	SGP Maximum 24-hr Concentration (µg/m³)	AAC (µg/m³)	TAP Compliance
7429-90-5	Aluminum	W5	6.17	500	Yes
7440-39-3	Barium	W5	0.07	25	Yes
1317-65-3	Calcium Carbonate	W5	1.22	500	Yes
1305-78-8	Calcium Oxide	ALL	0.15	100	Yes
592-01-8	Cyanide	ALL	0.20	250	Yes
7439-89-6	Iron	W5	1.58	50	Yes
7439-96-5	Manganese	W5	0.03	250	Yes
7723-14-0	Phosphorus	W5	0.06	5	Yes
7664-93-9	Sulfuric Acid	ALL	0.41	50	Yes
7440-28-0	Thallium	W5	0.001	5	Yes
7440-62-2	Vanadium	W5	0.002	2.5	Yes

The modeled emissions for each modeling scenario and source are provided in Appendix B. The modeled concentration per modeling scenario is provided in Appendix C. The predicted locations of the maximum concentrations for each non-carcinogenic TAP are presented in Figure 1.

Figure 1. Non-Carcinogenic Maximum TAP Concentration (µg/m³) Locations



3.4.3 Modeling Carcinogenic TAPs

The carcinogenic TAPs subject to the acceptable ambient concentrations for carcinogens (AACC) per IDAPA 58.01.01.586 were modeled using an emission inventory that includes the following T-RACT controls, long-term mining production limits, and other emission inventory refinements, as described below:

- Installing and operating dust collection systems on drilling rigs (T-RACT)
- Capping the haul roads that are outside of the pits and development rock storage facilities (DRSFs) with clean development rock (T-RACT)
- Limiting long-term mining production to 135,000 T/day (5-year rolling total)
- Constructing the Burntlog access road with offsite materials containing background level arsenic concentrations
- Updating the bulldozing emission factor using the SGP site-specific silt content.

The above emission inventory reductions are discussed in more detail in Section 5.0. The T-RACT analysis is provided in Section 6.0. A comparison of the 180,000 T/day TAP emissions shown in Table 3 and the T-RACT TAP emissions is shown in Table 7.

Table 7. Comparison of 180,000 T/day and T-RACT Emissions

CAS	TAP Name	Carcinogenic	180,000 T/day Emissions (lb/hr) [1]	T-RACT Emissions (lb/hr) [2]
7440-38-2	Arsenic	Yes	0.544	0.232
7440-41-7	Beryllium	Yes	0.00261	0.00185
7440-43-9	Cadmium	Yes	0.000435	0.000317
50-00-0	Formaldehyde	Yes	0.00189	0.00189
7440-02-0	Nickel	Yes	0.00169	0.00121

[1] Model Scenario W3 emissions from Table 3
[2] T-RACT emission levels for the demonstration of carcinogenic TAP compliance. See Table A-W3, T-RACT Emissions in Appendix A, pp. A-45 to A-49.

The maximum modeled concentration for each of the 14 modeling scenarios demonstrated compliance with the applicable AACC, as summarized in Table 8. The AACCs listed in Table 8 were increased by a factor of ten (10) per IDAPA 58.01.01.210.12(b); T-RACT adjustment. The SGP maximum concentrations were adjusted to account for the life-of-mine (LOM) production limits, which affect the lifetime exposure, and to account for the elimination of Modeling Scenario W5. See Sections 3.4.4 and 3.4.5 for more detail.

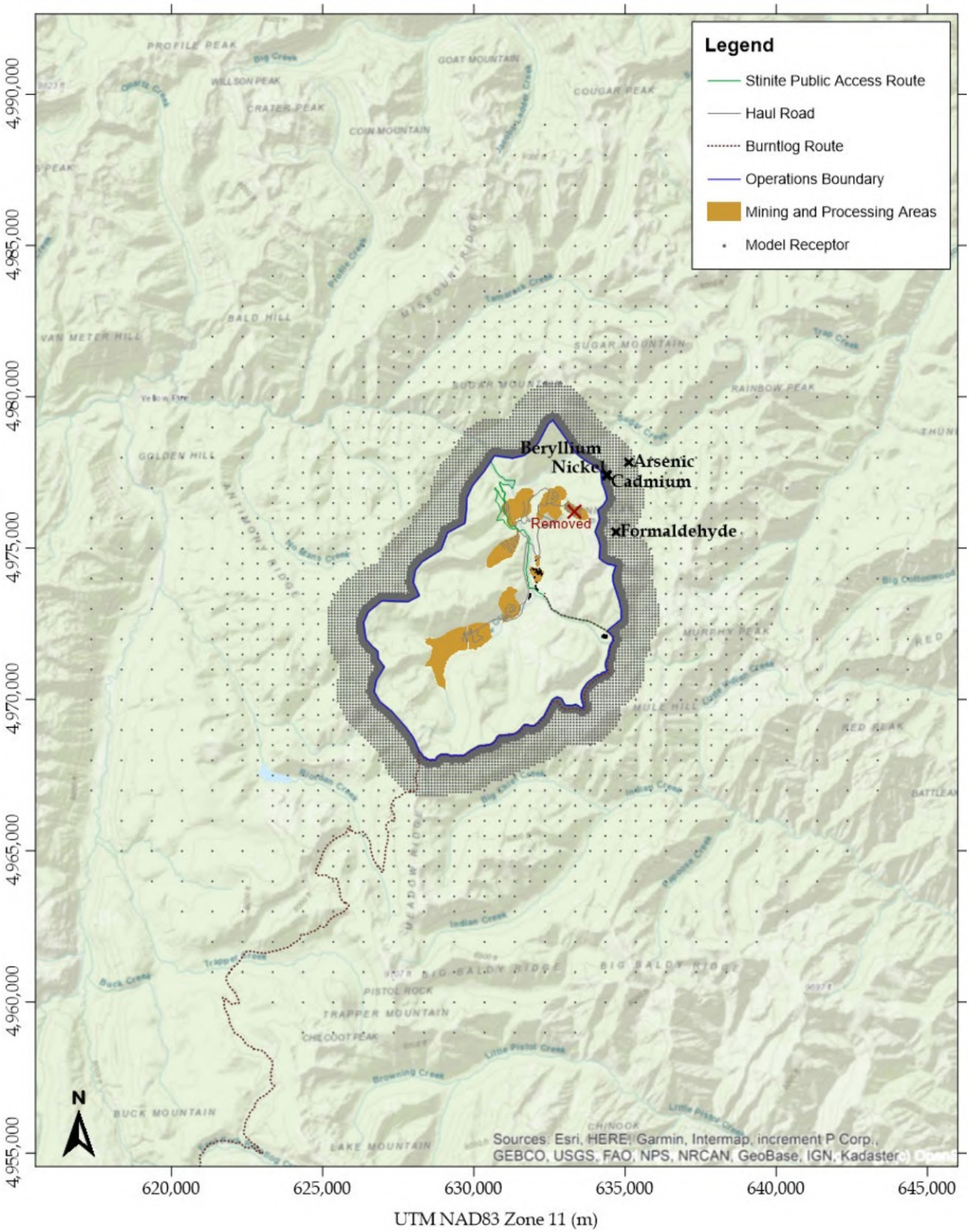
Table 8. Compliance Demonstration for Carcinogenic TAPs

CAS	TAP Name	Model Scenario	SGP Maximum Lifetime Exposure Concentration (µg/m³) [1]	AACC (µg/m³) [2]	TAP Compliance
7440-38-2	Arsenic	W2	0.00095	0.0023	Yes
7440-41-7	Beryllium	W1	0.00001	0.042	Yes
7440-43-9	Cadmium	W1	0.000002	0.0056	Yes
50-00-0	Formaldehyde	ALL	0.00007	0.77	Yes
7440-02-0	Nickel	W1	0.00001	0.42	Yes

[1] The lifetime exposure concentrations are based on the proposed restrictions discussed in Sections 3.4.4 and 3.4.5.
[2] The AACCs are increased by a factor of ten per IDAPA 58.01.01.210.12(b); T-RACT adjustment.

The modeled emissions for each modeling scenario and source are provided in Appendix B. The modeled concentration per modeling scenario is provided in Appendix C. The locations of the maximum concentrations for each carcinogenic TAP are presented in Figure 2.

Figure 2. Carcinogenic Maximum TAP Concentration (µg/m³) Locations



3.4.4 Carcinogenic TAP Modeling Lifetime Exposure Adjustment

The AACCs provided in IDAPA 58.01.01.586 were developed *based on the probability of developing excess cancers over a seventy (70) year lifetime exposure to one (1) microgram per cubic meter (1 ug/m3) of a given carcinogen and expressed in terms of a screening emission level or an acceptable ambient concentration for a carcinogenic toxic air pollutant* (IDAPA 58.01.01.006.125). Therefore, the highest modeled annual carcinogenic TAP concentration from each of the 14 modeling scenarios was evaluated for lifetime exposure as follows:

$$Lifetime\ expsoure\ \left(\frac{\mu g}{m^3}\right) = \frac{Highest\ annual\ concentration\ \left(\frac{\mu g}{m^3}\right) \times 16\ (mine\ operation\ years)}{70\ (years, lifetime\ exposure)}$$

This equation conservatively assumes that the highest annual concentration from the 14 modeling scenarios is repeated for 16 years of mining operation. This is then averaged over 70 years to calculate the 70-year lifetime exposure.

Calculating lifetime exposure based on 16 years of mining operation is also conservative. The annual emissions for carcinogenic TAP modeling are based on 135,000 T/day (see Section 3.4.3) and 365 days per year. Over 16 years, this equates to a potential mining production of 788.4 million tons:

$$\frac{135{,}000\left(\frac{ton}{day}\right) \times 365\left(\frac{day}{year}\right) \times 16\ years}{1{,}000{,}000\left(\frac{ton}{million\ ton}\right)} = 788.4\ million\ tons$$

The actual LOM total production as described in the SGP Refined Proposed Action (ModPRO2) mine plan is only 402.86 million tons (Perpetua 2021a), which is 51.1% of the potential LOM production represented in the above equation and related emissions evaluations.

3.4.5 Arsenic Compliance Demonstration for Modeling Scenarios W1–W5

To demonstrate compliance with the AACC for arsenic, two addition operating limitations were applied:

- The removal of Modeling Scenario W5 as a potential operating scenario
- Limiting the West End pit's LOM potential mining production to 50% of the total LOM potential mining production of 788.4 million tons: 50% * 788.4 = 394.2 million tons

Perpetua Resources has determined that the West End DRSF will not be constructed. This change eliminated Modeling Scenario W5 from the arsenic modeling evaluation. The remaining four West End pit modeling scenarios (W1–W4) are evaluated using the 70-year lifetime exposure equation from Section 3.4.4 and adjusting for the proposed West End pit LOM production limit of 50% of the total production as follows:

$$lifetime\ expsoure\ \left(\frac{\mu g}{m^3}\right) = \left(\frac{\left[Wi\left(\frac{\mu g}{m^3}\right)(50\%) + nonW\left(\frac{\mu g}{m^3}\right)(50\%)\right] \times 16\ (mine\ operation\ years)}{70\ (years, lifetime\ exposure)}\right)$$

Where:

$Wi = the\ modeled\ annual\ arsenic\ concentration\ from\ Scenario\ Wi;\ i = 1\ to\ 4$

$nonW = the\ modeled\ annual\ arsenic\ concentration\ of\ the\ highest\ nonW\ scenario;$

B1, B2, H1, H2, H3, H4, Y1, Y2, or Y3

The above equation was used to calculate the lifetime arsenic exposure from the West End pit scenarios (W1–W4) on a receptor-by-receptor basis. Combining the concentrations from Modeling Scenarios W1–W4 with the highest concentration from the remaining non-West End pit scenarios (B1, B2, H1, H2, H3, H4, Y1, Y2, or Y3) ensures that the maximum concentration is evaluated.

Calculating lifetime arsenic exposure based on the proposed West End pit LOM production limit of 50% of the total production is conservative. The actual LOM total production from the West End pit as described in the ModPRO2 mine plan is only 198.26 million tons (Perpetua 2021a), which is 50.3% of the proposed West End pit LOM production limit of 394.2 million tons.

4.0 COMPARISON OF ACTUAL ARSENIC MODELING TO POTENTIAL ARSENIC MODELING

Additional analyses of arsenic emissions were prompted by public comments on the draft PTC. IDEQ requested that Perpetua Resources conduct an arsenic modeling analysis based on the actual mining operation and production described in the ModPRO2 mine plan. Those modeling results were submitted to IDEQ in a report on July 8, 2021, titled "Stibnite Gold Project Permit to Construct Application Arsenic Modeling Addendum" (Air Sciences 2021).

While that report provided an assessment of the actual arsenic concentrations expected from the actual mining operation and production over the life of the SGP ("actual analysis"), the analysis described in Section 3.0 above is based on potential operating scenarios ("potential analysis"). These analyses ensure that public health is protected under all operating conditions.

A comparison between the actual analysis and the potential analysis for the lifetime exposure of arsenic is summarized in Table 9.

Table 9. Actual Analysis vs. Potential Analysis for Arsenic Lifetime Exposure

Model Parameter	Actual Data	Potential Data	Actual Data Basis	Potential Data Basis
Process emissions (lb/hr)	0.004514	0.004514	Equipment design rate	Equipment design rate
Mining emissions (lb/hr); varies	Max: 0.0854 Min: 0.0058 Avg: 0.0451	Max: 0.232 Min: 0.061	ModPRO2 – 16 years of operation	14 potential worst-case scenarios
Emissions included in modeling (lb/yr)	100%	98%	Actual analysis of all emissions	Includes IDAPA 58.01.01.210.20
LOM production (million tons)	402.86	788.4	ModPRO2	135,000 ton/day * 365 day/yr * 16 years
Lifetime exposure modeling	Average concentration over 16 years of operation	Highest scenario concentration assumed for 16 years	Actual analysis	Potential worst-case analysis
Maximum modeled concentration ($\mu g/m^3$)	0.00015	0.00095	Actual analysis	Potential worst-case analysis
Applicable AACC ($\mu g/m^3$)	0.0023	0.0023	IDAPA 58.01.01. 210.12(b) and .586	IDAPA 58.01.01. 210.12(b) and .586

A brief discussion of Table 9 is provided below:

- AACC Results: In both the actual and potential analyses, the maximum modeled arsenic concentrations are below the AACC, demonstrating compliance with IDAPA 58.01.01.210.

- Process emissions: The process arsenic emissions in both analyses are identical. This is because both emission inventories were based on the maximum design rates of the process equipment.

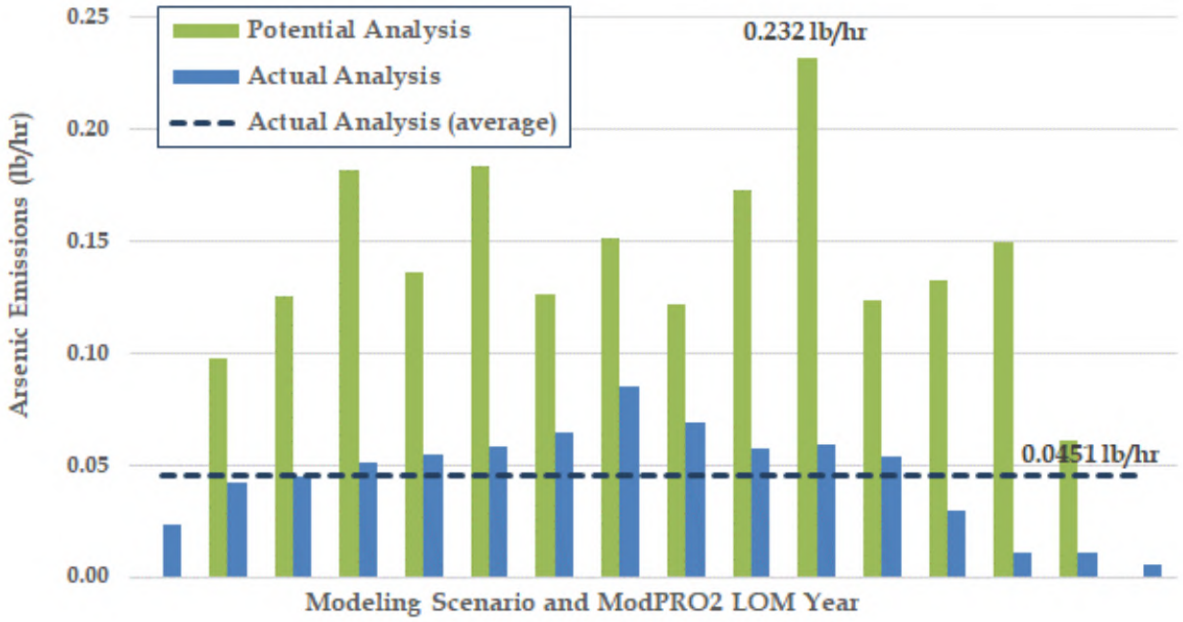
- Mining emissions: The arsenic emissions in the actual analysis (0.0451 lb/hr average) are only 19% of the arsenic emissions in the potential analysis (0.232 lb/hr highest scenario). This is because the actual mining operation and production activities (e.g., drilling, blasting, material product, hauling miles, etc.) in ModPRO2 are far less than the potential mining (PTC) operating scenarios. Figure 3 compares the ModPRO2 arsenic emissions from mining for each year of operation (actual analysis) to the PTC arsenic emissions from mining for each worst-case operating scenario (potential analysis).

- In both analyses, all the arsenic emissions are included in the modeling, except emissions from covered or addressed sources, IDAPA 58.01.01210.20(a) and (b). See Section 3.1.

- The actual analysis LOM production of 402.86 million tons is 51.1% of the potential analysis production of 788.4 million tons.

- When modeling the lifetime arsenic exposure, the actual analysis is based on modeling each year of the ModPRO2 mine plan and then averaging the yearly results on a receptor-by-receptor basis. In addition to the lower actual arsenic emissions, the mining activity locations vary, which reduced the average arsenic concentration at any given location outside the operations boundary. In contrast, the potential analysis is based on higher (potential) emissions and the highest modeling scenario, which are assumed to occur for 16 consecutive years. This potential approach resulted in significantly higher and more conservative arsenic hot-spot concentrations.

Figure 3. Actual Arsenic Mining Emissions vs. Potential Arsenic Mining Emissions



The concentrations and maximum locations of the arsenic lifetime exposure (70 years) are presented in Figure 4 for the actual analysis and Figure 5 for the potential analysis. As shown in these figures, the maximum arsenic concentrations are below the applicable AACC per IDAPA 58.01.01.210.12(b) and 586.

Figure 4. Actual Arsenic Concentrations (µg/m³) and Maximum Location

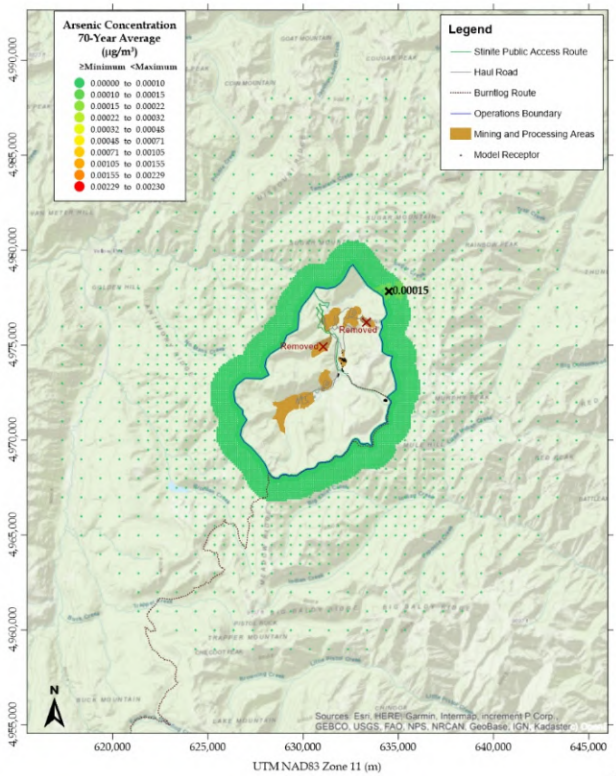
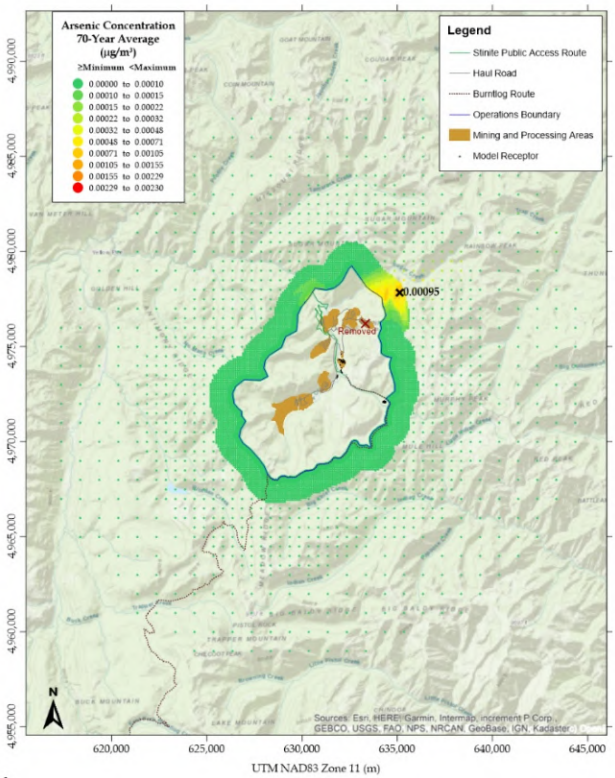


Figure 5. Potential Arsenic Concentrations (µg/m³) and Maximum Location



5.0 EMISSION INVENTORY FOR CARCINOGENIC TAPS

As discussed in Section 3.4.3, carcinogenic TAPs were modeled using an emission inventory adjusted for T-RACT controls, long-term mining production limits, and other refinements. These emission inventory changes are described in the following sections. The detailed emission calculations for the T-RACT emission inventory are provided in Appendix A (HAP/TAP Emission Calculations – Scenario W3, T-RACT Emissions).[8] The changes to these emission inventory inputs are highlighted on page A-41 of Appendix A.

5.1 Drilling Dust Control System

To reduce dust-related metal TAP emissions from drilling, Perpetua Resources will install and operate drilling rigs mounted with dust collection systems. *These systems have the ability to operate in various climates, i.e., they are not subject to freezing at lower temperatures as with the use of water, and they can be up to 99 percent efficient if properly maintained* (CDC 2012). The arsenic emissions inventory in Appendix A conservatively assumes a dust control efficiency of 90% for these systems.

5.2 Haul Road Capping

To reduce dust-related arsenic emissions from haul roads, Perpetua Resources will cap the haul roads that are outside of the pits and DRSFs with clean (low arsenic) development rock. Haul roads within the pits and DRSFs cannot be capped with this material because of steep grades and periodic road rerouting as mining areas develop. The median arsenic concentration of the clean development rock is 90 parts per million (ppm) (Perpetua 2021g).

5.3 Long-Term Mining Production Limits

To limit long-term dust-related metal TAP emissions, Perpetua Resources proposes limiting mining production to 135,000 T/day based on a 5-year rolling averaging period. This long-term mining production limit will be in addition to the current short-term daily limit of 180,000 T/day.

Limiting the long-term mining production limit to 135,000 T/day (5-year rolling average) is conservative. The highest 5-year rolling average mining production rate as described in ModPRO2 is only 95,700 T/day (Perpetua 2021a), which is 70.9% of the proposed limit.

[8] HAP/TAP Emission Calculations – Scenario W3, T-RACT: The HAP and TAP emissions based on T-RACT controls, a long-term mining production limit of 135,000 T/day (5-year rolling average), other refinements, and the highest emissions scenario (Modeling Scenario W3).

5.4 Burntlog Access Road Refinement

To reduce dust-related arsenic emissions from vehicle travel on the Burntlog access road, Perpetua Resources will construct this road with borrow material located outside of the mine site ambient air boundary. Analyses of the borrow sites show low arsenic levels of 2.5 ppm (ALS 2018), which are consistent with the background soil levels (DHHS 2007).

5.5 Bulldozing Refinement

Perpetua Resources and Air Sciences conducted a thorough review of the SGP emissions inventory to identify any potential dust-related metal TAP emission control measures (as discussed in the previous sections) and emission factor refinements. The only emission factor refinement identified was changing the bulldozing emission factor silt content from the EPA default of 6.9% to the SGP site-specific silt content of 4.0% (Midas Gold 2015). EPA recommends the use of site-specific data when available.[9]

[9] *In using the equations to estimate emissions from sources found in a specific western surface mine, it is necessary that reliable values for correction parameters be determined for the specific sources of interest if the assigned quality ratings of the equations are to be applicable. For example, actual silt content of coal or overburden measured at a facility should be used instead of estimated values. In the event that site-specific values for correction parameters cannot be obtained, the appropriate geometric mean values from Table 11.9-3 may be used, but the assigned quality rating of each emission factor equation should be reduced by 1 level (e.g., A to B)* (EPA 1998).

6.0 T-RACT ANALYSIS

Per IDAPA 58.01.01.210.14(a), this section documents the T-RACT control technologies.

6.1 Drilling Dust Control System

As discussed in Section 5.1, Perpetua Resources will install and operate drilling rigs mounted with dust collection systems. The following paragraphs evaluate this control as T-RACT:

Identification of all possible control technologies

Drilling operations create dust-related metal TAP emissions. The possible control technologies for these emissions are as follows:

- Applying best management practices
- Wet drilling with water injection
- Dry drilling with dust collectors

Best management practices include: (1) avoiding drilling operations during high dust conditions, and (2) shrouding drill areas to limit dust emissions.

Wet drilling includes injected water flows through the center of the drill and out though the drill bit to reduce dust emissions by 96% to 98%.[10]

Dry drilling includes rigs equipped with dust collection systems that shroud dust generated from the drilling area, capture, and remove dust through a dust collection system composed of an exhaust fan and filters that can achieve up to 99% control efficiency (CDC 2012).

Elimination of technologically infeasible or unreasonable technologies

Wet drilling at the SGP has the following disadvantages:

- It is subject to freezing at the low temperatures expected for the SGP location.
- It can result in drill bit plugging, drill rotation binding, and drill bit degradation.
- A wet drill hole can interfere with the blasting agent.

Based on the above disadvantages of wet drilling, it is considered an infeasible or unreasonable technology for the SGP.

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[10] *Testing has demonstrated that dust control efficiencies of up to 98 percent can be obtained using the water separator sub while dust control efficiencies of wet drilling without the water separator sub were 96 percent* (CDC 2012).

Ranking the remaining technologies by control effectiveness

The ranking of the possible control technologies for drilling by control effectiveness is as follows (highest to lowest):

1. Dry drilling with dust collectors – up to 99% control efficiency
2. Best management practices

Evaluation of the most effective control technology and selection of T-RACT

Perpetua Resources selects the top (most effective) control technology of dry drilling with dust collectors as T-RACT. Selecting the top control negates the need for considering economic, energy, and environmental impacts regarding the other control technologies.

6.2 Haul Road Dust and Arsenic Control

Dust emissions from unpaved roads are caused by vehicle traffic on these roads. Particles are lifted and dropped from the rolling wheels, and the turbulent wake behind the vehicles causes these particulates to become air borne. Dust control options include surface improvement (paving) or surface treatment (chemical suppressant application or watering).

As discussed in the SOB from February 18, 2021, Perpetua Resources will control dust emissions from haul roads by treating the surface with frequent watering and the periodic application of a chemical suppressant. Reducing dust emissions reduces dust-related metal TAP emissions. In addition, Perpetua Resources will reduce arsenic emissions by capping the haul roads outside of the pits and DRSFs with clean (low arsenic) development rock, as discussed in Section 5.2. The following sections evaluate these control measures as T-RACT.

6.2.1 Dust Control Technologies

Identification of all possible control technologies

Vehicle traffic on unpaved haul roads creates dust-related metal TAP emissions. The possible control technologies for these emissions are as follows:

- Paving
- Application of a chemical dust suppressant
- Watering

Paving: *The control efficiencies achievable by paving can be estimated by comparing emission factors for unpaved and paved road conditions* (EPA 2006). The particulate emission factor for a paved road with a silt loading of 0.2 g/m^2 (based on the EPA default value for the SGP average daily traffic of 500–5,000 trips per day) (EPA 2011a) and the SGP average vehicle weight of 182.6 tons is

0.515 lb/VMT. The SGP unpaved road particulate emission factor is 14.43 lb/VMT (uncontrolled). Based on these emission factors, the estimated control efficiency of paving the haul roads is 96%.

Dust suppressant and watering: The SGP dust emissions from unpaved haul roads are calculated based on a surface treatment control efficiency of 90% (annual basis) for the application of a chemical dust suppressant supplemented with frequent watering. As discussed in the SGP Application, this control efficiency is supported by EPA's AP-42 13.2.2 referenced test reports, which show that a chemical dust suppressant alone can achieve 90% to 99% control efficiency and 98% for magnesium chloride in particular (Air Sciences 2020, Appendix A to Attachment A). A control efficiency of 90% is also supported by the control efficiency limits established under Reasonable Achievable Control Technology (RACT), Best Available Control Technology (BACT), and Lowest Achievable Emission Rate (LAER) determinations under EPA's New Source Review permitting program.

The EPA RACT/BACT/LAER Clearinghouse (RBLC) database contains case-specific information on the air pollution technologies required by major stationary sources seeking a permit under EPA's New Source Review (NSR) program. This database was queried for all listings of air pollution technologies for unpaved roads using chemical dust suppressants or a combination of chemical dust suppressants and watering. The results of the query identified 10 projects containing a control efficiency of 90% or greater for unpaved roads. These determinations are listed in Table 10.

Table 10. EPA RBLC Determinations for 90% or Greater Control Efficiency of Unpaved Roads

State	Facility Name	RBLC-ID	Dust Control	Dust Control Efficiency
AK	Donlin Gold Project	AK-0084	water/chem	90%
AR	Turk Power Plant	AR-0094	water/chem	90%
CO	Rio Grande Portland Cement Corp.	CO-0043	water/chem	90%
IN	Nucor Steel	IN-0034	chem	90%
LA	Nucor Steel Louisiana	LA-0239	water/chem	90%
MO	Lafarge Corp.	MO-0048	chem	90%
NV	Sloan Quarry	NV-0045	chem	98%
NV	Nellis Air Force Base	NV-0047	water/chem	90%
OH	Unlimited Concrete	OH-0126	water/chem	90%
OH	Unlimited Concrete	OH-0131	water/chem	90%

(EPA 2021)

Elimination of technologically infeasible or unreasonable technologies

Paving haul roads at the SGP has the following disadvantages:

- The paving of haul roads is not conventional practice at mining operations.
- Paved highway weight limits are only approximately 20,000 pounds (10 tons).
- Paving is costly.

The conventional practice for mining operations is to utilize unpaved haul roads with treated surfaces to control fugitive dust. Haul trucks are single axle vehicles with a gross loaded weight of 60 tons to 685 tons. The loaded weight range for the SGP haul trucks is 60 to 260 tons. These weights significantly exceed regulatory weight limits for paved highways of 10 tons. Furthermore, the SGP mining activity locations move as mining progresses. This requires haul roads to be rerouted as necessary. Due to the temporary nature of hauling routes and the heavy weight of haul trucks, paving is considered an infeasible or unreasonable technology for the SGP.

Ranking the remaining technologies by control effectiveness

The ranking of the possible control technologies for drilling by control effectiveness is as follows (highest to lowest):

1. Application of a chemical dust suppressant – 90% to 99% control efficiency

2. Watering – 75% to 95% control efficiency (EPA 2006, Figure 13.2.2-2)

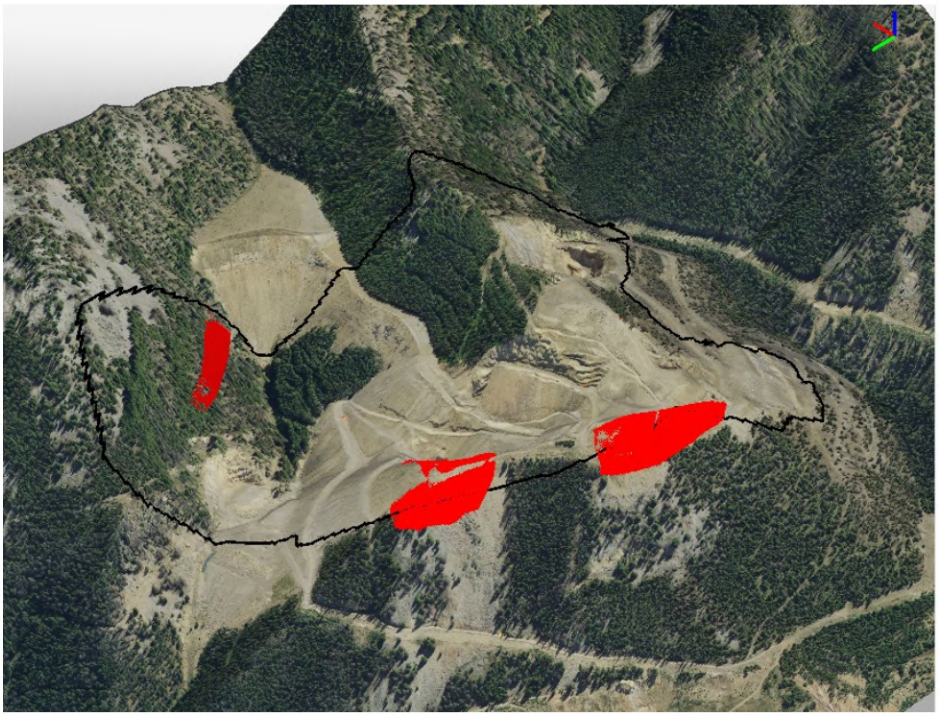
Evaluation of the most effective control technology and selection of T-RACT

After eliminating paving as a viable control option, Perpetua Resources selects the next most effective control technologies of the application of a chemical dust suppressant supplemented with frequent watering as T-RACT.

6.2.2 Arsenic Control Technologies

After applying T-RACT for dust control, as discussed in Section 6.2.1, dust-related arsenic emissions can only be further reduced by capping the haul roads with clean (low-arsenic) development rock. The median arsenic concentration of the SPG onsite material is 667 ppm (Midas Gold 2017c). However, there are quartzite rock deposits at the West End pit that have significantly lower mineralization and, thus, lower arsenic levels. The median arsenic concentration of this quartzite rock is 90 ppm (Perpetua 2021g), and there is approximately 3 million tons of this material available. Figure 6 shows the locations of the quartzite rock deposits.

Figure 6. Quartzite Rock Areas



Perpetua Resources proposes capping the haul roads that are outside of the pits and DRSFs with clean (low-arsenic) development rock as a T-RACT work practice, in addition to the T-RACT dust control measures discussed in Section 6.2.1. Haul roads within the pits and DRSFs cannot be capped with this material because of steep grades and periodic road rerouting as mining areas develop.

7.0 PROPOSED PERMIT CONDITIONS FOR CARCINOGENIC TAP COMPLIANCE

IDEQ is required to establish limits and standards as part of the permit to construct to ensure compliance with the TAP provisions in accordance with IDAPA 58.01.01.210.12(d) and 14(e). Per these two rules, Perpetua Resources proposes the following permit conditions:

7.1 Conditions per IDAPA 58.01.01.210.12(d)

Per IDAPA 58.01.01.210.12(d), *[t]he Department shall include emission limits and other permit terms for the toxic air pollutant in the permit to construct that assure that the facility will be operated in the manner described in the preconstruction compliance demonstration*. As discussed in Section 5.2, Perpetua Resources is proposing long-term mining production limits to demonstrate compliance with carcinogenic TAPs. The following are proposed permit conditions to address this TAP provision:

- The permittee shall haul no more than 135,000 tons per day (T/day) of ore and rock, based on a 5-year rolling average.
    - Each year, the permittee shall monitor and record the amount of ore and rock transported on haul trucks in tons per year (T/yr), and calculate the 5-year rolling average (T/day) based on 365 days per year.
- The permittee shall haul no more than 788.4 million tons (MT) of ore and rock from all deposits over the life of the mine.
- The permittee shall haul no more than 394.2 MT of ore and rock from the West End deposit over the life of the mine.
    - Each year, the permittee shall monitor and record the amount of ore and rock transported on haul trucks (T/yr) from all deposits and the amount of ore and rock transported on haul trucks (T/yr) from the West End deposit, and calculate the life-of-mine rolling total (MT) for each.

7.2 Conditions per IDAPA 58.01.01.210.14(e)

Per IDAPA 58.01.01.210.14(e), *[i]f the Department determines that the applicant has proposed T-RACT, the Department shall determine which of the options, or combination of options, will result in the lowest emission of toxic air pollutants, develop the emission standards constituting T-RACT and incorporate the emission standards into the permit to construct.* As discussed in Section 6.2, Perpetua Resources is proposing T-RACT controls to demonstrate compliance with carcinogenic TAPs. The following are proposed permit conditions to address this TAP provision:

- The permittee shall use drilling rigs equipped with dust collection systems. Control efficiency: 90%.
    - Within 60 days after startup, the permittee shall develop and maintain an Operation and Maintenance (O&M) manual. The O&M manual shall be a permittee-developed document based upon, but independent from, manufacturer-supplied operating manuals. The permittee shall operate the dust collection systems in accordance with the O&M manual at all times. The requirements in the O&M manual shall be incorporated by reference to this permit and shall be enforceable permit conditions. The O&M manual shall be submitted to DEQ within 60 days after initial startup.
- The permittee shall cap haul roads that are outside of the pits and DRSFs with low-arsenic material.
    - The permittee shall develop and maintain a plan that:
        - identifies the low-arsenic quartzite rock deposits in the West End pit based on core sample analyses,
        - requires periodic inspections (at least quarterly) of the capped haul roads and recapping as needed, and
        - includes record keeping of the inspections and any recapping of roads, noting the date and road section.
    - The permittee shall use the low-arsenic quartzite rock deposits from the West End pit, or other material with equal or lower arsenic concentration, as capping material.
        - If other material is used, it must be analyzed for arsenic concentration and a record of the median arsenic concentration shall be maintained.

The Draft PTC currently includes conditions for treating haul road surfaces with a chemical suppressant and water to control 90% of the dust (on an annual basis). See Conditions 1.2, 2.1–2.6, 2.8, 3.2, and 3.9. Therefore, no new conditions are needed or proposed for this dust control practice.

8.0 MERCURY EMISSIONS ANALYSIS

A complete inventory of mercury emissions is provided in Appendix A, as discussed in Section 2.0. This section categorizes these emissions into mercury emissions covered or not covered by IDAPA 58.01.01.215. According to IDAPA 58.01.01.215:

No owner or operator may commence construction or modification of a stationary source or facility that results in an increase in annual potential emissions of mercury of twenty-five (25) pounds or more unless the owner or operator has obtained a permit to construct under Sections 200 through 228 of these rules. The permit to construct application shall include an MBACT analysis for the new source or sources for review and approval by the Department. A determination of applicability under Section 215 shall be based upon the best available information. Fugitive emissions shall not be included in a determination of applicability under Section 215.

01. Exemptions. New or modified stationary sources within a source category subject to 40 CFR Part 63 are exempt from the requirements of Section 215.

Table 11 summarizes the SGP mercury sources and potential emissions for the highest emissions year (Model Scenario W3, 180,000 T/day Emissions). This table also provides the mercury emissions without considering the above exemptions, the exemption criteria, and the non-exempt mercury emissions for each source. As shown in this table, under IDAPA 58.01.01.215.01, the total potential non-exempt mercury emissions are 5.40E-5 ton/yr (0.108 lb/yr), which is well below the 25 lb/yr emission threshold.

Table 11. Mercury Source and Emissions Summary

Source	All Emissions ton/yr	Fugitive/ NESHAP Exemption	Non-Exempt Emissions ton/yr
Mining			
Fugitive Dust (drilling, blasting, excavating, hauling, etc.)	0.0021	Fugitive	0
Fugitive Evaporative (pits, tailings, DRSFs, stockpiles)	0.0036	Fugitive	0
Ore Processing			
Crushing, Screening, and Transfers	2.47E-05		2.47E-05
Prill Silos	0		0
Ore Concentration and Refining			
Autoclave	0.00010	7E	0
EW, Pregnant Tank, Retort, Furnace, Carbon Kiln	0.0017	7E	0
Process Heating			
POX, Carbon Kiln, Propane Vaporizers, Solution Heater	8.28E-06		8.28E-06
Lime Production			
Lime Kiln Combustion	2.09E-05	5A	0
Limestone Crushers, Screens, Mill, and Transfers	3.86E-07		3.86E-07
Lime Kiln, Kiln Feed, Lime Mill, and Pebble Lime Silo	0.0010	5A	0
Lime Silos and Lime Mill Crushing	4.05E-09		4.05E-09
Aggregate Production			
Portable Crushers, Screens, and Transfers	1.10E-07		1.10E-07
Concrete Production			
Central Mixer	0		0
Cement Silo Loading and Unloading	0		0
Aggregate Bin	6.90E-08		6.90E-08
HVAC			
Heaters	2.04E-05		2.04E-05
Emergency Power			
Emergency Generators and Fire Pump	0	4Z	0
Fuel Storage			
Gasoline Fuel Tanks	0	6C	0
Total	**0.00863**		**5.40E-05**

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Appendix A – HAP/TAP Emission Calculations

Appendix A Table of Contents

HAP/TAP Emission Calculations – Scenario W3, 180,000 T/day Emissions A-2

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HAP/TAP Emission Calculations – Scenario W3, T-RACT Emissions A-26

Table A-W3. HAP/TAP Emissions and Exemptions – Scenario W3, T-RACT Emissions A-45

Air Sciences Inc.	PROJECT TITLE: Stibnite Gold Project	BY: K. Lewis
	PROJECT NO: 335-20-3	PAGE: 1 OF: 19 SHEET: Calcs
AIR EMISSION CALCULATIONS	SUBJECT: HAP/TAP Emission Calculations	DATE: October 4, 2021

Model Scenario W3 180,000 T/day Emissions

Hazardous Air Pollutants (HAP)/Toxic Air Pollutants (TAP) Emissions Summary

		Emissions[1]									
		Fuel Combustion		Process/Prod/Leach		Mining		Total			
CAS	HAP/TAP	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	HAP	TAP
106-99-0	1,3-Butadiene	8.4E-07	3.7E-06	0	0	0	0	8.4E-07	3.7E-06	Y	Y
91-57-6	2-Methylnaphthalene	1.1E-06	4.6E-06	0	0	0	0	1.1E-06	4.6E-06	Y	N
56-49-5	3-Methylchloranthrene	7.8E-08	3.4E-07	0	0	0	0	7.8E-08	3.4E-07	Y	Y
57-97-6	7,12-Dimethylbenz(a)anthracene	7.6E-07	3.0E-06	0	0	0	0	7.6E-07	3.0E-06	Y	N
83-32-9	Acenaphthene	5.7E-06	7.1E-06	0	0	0	0	5.7E-06	7.1E-06	Y	N
208-96-8	Acenaphthylene	1.1E-05	1.4E-05	0	0	0	0	1.1E-05	1.4E-05	Y	N
75-07-0	Acetaldehyde	2.5E-05	1.1E-04	0	0	0	0	2.5E-05	1.1E-04	Y	Y
107-02-8	Acrolein	1.6E-05	2.0E-05	0	0	0	0	1.6E-05	2.0E-05	Y	Y
120-12-7	Anthracene	1.7E-06	2.4E-06	0	0	0	0	1.7E-06	2.4E-06	Y	N
7440-36-0	Antimony	0	0	5.7E-04	2.5E-03	1.9E-02	8.2E-02	1.9E-02	8.5E-02	Y	Y
7440-38-2	Arsenic	8.7E-06	3.8E-05	4.5E-03	2.0E-02	0.54	2.38	0.55	2.40	Y	Y
56-55-3	Benz(a)anthracene	3.1E-07	1.4E-06	0	0	0	0	3.1E-07	1.4E-06	Y	Y
71-43-2	Benzene	3.6E-04	1.6E-03	7.0E-03	3.1E-02	0	0	7.4E-03	3.2E-02	Y	Y
50-32-8	Benzo(a)pyrene	1.4E-07	6.1E-07	0	0	0	0	1.4E-07	6.1E-07	Y	Y
205-99-2	Benzo(b)fluoranthene	4.4E-07	1.9E-06	0	0	0	0	4.4E-07	1.9E-06	Y	Y
191-24-2	Benzo(g,h,i)perylene	7.5E-07	1.1E-06	0	0	0	0	7.5E-07	1.1E-06	Y	N
207-08-9	Benzo(k)fluoranthene	1.5E-07	6.6E-07	0	0	0	0	1.5E-07	6.6E-07	Y	Y
7440-41-7	Beryllium	5.2E-07	2.3E-06	4.3E-04	1.9E-03	2.6E-03	1.1E-02	3.0E-03	1.3E-02	Y	Y
92-52-4	Biphenyl	0	0	4.4E-05	1.9E-04	0	0	4.4E-05	1.9E-04	Y	Y
7440-43-9	Cadmium	4.8E-05	2.1E-04	4.1E-04	1.8E-03	4.1E-04	1.8E-03	8.7E-04	3.8E-03	Y	Y
75-15-0	Carbon Disulfide	0	0	1.4E-02	6.3E-02	0	0	1.4E-02	6.3E-02	Y	Y
7440-47-3	Chromium	6.6E-05	2.7E-04	6.1E-04	2.5E-03	7.3E-03	3.2E-02	8.0E-03	3.5E-02	Y	Y
18540-29-9	Cr (VI)	0	0	3.4E-07	1.5E-06	0	0	3.4E-07	1.5E-06	Y	Y
218-01-9	Chrysene	5.8E-07	2.5E-06	0	0	0	0	5.8E-07	2.5E-06	Y	Y
7440-48-4	Cobalt	4.0E-06	1.6E-05	4.7E-04	2.0E-03	3.3E-03	1.4E-02	3.7E-03	1.6E-02	Y	Y
592-01-8	Cyanide	0	0	0.45	1.99	0	0	0.45	1.99	Y	Y
53-70-3	Dibenzo(a,h)anthracene	1.8E-07	7.7E-07	0	0	0	0	1.8E-07	7.7E-07	Y	Y
106-46-7	Dichlorobenzene	5.7E-05	2.3E-04	0	0	0	0	5.7E-05	2.3E-04	Y	Y
206-44-0	Fluoranthene	5.5E-06	7.0E-06	0	0	0	0	5.5E-06	7.0E-06	Y	N
86-73-7	Fluorene	1.7E-05	2.1E-05	0	0	0	0	1.7E-05	2.1E-05	Y	N
50-00-0	Formaldehyde	3.3E-03	1.5E-02	0	0	0	0	3.3E-03	1.5E-02	Y	Y
110-54-3	Hexane	8.5E-02	0.34	3.1E-02	0.14	0	0	0.12	0.48	Y	Y
7647-01-0	Hydrogen Chloride	0	0	0.99	3.67	0	0	0.99	**3.67**	Y	Y
193-39-5	Indeno(1,2,3-cd)pyrene	2.2E-07	9.6E-07	0	0	0	0	2.2E-07	9.6E-07	Y	Y
7439-92-1	Lead	0	0	4.8E-04	2.1E-03	6.5E-03	2.9E-02	7.0E-03	3.1E-02	Y	N
7439-96-5	Manganese	1.8E-05	7.2E-05	4.6E-03	1.7E-02	0.24	1.07	0.25	1.08	Y	Y
7439-97-6	Mercury	1.2E-05	5.0E-05	6.9E-04	2.9E-03	1.3E-03	5.7E-03	2.0E-03	8.6E-03	Y	N
91-20-3	Naphthalene	1.9E-04	3.1E-04	1.9E-03	8.5E-03	0	0	2.1E-03	8.8E-03	Y	Y
7440-02-0	Nickel	9.1E-05	4.0E-04	4.6E-04	2.0E-03	1.6E-03	7.1E-03	2.2E-03	9.5E-03	Y	Y
85-01-8	Phenanthrene	5.1E-05	6.3E-05	0	0	0	0	5.1E-05	6.3E-05	Y	N
108-95-2	Phenol	0	0	2.4E-04	1.1E-03	0	0	2.4E-04	1.1E-03	Y	Y
7723-14-0	Phosphorus	0	0	5.6E-03	2.3E-02	0.53	2.32	0.54	2.34	Y	Y
129-00-0	Pyrene	5.0E-06	6.6E-06	0	0	0	0	5.0E-06	6.6E-06	Y	N
7782-49-2	Selenium	1.1E-06	4.6E-06	4.1E-04	1.8E-03	3.3E-04	1.4E-03	7.4E-04	3.2E-03	Y	Y
108-88-3	Toluene	5.2E-04	1.1E-03	3.2E-02	0.14	0	0	3.2E-02	0.14	Y	Y
1330-20-7	Xylene	2.5E-04	3.0E-04	3.1E-02	0.14	0	0	3.2E-02	0.14	Y	Y
Total HAP		9.0E-02	0.36	1.58	6.25	1.36	5.95	3.03	12.56		

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

	0.2155	0.8650	8.3307	31.6474	86.1858	377.4936	94.7319	410.0060
TRUE	0.2155	0.8650	8.3307	31.6474	86.1858	377.4936	94.7319	410.0060
	chk	chk	chk-15	chk	chk	chk	chk	chk

Hazardous Air Pollutants (HAP)/Toxic Air Pollutants (TAP) Emissions Summary - continued

		Emissions[1]									
		Fuel Combustion		Process/Prod/Leach		Mining		Total			
CAS	Non-HAP TAP	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	HAP	TAP
7429-90-5	Aluminum	0	0	0.65	2.58	57.86	253.41	58.50	255.98	N	Y
7440-39-3	Barium	2.1E-04	8.4E-04	6.6E-03	2.7E-02	0.65	2.86	0.66	2.88	N	Y
1317-65-3	Calcium Carbonate	0	0	2.24	8.12	11.41	49.97	13.65	58.09	N	Y
1305-78-8	Calcium Oxide	0	0	0.70	0.95	0	0	0.70	0.95	N	Y
7440-50-8	Copper	4.0E-05	1.6E-04	4.9E-04	2.1E-03	4.1E-03	1.8E-02	4.6E-03	2.0E-02	N	Y
110-82-7	Cyclohexane	0	0	1.0E-03	4.6E-03	0	0	1.0E-03	4.6E-03	N	Y
7783-06-4	Hydrogen Sulfide	0	0	0.90	3.94	0	0	0.90	3.94	N	Y
7439-89-6	Iron	0	0	0.21	0.81	14.83	64.96	15.04	65.77	N	Y
7439-98-7	Molybdenum	5.2E-05	2.1E-04	4.2E-04	1.8E-03	8.1E-04	3.6E-03	1.3E-03	5.6E-03	N	Y
109-66-0	Pentane	0.12	0.50	0	0	0	0	0.12	0.50	N	Y
7440-22-4	Silver	0	0	4.1E-04	1.8E-03	4.1E-04	1.8E-03	8.2E-04	3.6E-03	N	Y
7664-93-9	Sulfuric Acid	0	0	2.03	8.89	0	0	2.03	8.89	N	Y
7440-28-0	Thallium	0	0	5.2E-04	2.2E-03	8.1E-03	3.6E-02	8.7E-03	3.8E-02	N	Y
7440-61-1	Uranium	0	0	5.2E-04	2.2E-03	8.1E-03	3.6E-02	8.7E-03	3.8E-02	N	Y
7440-62-2	Vanadium	1.1E-04	4.4E-04	7.3E-04	3.0E-03	2.3E-02	1.0E-01	2.4E-02	0.10	N	Y
25551-13-7	Trimethyl benzene	0	0	1.1E-02	4.8E-02	0	0	1.1E-02	4.8E-02	N	Y
7440-33-7	Tungsten	0	0	5.2E-04	2.2E-03	8.1E-03	3.6E-02	8.7E-03	3.8E-02	N	Y
7440-66-6	Zinc	1.4E-03	5.5E-03	8.0E-04	3.3E-03	2.9E-02	0.12	3.1E-02	0.13	N	Y
Total Non-HAP TAP		0.13	0.50	6.75	25.40	84.83	371.54	91.71	397.44		

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

Conversions
2,000 lb/ton
8,760 hr/yr
24 hr/day

PROPANE COMBUSTION

Source Data

Source ID	Description	MMBtu/day	MMBtu/yr
Lime Process Heating			
LKC	PFR Shaft Lime Kiln Combustion	529.0	163,935
Ore Process Heating			
ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	17.0	510
CKB	Carbon Regeneration Kiln (Burners)	54.1	19,754
PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	2.4	876
HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	120.0	43,800
Subtotal		193.5	64,940
HVAC			
H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	96.0	35,040
H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	96.0	35,040
HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	96.0	35,040
HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	6.0	2,190
HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	6.0	2,190
HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	6.0	2,190
HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	12.0	4,380
HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	48.0	17,520
HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	72.0	26,280
Subtotal		438.0	159,870

PROPANE COMBUSTION - CONTINUED

HAP/TAP Emission Factors and Emissions

O.Heat_pph O.Heat_tpy L.Heat_pph L.Heat_tpy HVAC_pph HVAC_tpy lb/hr ton/yr

		Emission Factor[2]		Emissions[1] Ore Proc Heat		Lime Proc Heat		HVAC		Total			
CAS	Pollutant	lb/MMscf	lb/MMBtu[3]	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	TAP	A/C
91-57-6	2-Methylnaphthalene	2.4E-05	2.35E-8	1.9E-07	7.6E-07	5.2E-07	1.9E-06	4.3E-07	1.9E-06	1.1E-06	4.6E-06	N	
56-49-5	3-Methylchloranthrene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
57-97-6	7,12-Dimethylbenz(a)ant	< 1.6E-05	1.57E-8	1.3E-07	5.1E-07	3.5E-07	1.3E-06	2.9E-07	1.3E-06	7.6E-07	3.0E-06	N	
83-32-9	Acenaphthene	< 1.8E-06	1.76E-9	1.4E-08	5.7E-08	3.9E-08	1.4E-07	3.2E-08	1.4E-07	8.5E-08	3.4E-07	N	
208-96-8	Acenaphthylene	< 1.8E-06	1.76E-9	1.4E-08	5.7E-08	3.9E-08	1.4E-07	3.2E-08	1.4E-07	8.5E-08	3.4E-07	N	
120-12-7	Anthracene	< 2.4E-06	2.35E-9	1.9E-08	7.6E-08	5.2E-08	1.9E-07	4.3E-08	1.9E-07	1.1E-07	4.6E-07	N	
7440-38-2	Arsenic	2.0E-04	1.96E-7	1.5E-06	6.4E-06	3.7E-06	1.6E-05	3.6E-06	1.6E-05	8.7E-06	3.8E-05	Y	C
56-55-3	Benz(a)anthracene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
71-43-2	Benzene	2.1E-03	2.06E-6	1.5E-05	6.7E-05	3.9E-05	1.7E-04	3.8E-05	1.6E-04	9.1E-05	4.0E-04	Y	C
50-32-8	Benzo(a)pyrene	< 1.2E-06	1.18E-9	8.7E-09	3.8E-08	2.2E-08	9.6E-08	2.1E-08	9.4E-08	5.2E-08	2.3E-07	Y	C
205-99-2	Benzo(b)fluoranthene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
191-24-2	Benzo(g,h,i)perylene	< 1.2E-06	1.18E-9	9.5E-09	3.8E-08	2.6E-08	9.6E-08	2.1E-08	9.4E-08	5.7E-08	2.3E-07	N	
207-08-9	Benzo(k)fluoranthene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
7440-41-7	Beryllium	< 1.2E-05	1.18E-8	8.7E-08	3.8E-07	2.2E-07	9.6E-07	2.1E-07	9.4E-07	5.2E-07	2.3E-06	Y	C
7440-43-9	Cadmium	1.1E-03	1.08E-6	8.0E-06	3.5E-05	2.0E-05	8.8E-05	2.0E-05	8.6E-05	4.8E-05	2.1E-04	Y	C
7440-47-3	Chromium	1.4E-03	1.37E-6	1.1E-05	4.5E-05	3.0E-05	1.1E-04	2.5E-05	1.1E-04	6.6E-05	2.7E-04	Y	A
218-01-9	Chrysene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
7440-48-4	Cobalt	8.4E-05	8.24E-8	6.6E-07	2.7E-06	1.8E-06	6.8E-06	1.5E-06	6.6E-06	4.0E-06	1.6E-05	Y	A
53-70-3	Dibenzo(a,h)anthracene	< 1.2E-06	1.18E-9	8.7E-09	3.8E-08	2.2E-08	9.6E-08	2.1E-08	9.4E-08	5.2E-08	2.3E-07	Y	C
106-46-7	Dichlorobenzene	1.2E-03	1.18E-6	9.5E-06	3.8E-05	2.6E-05	9.6E-05	2.1E-05	9.4E-05	5.7E-05	2.3E-04	Y	A
206-44-0	Fluoranthene	3.0E-06	2.94E-9	2.4E-08	9.5E-08	6.5E-08	2.4E-07	5.4E-08	2.4E-07	1.4E-07	5.7E-07	N	
86-73-7	Fluorene	2.8E-06	2.75E-9	2.2E-08	8.9E-08	6.1E-08	2.3E-07	5.0E-08	2.2E-07	1.3E-07	5.3E-07	N	
50-00-0	Formaldehyde	7.5E-02	7.35E-5	5.5E-04	2.4E-03	1.4E-03	6.0E-03	1.3E-03	5.9E-03	3.3E-03	1.4E-02	Y	C
110-54-3	Hexane	1.8E+00	1.76E-3	1.4E-02	5.7E-02	3.9E-02	1.4E-01	3.2E-02	1.4E-01	8.5E-02	3.4E-01	Y	A
193-39-5	Indeno(1,2,3-cd)pyrene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
7439-96-5	Manganese	3.8E-04	3.73E-7	3.0E-06	1.2E-05	8.2E-06	3.1E-05	6.8E-06	3.0E-05	1.8E-05	7.2E-05	Y	A
7439-97-6	Mercury	2.6E-04	2.55E-7	2.1E-06	8.3E-06	5.6E-06	2.1E-05	4.7E-06	2.0E-05	1.2E-05	5.0E-05	N	
91-20-3	Naphthalene	6.1E-04	5.98E-7	4.8E-06	1.9E-05	1.3E-05	4.9E-05	1.1E-05	4.8E-05	2.9E-05	1.2E-04	Y	A
7440-02-0	Nickel	2.1E-03	2.06E-6	1.5E-05	6.7E-05	3.9E-05	1.7E-04	3.8E-05	1.6E-04	9.1E-05	4.0E-04	Y	C
85-01-8	Phenanthrene	1.7E-05	1.67E-8	1.3E-07	5.4E-07	3.7E-07	1.4E-06	3.0E-07	1.3E-06	8.1E-07	3.2E-06	N	
129-00-0	Pyrene	5.0E-06	4.90E-9	4.0E-08	1.6E-07	1.1E-07	4.0E-07	8.9E-08	3.9E-07	2.4E-07	9.5E-07	N	
7782-49-2	Selenium	< 2.4E-05	2.35E-8	1.9E-07	7.6E-07	5.2E-07	1.9E-06	4.3E-07	1.9E-06	1.1E-06	4.6E-06	Y	A
108-88-3	Toluene	3.4E-03	3.33E-6	2.7E-05	1.1E-04	7.3E-05	2.7E-04	6.1E-05	2.7E-04	1.6E-04	6.5E-04	Y	A
109-66-0	Pentane	2.6E+00	2.55E-3	2.1E-02	8.3E-02	5.6E-02	2.1E-01	4.7E-02	2.0E-01	1.2E-01	5.0E-01	Y	A
7440-39-3	Barium	4.4E-03	4.31E-6	3.5E-05	1.4E-04	9.5E-05	3.5E-04	7.9E-05	3.4E-04	2.1E-04	8.4E-04	Y	A
7440-50-8	Copper	8.5E-04	8.33E-7	6.7E-06	2.7E-05	1.8E-05	6.8E-05	1.5E-05	6.7E-05	4.0E-05	1.6E-04	Y	A
7439-98-7	Molybdenum	1.1E-03	1.08E-6	8.7E-06	3.5E-05	2.4E-05	8.8E-05	2.0E-05	8.6E-05	5.2E-05	2.1E-04	Y	A
7440-62-2	Vanadium	2.3E-03	2.25E-6	1.8E-05	7.3E-05	5.0E-05	1.8E-04	4.1E-05	1.8E-04	1.1E-04	4.4E-04	Y	A
7440-66-6	Zinc	2.9E-02	2.84E-5	2.3E-04	9.2E-04	6.3E-04	2.3E-03	5.2E-04	2.3E-03	1.4E-03	5.5E-03	Y	A
Total				3.6E-02	1.4E-01	9.8E-02	3.6E-01	8.1E-02	3.5E-01	2.1E-01	8.6E-01		

(1) *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

(2) *AP-42, Table 1.4-3 & 1.4-4 (7/98) Natural Gas Combustion* 1.07e6 1.07e6

(3) *Natural Gas Higher Heating Value* 1,020 *MMBtu/MMscf* chk

DIESEL COMBUSTION

Source Data

Source ID	Description	Power Rating kW	Power Rating hp	Operation hr/day	Operation hr/yr	Fuel Consumption[1] & [2] MMBtu/day	Fuel Consumption[1] & [2] MMBtu/yr
EDG1	Camp Emergency Generator	1,000	1,341	1	100	9.39	938.70
EDG2	Plant Emergency Generator #1	1,000	1,341	1	100	9.39	938.7
EDG3	Plant Emergency Generator #2	1,000	1,341	1	100	9.39	938.7
EDFP	Mill Fire Pump	200	268	1	100	1.88	187.7
Total						30.0	3,003.8

[1] *Based on brake specific fuel consumption for diesel generators* 7,000 *Btu/hp-hr* *AP-42 Tbl 3.3-1*

[2] *Heat Content of* 0.137 *MMBtu/gal* 1E+6 *Btu/MMBtu* 1.341 *hp/kW*

HAP/TAP Emission Factors and Emissions

	Pollutant	Factor (lb/MMBtu) ≤600 hp[2]	Factor (lb/MMBtu) >600hp[3]	Emissions (≤600 hp) lb/hr	Emissions (≤600 hp) ton/yr	Emissions (>600 hp) lb/hr	Emissions (>600 hp) ton/yr	Total Emissions[1] lb/hr	Total Emissions[1] ton/yr	TAP	A/C
106-99-0	1,3-Butadiene	< 3.9E-05		8.4E-07	3.7E-06	0.0E+00	0.0E+00	8.4E-07	3.7E-06	Y	C
83-32-9	Acenaphthene	< 1.4E-06	4.7E-06	1.1E-07	1.3E-07	5.5E-06	6.6E-06	5.6E-06	6.7E-06	N	
208-96-8	Acenaphthylene	< 5.1E-06	9.2E-06	4.0E-07	4.7E-07	1.1E-05	1.3E-05	1.1E-05	1.3E-05	N	
75-07-0	Acetaldehyde	7.7E-04	2.5E-05	1.6E-05	7.2E-05	8.1E-06	3.5E-05	2.5E-05	1.1E-04	Y	C
107-02-8	Acrolein	< 9.3E-05	7.9E-06	7.2E-06	8.7E-06	9.2E-06	1.1E-05	1.6E-05	2.0E-05	Y	A
120-12-7	Anthracene	1.9E-06	1.2E-06	1.5E-07	1.8E-07	1.4E-06	1.7E-06	1.6E-06	1.9E-06	N	
56-55-3	Benz(a)anthracene	1.7E-06	6.2E-07	3.6E-08	1.6E-07	2.0E-07	8.8E-07	2.4E-07	1.0E-06	Y	C
71-43-2	Benzene	9.3E-04	7.8E-04	2.0E-05	8.8E-05	2.5E-04	1.1E-03	2.7E-04	1.2E-03	Y	C
50-32-8	Benzo(a)pyrene	< 1.9E-07	< 2.6E-07	4.0E-09	1.8E-08	8.3E-08	3.6E-07	8.7E-08	3.8E-07	Y	C
205-99-2	Benzo(b)fluoranthene	< 9.9E-08	< 1.1E-06	2.1E-09	9.3E-09	3.6E-07	1.6E-06	3.6E-07	1.6E-06	Y	C
191-24-2	Benzo(g,h,i)perylene	< 4.9E-07	< 5.6E-07	3.8E-08	4.6E-08	6.5E-07	7.8E-07	6.9E-07	8.3E-07	N	
207-08-9	Benzo(k)fluoranthene	< 1.6E-07	< 2.2E-07	3.3E-09	1.5E-08	7.0E-08	3.1E-07	7.3E-08	3.2E-07	Y	C
218-01-9	Chrysene	3.5E-07	1.5E-06	7.6E-09	3.3E-08	4.9E-07	2.2E-06	5.0E-07	2.2E-06	Y	C
53-70-3	Dibenzo(a,h)anthracene	< 5.8E-07	< 3.5E-07	1.2E-08	5.5E-08	1.1E-07	4.9E-07	1.2E-07	5.4E-07	Y	C
206-44-0	Fluoranthene	7.6E-06	4.0E-06	6.0E-07	7.1E-07	4.7E-06	5.7E-06	5.3E-06	6.4E-06	N	
86-73-7	Fluorene	2.9E-05	1.3E-05	2.3E-06	2.7E-06	1.5E-05	1.8E-05	1.7E-05	2.1E-05	N	
50-00-0	Formaldehyde	1.2E-03	7.9E-05	2.5E-05	1.1E-04	2.5E-05	1.1E-04	5.1E-05	2.2E-04	Y	C
193-39-5	Indeno(1,2,3-cd)pyrene	< 3.8E-07	< 4.1E-07	8.0E-09	3.5E-08	1.3E-07	5.8E-07	1.4E-07	6.2E-07	Y	C
91-20-3	Naphthalene	8.5E-05	1.3E-04	6.6E-06	8.0E-06	1.5E-04	1.8E-04	1.6E-04	1.9E-04	Y	A
85-01-8	Phenanthrene	2.9E-05	4.1E-05	2.3E-06	2.8E-06	4.8E-05	5.7E-05	5.0E-05	6.0E-05	N	
129-00-0	Pyrene	4.8E-06	3.7E-06	3.7E-07	4.5E-07	4.4E-06	5.2E-06	4.7E-06	5.7E-06	N	
108-88-3	Toluene	4.1E-04	2.8E-04	3.2E-05	3.8E-05	3.3E-04	4.0E-04	3.6E-04	4.3E-04	Y	A
1330-20-7	Xylene	2.9E-04	1.9E-04	2.2E-05	2.7E-05	2.3E-04	2.7E-04	2.5E-04	3.0E-04	Y	A
Total				1.4E-04	3.6E-04	1.1E-03	2.2E-03	1.2E-03	2.6E-03		

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

[2] *AP-42, Tab. 3.3-2, 10/96, diesel engines (≤ 600 hp)*

[3] *AP-42, Tabs. 3.4-3 & 3.4-4, 10/96, large diesel engines (> 600 hp)*

ORE PROCESSING

Source Data

Source ID	Description	PM Emissions lb/day	PM Emissions ton/yr
OC1	Loader Transfer of Ore to Grizzly	3.500	0.639
OC2	Grizzly to Apron Feeder	3.500	0.639
OC3	Apron Feeder to Dribble Conveyor	3.500	0.639
OC4	Apron Feeder to Vibrating Grizzly	3.500	0.639
OC5	Dribble Conveyor to Vibrating Grizzly	3.500	0.639
OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	3.500	0.639
OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	30.000	5.475
OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	3.500	0.639
OC9	Stockpile Transfers to Reclaim Conveyors	16.560	3.022
OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	16.560	3.022
OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	16.560	3.022
OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge C	33.120	6.044
OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	3.864	0.705
Total		141.164	25.762

HAP/TAP Emission Factors and Emissions

CAS No.	Pollutant	Concentration ppm[2]	Emissions[1] lb/hr	Emissions[1] ton/yr	TAP	A/C
7440-38-2	Arsenic	667	3.9E-03	1.7E-02	Y	C
7440-41-7	Beryllium	3.2	1.9E-05	8.2E-05	Y	C
7440-43-9	Cadmium	0.50	2.9E-06	1.3E-05	Y	C
7440-48-4	Cobalt	4	2.4E-05	1.0E-04	Y	A
7440-47-3	Chromium	9	5.3E-05	2.3E-04	Y	A
7439-97-6	Mercury [3]	0.96	5.6E-06	2.5E-05	N	
7439-96-5	Manganese	299	1.8E-03	7.7E-03	Y	A
7440-02-0	Nickel	2	1.2E-05	5.2E-05	Y	C
7439-92-1	Lead	8	4.7E-05	2.1E-04	N	
7440-36-0	Antimony	23	1.4E-04	5.9E-04	Y	A
7723-14-0	Phosphorus	650	3.8E-03	1.7E-02	Y	A
7782-49-2	Selenium [4]	0.40	2.4E-06	1.0E-05	Y	A
7440-22-4	Silver	0.50	2.9E-06	1.3E-05	Y	A
7429-90-5	Aluminum	71,000	4.2E-01	1.8E+00	Y	A
7440-39-3	Barium	800	4.7E-03	2.1E-02	Y	A
1317-65-3	Calcium Carbonate	14,000	8.2E-02	3.6E-01	Y	A
7440-50-8	Copper	5	2.9E-05	1.3E-04	Y	A
7439-89-6	Iron [4]	18,200	1.1E-01	4.7E-01	Y	A
7439-98-7	Molybdenum	1	5.9E-06	2.6E-05	Y	A
7440-28-0	Thallium	10	5.9E-05	2.6E-04	Y	A
7440-61-1	Uranium	10	5.9E-05	2.6E-04	Y	A
7440-62-2	Vanadium	28	1.6E-04	7.2E-04	Y	A
7440-33-7	Tungsten	10	5.9E-05	2.6E-04	Y	A
7440-66-6	Zinc	35	2.1E-04	9.0E-04	Y	A
Total			6.2E-01	2.7E+00		

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

[2] *(Midas Gold 2017c) Median concentration of 55,000 SGP samples.*

[3] *(Midas Gold 2018e) Median ore concentration of 151,000 SGP samples; resource block model.*

[4] *(Midas Gold 2020) Median concentration of 56,000 SGP samples for Fe and 1,500 SGP samples for Se.*

1E+6 parts/ppm

Air Sciences Inc.	PROJECT TITLE: Stibnite Gold Project	BY: K. Lewis
	PROJECT NO: 335-20-3	PAGE: 7 OF: 19 SHEET: Calcs
AIR EMISSION CALCULATIONS	SUBJECT: HAP/TAP Emission Calculations	DATE: October 4, 2021

ORE CONCETRATION AND REFINING

Source Data

Source ID	Description	Subpart 7E Allowable Limit lb/yr[1]	Oper. hr/yr	% of Subpart 7E for Controlled Systems %	Controlled Hg Emissions lb/hr	ton/yr	lb/yr
AC	Autoclave	213.4	8,760	[2]	0.000023	0.00010	0.20
EW,MR,MF,CKD	Refinery Sources (C. Kiln, EW, Retort, Furr	16.8		20% [3]	0.000384	0.00168	3.36
7439-97-6 Mercury	Total	230.2			0.000407	0.00178	3.56

[1] *Subpart 7E Limit - Ore Pretreatment Processes (CFR 2018b)*

$$\frac{84\ lb}{MMton} \times \frac{2{,}540{,}400\ ton}{yr} \times \frac{MMton}{1.0E{+}6\ ton} = \frac{213.4\ lb}{yr}$$

[1] *Subpart 7E Limit - Carbon Processes with Mercury Retorts*

$$\frac{0.8\ lb}{ton} \times \frac{21\ ton}{yr} = \frac{16.8\ lb}{yr}$$

[2] *Controlled SysCAD modeled emissions from Autoclave:* 0.0105 g/hr 2.3E-05 lb/hr 0.20 lb/yr (M3 2019)

[3] *Based on similar source (but with much higher ore Hg content) Hg reporting levels provided below:*

Goldstrike Refinery (2015 & 2016 Hg Reports) (NDEP 2015a) (NDEP 2016)

$$\frac{28.79\ lb}{yr} \times \frac{yr}{251.00\ ton} = \frac{0.11\ lb}{MMton} \times \frac{ton}{0.8\ lb} = 14.3\%$$

Twin Creeks Refinery (2015 & 2016 Hg Reports) (NDEP 2015a) (NDEP 2016)

$$\frac{31.27\ lb}{yr} \times \frac{yr}{142.77\ ton} = \frac{0.22\ lb}{MMton} \times \frac{ton}{0.8\ lb} = 27.4\%$$

HAP/TAP Emission Factors and Emission

AC_pph AC_tpy Refin_pph Refin_tpy lb/hr ton/yr

CAS No.	Pollutant	Emission Factor[1]	Autoclave lb/hr	Autoclave ton/yr	Refinery lb/hr	Refinery ton/yr	Total Emissions lb/hr	Total Emissions ton/yr	TAP	A/C
7440-38-2	Arsenic	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	C
7440-41-7	Beryllium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	C
7440-43-9	Cadmium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	C
7440-48-4	Cobalt	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-47-3	Chromium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7439-97-6	Mercury	see above	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	N	
7439-96-5	Manganese	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-02-0	Nickel	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	C
7439-92-1	Lead	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	N	
7440-36-0	Antimony	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7723-14-0	Phosphorus	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7782-49-2	Selenium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-22-4	Silver	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7429-90-5	Aluminum	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-39-3	Barium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
1317-65-3	Calcium Carbonate	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-50-8	Copper	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7439-89-6	Iron	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7439-98-7	Molybdenum	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-28-0	Thallium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-61-1	Uranium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-62-2	Vanadium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-33-7	Tungsten	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-66-6	Zinc	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
Total			5.5E-04	2.4E-03	9.2E-03	4.0E-02	9.8E-03	4.3E-02		

[1] *Hg is the most difficult metal to control due to it existing in both particulate and gaseous form. Therefore, all other metals are conservatively estimated to be equal to or less than the Hg emissions.*

0.0525 0.0525 chk

7664-93-9	Sulfuric Acid	Autoclave	2.03	8.89			2.03	8.89
7783-06-4	Hydrogen Sulfic	Autoclave	0.90	3.94			0.90	3.94
592-01-8	Cyanide	Point Sources - 5 EW Cells			0.0012	0.0053	0.00	0.01
Total			2.93	12.84	0.01	0.05	2.94	12.88

ORE CONCETRATION AND REFINING - CONTINUED

Source Data

Source ID	Description	Throughput ton/day	Throughput ton/yr	Operation hr/day	Operation hr/yr
AC	Autoclave	6,960	2,540,400	24	8,760

Autoclave HAP/TAP Emission Factors and Emission lb/hr ton/yr

CAS No.	Pollutant	Emission Factor		Emissions[1] lb/hr	Emissions[1] ton/yr
7664-93-9	Sulfuric Acid	0.007	lb/ton[2]	2.03	8.89
7783-06-4	Hydrogen Sulfide	0.9	lb/hr[3]	0.90	3.94

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

[2] *H2SO4 is based on Acidic Autoclave test data (APT 2010)*

[3] *H2S is based on Acidic Autoclave test data (APT 2013)*

LEACHING OPERATION

Cyanide (HCN) Source Data, Emission Factors, and Emissions

Source ID	Description	Dia. ft[1]	pH[1]	Free CN- g/m3[1]	T C[1]	pKa	a0	H	kG[2] m/s	Fa*Fw	g/s	lb/hr	ton/yr
TSF	***Fugitive Sources***												
TSF	Tailings Maint. Pond	76	7.75	1	3.74	9.803	0.9912	0.0025	1.89E-05	0.641	1.27E-05	0.0001	0.0004
MILLTA	CN Detox Tank 1	40	8.5	25	25	9.250	0.8490	0.0055	0.000311	0.688	0.002891	0.0229	0.101
MILLTA	CN Detox Tank 2	40	8.5	25	25	9.250	0.8490	0.0055	0.000311	0.688	0.002891	0.0229	0.101
MILLTA	CIP Leach Tank 1	52	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.668	0.001435	0.0114	0.050
MILLTA	CIP Leach Tank 2	52	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.668	0.001435	0.0114	0.050
MILLTA	CIP Leach Tank 3	52	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.668	0.001435	0.0114	0.050
MILLTA	CIP Leach Tank 4	52	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.668	0.001435	0.0114	0.050
MILLTA	CIL Tank 1	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA	CIL Tank 2	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA	CIL Tank 3	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA	CIL Tank 4	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA	CIL Tank 5	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA	CIL Tank 6	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA	CIP Tank 1	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
MILLTA	CIP Tank 2	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
MILLTA	CIP Tank 3	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
MILLTA	CIP Tank 4	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
MILLTA	CIP Tank 5	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
MILLTA	CIP Tank 6	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
		Acres[1]											
TSF	Tails, Aqueous Surface	110.222	7.75	1	3.74	9.803	0.9912	0.0025	1.89E-05	0.421	0.008845	0.0702	0.307
TSF	Tails, Wet Sediment	110.222							5.31E-08	0.421	0.009961	0.0791	0.346
TSF	Tails, Dry Sediment	110.222							2.33E-08	1	0.010375	0.0823	0.361
		330.666											
592-01-8	Cyanide Fugitive Sources - Subtotal											0.4527	1.983
75-15-0	Carbon Disulfide											0.01446	0.06332
	Point Sources												
EW	EW Cells	[3]										0.0006	0.003
EW	Preg/Barren Tanks	[3]										0.0006	0.003
592-01-8	Cyanide Point Sources - Subtotal											0.0012	0.0053
	Total											0.454	1.988

[1] *(Midas Gold 2016)(M3 2017c)(M3 2017d)*

[2] *The emission factors and caculation methodology are from the EPA directed HCN study: (Card, T. 2009)(EPA 2009)(Schmidt 2010)*

[3] *(APT 2009)*

Carbon Disulfide Emissions from Xanthate Decomposition

CAS No.	Pollutant	Xanthate[1] ton/yr	Molar Decomp.[2]	CS_2 MW Ratio	Temperature Adj. Factor[3]	Emissions lb/hr	Emissions ton/yr
75-15-0	Carbon Disulfide	1,700	0.99%	0.376	1%	0.0145	0.063

	MW	
Xanthate (PAX)	202.37	$C6H11KOS_2$
Carbon disulfide	76.139	CS_2

[1] *(Midas Gold 2016) p. 12-11*

[2] *(Air Sciences 2020) molar decomposition of xanthate in solution to CS2 gas*

[3] *(Air Sciences 2020) based on the comparison of CS2 generation at 25C and 70C*

Conversions

8,760	hr/yr	453.5929	g/lb	Wind adjustment factor Fw	1
2,000	lb/ton	3.28084	ft/m		
4,046.86	m2/acre	3,600	s/hr		

Air Sciences Inc.	PROJECT TITLE: Stibnite Gold Project	BY: K. Lewis		
	PROJECT NO: 335-20-3	PAGE: 10	OF: 19	SHEET: Calcs
AIR EMISSION CALCULATIONS	SUBJECT: HAP/TAP Emission Calculations	DATE: October 4, 2021		

LIME PRODUCTION

Source Data

Source ID	Description	Throughput ton/day	Throughput ton/yr	PM Emissions lb/day	PM Emissions ton/yr
LS1	Limestone transfer to Primary Crusher Hopper			3.39	0.48
LS2	Primary Crushing and Associated Transfers In and Out			6.10	0.86
LS3	Primary Screening and Associated Transfers In and Out			28.25	3.97
LS4	Secondary Crushing and Associated Transfers In and Out			6.10	0.86
LS5	Secondary Screening and Associated Transfers In and Out			28.25	3.97
LS6	Limestone transfer to Ball Mill Feed Bin			3.39	0.48
LS7	Limestone transfer to Ball Mill Feed Conveyor			3.39	0.48
LS8	Ball Mill Feed transfer to Ball Mill			3.39	0.48
LSBM	Limestone Ball Mill			45.65	6.42
LS9	Limestone transfer to Kiln Feed Bin			0.80	0.12
LS10	Limestone transfer to Lime Kiln Feed Conveyor			0.80	0.12
LS11	Fines Screening and Associated Transfers In and Out			6.68	1.03
Subtotal LS1-11				136.18	19.28
LS12	Kiln Feed transfer to PFR Shaft Lime Kiln			0.80	0.12
LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	169	52,377	21.97	3.40
Subtotal LS12,LK				22.77	3.53
Total				158.95	22.80

HAP/TAP Emission Factors and Emissions

LS_pph LS_tpy LS12_pph LS12_tpy LK_pph LK_tpy lb/hr ton/yr

CAS No.	Pollutant	Concentration ppm[2]	LS1-11,LSBM lb/hr	LS1-11,LSBM ton/yr	LS12 lb/hr	LS12 ton/yr	Lime Kiln lb/hr	Lime Kiln ton/yr	Emissions[1] lb/hr	Emissions[1] ton/yr	TAP	A/C
7440-38-2	Arsenic	23	1.01E-04	4.43E-04	6.51E-07	2.85E-06	1.79E-05	7.83E-05	1.20E-04	5.24E-04	Y	C
7440-41-7	Beryllium	0.8	3.52E-06	1.54E-05	2.27E-08	9.92E-08	6.22E-07	2.72E-06	4.17E-06	1.82E-05	Y	C
7440-43-9	Cadmium	0.25	1.10E-06	4.82E-06	7.08E-09	3.10E-08	1.94E-07	8.51E-07	1.30E-06	5.70E-06	Y	C
7440-48-4	Cobalt	4	2.27E-05	7.71E-05	1.34E-07	4.96E-07	3.66E-06	1.36E-05	2.65E-05	9.12E-05	Y	A
7440-47-3	Chromium	15	8.51E-05	2.89E-04	5.01E-07	1.86E-06	1.37E-05	5.11E-05	9.93E-05	3.42E-04	Y	A
7439-97-6	Mercury [3]	0.02	1.13E-07	3.86E-07	6.68E-10	2.48E-09	2.82E-04	1.05E-03	2.82E-04	1.05E-03	N	
7439-96-5	Manganese	236.5	1.34E-03	4.56E-03	7.89E-06	2.93E-05	2.16E-04	8.05E-04	1.57E-03	5.39E-03	Y	A
7440-02-0	Nickel	5	2.20E-05	9.64E-05	1.42E-07	6.20E-07	3.89E-06	1.70E-05	2.60E-05	1.14E-04	Y	C
7439-92-1	Lead	3	1.70E-05	5.78E-05	1.00E-07	3.72E-07	2.75E-06	1.02E-05	1.99E-05	6.84E-05	N	
7440-36-0	Antimony	2.5	1.42E-05	4.82E-05	8.34E-08	3.10E-07	2.29E-06	8.51E-06	1.66E-05	5.70E-05	Y	A
7723-14-0	Phosphorus	130	7.38E-04	2.51E-03	4.34E-06	1.61E-05	1.19E-04	4.43E-04	8.61E-04	2.96E-03	Y	A
7440-22-4	Silver	0	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	Y	A
7429-90-5	Aluminum	22600	1.28E-01	4.36E-01	7.54E-04	2.80E-03	2.07E-02	7.69E-02	1.50E-01	5.15E-01	Y	A
7440-39-3	Barium	145	8.23E-04	2.79E-03	4.84E-06	1.80E-05	1.33E-04	4.94E-04	9.60E-04	3.31E-03	Y	A
1317-65-3	Calcium Carbonate	274500	1.56E+00	5.29E+00	9.16E-03	3.40E-02	2.51E-01	9.35E-01	1.82E+00	6.26E+00	Y	A
7440-50-8	Copper	5	2.84E-05	9.64E-05	1.67E-07	6.20E-07	4.58E-06	1.70E-05	3.31E-05	1.14E-04	Y	A
7439-89-6	Iron	10350	5.87E-02	1.99E-01	3.45E-04	1.28E-03	9.47E-03	3.52E-02	6.85E-02	2.36E-01	Y	A
7439-98-7	Molybdenum	0.5	2.84E-06	9.64E-06	1.67E-08	6.20E-08	4.58E-07	1.70E-06	3.31E-06	1.14E-05	Y	A
7440-28-0	Thallium	5	2.84E-05	9.64E-05	1.67E-07	6.20E-07	4.58E-06	1.70E-05	3.31E-05	1.14E-04	Y	A
7440-61-1	Uranium	5	2.84E-05	9.64E-05	1.67E-07	6.20E-07	4.58E-06	1.70E-05	3.31E-05	1.14E-04	Y	A
7440-62-2	Vanadium	15.5	8.79E-05	2.99E-04	5.17E-07	1.92E-06	1.42E-05	5.28E-05	1.03E-04	3.53E-04	Y	A
7440-33-7	Tungsten	5	2.84E-05	9.64E-05	1.67E-07	6.20E-07	4.58E-06	1.70E-05	3.31E-05	1.14E-04	Y	A
7440-66-6	Zinc	18	1.02E-04	3.47E-04	6.01E-07	2.23E-06	1.65E-05	6.13E-05	1.19E-04	4.10E-04	Y	A
Subtotal			1.75E+00	5.94E+00	1.03E-02	3.82E-02	2.82E-01	1.05E+00	2.04E+00	7.03E+00	9.0667	9.0667
7647-01-0	Hydrogen Chloride	0.14 lb/ton product[4]					0.99	3.67	0.99	3.67		chk

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

[2] *(M3 2018) Median concentrations of SGP limestone material. Metals with medians below the detection limit (DL) are set to 1/2DL.*

[3] *Hg emissions from the Lime Kiln are conservatively estimated assuming 100% volatilization of all Hg in the limestone*

[4] *(EPA 1999b)*

1E+6 parts/ppm

LIME PRODUCTION - CONTINUED

Source Data

Source ID	Description	PM Emissions lb/day (PM_ppd)	PM Emissions ton/yr (PM_tpy)
LS1L	Mill Lime Silo #1 Loading	0.248	0.002
LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	1.200	0.011
MillS2L	Mill Lime Silo #2 Loading	0.248	0.002
MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	1.200	0.011
ACS1L	AC Lime Silo #1 Loading	0.990	0.009
ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.304	0.042
ACS2L	AC Lime Silo #2 Loading	0.990	0.009
ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.304	0.042
ACS3L	AC Lime Silo #3 Loading	0.990	0.009
ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.304	0.042
ACS4L	AC Lime Silo #4 Loading	0.495	0.004
ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	2.304	0.021
Subtotal - Mill & AC Lime Silos		15.576	0.203
LCR	Lime Mill Crushing and associated transfers In and Out	6.828	1.058
LSL	Pebble Lime Silo Loading via Bucket Elevator	0.149	0.023
LSU	Pebble Lime Silo discharge to Lime Slaker	0.015	0.002
Subtotal - Lime Mfg		6.991	1.083
Total		22.567	1.286

HAP/TAP Emission Factors and Emissions

CAS No.	Pollutant	Concentration ppm[2]	Mill and AC lb/hr (MillAC_pph)	Mill and AC ton/yr (MillAC_tpy)	Lime Mfg lb/hr (LimeM_pph)	Lime Mfg ton/yr (LimeM_tpy)	Emissions[1] lb/hr	Emissions[1] ton/yr	TAP	A/C
7440-38-2	Arsenic	23	1.06E-06	4.66E-06	5.69E-06	2.49E-05	6.75E-06	2.96E-05	Y	C
7440-41-7	Beryllium	0.8	3.70E-08	1.62E-07	1.98E-07	8.67E-07	2.35E-07	1.03E-06	Y	C
7440-43-9	Cadmium	0.25	1.16E-08	5.07E-08	6.18E-08	2.71E-07	7.34E-08	3.22E-07	Y	C
7440-48-4	Cobalt	4	2.60E-06	8.11E-07	1.17E-06	4.33E-06	3.76E-06	5.14E-06	Y	A
7440-47-3	Chromium	15	9.74E-06	3.04E-06	4.37E-06	1.63E-05	1.41E-05	1.93E-05	Y	A
7439-97-6	Mercury	0.02	1.30E-08	4.05E-09	5.83E-09	2.17E-08	1.88E-08	2.57E-08	N	
7439-96-5	Manganese	236.5	1.53E-04	4.79E-05	6.89E-05	2.56E-04	2.22E-04	3.04E-04	Y	A
7440-02-0	Nickel	5	2.31E-07	1.01E-06	1.24E-06	5.42E-06	1.47E-06	6.43E-06	Y	C
7439-92-1	Lead	3	1.95E-06	6.08E-07	8.74E-07	3.25E-06	2.82E-06	3.86E-06	N	
7440-36-0	Antimony	2.5	1.62E-06	5.07E-07	7.28E-07	2.71E-06	2.35E-06	3.22E-06	Y	A
7723-14-0	Phosphorus	130	8.44E-05	2.63E-05	3.79E-05	1.41E-04	1.22E-04	1.67E-04	Y	A
7440-22-4	Silver	0	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	Y	A
7429-90-5	Aluminum	22,600	1.47E-02	4.58E-03	6.58E-03	2.45E-02	2.13E-02	2.91E-02	Y	A
7440-39-3	Barium	145	9.41E-05	2.94E-05	4.22E-05	1.57E-04	1.36E-04	1.86E-04	Y	A
1305-78-8	Calcium Oxide	740,000 [3]	4.80E-01	1.50E-01	2.16E-01	8.02E-01	6.96E-01	9.52E-01	Y	A
7440-50-8	Copper	5	3.25E-06	1.01E-06	1.46E-06	5.42E-06	4.70E-06	6.43E-06	Y	A
7439-89-6	Iron	10350	6.72E-03	2.10E-03	3.01E-03	1.12E-02	9.73E-03	1.33E-02	Y	A
7439-98-7	Molybdenum	0.5	3.25E-07	1.01E-07	1.46E-07	5.42E-07	4.70E-07	6.43E-07	Y	A
7440-28-0	Thallium	5	3.25E-06	1.01E-06	1.46E-06	5.42E-06	4.70E-06	6.43E-06	Y	A
7440-61-1	Uranium	5	3.25E-06	1.01E-06	1.46E-06	5.42E-06	4.70E-06	6.43E-06	Y	A
7440-62-2	Vanadium	15.5	1.01E-05	3.14E-06	4.52E-06	1.68E-05	1.46E-05	1.99E-05	Y	A
7440-33-7	Tungsten	5	3.25E-06	1.01E-06	1.46E-06	5.42E-06	4.70E-06	6.43E-06	Y	A
7440-66-6	Zinc	18	1.17E-05	3.65E-06	5.24E-06	1.95E-05	1.69E-05	2.31E-05	Y	A
Total			5.02E-01	1.57E-01	2.25E-01	8.38E-01	7.27E-01	9.95E-01		

(1) *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

(2) *See LIME PRODUCTION, page 10*

(3) *(NLA 2007) 40% to 74% CaO in lime*

1E+6 parts/ppm

AGGREGATE PRODUCTION

Source Data

Source ID	Description (description)	PM Emissions lb/day (PM_ppd)	PM Emissions ton/yr (PM_tpy)
PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conve	15.00	2.74
PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conve	15.00	2.74
Total		30.00	5.48

HAP/TAP Emission Factors and Emissions

CAS No.	Pollutant	Concentration ppm[2]	Emissions[1] lb/hr (lb/hr)	Emissions[1] ton/yr (ton/yr)	TAP	A/C
7440-38-2	Arsenic	23	2.88E-05	1.26E-04	Y	C
7440-41-7	Beryllium	0.8	1.00E-06	4.38E-06	Y	C
7440-43-9	Cadmium	0.25	3.13E-07	1.37E-06	Y	C
7440-48-4	Cobalt	4	5.00E-06	2.19E-05	Y	A
7440-47-3	Chromium	15	1.88E-05	8.21E-05	Y	A
7439-97-6	Mercury	0.02	2.50E-08	1.10E-07	N	
7439-96-5	Manganese	236.5	2.96E-04	1.29E-03	Y	A
7440-02-0	Nickel	5	6.25E-06	2.74E-05	Y	C
7439-92-1	Lead	3	3.75E-06	1.64E-05	N	
7440-36-0	Antimony	2.5	3.13E-06	1.37E-05	Y	A
7723-14-0	Phosphorus	130	1.63E-04	7.12E-04	Y	A
7440-22-4	Silver	0	0.00E+00	0.00E+00	Y	A
7429-90-5	Aluminum	22600	2.83E-02	1.24E-01	Y	A
7440-39-3	Barium	145	1.81E-04	7.94E-04	Y	A
1317-65-3	Calcium Carbonate	274500	3.43E-01	1.50E+00	Y	A
7440-50-8	Copper	5	6.25E-06	2.74E-05	Y	A
7439-89-6	Iron	10350	1.29E-02	5.67E-02	Y	A
7439-98-7	Molybdenum	0.5	6.25E-07	2.74E-06	Y	A
7440-28-0	Thallium	5	6.25E-06	2.74E-05	Y	A
7440-61-1	Uranium	5	6.25E-06	2.74E-05	Y	A
7440-62-2	Vanadium	15.5	1.94E-05	8.49E-05	Y	A
7440-33-7	Tungsten	5	6.25E-06	2.74E-05	Y	A
7440-66-6	Zinc	18	2.25E-05	9.86E-05	Y	A
Total			3.85E-01	1.69E+00		

(1) *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

(2) *See LIME PRODUCTION, page 10*

1E+6 parts/ppm

Air Sciences Inc.	PROJECT TITLE: Stibnite Gold Project	BY: K. Lewis
	PROJECT NO: 335-20-3	PAGE: 13 OF: 19 SHEET: Calcs
AIR EMISSION CALCULATIONS	SUBJECT: HAP/TAP Emission Calculations	DATE: October 4, 2021

CONCRETE PRODUCTION

Source Data

TP_unit/day TP_unit/yr

description

Source ID	Description	Throughput ton/day	Throughput ton/yr
CS1L	Cement/Shotcrete Silo #1 Loading	164	60,000
CS1U	Cement/Shotcrete Silo #1 Unloading	164	60,000
CS2L	Cement/Shotcrete Silo #2 Loading	164	60,000
CS2U	Cement/Shotcrete Silo #2 Unloading	164	60,000
CM	Central Mixer Loading	164	60,000
	Subtotal Cement Silo Filling	658	240,000
	Subtotal Central Mix Batching	164	60,000

HAP/TAP Emission Factors and Emissions

CF_pph CF_tpy CM_pph CM_tpy lb/hr ton/yr

CAS No.	HAP/TAP	Silo Fill lb/ton[2]	Central Mixer lb/ton[3]	Cement Silo L/U lb/hr	Cement Silo L/U ton/yr	Central Mix Batching lb/hr	Central Mix Batching ton/yr	Total Emissions[3] lb/hr	Total Emissions[3] ton/yr	TAP	A/C
7440-38-2	Arsenic	4.24E-09	2.96E-07	1.16E-7	5.09E-7	2.03E-6	8.88E-6	2.14E-6	9.39E-6	Y	C
7440-41-7	Beryllium	4.86E-10		1.33E-8	5.83E-8	--	--	1.33E-8	5.83E-8	Y	C
7440-43-9	Cadmium		7.10E-10	--	--	4.86E-9	2.13E-8	4.86E-9	2.13E-8	Y	C
7440-47-3	Chromium	2.90E-08	1.27E-07	7.95E-7	3.48E-6	8.70E-7	3.81E-6	1.66E-6	7.29E-6	Y	A
18540-29-9	Cr (VI)	5.80E-09	2.70E-08	1.59E-7	6.96E-7	1.85E-7	8.11E-7	3.44E-7	1.51E-6	Y	C
7439-92-1	Lead	1.09E-08	3.66E-08	2.99E-7	1.31E-6	2.51E-7	1.10E-6	5.49E-7	2.41E-6	N	
7439-96-5	Manganese	1.17E-07	3.78E-06	3.21E-6	1.40E-5	2.59E-5	1.13E-4	2.91E-5	1.27E-4	Y	A
7440-02-0	Nickel	4.18E-08	2.48E-07	1.15E-6	5.02E-6	1.70E-6	7.44E-6	2.84E-6	1.25E-5	Y	C
7723-14-0	Phosphorus		1.20E-06	--	--	8.22E-6	3.60E-5	8.22E-6	3.60E-5	Y	A
Total				5.73E-6	2.51E-5	3.91E-5	1.71E-4	4.49E-5	1.97E-4		

(1) *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

(2) *AP-42, Table 11.12-8, (06/06) Cement Silo Filing, Controlled.* 20% *Cr (VI), IDEQ email on 11/23/2020* 0.0002 0.0002

(3) *AP-42, Table 11.12-8, (06/06) Central Mix Batching, Controlled.* 21.29% *Cr (VI), IDEQ email on 11/23/2020* chk

Conversions

24 hr/day

CONCRETE PRODUCTION - CONTINUED

Source Data PM_ppd PM_tpy

Source ID	description Description	PM Emissions lb/day	ton/yr
CAL	Aggregate Bin Loading	16.56	1.73
CAU	Aggregate Bin Unloading	16.56	1.73
Total		33.12	3.45

HAP/TAP Emission Factors and Emissions lb/hr ton/yr

CAS No.	Pollutant	Concentration ppm[2]	Emissions[1] lb/hr	ton/yr	TAP	A/C
7440-38-2	Arsenic	23	1.81E-05	7.94E-05	Y	C
7440-41-7	Beryllium	0.8	6.30E-07	2.76E-06	Y	C
7440-43-9	Cadmium	0.25	1.97E-07	8.63E-07	Y	C
7440-48-4	Cobalt	4	5.52E-06	1.38E-05	Y	A
7440-47-3	Chromium	15	2.07E-05	5.18E-05	Y	A
7439-97-6	Mercury	0.02	2.76E-08	6.90E-08	N	
7439-96-5	Manganese	236.5	3.26E-04	8.16E-04	Y	A
7440-02-0	Nickel	5	3.94E-06	1.73E-05	Y	C
7439-92-1	Lead	3	4.14E-06	1.04E-05	N	
7440-36-0	Antimony	2.5	3.45E-06	8.63E-06	Y	A
7723-14-0	Phosphorus	130	1.79E-04	4.49E-04	Y	A
7440-22-4	Silver	0	0.00E+00	0.00E+00	Y	A
7429-90-5	Aluminum	22600	3.12E-02	7.80E-02	Y	A
7440-39-3	Barium	145	2.00E-04	5.00E-04	Y	A
7440-50-8	Copper	5	6.90E-06	1.73E-05	Y	A
7439-89-6	Iron	10350	1.43E-02	3.57E-02	Y	A
7439-98-7	Molybdenum	0.5	6.90E-07	1.73E-06	Y	A
7440-28-0	Thallium	5	6.90E-06	1.73E-05	Y	A
7440-61-1	Uranium	5	6.90E-06	1.73E-05	Y	A
7440-62-2	Vanadium	15.5	2.14E-05	5.35E-05	Y	A
7440-33-7	Tungsten	5	6.90E-06	1.73E-05	Y	A
7440-66-6	Zinc	18	2.48E-05	6.21E-05	Y	A
Total			4.63E-02	1.16E-01		

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

[2] *See LIME PRODUCTION, page 10*

1E+6 parts/ppm

FUEL STORAGE - GASOLINE

Source Data

Source ID	Description	VOC Emissions lb/day	VOC Emissions ton/yr
TG1	Mine Site Gasoline Tank #1	5.25	0.96
TG2	Mine Site Gasoline Tank #2	5.25	0.96
Total		10.49	1.91

HAP/TAP Emission Factors and Emissions

CAS No.	Pollutant	Concentration wt. %[2]	Emissions[1] lb/hr	Emissions[1] ton/yr	TAP	A/C
71-43-2	Benzene	1.608%	7.03E-03	3.08E-02	Y	C
92-52-4	Biphenyl	0.010%	4.37E-05	1.91E-04	Y	A
110-82-7	Cyclohexane	0.240%	1.05E-03	4.60E-03	Y	A
110-54-3	Hexane	7.138%	3.12E-02	1.37E-01	Y	A
91-20-3	Naphthalene	0.444%	1.94E-03	8.50E-03	Y	A
108-95-2	Phenol	0.055%	2.40E-04	1.05E-03	Y	A
108-88-3	Toluene	7.212%	3.15E-02	1.38E-01	Y	A
25551-13-7	Trimethyl benzene	2.500%	1.09E-02	4.79E-02	Y	A
1330-20-7	Xylene	7.170%	3.13E-02	1.37E-01	Y	A
Total			1.15E-01	5.05E-01		

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

[2] *(EPA 1999a)*

MINING FUGITIVE EMISSIONS

Dust Emissions

Source Data **Model Scenario** **W3** **180,000 T/day Emissions**

Operating schedule 365 day/yr

Clean rock cap (CR) >0% [1]

[1] *(Perpetua 2021h) Percent of VMTs on haul roads capped with CR*
Roads outside of the pits and DRSFs are capped with CR

Source ID	Description	PM Emissions lb/day	PM Emissions ton/yr
YPP	Yellow Pine Pit	--	--
HFP	Hangar Flats Pit	--	--
WEP	West End Pit	1,887.91	344.54
BT	Bradley Tailings	--	--
YPPBL	Yellow Pine Pit Blasting	--	--
HFPBL	Hangar Flats Pit Blasting	--	--
WEPBL	West End Pit Blasting	643.03	117.35
BTBL	Bradley Tailings Blasting	--	--
STKP	PC Stockpile	--	--
FDRSF	Fiddle DRSF	--	--
HFDRSF	Hangar Flats DRSF	289.91	52.91
YPDRSF	Yellow Pine DRSF	--	--
WEDRSF	West End DRSF	--	--
HR000	Haul Roads	16,697.74	3,047.34
TSF	Tailing Storage Facility	--	--
ACCRD	Access Roads	38.10	6.95
UGEXP	Scout Portal	0.008	0.002
Total		19,556.71	3,569.10

TSF, ACCRD, UGEXP 38.11 6.95 chk 3569.10

HAP/TAP Emission Factors		ORE	DR	CR	HRD	Borrow	AR
		Concentration					
CAS No.	Pollutant	ppm[1]	ppm[1]	ppm[3]	ppm[4]	ppm[5]	ppm
7440-38-2	Arsenic	667	667	90	667	2.5	667
7440-41-7	Beryllium	3.2	3.2		3.2		3.2
7440-43-9	Cadmium	0.5	0.5		0.5		0.5
7440-48-4	Cobalt	4	4		4		4
7440-47-3	Chromium	9	9		9		9
7439-97-6	Mercury [2]	0.96	0.6		0.6		0.6
7439-96-5	Manganese	299	299		299		299
7440-02-0	Nickel	2	2		2		2
7439-92-1	Lead	8	8		8		8
7440-36-0	Antimony	23	23		23		23
7723-14-0	Phosphorus	650	650		650		650
7782-49-2	Selenium	0.4	0.4		0.4		0.4
7440-22-4	Silver	0.5	0.5		0.5		0.5
7429-90-5	Aluminum	71000	71000		71000		71000
7440-39-3	Barium	800	800		800		800
1317-65-3	Calcium Carbonate	14000	14000		14000		14000
7440-50-8	Copper	5	5		5		5
7439-89-6	Iron	18200	18200		18200		18200
7439-98-7	Molybdenum	1	1		1		1
7440-28-0	Thallium	10	10		10		10
7440-61-1	Uranium	10	10		10		10
7440-62-2	Vanadium	28	28		28		28
7440-33-7	Tungsten	10	10		10		10
7440-66-6	Zinc	35	35		35		35

[1] *(Midas Gold 2017c)* *Median concentration of 55,000 SGP samples.* *1E+6 parts/ppm*
[2] *(Midas Gold 2018e)* *Median ore and development rock (DR) concentrations of 151,000 samples; resource block model.*
[3] *(Perpetua 2021g)* *Median concentration of 265 SGP samples.*
[4] *HRD: haul road - emissions calculated based on 0% of the total VMT occuring on CR*
[5] *(ALS 2018)* *Median concentration of 8 SGP samples.*

DR DR DR DR DR DR DR DR ORE DR DR DR DR HRD DR/AR

MINING FUGITIVE EMISSIONS - CONTINUED **Model Scenario W3** DR **180,000 T/day Emissions**

HAP/TAP Emissions

Hourly [1] YPP_pph HFP_pph WEP_pph BT_pph YPPBL_pph HFPBL_pph WEPBL_ppl BTBL_pph STKP_pph FDRSF_pph HFDRSF_pph YPDRSF_pph WEDRSF_pph HR000_pph CCRD, UGE lb/hr

CAS No.	Pollutant	YPP lb/hr	HFP lb/hr	WEP lb/hr	BT lb/hr	YPPBL lb/hr	HFPBL lb/hr	WEPBL lb/hr	BTBL lb/hr	STKP lb/hr	FDRSF lb/hr	HFDRSF lb/hr	YPDRSF lb/hr	WEDRSF lb/hr	HR000 lb/hr	TSF, ACCRD, UGEXP lb/hr	Total lb/hr
7440-38-2	Arsenic	0	0	0.052	0	0	0	0.018	0	0	0	8.1E-3	0	0	0.464	1.1E-3	0.544
7440-41-7	Beryllium	0	0	2.5E-4	0	0	0	8.6E-5	0	0	0	3.9E-5	0	0	2.2E-3	5.1E-6	2.6E-3
7440-43-9	Cadmium	0	0	3.9E-5	0	0	0	1.3E-5	0	0	0	6.0E-6	0	0	3.5E-4	7.9E-7	4.1E-4
7440-48-4	Cobalt	0	0	3.1E-4	0	0	0	1.1E-4	0	0	0	4.8E-5	0	0	2.8E-3	6.4E-6	3.3E-3
7440-47-3	Chromium	0	0	7.1E-4	0	0	0	2.4E-4	0	0	0	1.1E-4	0	0	6.3E-3	1.4E-5	7.3E-3
7439-97-6	Mercury	0	0	4.7E-5	0	0	0	1.6E-5	0	0	0	7.2E-6	0	0	4.2E-4	9.5E-7	4.9E-4
7439-96-5	Manganese	0	0	0.024	0	0	0	8.0E-3	0	0	0	3.6E-3	0	0	0.208	4.7E-4	0.244
7440-02-0	Nickel	0	0	1.6E-4	0	0	0	5.4E-5	0	0	0	2.4E-5	0	0	1.4E-3	3.2E-6	1.6E-3
7439-92-1	Lead	0	0	6.3E-4	0	0	0	2.1E-4	0	0	0	9.7E-5	0	0	5.6E-3	1.3E-5	6.5E-3
7440-36-0	Antimony	0	0	1.8E-3	0	0	0	6.2E-4	0	0	0	2.8E-4	0	0	0.016	3.7E-5	0.019
7723-14-0	Phosphorus	0	0	0.051	0	0	0	0.017	0	0	0	7.9E-3	0	0	0.452	1.0E-3	0.530
7782-49-2	Selenium	0	0	3.1E-5	0	0	0	1.1E-5	0	0	0	4.8E-6	0	0	2.8E-4	6.4E-7	3.3E-4
7440-22-4	Silver	0	0	3.9E-5	0	0	0	1.3E-5	0	0	0	6.0E-6	0	0	3.5E-4	7.9E-7	4.1E-4
7429-90-5	Aluminum	0	0	5.585	0	0	0	1.902	0	0	0	0.858	0	0	49.397	0.113	57.855
7440-39-3	Barium	0	0	0.063	0	0	0	0.021	0	0	0	9.7E-3	0	0	0.557	1.3E-3	0.652
1317-65-3	Calcium Ca:	0	0	1.101	0	0	0	0.375	0	0	0	0.169	0	0	9.740	0.022	11.408
7440-50-8	Copper	0	0	3.9E-4	0	0	0	1.3E-4	0	0	0	6.0E-5	0	0	3.5E-3	7.9E-6	4.1E-3
7439-89-6	Iron	0	0	1.432	0	0	0	0.488	0	0	0	0.220	0	0	12.662	0.029	14.831
7439-98-7	Molybdenu	0	0	7.9E-5	0	0	0	2.7E-5	0	0	0	1.2E-5	0	0	7.0E-4	1.6E-6	8.1E-4
7440-28-0	Thallium	0	0	7.9E-4	0	0	0	2.7E-4	0	0	0	1.2E-4	0	0	7.0E-3	1.6E-5	8.1E-3
7440-61-1	Uranium	0	0	7.9E-4	0	0	0	2.7E-4	0	0	0	1.2E-4	0	0	7.0E-3	1.6E-5	8.1E-3
7440-62-2	Vanadium	0	0	2.2E-3	0	0	0	7.5E-4	0	0	0	3.4E-4	0	0	0.019	4.4E-5	0.023
7440-33-7	Tungsten	0	0	7.9E-4	0	0	0	2.7E-4	0	0	0	1.2E-4	0	0	7.0E-3	1.6E-5	8.1E-3
7440-66-6	Zinc	0	0	2.8E-3	0	0	0	9.4E-4	0	0	0	4.2E-4	0	0	0.024	5.6E-5	0.029
Total		0	0	8.320	0	0	0	2.834	0	0	0	1.278	0	0	73.586	0.168	86.185

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.* chk 86.1849 86.1849

DR DR DR DR DR DR DR DR ORE DR DR DR DR HRD DR/AR

MINING FUGITIVE EMISSIONS - CONTINUED **Model Scenario W3** DR **180,000 T/day Emissions**

HAP/TAP Emissions

Annual

		YPP_tpy	HFP_tpy	WEP_tpy	BT_tpy	YPPBL_tpy	HFPBL_tpy	WEPBL_tpy	BTBL_tpy	STKP_tpy	FDRSF_tpy	HFDRSF_tpy	YPDRSF_tpy	WEDRSF_tpy	HR000_tpy	CCRD, UGE	ton/yr
		YPP	HFP	WEP	BT	YPPBL	HFPBL	WEPBL	BTBL	STKP	FDRSF	HFDRSF	YPDRSF	WEDRSF	HR000	TSF, ACCRD, UGEXP	Total
CAS No.	Pollutant	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr
7440-38-2	Arsenic	0	0	0.230	0	0	0	0.078	0	0	0	0.035	0	0	2.033	4.6E-3	2.381
7440-41-7	Beryllium	0	0	1.1E-3	0	0	0	3.8E-4	0	0	0	1.7E-4	0	0	9.8E-3	2.2E-5	0.011
7440-43-9	Cadmium	0	0	1.7E-4	0	0	0	5.9E-5	0	0	0	2.6E-5	0	0	1.5E-3	3.5E-6	1.8E-3
7440-48-4	Cobalt	0	0	1.4E-3	0	0	0	4.7E-4	0	0	0	2.1E-4	0	0	0.012	2.8E-5	0.014
7440-47-3	Chromium	0	0	3.1E-3	0	0	0	1.1E-3	0	0	0	4.8E-4	0	0	0.027	6.3E-5	0.032
7439-97-6	Mercury	0	0	2.1E-4	0	0	0	7.0E-5	0	0	0	3.2E-5	0	0	1.8E-3	4.2E-6	2.1E-3
7439-96-5	Manganese	0	0	0.103	0	0	0	0.035	0	0	0	0.016	0	0	0.911	2.1E-3	1.067
7440-02-0	Nickel	0	0	6.9E-4	0	0	0	2.3E-4	0	0	0	1.1E-4	0	0	6.1E-3	1.4E-5	7.1E-3
7439-92-1	Lead	0	0	2.8E-3	0	0	0	9.4E-4	0	0	0	4.2E-4	0	0	0.024	5.6E-5	0.029
7440-36-0	Antimony	0	0	7.9E-3	0	0	0	2.7E-3	0	0	0	1.2E-3	0	0	0.070	1.6E-4	0.082
7723-14-0	Phosphorus	0	0	0.224	0	0	0	0.076	0	0	0	0.034	0	0	1.981	4.5E-3	2.320
7782-49-2	Selenium	0	0	1.4E-4	0	0	0	4.7E-5	0	0	0	2.1E-5	0	0	1.2E-3	2.8E-6	1.4E-3
7440-22-4	Silver	0	0	1.7E-4	0	0	0	5.9E-5	0	0	0	2.6E-5	0	0	1.5E-3	3.5E-6	1.8E-3
7429-90-5	Aluminum	0	0	24.463	0	0	0	8.332	0	0	0	3.756	0	0	216	0.494	253
7440-39-3	Barium	0	0	0.276	0	0	0	0.094	0	0	0	0.042	0	0	2.438	5.6E-3	2.855
1317-65-3	Calcium Ca:	0	0	4.824	0	0	0	1.643	0	0	0	0.741	0	0	42.663	0.097	49.967
7440-50-8	Copper	0	0	1.7E-3	0	0	0	5.9E-4	0	0	0	2.6E-4	0	0	0.015	3.5E-5	0.018
7439-89-6	Iron	0	0	6.271	0	0	0	2.136	0	0	0	0.963	0	0	55.462	0.127	64.958
7439-98-7	Molybdenu	0	0	3.4E-4	0	0	0	1.2E-4	0	0	0	5.3E-5	0	0	3.0E-3	7.0E-6	3.6E-3
7440-28-0	Thallium	0	0	3.4E-3	0	0	0	1.2E-3	0	0	0	5.3E-4	0	0	0.030	7.0E-5	0.036
7440-61-1	Uranium	0	0	3.4E-3	0	0	0	1.2E-3	0	0	0	5.3E-4	0	0	0.030	7.0E-5	0.036
7440-62-2	Vanadium	0	0	9.6E-3	0	0	0	3.3E-3	0	0	0	1.5E-3	0	0	0.085	1.9E-4	0.100
7440-33-7	Tungsten	0	0	3.4E-3	0	0	0	1.2E-3	0	0	0	5.3E-4	0	0	0.030	7.0E-5	0.036
7440-66-6	Zinc	0	0	0.012	0	0	0	4.1E-3	0	0	0	1.9E-3	0	0	0.107	2.4E-4	0.125
Total		0	0	36.441	0	0	0	12.412	0	0	0	5.596	0	0	322	0.736	377
															chk	377.4900	377.4900

MINING FUGITIVE EMISSIONS - CONTINUED

Mercury Evaporative Flux Emissions

Fugitive Mercury Flux and Emissions

			Area		Hg Flux	Emissions[1] lb/hr	Emissions[1] ton/yr	Emissions[1] lb/yr
CAS No.	Pollutant	Source	m^2	ha	$\mu g/m^2$-yr	lb/hr	ton/yr	lb/yr
		Stockpiles	52,623	5.3	556	7.37E-6	3.2E-5	6.5E-2
		Rock Dumps	2,063,990	206.4	76.2	3.96E-5	1.7E-4	0.35
		Tailings	1,338,158	133.8	2,144	7.22E-4	3.2E-3	6.32
		Pits	1,504,919	150.5	132.3	5.01E-5	2.2E-4	0.44
7439-97-6	Mercury					8.2E-4	3.6E-3	7.17

(1) *Hourly emissions based on:* 8,760 *hours per year of operation*

Fugitive Mercury Emission Factors

	Twin Creeks (TC)		Ore Hg Adjusted	Stibnite	
	Hg Flux (1)	Hg (2)	$\mu g/m^2$/yr	Hg Flux (3)	Hg (4)
Source	$\mu g/m^2$-yr	µg/g	TC	$\mu g/m^2$-yr	µg/g
Stockpiles	5,609	33	556	556	0.96
Rock Dumps	768	3.5	76.2	76.2	0.60
Tailings	21,621	33	2,144	2,144	0.96
Pits	1,334	9.5	132	132.3	0.60

(1) *(Eckley 2010)* *Table 1: Hg flux* $\mu g/m^2$*-yr*

(2) *(Eckley 2010)* *Table 1: Average Hg flux mg/g: " Stockpiles - high-grade stockpiles, Rock Dumps - waste rock dumps, Tailings - high-grade stockpiles as a surrogate; Pits - pit"*

(3) *(Eckley 2010)* *Figure 2: log(y) = m*log(x) + b*

y = Hg Flux (ng/m^2*-d)*
x = material Hg concentration (µg/g)]

Slope =	*Solar*	*TC*
	Low	*0.59*
	Medium	*0.6*
	High	*0.77*
	Average	*0.65*

(4) *(Midas Gold 2018e)*

Sample Calculation: $m = \log(y1/y2) / \log(x1/x2)$

m=	0.65	unitless
y1=	5,609	$\mu g/m^2$-yr
x1=	33	$\mu g/m^2$-yr
x2=	0.96	$\mu g/m^2$-yr
log(x1/x2)=	1.536243	unitless
log(y1/y2)=	1.003679	unitless
y1/y2=	10.08506	unitless
y2=	556.2	$\mu g/m^2$-yr

Conversions

2,000	lb/ton
10,000	m2/ha
453.593	g/lb

TABLE A-W3. HAP/TAP Emissions and Exemptions

180,000 T/day Emissions						MINING										LEACHING	
chk						*Mining*	*Model Scenario W3*									*CN Leach/PAX*	
						YPP,HFP,WEP,BT		YPPBL,HFPBL,WEPBL,BTBL		HR000		STKP, FDRSF, HFDRSF, YPDRSF, WEDRSF		TSF,ACCRD,UGEXP			
CAS	HAP/TAP	HAP	TAP			Pits		Blasting		Haul Roads		Stockpiles and DRFS		Tails, Access Road, Exploration		CN Leach and PAX	
	NSPS or NESHAP HAP/TAP -->			*Y*													
	Non-Carcinogenic Acute (A) or Carcinogenic (C) -->				*A/C*	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr
106-99-0	1,3-Butadiene	Y	Y	Y	C				0	0	0		0				
91-57-6	2-Methylnaphthalene	Y	N	n/a								0					
56-49-5	3-Methylchloranthrene	Y	Y	Y	C												
57-97-6	7,12-Dimethylbenz(a)anthracene	Y	N	n/a													
83-32-9	Acenaphthene	Y	N	n/a													
208-96-8	Acenaphthylene	Y	N	n/a													
75-07-0	Acetaldehyde	Y	Y	Y	C												
107-02-8	Acrolein	Y	Y	Y	A												
120-12-7	Anthracene	Y	N	n/a													
7440-36-0	Antimony	Y	Y	Y	A	1.8E-3	7.9E-3	6.2E-4	2.7E-3	0.016	0.070	2.8E-4	1.2E-3	3.7E-5	1.6E-4		
7440-38-2	Arsenic	Y	Y	Y	C	0.052	0.230	0.018	0.078	0.464	2.033	8.1E-3	0.035	1.1E-3	4.6E-3		
71-43-2	Benzene	Y	Y	Y	C												
50-32-8	Benzo(a)pyrene	Y	Y	Y	C												
56-55-3	Benz(a)anthracene	Y	Y	Y	C												
205-99-2	Benzo(b)fluoranthene	Y	Y	Y	C												
207-08-9	Benzo(k)fluoranthene	Y	Y	Y	C												
218-01-9	Chrysene	Y	Y	Y	C												
53-70-3	Dibenzo(a,h)anthracene	Y	Y	Y	C												
193-39-5	Indeno(1,2,3-cd)pyrene	Y	Y	Y	C												
191-24-2	Benzo(g,h,i)perylene	Y	N	n/a													
7440-41-7	Beryllium	Y	Y	Y	C	2.5E-4	1.1E-3	8.6E-5	3.8E-4	2.2E-3	9.8E-3	3.9E-5	1.7E-4	5.1E-6	2.2E-5		
92-52-4	Biphenyl	Y	Y	Y	A												
7440-43-9	Cadmium	Y	Y	Y	C	3.9E-5	1.7E-4	1.3E-5	5.9E-5	3.5E-4	1.5E-3	6.0E-6	2.6E-5	7.9E-7	3.5E-6		
75-15-0	Carbon Disulfide	Y	Y	Y	A											0.014	0.063
7440-47-3	Chromium	Y	Y	Y	A	7.1E-4	3.1E-3	2.4E-4	1.1E-3	6.3E-3	0.027	1.1E-4	4.8E-4	1.4E-5	6.3E-5		
18540-29-9	Cr (VI)	Y	Y	Y	C												
7440-48-4	Cobalt	Y	Y	Y	A	3.1E-4	1.4E-3	1.1E-4	4.7E-4	2.8E-3	0.012	4.8E-5	2.1E-4	6.4E-6	2.8E-5		
592-01-8	Cyanide	Y	Y	Y	A											0.453	1.983
106-46-7	Dichlorobenzene	Y	Y	Y	A												
206-44-0	Fluoranthene	Y	N	n/a													
86-73-7	Fluorene	Y	N	n/a													
50-00-0	Formaldehyde	Y	Y	Y	C												
110-54-3	Hexane	Y	Y	Y	A												
7647-01-0	Hydrogen Chloride	Y	Y	Y	A												
7439-92-1	Lead	Y	N	n/a		6.3E-4	2.8E-3	2.1E-4	9.4E-4	5.6E-3	0.024	9.7E-5	4.2E-4	1.3E-5	5.6E-5		
7439-96-5	Manganese	Y	Y	Y	A	0.024	0.103	8.0E-3	0.035	0.208	0.911	3.6E-3	0.016	4.7E-4	2.1E-3		
7439-97-6	Mercury	Y	N	n/a		9.7E-5	4.3E-4	1.6E-5	7.0E-5	4.2E-4	1.8E-3	5.4E-5	2.4E-4	7.2E-4	3.2E-3		
91-20-3	Naphthalene	Y	Y	Y	A												
7440-02-0	Nickel	Y	Y	Y	C	1.6E-4	6.9E-4	5.4E-5	2.3E-4	1.4E-3	6.1E-3	2.4E-5	1.1E-4	3.2E-6	1.4E-5		
85-01-8	Phenanthrene	Y	N	n/a													
108-95-2	Phenol	Y	Y	Y	A												
7723-14-0	Phosphorus	Y	Y	Y	A	0.051	0.224	0.017	0.076	0.452	1.981	7.9E-3	0.034	1.0E-3	4.5E-3		
129-00-0	Pyrene	Y	N	n/a													
7782-49-2	Selenium	Y	Y	Y	A	3.1E-5	1.4E-4	1.1E-5	4.7E-5	2.8E-4	1.2E-3	4.8E-6	2.1E-5	6.4E-7	2.8E-6		
108-88-3	Toluene	Y	Y	Y	A												
1330-20-7	Xylene	Y	Y	Y	A												
7429-90-5	Aluminum	N	Y	N	A	5.585	24.463	1.902	8.332	49.397	216	0.858	3.756	0.113	0.494		
7440-39-3	Barium	N	Y	N	A	0.063	0.276	0.021	0.094	0.557	2.438	9.7E-3	0.042	1.3E-3	5.6E-3		
1317-65-3	Calcium Carbonate	N	Y	N	A	1.101	4.824	0.375	1.643	9.740	42.663	0.169	0.741	0.022	0.097		
1305-78-8	Calcium Oxide	N	Y	N	A												
7440-50-8	Copper	N	Y	N	A	3.9E-4	1.7E-3	1.3E-4	5.9E-4	3.5E-3	0.015	6.0E-5	2.6E-4	7.9E-6	3.5E-5		
110-82-7	Cyclohexane	N	Y	N	A												
7783-06-4	Hydrogen Sulfide	N	Y	N	A												
7439-89-6	Iron	N	Y	N	A	1.432	6.271	0.488	2.136	12.662	55.462	0.220	0.963	0.029	0.127		
7439-98-7	Molybdenum	N	Y	N	A	7.9E-5	3.4E-4	2.7E-5	1.2E-4	7.0E-4	3.0E-3	1.2E-5	5.3E-5	1.6E-6	7.0E-6		
109-66-0	Pentane	N	Y	N	A												
7440-22-4	Silver	N	Y	N	A	3.9E-5	1.7E-4	1.3E-5	5.9E-5	3.5E-4	1.5E-3	6.0E-6	2.6E-5	7.9E-7	3.5E-6		
7664-93-9	Sulfuric Acid	N	Y	N	A												
7440-28-0	Thallium	N	Y	N	A	7.9E-4	3.4E-3	2.7E-4	1.2E-3	7.0E-3	0.030	1.2E-4	5.3E-4	1.6E-5	7.0E-5		
7440-61-1	Uranium	N	Y	N	A	7.9E-4	3.4E-3	2.7E-4	1.2E-3	7.0E-3	0.030	1.2E-4	5.3E-4	1.6E-5	7.0E-5		
7440-62-2	Vanadium	N	Y	N	A	2.2E-3	9.6E-3	7.5E-4	3.3E-3	0.019	0.085	3.4E-4	1.5E-3	4.4E-5	1.9E-4		
25551-13-7	Trimethyl benzene	N	Y	N	A												
7440-33-7	Tungsten	N	Y	N	A	7.9E-4	3.4E-3	2.7E-4	1.2E-3	7.0E-3	0.030	1.2E-4	5.3E-4	1.6E-5	7.0E-5		
7440-66-6	Zinc	N	Y	N	A	2.8E-3	0.012	9.4E-4	4.1E-3	0.024	0.107	4.2E-4	1.9E-3	5.6E-5	2.4E-4		
HAP TOTAL						***0.131***	***0.574***	***0.045***	***0.196***	***1.160***	***5.079***	***0.020***	***0.088***	***3.4E-3***	***0.015***	***0.467***	***2.046***
MERCURY TOTAL (exempt)						***9.7E-5***	***4.3E-4***	***1.6E-5***	***7.0E-5***	***4.2E-4***	***1.8E-3***	***5.4E-5***	***2.4E-4***	***7.2E-4***	***3.2E-3***		
MERCURY TOTAL (non-exempt)																	
TAP TOTAL (HAP-TAP addressed by NSPS/NESHAP)																	
TAP TOTAL (For EL Evaluation)						***8.319***	***36.438***	***2.834***	***12.411***	***73.580***	***322***	***1.278***	***5.595***	***0.168***	***0.735***	***0.467***	***2.046***

TABLE A-W3. HAP/TAP Emissions and Exemptions

180,000 T/day Emissions						PROCESSING AND PRODUCTION											
chk						*Ore Processing*				*Ore Concentration and Refining*				*Process Heating*			
						OC1-13		PS		AC		EW,MR,MF,CKD		ACB, CKB, PV, HS		LKC	
CAS	HAP/TAP	HAP	TAP			Crushers & Xfers		Prill Silos		Autoclave		EW, Preg Tank, Retort, Furnace, Carbon Kiln		POX Boiler, C. Kiln Comb., Prop. Vap., Sol'n Heater		Lime Kiln Combustion	
	NSPS or NESHAP HAP/TAP -->			*Y*		*LL*	*LL*			*7E*	*7E*	*7E*	*7E*			*5A*	*5A*
	Non-Carcinogenic Acute (A) or Carcinogenic (C) -->				*A/C*	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr
106-99-0	1,3-Butadiene	Y	Y	Y	C												
91-57-6	2-Methylnaphthalene	Y	N	n/a										1.9E-7	7.6E-7	5.2E-7	1.9E-6
56-49-5	3-Methylchloranthrene	Y	Y	Y	C									1.3E-8	5.7E-8	3.3E-8	1.4E-7
57-97-6	7,12-Dimethylbenz(a)anthracene	Y	N	n/a										1.3E-7	5.1E-7	3.5E-7	1.3E-6
83-32-9	Acenaphthene	Y	N	n/a										1.4E-8	5.7E-8	3.9E-8	1.4E-7
208-96-8	Acenaphthylene	Y	N	n/a										1.4E-8	5.7E-8	3.9E-8	1.4E-7
75-07-0	Acetaldehyde	Y	Y	Y	C												
107-02-8	Acrolein	Y	Y	Y	A												
120-12-7	Anthracene	Y	N	n/a										1.9E-8	7.6E-8	5.2E-8	1.9E-7
7440-36-0	Antimony	Y	Y	Y	A	1.4E-4	5.9E-4			2.3E-5	1.0E-4	3.8E-4	1.7E-3				
7440-38-2	Arsenic	Y	Y	Y	C	3.9E-3	0.017			2.3E-5	1.0E-4	3.8E-4	1.7E-3	1.5E-6	6.4E-6	3.7E-6	1.6E-5
71-43-2	Benzene	Y	Y	Y	C									1.5E-5	6.7E-5	3.9E-5	1.7E-4
50-32-8	Benzo(a)pyrene	Y	Y	Y	C									8.7E-9	3.8E-8	2.2E-8	9.6E-8
56-55-3	Benz(a)anthracene	Y	Y	Y	C									1.3E-8	5.7E-8	3.3E-8	1.4E-7
205-99-2	Benzo(b)fluoranthene	Y	Y	Y	C									1.3E-8	5.7E-8	3.3E-8	1.4E-7
207-08-9	Benzo(k)fluoranthene	Y	Y	Y	C									1.3E-8	5.7E-8	3.3E-8	1.4E-7
218-01-9	Chrysene	Y	Y	Y	C									1.3E-8	5.7E-8	3.3E-8	1.4E-7
53-70-3	Dibenzo(a,h)anthracene	Y	Y	Y	C									8.7E-9	3.8E-8	2.2E-8	9.6E-8
193-39-5	Indeno(1,2,3-cd)pyrene	Y	Y	Y	C									1.3E-8	5.7E-8	3.3E-8	1.4E-7
191-24-2	Benzo(g,h,i)perylene	Y	N	n/a										9.5E-9	3.8E-8	2.6E-8	9.6E-8
7440-41-7	Beryllium	Y	Y	Y	C	1.9E-5	8.2E-5			2.3E-5	1.0E-4	3.8E-4	1.7E-3	8.7E-8	3.8E-7	2.2E-7	9.6E-7
92-52-4	Biphenyl	Y	Y	Y	A												
7440-43-9	Cadmium	Y	Y	Y	C	2.9E-6	1.3E-5			2.3E-5	1.0E-4	3.8E-4	1.7E-3	8.0E-6	3.5E-5	2.0E-5	8.8E-5
75-15-0	Carbon Disulfide	Y	Y	Y	A												
7440-47-3	Chromium	Y	Y	Y	A	5.3E-5	2.3E-4			2.3E-5	1.0E-4	3.8E-4	1.7E-3	1.1E-5	4.5E-5	3.0E-5	1.1E-4
18540-29-9	Cr (VI)	Y	Y	Y	C												
7440-48-4	Cobalt	Y	Y	Y	A	2.4E-5	1.0E-4			2.3E-5	1.0E-4	3.8E-4	1.7E-3	6.6E-7	2.7E-6	1.8E-6	6.8E-6
592-01-8	Cyanide	Y	Y	Y	A							1.2E-3	5.3E-3				
106-46-7	Dichlorobenzene	Y	Y	Y	A									9.5E-6	3.8E-5	2.6E-5	9.6E-5
206-44-0	Fluoranthene	Y	N	n/a										2.4E-8	9.5E-8	6.5E-8	2.4E-7
86-73-7	Fluorene	Y	N	n/a										2.2E-8	8.9E-8	6.1E-8	2.3E-7
50-00-0	Formaldehyde	Y	Y	Y	C									5.5E-4	2.4E-3	1.4E-3	6.0E-3
110-54-3	Hexane	Y	Y	Y	A									0.014	0.057	0.039	0.145
7647-01-0	Hydrogen Chloride	Y	Y	Y	A												
7439-92-1	Lead	Y	N	n/a		4.7E-5	2.1E-4			2.3E-5	1.0E-4	3.8E-4	1.7E-3				
7439-96-5	Manganese	Y	Y	Y	A	1.8E-3	7.7E-3			2.3E-5	1.0E-4	3.8E-4	1.7E-3	3.0E-6	1.2E-5	8.2E-6	3.1E-5
7439-97-6	Mercury	Y	N	n/a		5.6E-6	2.5E-5			2.3E-5	1.0E-4	3.8E-4	1.7E-3	2.1E-6	8.3E-6	5.6E-6	2.1E-5
91-20-3	Naphthalene	Y	Y	Y	A									4.8E-6	1.9E-5	1.3E-5	4.9E-5
7440-02-0	Nickel	Y	Y	Y	C	1.2E-5	5.2E-5			2.3E-5	1.0E-4	3.8E-4	1.7E-3	1.5E-5	6.7E-5	3.9E-5	1.7E-4
85-01-8	Phenanthrene	Y	N	n/a										1.3E-7	5.4E-7	3.7E-7	1.4E-6
108-95-2	Phenol	Y	Y	Y	A												
7723-14-0	Phosphorus	Y	Y	Y	A	3.8E-3	0.017			2.3E-5	1.0E-4	3.8E-4	1.7E-3				
129-00-0	Pyrene	Y	N	n/a										4.0E-8	1.6E-7	1.1E-7	4.0E-7
7782-49-2	Selenium	Y	Y	Y	A	2.4E-6	1.0E-5			2.3E-5	1.0E-4	3.8E-4	1.7E-3	1.9E-7	7.6E-7	5.2E-7	1.9E-6
108-88-3	Toluene	Y	Y	Y	A									2.7E-5	1.1E-4	7.3E-5	2.7E-4
1330-20-7	Xylene	Y	Y	Y	A												
7429-90-5	Aluminum	N	Y	N	A	0.418	1.829			2.3E-5	1.0E-4	3.8E-4	1.7E-3				
7440-39-3	Barium	N	Y	N	A	4.7E-3	0.021			2.3E-5	1.0E-4	3.8E-4	1.7E-3	3.5E-5	1.4E-4	9.5E-5	3.5E-4
1317-65-3	Calcium Carbonate	N	Y	N	A	0.082	0.361			2.3E-5	1.0E-4	3.8E-4	1.7E-3				
1305-78-8	Calcium Oxide	N	Y	N	A												
7440-50-8	Copper	N	Y	N	A	2.9E-5	1.3E-4			2.3E-5	1.0E-4	3.8E-4	1.7E-3	6.7E-6	2.7E-5	1.8E-5	6.8E-5
110-82-7	Cyclohexane	N	Y	N	A												
7783-06-4	Hydrogen Sulfide	N	Y	N	A					0.900	3.942						
7439-89-6	Iron	N	Y	N	A	0.107	0.469			2.3E-5	1.0E-4	3.8E-4	1.7E-3				
7439-98-7	Molybdenum	N	Y	N	A	5.9E-6	2.6E-5			2.3E-5	1.0E-4	3.8E-4	1.7E-3	8.7E-6	3.5E-5	2.4E-5	8.8E-5
109-66-0	Pentane	N	Y	N	A									0.021	0.083	0.056	0.209
7440-22-4	Silver	N	Y	N	A	2.9E-6	1.3E-5			2.3E-5	1.0E-4	3.8E-4	1.7E-3				
7664-93-9	Sulfuric Acid	N	Y	N	A					2.030	8.891						
7440-28-0	Thallium	N	Y	N	A	5.9E-5	2.6E-4			2.3E-5	1.0E-4	3.8E-4	1.7E-3				
7440-61-1	Uranium	N	Y	N	A	5.9E-5	2.6E-4			2.3E-5	1.0E-4	3.8E-4	1.7E-3				
7440-62-2	Vanadium	N	Y	N	A	1.6E-4	7.2E-4			2.3E-5	1.0E-4	3.8E-4	1.7E-3	1.8E-5	7.3E-5	5.0E-5	1.8E-4
25551-13-7	Trimethyl benzene	N	Y	N	A												
7440-33-7	Tungsten	N	Y	N	A	5.9E-5	2.6E-4			2.3E-5	1.0E-4	3.8E-4	1.7E-3				
7440-66-6	Zinc	N	Y	N	A	2.1E-4	9.0E-4			2.3E-5	1.0E-4	3.8E-4	1.7E-3	2.3E-4	9.2E-4	6.3E-4	2.3E-3
HAP TOTAL						***9.8E-3***	***0.043***			***2.8E-4***	***1.2E-3***	***5.8E-3***	***0.025***	***0.015***	***0.060***	***0.041***	***0.152***
MERCURY TOTAL (exempt)										***2.3E-5***	***1.0E-4***	***3.8E-4***	***1.7E-3***			***5.6E-6***	***2.1E-5***
MERCURY TOTAL (non-exempt)						***5.6E-6***	***2.5E-5***							***2.1E-6***	***8.3E-6***		
TAP TOTAL (HAP-TAP addressed by NSPS/NESHAP)						***9.8E-3***	***0.043***			***2.3E-4***	***1.0E-3***	***5.0E-3***	***0.022***			***0.041***	***0.152***
TAP TOTAL (For EL Evaluation)						***0.612***	***2.682***			***2.930***	***12.835***	***4.6E-3***	***0.020***	***0.036***	***0.144***	***0.057***	***0.212***

TABLE A-W3. HAP/TAP Emissions and Exemptions

180,000 T/day Emissions						PROCESSING AND PRODUCTION - Continued													
chk						*Lime Production*						*Aggregate Prod.*		*Concrete Production*					
CAS	HAP/TAP	HAP	TAP			LS1-11,LSBM		LK,LS12,LCR,LS-L/U		LS1-L/U,MillS2-L/U,ACS1-4		PCSP1,PCSP2		CM		CS1L,CS1U,CS2L, CS2U		CA-L/U	
						Limestone Crushers, Screens, Mill, Xfers		Lime Kiln, Kiln Feed, Lime Mill, Pebble Lime Silo		Lime Silos and Lime Mill Crushing		Portable Crushers, Screens, Xfers		Central Mixer		Cement Silo #1 and #2 L/U		Aggregate Bin	
	NSPS or NESHAP HAP/TAP -->			*Y*		*OOO*	*OOO*	*5A*	*5A*			*OOO*	*OOO*					*OOO*	*OOO*
	Non-Carcinogenic Acute (A) or Carcinogenic (C) -->				*A/C*	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr
106-99-0	1,3-Butadiene	Y	Y	Y	C														
91-57-6	2-Methylnaphthalene	Y	N	n/a															
56-49-5	3-Methylchloranthrene	Y	Y	Y	C														
57-97-6	7,12-Dimethylbenz(a)anthracene	Y	N	n/a															
83-32-9	Acenaphthene	Y	N	n/a															
208-96-8	Acenaphthylene	Y	N	n/a															
75-07-0	Acetaldehyde	Y	Y	Y	C														
107-02-8	Acrolein	Y	Y	Y	A														
120-12-7	Anthracene	Y	N	n/a															
7440-36-0	Antimony	Y	Y	Y	A	1.4E-5	4.8E-5	3.1E-6	1.2E-5	1.6E-6	5.1E-7	3.1E-6	1.4E-5					3.5E-6	8.6E-6
7440-38-2	Arsenic	Y	Y	Y	C	1.0E-4	4.4E-4	2.4E-5	1.1E-4	1.1E-6	4.7E-6	2.9E-5	1.3E-4	2.0E-6	8.9E-6	1.2E-7	5.1E-7	1.8E-5	7.9E-5
71-43-2	Benzene	Y	Y	Y	C														
50-32-8	Benzo(a)pyrene	Y	Y	Y	C														
56-55-3	Benz(a)anthracene	Y	Y	Y	C														
205-99-2	Benzo(b)fluoranthene	Y	Y	Y	C														
207-08-9	Benzo(k)fluoranthene	Y	Y	Y	C														
218-01-9	Chrysene	Y	Y	Y	C														
53-70-3	Dibenzo(a,h)anthracene	Y	Y	Y	C														
193-39-5	Indeno(1,2,3-cd)pyrene	Y	Y	Y	C														
191-24-2	Benzo(g,h,i)perylene	Y	N	n/a															
7440-41-7	Beryllium	Y	Y	Y	C	3.5E-6	1.5E-5	8.4E-7	3.7E-6	3.7E-8	1.6E-7	1.0E-6	4.4E-6			1.3E-8	5.8E-8	6.3E-7	2.8E-6
92-52-4	Biphenyl	Y	Y	Y	A														
7440-43-9	Cadmium	Y	Y	Y	C	1.1E-6	4.8E-6	2.6E-7	1.2E-6	1.2E-8	5.1E-8	3.1E-7	1.4E-6	4.9E-9	2.1E-8			2.0E-7	8.6E-7
75-15-0	Carbon Disulfide	Y	Y	Y	A														
7440-47-3	Chromium	Y	Y	Y	A	8.5E-5	2.9E-4	1.9E-5	6.9E-5	9.7E-6	3.0E-6	1.9E-5	8.2E-5	8.7E-7	3.8E-6	7.9E-7	3.5E-6	2.1E-5	5.2E-5
18540-29-9	Cr (VI)	Y	Y	Y	C									1.9E-7	8.1E-7	1.6E-7	7.0E-7		
7440-48-4	Cobalt	Y	Y	Y	A	2.3E-5	7.7E-5	5.0E-6	1.8E-5	2.6E-6	8.1E-7	5.0E-6	2.2E-5					5.5E-6	1.4E-5
592-01-8	Cyanide	Y	Y	Y	A														
106-46-7	Dichlorobenzene	Y	Y	Y	A														
206-44-0	Fluoranthene	Y	N	n/a															
86-73-7	Fluorene	Y	N	n/a															
50-00-0	Formaldehyde	Y	Y	Y	C														
110-54-3	Hexane	Y	Y	Y	A														
7647-01-0	Hydrogen Chloride	Y	Y	Y	A	0	0	0.986	3.666										
7439-92-1	Lead	Y	N	n/a		1.7E-5	5.8E-5	3.7E-6	1.4E-5	1.9E-6	6.1E-7	3.8E-6	1.6E-5	2.5E-7	1.1E-6	3.0E-7	1.3E-6	4.1E-6	1.0E-5
7439-96-5	Manganese	Y	Y	Y	A	1.3E-3	4.6E-3	2.9E-4	1.1E-3	1.5E-4	4.8E-5	3.0E-4	1.3E-3	2.6E-5	1.1E-4	3.2E-6	1.4E-5	3.3E-4	8.2E-4
7439-97-6	Mercury	Y	N	n/a		1.1E-7	3.9E-7	2.8E-4	1.0E-3	1.3E-8	4.1E-9	2.5E-8	1.1E-7					2.8E-8	6.9E-8
91-20-3	Naphthalene	Y	Y	Y	A														
7440-02-0	Nickel	Y	Y	Y	C	2.2E-5	9.6E-5	5.3E-6	2.3E-5	2.3E-7	1.0E-6	6.3E-6	2.7E-5	1.7E-6	7.4E-6	1.1E-6	5.0E-6	3.9E-6	1.7E-5
85-01-8	Phenanthrene	Y	N	n/a															
108-95-2	Phenol	Y	Y	Y	A														
7723-14-0	Phosphorus	Y	Y	Y	A	7.4E-4	2.5E-3	1.6E-4	6.0E-4	8.4E-5	2.6E-5	1.6E-4	7.1E-4	8.2E-6	3.6E-5			1.8E-4	4.5E-4
129-00-0	Pyrene	Y	N	n/a															
7782-49-2	Selenium	Y	Y	Y	A														
108-88-3	Toluene	Y	Y	Y	A														
1330-20-7	Xylene	Y	Y	Y	A														
7429-90-5	Aluminum	N	Y	N	A	0.128	0.436	0.028	0.104	0.015	4.6E-3	0.028	0.124					0.031	0.078
7440-39-3	Barium	N	Y	N	A	8.2E-4	2.8E-3	1.8E-4	6.7E-4	9.4E-5	2.9E-5	1.8E-4	7.9E-4					2.0E-4	5.0E-4
1317-65-3	Calcium Carbonate	N	Y	N	A	1.558	5.291	0.260	0.969			0.343	1.503						
1305-78-8	Calcium Oxide	N	Y	N	A			0.216	0.802	0.480	0.150								
7440-50-8	Copper	N	Y	N	A	2.8E-5	9.6E-5	6.2E-6	2.3E-5	3.2E-6	1.0E-6	6.3E-6	2.7E-5					6.9E-6	1.7E-5
110-82-7	Cyclohexane	N	Y	N	A														
7783-06-4	Hydrogen Sulfide	N	Y	N	A														
7439-89-6	Iron	N	Y	N	A	0.059	0.199	0.013	0.048	6.7E-3	2.1E-3	0.013	0.057					0.014	0.036
7439-98-7	Molybdenum	N	Y	N	A	2.8E-6	9.6E-6	6.2E-7	2.3E-6	3.2E-7	1.0E-7	6.3E-7	2.7E-6					6.9E-7	1.7E-6
109-66-0	Pentane	N	Y	N	A														
7440-22-4	Silver	N	Y	N	A	0	0												
7664-93-9	Sulfuric Acid	N	Y	N	A														
7440-28-0	Thallium	N	Y	N	A	2.8E-5	9.6E-5	6.2E-6	2.3E-5	3.2E-6	1.0E-6	6.3E-6	2.7E-5					6.9E-6	1.7E-5
7440-61-1	Uranium	N	Y	N	A	2.8E-5	9.6E-5	6.2E-6	2.3E-5	3.2E-6	1.0E-6	6.3E-6	2.7E-5					6.9E-6	1.7E-5
7440-62-2	Vanadium	N	Y	N	A	8.8E-5	3.0E-4	1.9E-5	7.1E-5	1.0E-5	3.1E-6	1.9E-5	8.5E-5					2.1E-5	5.3E-5
25551-13-7	Trimethyl benzene	N	Y	N	A														
7440-33-7	Tungsten	N	Y	N	A	2.8E-5	9.6E-5	6.2E-6	2.3E-5	3.2E-6	1.0E-6	6.3E-6	2.7E-5					6.9E-6	1.7E-5
7440-66-6	Zinc	N	Y	N	A	1.0E-4	3.5E-4	2.2E-5	8.3E-5	1.2E-5	3.6E-6	2.3E-5	9.9E-5					2.5E-5	6.2E-5
HAP TOTAL						***2.3E-3***	***8.1E-3***	***0.987***	***3.669***	***2.6E-4***	***8.5E-5***	***5.3E-4***	***2.3E-3***	***3.9E-5***	***1.7E-4***	***5.7E-6***	***2.5E-5***	***5.6E-4***	***1.4E-3***
MERCURY TOTAL (exempt)						***0***	***0***	***2.8E-4***	***1.0E-3***										
MERCURY TOTAL (non-exempt)						***1.1E-7***	***3.9E-7***			***1.3E-8***	***4.1E-9***	***2.5E-8***	***1.1E-7***					***2.8E-8***	***6.9E-8***
TAP TOTAL (HAP-TAP addressed by NSPS/NESHAP)						***2.3E-3***	***8.0E-3***	***0.986***	***3.668***			***5.2E-4***	***2.3E-3***					***5.6E-4***	***1.4E-3***
TAP TOTAL (For EL Evaluation)						***1.746***	***5.930***	***0.517***	***1.923***	***0.502***	***0.157***	***0.385***	***1.684***	***3.9E-5***	***1.7E-4***	***5.4E-6***	***2.4E-5***	***0.046***	***0.114***

TABLE A-W3. HAP/TAP Emissions and Exemptions

180,000 T/day Emissions						PROCESSING AND PRODUCTION - Continued						MINING and LEACHING - Totals									
chk						*HVAC*		*Emer. Power/Fire*		*Fuel Storage*		*HAP Total*		*Mercury Total*		*Mercury Total*		*TAP Total*		*TAP Total*	
						H1M,H2M,HM,HAC,HR,HA,HMO,HTS,HW		EDG1,EDG2,EDG3,EDFP		TG1,TG2				*Exempt*		*Non-Exempt*		*HAP-TAP addressed by NSPS/NESHAP*		*For EL Evaluation*	
CAS	HAP/TAP	HAP	TAP			Heaters		Emergency Generators and Fire Pump		Gasoline Fuel Tanks											
	NSPS or NESHAP HAP/TAP -->			*Y*				*4Z*	*4Z*	*6C*	*6C*										
	Non-Carcinogenic Acute (A) or Carcinogenic (C) -->				*A/C*	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr
106-99-0	1,3-Butadiene	Y	Y	Y	C			8.4E-7	3.7E-6			0	0					0	0	0	0
91-57-6	2-Methylnaphthalene	Y	N	n/a		4.3E-7	1.9E-6														
56-49-5	3-Methylchloranthrene	Y	Y	Y	C	3.2E-8	1.4E-7														
57-97-6	7,12-Dimethylbenz(a)anthracene	Y	N	n/a		2.9E-7	1.3E-6														
83-32-9	Acenaphthene	Y	N	n/a		3.2E-8	1.4E-7	5.6E-6	6.7E-6												
208-96-8	Acenaphthylene	Y	N	n/a		3.2E-8	1.4E-7	1.1E-5	1.3E-5												
75-07-0	Acetaldehyde	Y	Y	Y	C			2.5E-5	1.1E-4												
107-02-8	Acrolein	Y	Y	Y	A			1.6E-5	2.0E-5												
120-12-7	Anthracene	Y	N	n/a		4.3E-8	1.9E-7	1.6E-6	1.9E-6												
7440-36-0	Antimony	Y	Y	Y	A							0.019	0.082							0.019	0.082
7440-38-2	Arsenic	Y	Y	Y	C	3.6E-6	1.6E-5					0.544	2.381							0.544	2.381
71-43-2	Benzene	Y	Y	Y	C	3.8E-5	1.6E-4	2.7E-4	1.2E-3	7.0E-3	0.031										
50-32-8	Benzo(a)pyrene	Y	Y	Y	C	2.1E-8	9.4E-8	8.7E-8	3.8E-7												
56-55-3	Benz(a)anthracene	Y	Y	Y	C	3.2E-8	1.4E-7	2.4E-7	1.0E-6												
205-99-2	Benzo(b)fluoranthene	Y	Y	Y	C	3.2E-8	1.4E-7	3.6E-7	1.6E-6												
207-08-9	Benzo(k)fluoranthene	Y	Y	Y	C	3.2E-8	1.4E-7	7.3E-8	3.2E-7												
218-01-9	Chrysene	Y	Y	Y	C	3.2E-8	1.4E-7	5.0E-7	2.2E-6												
53-70-3	Dibenzo(a,h)anthracene	Y	Y	Y	C	2.1E-8	9.4E-8	1.2E-7	5.4E-7												
193-39-5	Indeno(1,2,3-cd)pyrene	Y	Y	Y	C	3.2E-8	1.4E-7	1.4E-7	6.2E-7												
191-24-2	Benzo(g,h,i)perylene	Y	N	n/a		2.1E-8	9.4E-8	6.9E-7	8.3E-7												
7440-41-7	Beryllium	Y	Y	Y	C	2.1E-7	9.4E-7					2.6E-3	0.011							2.6E-3	0.011
92-52-4	Biphenyl	Y	Y	Y	A					4.4E-5	1.9E-4										
7440-43-9	Cadmium	Y	Y	Y	C	2.0E-5	8.6E-5					4.1E-4	1.8E-3							4.1E-4	1.8E-3
75-15-0	Carbon Disulfide	Y	Y	Y	A							0.014	0.063							0.014	0.063
7440-47-3	Chromium	Y	Y	Y	A	2.5E-5	1.1E-4					7.3E-3	0.032							7.3E-3	0.032
18540-29-9	Cr (VI)	Y	Y	Y	C																
7440-48-4	Cobalt	Y	Y	Y	A	1.5E-6	6.6E-6					3.3E-3	0.014							3.3E-3	0.014
592-01-8	Cyanide	Y	Y	Y	A							0.453	1.983							0.453	1.983
106-46-7	Dichlorobenzene	Y	Y	Y	A	2.1E-5	9.4E-5														
206-44-0	Fluoranthene	Y	N	n/a		5.4E-8	2.4E-7	5.3E-6	6.4E-6												
86-73-7	Fluorene	Y	N	n/a		5.0E-8	2.2E-7	1.7E-5	2.1E-5												
50-00-0	Formaldehyde	Y	Y	Y	C	1.3E-3	5.9E-3	5.1E-5	2.2E-4												
110-54-3	Hexane	Y	Y	Y	A	0.032	0.141			0.031	0.137										
7647-01-0	Hydrogen Chloride	Y	Y	Y	A																
7439-92-1	Lead	Y	N	n/a								6.5E-3	0.029								
7439-96-5	Manganese	Y	Y	Y	A	6.8E-6	3.0E-5					0.244	1.067							0.244	1.067
7439-97-6	Mercury	Y	N	n/a		4.7E-6	2.0E-5					1.3E-3	5.7E-3	1.3E-3	5.7E-3	0	0	0	0	0	0
91-20-3	Naphthalene	Y	Y	Y	A	1.1E-5	4.8E-5	1.6E-4	1.9E-4	1.9E-3	8.5E-3	0	0					0	0	0	0
7440-02-0	Nickel	Y	Y	Y	C	3.8E-5	1.6E-4					1.6E-3	7.1E-3					0	0	1.6E-3	7.1E-3
85-01-8	Phenanthrene	Y	N	n/a		3.0E-7	1.3E-6	5.0E-5	6.0E-5			0	0					0	0	0	0
108-95-2	Phenol	Y	Y	Y	A					2.4E-4	1.1E-3	0	0					0	0	0	0
7723-14-0	Phosphorus	Y	Y	Y	A							0.530	2.320					0	0	0.530	2.320
129-00-0	Pyrene	Y	N	n/a		8.9E-8	3.9E-7	4.7E-6	5.7E-6			0	0					0	0	0	0
7782-49-2	Selenium	Y	Y	Y	A	4.3E-7	1.9E-6					3.3E-4	1.4E-3					0	0	3.3E-4	1.4E-3
108-88-3	Toluene	Y	Y	Y	A	6.1E-5	2.7E-4	3.6E-4	4.3E-4	0.032	0.138	0	0					0	0	0	0
1330-20-7	Xylene	Y	Y	Y	A			2.5E-4	3.0E-4	0.031	0.137	0	0					0	0	0	0
7429-90-5	Aluminum	N	Y	N	A							0	0					0	0	57.855	253
7440-39-3	Barium	N	Y	N	A	7.9E-5	3.4E-4					0	0					0	0	0.652	2.855
1317-65-3	Calcium Carbonate	N	Y	N	A							0	0					0	0	11.408	49.967
1305-78-8	Calcium Oxide	N	Y	N	A							0	0					0	0	0	0
7440-50-8	Copper	N	Y	N	A	1.5E-5	6.7E-5					0	0					0	0	4.1E-3	0.018
110-82-7	Cyclohexane	N	Y	N	A					1.0E-3	4.6E-3	0	0					0	0	0	0
7783-06-4	Hydrogen Sulfide	N	Y	N	A							0	0					0	0	0	0
7439-89-6	Iron	N	Y	N	A							0	0					0	0	14.831	64.958
7439-98-7	Molybdenum	N	Y	N	A	2.0E-5	8.6E-5					0	0					0	0	8.1E-4	3.6E-3
109-66-0	Pentane	N	Y	N	A	0.047	0.204					0	0					0	0	0	0
7440-22-4	Silver	N	Y	N	A							0	0					0	0	4.1E-4	1.8E-3
7664-93-9	Sulfuric Acid	N	Y	N	A							0	0					0	0	0	0
7440-28-0	Thallium	N	Y	N	A							0	0					0	0	8.1E-3	0.036
7440-61-1	Uranium	N	Y	N	A							0	0					0	0	8.1E-3	0.036
7440-62-2	Vanadium	N	Y	N	A	4.1E-5	1.8E-4					0	0					0	0	0.023	0.100
25551-13-7	Trimethyl benzene	N	Y	N	A					0.011	0.048	0	0					0	0	0	0
7440-33-7	Tungsten	N	Y	N	A							0	0					0	0	8.1E-3	0.036
7440-66-6	Zinc	N	Y	N	A	5.2E-4	2.3E-3					0	0					0	0	0.029	0.125
HAP TOTAL						***0.034***	***0.148***	***1.2E-3***	***2.6E-3***	***0.103***	***0.453***	***1.826***	***7.998***								
MERCURY TOTAL (exempt)														***1.3E-3***	***5.7E-3***						
MERCURY TOTAL (non-exempt)						***4.7E-6***	***2.0E-5***									***0***	***0***				
TAP TOTAL (HAP-TAP addressed by NSPS/NESHAP)								***1.1E-3***	***2.5E-3***	***0.103***	***0.453***							***0***	***0***		
TAP TOTAL (For EL Evaluation)						***0.081***	***0.355***			***0.012***	***0.052***									***86.645***	***380***

TABLE A-W3. HAP/TAP Emissions and Exemptions

180,000 T/day Emissions						PROCESSING AND PRODUCTION - Totals										ALL	ALL	ALL	TAP EL	
chk						*HAP Total*		*Mercury Total Exempt*		*Mercury Total Non-Exempt*		*TAP Total HAP-TAP addressed by NSPS/NESHAP*		*TAP Total For EL Evaluation*		*HAP*	*Hg Non-Exempt*	*TAP For EL Evaluation*	*TAP Emission Screening Level (EL)*	
CAS	HAP/TAP	HAP	TAP																	
	NSPS or NESHAP HAP/TAP -->			*Y*															Non-car	Carcin
	Non-Carcinogenic Acute (A) or Carcinogenic (C) -->				*A/C*	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	ton/yr	ton/yr	lb/hr	lb/hr	lb/hr
106-99-0	1,3-Butadiene	Y	Y	Y	C	8.4E-7	3.7E-6					8.4E-7	3.7E-6			3.7E-6		0	--	2.4E-5
91-57-6	2-Methylnaphthalene	Y	N	n/a		1.1E-6	4.6E-6									4.6E-6			--	--
56-49-5	3-Methylchloranthrene	Y	Y	Y	C	7.8E-8	3.4E-7					3.3E-8	1.4E-7	4.5E-8	2.0E-7	3.4E-7		4.5E-8	--	2.5E-6
57-97-6	7,12-Dimethylbenz(a)anthracene	Y	N	n/a		7.6E-7	3.0E-6									3.0E-6			--	--
83-32-9	Acenaphthene	Y	N	n/a		5.7E-6	7.1E-6									7.1E-6			--	--
208-96-8	Acenaphthylene	Y	N	n/a		1.1E-5	1.4E-5									1.4E-5			--	--
75-07-0	Acetaldehyde	Y	Y	Y	C	2.5E-5	1.1E-4					2.5E-5	1.1E-4			1.1E-4			--	3.0E-3
107-02-8	Acrolein	Y	Y	Y	A	1.6E-5	2.0E-5					1.6E-5	2.0E-5			2.0E-5			0.017	--
120-12-7	Anthracene	Y	N	n/a		1.7E-6	2.4E-6									2.4E-6			--	--
7440-36-0	Antimony	Y	Y	Y	A	5.7E-4	2.5E-3					5.7E-4	2.5E-3	1.6E-6	5.1E-7	0.085		0.019	0.033	--
7440-38-2	Arsenic	Y	Y	Y	C	4.5E-3	0.020					4.5E-3	0.020	8.2E-6	3.6E-5	2.400		0.544	--	1.5E-6
71-43-2	Benzene	Y	Y	Y	C	7.4E-3	0.032					7.3E-3	0.032	5.3E-5	2.3E-4	0.032		5.3E-5	--	8.0E-4
50-32-8	Benzo(a)pyrene	Y	Y	Y	C	1.4E-7	6.1E-7					1.1E-7	4.8E-7	3.0E-8	1.3E-7	6.1E-7				
56-55-3	Benz(a)anthracene	Y	Y	Y	C	3.1E-7	1.4E-6					2.7E-7	1.2E-6	4.5E-8	2.0E-7	1.4E-6				
205-99-2	Benzo(b)fluoranthene	Y	Y	Y	C	4.4E-7	1.9E-6					3.9E-7	1.7E-6	4.5E-8	2.0E-7	1.9E-6				
207-08-9	Benzo(k)fluoranthene	Y	Y	Y	C	1.5E-7	6.6E-7					1.1E-7	4.7E-7	4.5E-8	2.0E-7	6.6E-7		2.9E-7	--	2.0E-6
218-01-9	Chrysene	Y	Y	Y	C	5.8E-7	2.5E-6					5.3E-7	2.3E-6	4.5E-8	2.0E-7	2.5E-6				
53-70-3	Dibenzo(a,h)anthracene	Y	Y	Y	C	1.8E-7	7.7E-7					1.5E-7	6.4E-7	3.0E-8	1.3E-7	7.7E-7				
193-39-5	Indeno(1,2,3-cd)pyrene	Y	Y	Y	C	2.2E-7	9.6E-7					1.7E-7	7.6E-7	4.5E-8	2.0E-7	9.6E-7				
191-24-2	Benzo(g,h,i)perylene	Y	N	n/a		7.5E-7	1.1E-6									1.1E-6			--	--
7440-41-7	Beryllium	Y	Y	Y	C	4.3E-4	1.9E-3					4.3E-4	1.9E-3	3.5E-7	1.5E-6	0.013		2.6E-3	--	2.8E-5
92-52-4	Biphenyl	Y	Y	Y	A	4.4E-5	1.9E-4					4.4E-5	1.9E-4			1.9E-4			0.100	--
7440-43-9	Cadmium	Y	Y	Y	C	4.6E-4	2.0E-3					4.3E-4	1.9E-3	2.8E-5	1.2E-4	3.8E-3		4.4E-4	--	3.7E-6
75-15-0	Carbon Disulfide	Y	Y	Y	A											0.063		0.014	2.000	--
7440-47-3	Chromium	Y	Y	Y	A	6.8E-4	2.8E-3					6.3E-4	2.6E-3	4.8E-5	1.6E-4	0.035		7.4E-3	0.033	--
18540-29-9	Cr (VI)	Y	Y	Y	C	3.4E-7	1.5E-6							3.4E-7	1.5E-6	1.5E-6		3.4E-7	--	5.6E-7
7440-48-4	Cobalt	Y	Y	Y	A	4.7E-4	2.0E-3					4.7E-4	2.0E-3	4.8E-6	1.0E-5	0.016		3.3E-3	3.3E-3	--
592-01-8	Cyanide	Y	Y	Y	A	1.2E-3	5.3E-3					1.2E-3	5.3E-3			1.988		0.453	0.333	--
106-46-7	Dichlorobenzene	Y	Y	Y	A	5.7E-5	2.3E-4					2.6E-5	9.6E-5	3.1E-5	1.3E-4	2.3E-4		3.1E-5	30.000	--
206-44-0	Fluoranthene	Y	N	n/a		5.5E-6	7.0E-6									7.0E-6			--	--
86-73-7	Fluorene	Y	N	n/a		1.7E-5	2.1E-5									2.1E-5			--	--
50-00-0	Formaldehyde	Y	Y	Y	C	3.3E-3	0.015					1.4E-3	6.2E-3	1.9E-3	8.3E-3	0.015		1.9E-3	--	5.1E-4
110-54-3	Hexane	Y	Y	Y	A	0.117	0.480					0.070	0.281	0.046	0.198	0.480		0.046	12.000	--
7647-01-0	Hydrogen Chloride	Y	Y	Y	A	0.986	3.666					0.986	3.666			3.666			0.050	--
7439-92-1	Lead	Y	N	n/a		4.8E-4	2.1E-3									0.031			--	--
7439-96-5	Manganese	Y	Y	Y	A	4.6E-3	0.017					4.4E-3	0.017	1.9E-4	2.2E-4	1.085		0.244	0.067	--
7439-97-6	Mercury	Y	N	n/a		7.1E-4	2.9E-3	6.9E-4	2.8E-3	1.3E-5	5.4E-5					8.6E-3	5.4E-5		--	--
91-20-3	Naphthalene	Y	Y	Y	A	2.1E-3	8.8E-3					2.1E-3	8.7E-3	1.6E-5	6.7E-5	8.8E-3		1.6E-5	3.330	--
7440-02-0	Nickel	Y	Y	Y	C	5.5E-4	2.4E-3					4.9E-4	2.2E-3	5.6E-5	2.4E-4	9.5E-3		1.7E-3	--	2.7E-5
85-01-8	Phenanthrene	Y	N	n/a		5.1E-5	6.3E-5									6.3E-5			--	--
108-95-2	Phenol	Y	Y	Y	A	2.4E-4	1.1E-3					2.4E-4	1.1E-3			1.1E-3			1.270	--
7723-14-0	Phosphorus	Y	Y	Y	A	5.6E-3	0.023					5.5E-3	0.023	9.3E-5	6.2E-5	2.343		0.530	7.0E-3	--
129-00-0	Pyrene	Y	N	n/a		5.0E-6	6.6E-6									6.6E-6			--	--
7782-49-2	Selenium	Y	Y	Y	A	4.1E-4	1.8E-3					4.1E-4	1.8E-3	6.2E-7	2.6E-6	3.2E-3		3.3E-4	0.013	--
108-88-3	Toluene	Y	Y	Y	A	0.032	0.139					0.032	0.139	8.8E-5	3.7E-4	0.139		8.8E-5	25.000	--
1330-20-7	Xylene	Y	Y	Y	A	0.032	0.138					0.032	0.138			0.138			29.000	--
7429-90-5	Aluminum	N	Y	N	A									0.648	2.577			58.504	0.667	--
7440-39-3	Barium	N	Y	N	A									6.8E-3	0.028			0.659	0.033	--
1317-65-3	Calcium Carbonate	N	Y	N	A									2.244	8.125			13.652	0.667	--
1305-78-8	Calcium Oxide	N	Y	N	A									0.696	0.952			0.696	0.133	--
7440-50-8	Copper	N	Y	N	A									5.3E-4	2.2E-3			4.6E-3	0.067	--
110-82-7	Cyclohexane	N	Y	N	A									1.0E-3	4.6E-3			1.0E-3	70.000	--
7783-06-4	Hydrogen Sulfide	N	Y	N	A									0.900	3.942			0.900	0.933	--
7439-89-6	Iron	N	Y	N	A									0.213	0.812			15.043	0.067	--
7439-98-7	Molybdenum	N	Y	N	A									4.7E-4	2.0E-3			1.3E-3	0.333	--
109-66-0	Pentane	N	Y	N	A									0.123	0.495			0.123	118	--
7440-22-4	Silver	N	Y	N	A									4.1E-4	1.8E-3			8.2E-4	7.0E-3	--
7664-93-9	Sulfuric Acid	N	Y	N	A									2.030	8.891			2.030	0.067	--
7440-28-0	Thallium	N	Y	N	A									5.2E-4	2.2E-3			8.7E-3	7.0E-3	--
7440-61-1	Uranium	N	Y	N	A									5.2E-4	2.2E-3			8.7E-3	0.013	--
7440-62-2	Vanadium	N	Y	N	A									8.4E-4	3.5E-3			0.024	3.0E-3	--
25551-13-7	Trimethyl benzene	N	Y	N	A									0.011	0.048			0.011	8.200	--
7440-33-7	Tungsten	N	Y	N	A									5.2E-4	2.2E-3	0		8.7E-3	0.333	--
7440-66-6	Zinc	N	Y	N	A									2.2E-3	8.8E-3	0		0.031	0.667	--
HAP TOTAL						*1.200*	*4.566*									*12.564*				
MERCURY TOTAL (exempt)								*6.9E-4*	*2.8E-3*											
MERCURY TOTAL (non-exempt)										*1.3E-5*	*5.4E-5*						*5.4E-5*			
TAP TOTAL (HAP-TAP addressed by NSPS/NESHAP)												*1.150*	*4.353*							
TAP TOTAL (For EL Evaluation)														*6.928*	*26.109*			*93.573*		

Air Sciences Inc.	PROJECT TITLE: Stibnite Gold Project	BY: K. Lewis
	PROJECT NO: 335-20-3	PAGE: 1 OF: 19 SHEET: Calcs
AIR EMISSION CALCULATIONS	SUBJECT: HAP/TAP Emission Calculations	DATE: October 4, 2021

Model Scenario W3 T-RACT Emissions

Hazardous Air Pollutants (HAP)/Toxic Air Pollutants (TAP) Emissions Summary

		Emissions[1]									
		Fuel Combustion		Process/Prod/Leach		Mining		Total			
CAS	HAP/TAP	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	HAP	TAP
106-99-0	1,3-Butadiene	8.4E-07	3.7E-06	0	0	0	0	8.4E-07	3.7E-06	Y	Y
91-57-6	2-Methylnaphthalene	1.1E-06	4.6E-06	0	0	0	0	1.1E-06	4.6E-06	Y	N
56-49-5	3-Methylchloranthrene	7.8E-08	3.4E-07	0	0	0	0	7.8E-08	3.4E-07	Y	Y
57-97-6	7,12-Dimethylbenz(a)anthracene	7.6E-07	3.0E-06	0	0	0	0	7.6E-07	3.0E-06	Y	N
83-32-9	Acenaphthene	5.7E-06	7.1E-06	0	0	0	0	5.7E-06	7.1E-06	Y	N
208-96-8	Acenaphthylene	1.1E-05	1.4E-05	0	0	0	0	1.1E-05	1.4E-05	Y	N
75-07-0	Acetaldehyde	2.5E-05	1.1E-04	0	0	0	0	2.5E-05	1.1E-04	Y	Y
107-02-8	Acrolein	1.6E-05	2.0E-05	0	0	0	0	1.6E-05	2.0E-05	Y	Y
120-12-7	Anthracene	1.7E-06	2.4E-06	0	0	0	0	1.7E-06	2.4E-06	Y	N
7440-36-0	Antimony	0	0	5.7E-04	2.5E-03	1.3E-02	5.8E-02	1.4E-02	6.1E-02	Y	Y
7440-38-2	Arsenic	8.7E-06	3.8E-05	4.5E-03	2.0E-02	0.23	1.02	0.24	1.04	Y	Y
56-55-3	Benz(a)anthracene	3.1E-07	1.4E-06	0	0	0	0	3.1E-07	1.4E-06	Y	Y
71-43-2	Benzene	3.6E-04	1.6E-03	7.0E-03	3.1E-02	0	0	7.4E-03	3.2E-02	Y	Y
50-32-8	Benzo(a)pyrene	1.4E-07	6.1E-07	0	0	0	0	1.4E-07	6.1E-07	Y	Y
205-99-2	Benzo(b)fluoranthene	4.4E-07	1.9E-06	0	0	0	0	4.4E-07	1.9E-06	Y	Y
191-24-2	Benzo(g,h,i)perylene	7.5E-07	1.1E-06	0	0	0	0	7.5E-07	1.1E-06	Y	N
207-08-9	Benzo(k)fluoranthene	1.5E-07	6.6E-07	0	0	0	0	1.5E-07	6.6E-07	Y	Y
7440-41-7	Beryllium	5.2E-07	2.3E-06	4.3E-04	1.9E-03	1.9E-03	8.1E-03	2.3E-03	1.0E-02	Y	Y
92-52-4	Biphenyl	0	0	4.4E-05	1.9E-04	0	0	4.4E-05	1.9E-04	Y	Y
7440-43-9	Cadmium	4.8E-05	2.1E-04	4.1E-04	1.8E-03	2.9E-04	1.3E-03	7.5E-04	3.3E-03	Y	Y
75-15-0	Carbon Disulfide	0	0	1.4E-02	6.3E-02	0	0	1.4E-02	6.3E-02	Y	Y
7440-47-3	Chromium	6.6E-05	2.7E-04	6.1E-04	2.5E-03	5.2E-03	2.3E-02	5.9E-03	2.6E-02	Y	Y
18540-29-9	Cr (VI)	0	0	3.4E-07	1.5E-06	0	0	3.4E-07	1.5E-06	Y	Y
218-01-9	Chrysene	5.8E-07	2.5E-06	0	0	0	0	5.8E-07	2.5E-06	Y	Y
7440-48-4	Cobalt	4.0E-06	1.6E-05	4.7E-04	2.0E-03	2.3E-03	1.0E-02	2.8E-03	1.2E-02	Y	Y
592-01-8	Cyanide	0	0	0.45	1.99	0	0	0.45	1.99	Y	Y
53-70-3	Dibenzo(a,h)anthracene	1.8E-07	7.7E-07	0	0	0	0	1.8E-07	7.7E-07	Y	Y
106-46-7	Dichlorobenzene	5.7E-05	2.3E-04	0	0	0	0	5.7E-05	2.3E-04	Y	Y
206-44-0	Fluoranthene	5.5E-06	7.0E-06	0	0	0	0	5.5E-06	7.0E-06	Y	N
86-73-7	Fluorene	1.7E-05	2.1E-05	0	0	0	0	1.7E-05	2.1E-05	Y	N
50-00-0	Formaldehyde	3.3E-03	1.5E-02	0	0	0	0	3.3E-03	1.5E-02	Y	Y
110-54-3	Hexane	8.5E-02	0.34	3.1E-02	0.14	0	0	0.12	0.48	Y	Y
7647-01-0	Hydrogen Chloride	0	0	0.99	3.67	0	0	0.99	**3.67**	Y	Y
193-39-5	Indeno(1,2,3-cd)pyrene	2.2E-07	9.6E-07	0	0	0	0	2.2E-07	9.6E-07	Y	Y
7439-92-1	Lead	0	0	4.8E-04	2.1E-03	4.6E-03	2.0E-02	5.1E-03	2.2E-02	Y	N
7439-96-5	Manganese	1.8E-05	7.2E-05	4.6E-03	1.7E-02	0.17	0.76	0.18	0.78	Y	Y
7439-97-6	Mercury	1.2E-05	5.0E-05	6.9E-04	2.9E-03	1.2E-03	5.1E-03	1.9E-03	8.0E-03	Y	N
91-20-3	Naphthalene	1.9E-04	3.1E-04	1.9E-03	8.5E-03	0	0	2.1E-03	8.8E-03	Y	Y
7440-02-0	Nickel	9.1E-05	4.0E-04	4.6E-04	2.0E-03	1.2E-03	5.1E-03	1.7E-03	7.5E-03	Y	Y
85-01-8	Phenanthrene	5.1E-05	6.3E-05	0	0	0	0	5.1E-05	6.3E-05	Y	N
108-95-2	Phenol	0	0	2.4E-04	1.1E-03	0	0	2.4E-04	1.1E-03	Y	Y
7723-14-0	Phosphorus	0	0	5.6E-03	2.3E-02	0.38	1.65	0.38	1.67	Y	Y
129-00-0	Pyrene	5.0E-06	6.6E-06	0	0	0	0	5.0E-06	6.6E-06	Y	N
7782-49-2	Selenium	1.1E-06	4.6E-06	4.1E-04	1.8E-03	2.3E-04	1.0E-03	6.4E-04	2.8E-03	Y	Y
108-88-3	Toluene	5.2E-04	1.1E-03	3.2E-02	0.14	0	0	3.2E-02	0.14	Y	Y
1330-20-7	Xylene	2.5E-04	3.0E-04	3.1E-02	0.14	0	0	3.2E-02	0.14	Y	Y
Total HAP		9.0E-02	0.36	1.58	6.25	0.81	3.56	2.48	10.17		

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

	0.2155	0.8650	8.3307	31.6474	61.0803	267.5316	69.6264	300.0439
TRUE	0.2155	0.8650	8.3307	31.6474	61.0803	267.5316	69.6264	300.0439
	chk	chk	chk-15	chk	chk	chk	chk-14	chk

Hazardous Air Pollutants (HAP)/Toxic Air Pollutants (TAP) Emissions Summary - continued

		Emissions[1]									
		Fuel Combustion		Process/Prod/Leach		Mining		Total			
CAS	**Non-HAP TAP**	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	HAP	TAP
7429-90-5	Aluminum	0	0	0.65	2.58	41.11	180.04	41.75	182.62	N	Y
7440-39-3	Barium	2.1E-04	8.4E-04	6.6E-03	2.7E-02	0.46	2.03	0.47	2.06	N	Y
1317-65-3	Calcium Carbonate	0	0	2.24	8.12	8.11	35.50	10.35	43.63	N	Y
1305-78-8	Calcium Oxide	0	0	0.70	0.95	0	0	0.70	0.95	N	Y
7440-50-8	Copper	4.0E-05	1.6E-04	4.9E-04	2.1E-03	2.9E-03	1.3E-02	3.4E-03	1.5E-02	N	Y
110-82-7	Cyclohexane	0	0	1.0E-03	4.6E-03	0	0	1.0E-03	4.6E-03	N	Y
7783-06-4	Hydrogen Sulfide	0	0	0.90	3.94	0	0	0.90	3.94	N	Y
7439-89-6	Iron	0	0	0.21	0.81	10.54	46.15	10.75	46.96	N	Y
7439-98-7	Molybdenum	5.2E-05	2.1E-04	4.2E-04	1.8E-03	5.8E-04	2.5E-03	1.0E-03	4.6E-03	N	Y
109-66-0	Pentane	0.12	0.50	0	0	0	0	0.12	0.50	N	Y
7440-22-4	Silver	0	0	4.1E-04	1.8E-03	2.9E-04	1.3E-03	7.0E-04	3.1E-03	N	Y
7664-93-9	Sulfuric Acid	0	0	2.03	8.89	0	0	2.03	8.89	N	Y
7440-28-0	Thallium	0	0	5.2E-04	2.2E-03	5.8E-03	2.5E-02	6.3E-03	2.8E-02	N	Y
7440-61-1	Uranium	0	0	5.2E-04	2.2E-03	5.8E-03	2.5E-02	6.3E-03	2.8E-02	N	Y
7440-62-2	Vanadium	1.1E-04	4.4E-04	7.3E-04	3.0E-03	1.6E-02	7.1E-02	1.7E-02	7.4E-02	N	Y
25551-13-7	Trimethyl benzene	0	0	1.1E-02	4.8E-02	0	0	1.1E-02	4.8E-02	N	Y
7440-33-7	Tungsten	0	0	5.2E-04	2.2E-03	5.8E-03	2.5E-02	6.3E-03	2.8E-02	N	Y
7440-66-6	Zinc	1.4E-03	5.5E-03	8.0E-04	3.3E-03	2.0E-02	8.9E-02	2.2E-02	9.8E-02	N	Y
Total Non-HAP TAP		0.13	0.50	6.75	25.40	60.27	263.98	67.15	289.88		

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

Conversions

2,000 lb/ton
8,760 hr/yr
24 hr/day

PROPANE COMBUSTION

Source Data

Source ID	Description	MMBtu/day	MMBtu/yr
Lime Process Heating			
LKC	PFR Shaft Lime Kiln Combustion	529.0	163,935
Ore Process Heating			
ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	17.0	510
CKB	Carbon Regeneration Kiln (Burners)	54.1	19,754
PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	2.4	876
HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	120.0	43,800
Subtotal		193.5	64,940
HVAC			
H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	96.0	35,040
H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	96.0	35,040
HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	96.0	35,040
HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	6.0	2,190
HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	6.0	2,190
HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	6.0	2,190
HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	12.0	4,380
HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	48.0	17,520
HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	72.0	26,280
Subtotal		438.0	159,870

PROPANE COMBUSTION - CONTINUED

HAP/TAP Emission Factors and Emissions

O.Heat_pph O.Heat_tpy L.Heat_pph L.Heat_tpy HVAC_pph HVAC_tpy lb/hr ton/yr

		Emission Factor[2]		Emissions[1] Ore Proc Heat		Lime Proc Heat		HVAC		Total			
CAS	Pollutant	lb/MMscf	lb/MMBtu[3]	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	TAP	A/C
91-57-6	2-Methylnaphthalene	2.4E-05	2.35E-8	1.9E-07	7.6E-07	5.2E-07	1.9E-06	4.3E-07	1.9E-06	1.1E-06	4.6E-06	N	
56-49-5	3-Methylchloranthrene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
57-97-6	7,12-Dimethylbenz(a)ant	< 1.6E-05	1.57E-8	1.3E-07	5.1E-07	3.5E-07	1.3E-06	2.9E-07	1.3E-06	7.6E-07	3.0E-06	N	
83-32-9	Acenaphthene	< 1.8E-06	1.76E-9	1.4E-08	5.7E-08	3.9E-08	1.4E-07	3.2E-08	1.4E-07	8.5E-08	3.4E-07	N	
208-96-8	Acenaphthylene	< 1.8E-06	1.76E-9	1.4E-08	5.7E-08	3.9E-08	1.4E-07	3.2E-08	1.4E-07	8.5E-08	3.4E-07	N	
120-12-7	Anthracene	< 2.4E-06	2.35E-9	1.9E-08	7.6E-08	5.2E-08	1.9E-07	4.3E-08	1.9E-07	1.1E-07	4.6E-07	N	
7440-38-2	Arsenic	2.0E-04	1.96E-7	1.5E-06	6.4E-06	3.7E-06	1.6E-05	3.6E-06	1.6E-05	8.7E-06	3.8E-05	Y	C
56-55-3	Benz(a)anthracene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
71-43-2	Benzene	2.1E-03	2.06E-6	1.5E-05	6.7E-05	3.9E-05	1.7E-04	3.8E-05	1.6E-04	9.1E-05	4.0E-04	Y	C
50-32-8	Benzo(a)pyrene	< 1.2E-06	1.18E-9	8.7E-09	3.8E-08	2.2E-08	9.6E-08	2.1E-08	9.4E-08	5.2E-08	2.3E-07	Y	C
205-99-2	Benzo(b)fluoranthene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
191-24-2	Benzo(g,h,i)perylene	< 1.2E-06	1.18E-9	9.5E-09	3.8E-08	2.6E-08	9.6E-08	2.1E-08	9.4E-08	5.7E-08	2.3E-07	N	
207-08-9	Benzo(k)fluoranthene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
7440-41-7	Beryllium	< 1.2E-05	1.18E-8	8.7E-08	3.8E-07	2.2E-07	9.6E-07	2.1E-07	9.4E-07	5.2E-07	2.3E-06	Y	C
7440-43-9	Cadmium	1.1E-03	1.08E-6	8.0E-06	3.5E-05	2.0E-05	8.8E-05	2.0E-05	8.6E-05	4.8E-05	2.1E-04	Y	C
7440-47-3	Chromium	1.4E-03	1.37E-6	1.1E-05	4.5E-05	3.0E-05	1.1E-04	2.5E-05	1.1E-04	6.6E-05	2.7E-04	Y	A
218-01-9	Chrysene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
7440-48-4	Cobalt	8.4E-05	8.24E-8	6.6E-07	2.7E-06	1.8E-06	6.8E-06	1.5E-06	6.6E-06	4.0E-06	1.6E-05	Y	A
53-70-3	Dibenzo(a,h)anthracene	< 1.2E-06	1.18E-9	8.7E-09	3.8E-08	2.2E-08	9.6E-08	2.1E-08	9.4E-08	5.2E-08	2.3E-07	Y	C
106-46-7	Dichlorobenzene	1.2E-03	1.18E-6	9.5E-06	3.8E-05	2.6E-05	9.6E-05	2.1E-05	9.4E-05	5.7E-05	2.3E-04	Y	A
206-44-0	Fluoranthene	3.0E-06	2.94E-9	2.4E-08	9.5E-08	6.5E-08	2.4E-07	5.4E-08	2.4E-07	1.4E-07	5.7E-07	N	
86-73-7	Fluorene	2.8E-06	2.75E-9	2.2E-08	8.9E-08	6.1E-08	2.3E-07	5.0E-08	2.2E-07	1.3E-07	5.3E-07	N	
50-00-0	Formaldehyde	7.5E-02	7.35E-5	5.5E-04	2.4E-03	1.4E-03	6.0E-03	1.3E-03	5.9E-03	3.3E-03	1.4E-02	Y	C
110-54-3	Hexane	1.8E+00	1.76E-3	1.4E-02	5.7E-02	3.9E-02	1.4E-01	3.2E-02	1.4E-01	8.5E-02	3.4E-01	Y	A
193-39-5	Indeno(1,2,3-cd)pyrene	< 1.8E-06	1.76E-9	1.3E-08	5.7E-08	3.3E-08	1.4E-07	3.2E-08	1.4E-07	7.8E-08	3.4E-07	Y	C
7439-96-5	Manganese	3.8E-04	3.73E-7	3.0E-06	1.2E-05	8.2E-06	3.1E-05	6.8E-06	3.0E-05	1.8E-05	7.2E-05	Y	A
7439-97-6	Mercury	2.6E-04	2.55E-7	2.1E-06	8.3E-06	5.6E-06	2.1E-05	4.7E-06	2.0E-05	1.2E-05	5.0E-05	N	
91-20-3	Naphthalene	6.1E-04	5.98E-7	4.8E-06	1.9E-05	1.3E-05	4.9E-05	1.1E-05	4.8E-05	2.9E-05	1.2E-04	Y	A
7440-02-0	Nickel	2.1E-03	2.06E-6	1.5E-05	6.7E-05	3.9E-05	1.7E-04	3.8E-05	1.6E-04	9.1E-05	4.0E-04	Y	C
85-01-8	Phenanthrene	1.7E-05	1.67E-8	1.3E-07	5.4E-07	3.7E-07	1.4E-06	3.0E-07	1.3E-06	8.1E-07	3.2E-06	N	
129-00-0	Pyrene	5.0E-06	4.90E-9	4.0E-08	1.6E-07	1.1E-07	4.0E-07	8.9E-08	3.9E-07	2.4E-07	9.5E-07	N	
7782-49-2	Selenium	< 2.4E-05	2.35E-8	1.9E-07	7.6E-07	5.2E-07	1.9E-06	4.3E-07	1.9E-06	1.1E-06	4.6E-06	Y	A
108-88-3	Toluene	3.4E-03	3.33E-6	2.7E-05	1.1E-04	7.3E-05	2.7E-04	6.1E-05	2.7E-04	1.6E-04	6.5E-04	Y	A
109-66-0	Pentane	2.6E+00	2.55E-3	2.1E-02	8.3E-02	5.6E-02	2.1E-01	4.7E-02	2.0E-01	1.2E-01	5.0E-01	Y	A
7440-39-3	Barium	4.4E-03	4.31E-6	3.5E-05	1.4E-04	9.5E-05	3.5E-04	7.9E-05	3.4E-04	2.1E-04	8.4E-04	Y	A
7440-50-8	Copper	8.5E-04	8.33E-7	6.7E-06	2.7E-05	1.8E-05	6.8E-05	1.5E-05	6.7E-05	4.0E-05	1.6E-04	Y	A
7439-98-7	Molybdenum	1.1E-03	1.08E-6	8.7E-06	3.5E-05	2.4E-05	8.8E-05	2.0E-05	8.6E-05	5.2E-05	2.1E-04	Y	A
7440-62-2	Vanadium	2.3E-03	2.25E-6	1.8E-05	7.3E-05	5.0E-05	1.8E-04	4.1E-05	1.8E-04	1.1E-04	4.4E-04	Y	A
7440-66-6	Zinc	2.9E-02	2.84E-5	2.3E-04	9.2E-04	6.3E-04	2.3E-03	5.2E-04	2.3E-03	1.4E-03	5.5E-03	Y	A
Total				3.6E-02	1.4E-01	9.8E-02	3.6E-01	8.1E-02	3.5E-01	2.1E-01	8.6E-01		

(1) *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

(2) *AP-42, Table 1.4-3 & 1.4-4 (7/98) Natural Gas Combustion* 1.0766 1.0766

(3) *Natural Gas Higher Heating Value* 1,020 *MMBtu/MMscf* chk

Air Sciences Inc.	PROJECT TITLE: Stibnite Gold Project	BY: K. Lewis
	PROJECT NO: 335-20-3	PAGE: 5 OF: 19 SHEET: Calcs
AIR EMISSION CALCULATIONS	SUBJECT: HAP/TAP Emission Calculations	DATE: October 4, 2021

DIESEL COMBUSTION

Source Data

Source ID	Description	Power Rating kW	Power Rating hp	Operation hr/day	Operation hr/yr	Fuel Consumption[1] & [2] MMBtu/day	Fuel Consumption[1] & [2] MMBtu/yr
EDG1	Camp Emergency Generator	1,000	1,341	1	100	9.39	938.70
EDG2	Plant Emergency Generator #1	1,000	1,341	1	100	9.39	938.7
EDG3	Plant Emergency Generator #2	1,000	1,341	1	100	9.39	938.7
EDFP	Mill Fire Pump	200	268	1	100	1.88	187.7
Total						30.0	3,003.8

[1] *Based on brake specific fuel consumption for diesel generators* 7,000 *Btu/hp-hr* *AP-42 Tbl 3.3-1*

[2] *Heat Content of* 0.137 *MMBtu/gal* 1E+6 *Btu/MMBtu* 1.341 *hp/kW*

HAP/TAP Emission Factors and Emissions

lb/hr ton/yr

	Pollutant	Factor (lb/MMBtu) ≤600 hp[2]	Factor (lb/MMBtu) >600hp[3]	Emissions (≤600 hp) lb/hr	Emissions (≤600 hp) ton/yr	Emissions (>600 hp) lb/hr	Emissions (>600 hp) ton/yr	Total Emissions[1] lb/hr	Total Emissions[1] ton/yr	TAP	A/C
106-99-0	1,3-Butadiene	< 3.9E-05		8.4E-07	3.7E-06	0.0E+00	0.0E+00	8.4E-07	3.7E-06	Y	C
83-32-9	Acenaphthene	< 1.4E-06	4.7E-06	1.1E-07	1.3E-07	5.5E-06	6.6E-06	5.6E-06	6.7E-06	N	
208-96-8	Acenaphthylene	< 5.1E-06	9.2E-06	4.0E-07	4.7E-07	1.1E-05	1.3E-05	1.1E-05	1.3E-05	N	
75-07-0	Acetaldehyde	7.7E-04	2.5E-05	1.6E-05	7.2E-05	8.1E-06	3.5E-05	2.5E-05	1.1E-04	Y	C
107-02-8	Acrolein	< 9.3E-05	7.9E-06	7.2E-06	8.7E-06	9.2E-06	1.1E-05	1.6E-05	2.0E-05	Y	A
120-12-7	Anthracene	1.9E-06	1.2E-06	1.5E-07	1.8E-07	1.4E-06	1.7E-06	1.6E-06	1.9E-06	N	
56-55-3	Benz(a)anthracene	1.7E-06	6.2E-07	3.6E-08	1.6E-07	2.0E-07	8.8E-07	2.4E-07	1.0E-06	Y	C
71-43-2	Benzene	9.3E-04	7.8E-04	2.0E-05	8.8E-05	2.5E-04	1.1E-03	2.7E-04	1.2E-03	Y	C
50-32-8	Benzo(a)pyrene	< 1.9E-07	< 2.6E-07	4.0E-09	1.8E-08	8.3E-08	3.6E-07	8.7E-08	3.8E-07	Y	C
205-99-2	Benzo(b)fluoranthene	< 9.9E-08	< 1.1E-06	2.1E-09	9.3E-09	3.6E-07	1.6E-06	3.6E-07	1.6E-06	Y	C
191-24-2	Benzo(g,h,i)perylene	< 4.9E-07	< 5.6E-07	3.8E-08	4.6E-08	6.5E-07	7.8E-07	6.9E-07	8.3E-07	N	
207-08-9	Benzo(k)fluoranthene	< 1.6E-07	< 2.2E-07	3.3E-09	1.5E-08	7.0E-08	3.1E-07	7.3E-08	3.2E-07	Y	C
218-01-9	Chrysene	3.5E-07	1.5E-06	7.6E-09	3.3E-08	4.9E-07	2.2E-06	5.0E-07	2.2E-06	Y	C
53-70-3	Dibenzo(a,h)anthracene	< 5.8E-07	< 3.5E-07	1.2E-08	5.5E-08	1.1E-07	4.9E-07	1.2E-07	5.4E-07	Y	C
206-44-0	Fluoranthene	7.6E-06	4.0E-06	6.0E-07	7.1E-07	4.7E-06	5.7E-06	5.3E-06	6.4E-06	N	
86-73-7	Fluorene	2.9E-05	1.3E-05	2.3E-06	2.7E-06	1.5E-05	1.8E-05	1.7E-05	2.1E-05	N	
50-00-0	Formaldehyde	1.2E-03	7.9E-05	2.5E-05	1.1E-04	2.5E-05	1.1E-04	5.1E-05	2.2E-04	Y	C
193-39-5	Indeno(1,2,3-cd)pyrene	< 3.8E-07	< 4.1E-07	8.0E-09	3.5E-08	1.3E-07	5.8E-07	1.4E-07	6.2E-07	Y	C
91-20-3	Naphthalene	8.5E-05	1.3E-04	6.6E-06	8.0E-06	1.5E-04	1.8E-04	1.6E-04	1.9E-04	Y	A
85-01-8	Phenanthrene	2.9E-05	4.1E-05	2.3E-06	2.8E-06	4.8E-05	5.7E-05	5.0E-05	6.0E-05	N	
129-00-0	Pyrene	4.8E-06	3.7E-06	3.7E-07	4.5E-07	4.4E-06	5.2E-06	4.7E-06	5.7E-06	N	
108-88-3	Toluene	4.1E-04	2.8E-04	3.2E-05	3.8E-05	3.3E-04	4.0E-04	3.6E-04	4.3E-04	Y	A
1330-20-7	Xylene	2.9E-04	1.9E-04	2.2E-05	2.7E-05	2.3E-04	2.7E-04	2.5E-04	3.0E-04	Y	A
Total				1.4E-04	3.6E-04	1.1E-03	2.2E-03	1.2E-03	2.6E-03		

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

[2] *AP-42, Tab. 3.3-2, 10/96, diesel engines (≤ 600 hp)* chk chk

[3] *AP-42, Tabs. 3.4-3 & 3.4-4, 10/96, large diesel engines (> 600 hp)*

ORE PROCESSING

Source Data

Source ID	Description	PM Emissions lb/day	PM Emissions ton/yr
OC1	Loader Transfer of Ore to Grizzly	3.500	0.639
OC2	Grizzly to Apron Feeder	3.500	0.639
OC3	Apron Feeder to Dribble Conveyor	3.500	0.639
OC4	Apron Feeder to Vibrating Grizzly	3.500	0.639
OC5	Dribble Conveyor to Vibrating Grizzly	3.500	0.639
OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	3.500	0.639
OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	30.000	5.475
OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	3.500	0.639
OC9	Stockpile Transfers to Reclaim Conveyors	16.560	3.022
OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	16.560	3.022
OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	16.560	3.022
OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge C	33.120	6.044
OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	3.864	0.705
Total		141.164	25.762

HAP/TAP Emission Factors and Emissions

CAS No.	Pollutant	Concentration ppm[2]	Emissions[1] lb/hr	Emissions[1] ton/yr	TAP	A/C
7440-38-2	Arsenic	667	3.9E-03	1.7E-02	Y	C
7440-41-7	Beryllium	3.2	1.9E-05	8.2E-05	Y	C
7440-43-9	Cadmium	0.50	2.9E-06	1.3E-05	Y	C
7440-48-4	Cobalt	4	2.4E-05	1.0E-04	Y	A
7440-47-3	Chromium	9	5.3E-05	2.3E-04	Y	A
7439-97-6	Mercury [3]	0.96	5.6E-06	2.5E-05	N	
7439-96-5	Manganese	299	1.8E-03	7.7E-03	Y	A
7440-02-0	Nickel	2	1.2E-05	5.2E-05	Y	C
7439-92-1	Lead	8	4.7E-05	2.1E-04	N	
7440-36-0	Antimony	23	1.4E-04	5.9E-04	Y	A
7723-14-0	Phosphorus	650	3.8E-03	1.7E-02	Y	A
7782-49-2	Selenium [4]	0.40	2.4E-06	1.0E-05	Y	A
7440-22-4	Silver	0.50	2.9E-06	1.3E-05	Y	A
7429-90-5	Aluminum	71,000	4.2E-01	1.8E+00	Y	A
7440-39-3	Barium	800	4.7E-03	2.1E-02	Y	A
1317-65-3	Calcium Carbonate	14,000	8.2E-02	3.6E-01	Y	A
7440-50-8	Copper	5	2.9E-05	1.3E-04	Y	A
7439-89-6	Iron [4]	18,200	1.1E-01	4.7E-01	Y	A
7439-98-7	Molybdenum	1	5.9E-06	2.6E-05	Y	A
7440-28-0	Thallium	10	5.9E-05	2.6E-04	Y	A
7440-61-1	Uranium	10	5.9E-05	2.6E-04	Y	A
7440-62-2	Vanadium	28	1.6E-04	7.2E-04	Y	A
7440-33-7	Tungsten	10	5.9E-05	2.6E-04	Y	A
7440-66-6	Zinc	35	2.1E-04	9.0E-04	Y	A
Total			6.2E-01	2.7E+00		

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

[2] *(Midas Gold 2017c) Median concentration of 55,000 SGP samples.*

[3] *(Midas Gold 2018e) Median ore concentration of 151,000 SGP samples; resource block model.*

[4] *(Midas Gold 2020) Median concentration of 56,000 SGP samples for Fe and 1,500 SGP samples for Se.*

1E+6 parts/ppm

Air Sciences Inc.	PROJECT TITLE: Stibnite Gold Project	BY: K. Lewis
	PROJECT NO: 335-20-3	PAGE: 7 OF: 19 SHEET: Calcs
AIR EMISSION CALCULATIONS	SUBJECT: HAP/TAP Emission Calculations	DATE: October 4, 2021

ORE CONCETRATION AND REFINING

Source Data

Source ID	Description	Subpart 7E Allowable Limit lb/yr[1]	Oper. hr/yr	% of Subpart 7E for Controlled Systems %	Controlled Hg Emissions lb/hr	ton/yr	lb/yr
AC	Autoclave	213.4	8,760	[2]	0.000023	0.00010	0.20
EW,MR,MF,CKD	Refinery Sources (C. Kiln, EW, Retort, Furn	16.8		20% [3]	0.000384	0.00168	3.36
7439-97-6 Mercury	Total	230.2			0.000407	0.00178	3.56

[1] *Subpart 7E Limit - Ore Pretreatment Processes (CFR 2018b)*

$$\frac{84\ lb}{MMton} \times \frac{2{,}540{,}400\ ton}{yr} \times \frac{MMton}{1.0E{+}6\ ton} = \frac{213.4\ lb}{yr}$$

[1] *Subpart 7E Limit - Carbon Processes with Mercury Retorts*

$$\frac{0.8\ lb}{ton} \times \frac{21\ ton}{yr} = \frac{16.8\ lb}{yr}$$

[2] *Controlled SysCAD modeled emissions from Autoclave:* 0.0105 g/hr 2.3E-05 lb/hr 0.20 lb/yr (M3 2019)

[3] *Based on similar source (but with much higher ore Hg content) Hg reporting levels provided below:*

Goldstrike Refinery (2015 & 2016 Hg Reports) (NDEP 2015a) (NDEP 2016)

$$\frac{28.79\ lb}{yr} \times \frac{yr}{251.00\ ton} = \frac{0.11\ lb}{MMton} \times \frac{ton}{0.8\ lb} = 14.3\%$$

Twin Creeks Refinery (2015 & 2016 Hg Reports) (NDEP 2015a) (NDEP 2016)

$$\frac{31.27\ lb}{yr} \times \frac{yr}{142.77\ ton} = \frac{0.22\ lb}{MMton} \times \frac{ton}{0.8\ lb} = 27.4\%$$

HAP/TAP Emission Factors and Emission

AC_pph AC_tpy Refin_pph Refin_tpy lb/hr ton/yr

CAS No.	Pollutant	Emission Factor[1]	Autoclave lb/hr	Autoclave ton/yr	Refinery lb/hr	Refinery ton/yr	Total Emissions lb/hr	Total Emissions ton/yr	TAP	A/C
7440-38-2	Arsenic	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	C
7440-41-7	Beryllium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	C
7440-43-9	Cadmium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	C
7440-48-4	Cobalt	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-47-3	Chromium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7439-97-6	Mercury	see above	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	N	
7439-96-5	Manganese	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-02-0	Nickel	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	C
7439-92-1	Lead	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	N	
7440-36-0	Antimony	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7723-14-0	Phosphorus	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7782-49-2	Selenium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-22-4	Silver	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7429-90-5	Aluminum	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-39-3	Barium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
1317-65-3	Calcium Carbonate	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-50-8	Copper	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7439-89-6	Iron	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7439-98-7	Molybdenum	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-28-0	Thallium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-61-1	Uranium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-62-2	Vanadium	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-33-7	Tungsten	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
7440-66-6	Zinc	same as Hg	2.3E-05	1.0E-04	3.8E-04	1.7E-03	4.1E-04	1.8E-03	Y	A
Total			5.5E-04	2.4E-03	9.2E-03	4.0E-02	9.8E-03	4.3E-02		

[1] *Hg is the most difficult metal to control due to it existing in both particulate and gaseous form. Therefore, all other metals are conservatively estimated to be equal to or less than the Hg emissions.*

0.0525 0.0525 chk

7664-93-9	Sulfuric Acid	Autoclave	2.03	8.89			2.03	8.89
7783-06-4	Hydrogen Sulfic	Autoclave	0.90	3.94			0.90	3.94
592-01-8	Cyanide	Point Sources - 5 EW Cells			0.0012	0.0053	0.00	0.01
Total			2.93	12.84	0.01	0.05	2.94	12.88

ORE CONCETRATION AND REFINING - CONTINUED

Source Data

Source ID	Description	Throughput ton/day	Throughput ton/yr	Operation hr/day	Operation hr/yr
AC	Autoclave	6,960	2,540,400	24	8,760

Autoclave HAP/TAP Emission Factors and Emission lb/hr ton/yr

CAS No.	Pollutant	Emission Factor		Emissions[1] lb/hr	Emissions[1] ton/yr
7664-93-9	Sulfuric Acid	0.007	lb/ton[2]	2.03	8.89
7783-06-4	Hydrogen Sulfide	0.9	lb/hr[3]	0.90	3.94

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

[2] *H2SO4 is based on Acidic Autoclave test data (APT 2010)*

[3] *H2S is based on Acidic Autoclave test data (APT 2013)*

LEACHING OPERATION

Cyanide (HCN) Source Data, Emission Factors, and Emissions

Source	II	Description	Dia. ft[1]	pH[1]	Free CN- g/m3[1]	T C[1]	pKa	a0	H	kG[2] m/s	Fa*Fw	g/s	lb/hr	ton/yr
TSF		***Fugitive Sources***												
TSF		Tailings Maint. Pond	76	7.75	1	3.74	9.803	0.9912	0.0025	1.89E-05	0.641	1.27E-05	0.0001	0.0004
MILLTA		CN Detox Tank 1	40	8.5	25	25	9.250	0.8490	0.0055	0.000311	0.688	0.002891	0.0229	0.101
MILLTA		CN Detox Tank 2	40	8.5	25	25	9.250	0.8490	0.0055	0.000311	0.688	0.002891	0.0229	0.101
MILLTA		CIP Leach Tank 1	52	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.668	0.001435	0.0114	0.050
MILLTA		CIP Leach Tank 2	52	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.668	0.001435	0.0114	0.050
MILLTA		CIP Leach Tank 3	52	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.668	0.001435	0.0114	0.050
MILLTA		CIP Leach Tank 4	52	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.668	0.001435	0.0114	0.050
MILLTA		CIL Tank 1	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA		CIL Tank 2	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA		CIL Tank 3	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA		CIL Tank 4	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA		CIL Tank 5	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA		CIL Tank 6	54	10.25	125	30	9.120	0.0690	0.0065	0.000311	0.666	0.002485	0.0197	0.086
MILLTA		CIP Tank 1	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
MILLTA		CIP Tank 2	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
MILLTA		CIP Tank 3	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
MILLTA		CIP Tank 4	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
MILLTA		CIP Tank 5	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
MILLTA		CIP Tank 6	20	10.25	125	52.5	8.535	0.0189	0.0148	0.000311	0.742	0.000236	0.0019	0.008
			Acres[1]											
TSF		Tails, Aqueous Surface	110.222	7.75	1	3.74	9.803	0.9912	0.0025	1.89E-05	0.421	0.008845	0.0702	0.307
TSF		Tails, Wet Sediment	110.222							5.31E-08	0.421	0.009961	0.0791	0.346
TSF		Tails, Dry Sediment	110.222							2.33E-08	1	0.010375	0.0823	0.361
			330.666											
592-01-8		Cyanide Fugitive Sources - Subtotal											0.4527	1.983
75-15-0		Carbon Disulfide											0.01446	0.06332
		Point Sources												
EW		EW Cells	[3]										0.0006	0.003
EW		Preg/Barren Tanks	[3]										0.0006	0.003
592-01-8		Cyanide Point Sources - Subtotal											0.0012	0.0053
Total													0.454	1.988

[1] *(Midas Gold 2016)(M3 2017c)(M3 2017d)*

[2] *The emission factors and caculation methodology are from the EPA directed HCN study: (Card, T. 2009)(EPA 2009)(Schmidt 2010)*

[3] *(APT 2009)*

Carbon Disulfide Emissions from Xanthate Decomposition

CAS No.	Pollutant	Xanthate[1] ton/yr	Molar Decomp.[2]	CS_2 MW Ratio	Temperature Adj. Factor[3]	Emissions lb/hr	Emissions ton/yr
75-15-0	Carbon Disulfide	1,700	0.99%	0.376	1%	0.0145	0.063

	MW	
Xanthate (PAX)	202.37	$C6H11KOS_2$
Carbon disulfide	76.139	CS_2

[1] *(Midas Gold 2016) p. 12-11*

[2] *(Air Sciences 2020) molar decomposition of xanthate in solution to CS2 gas*

[3] *(Air Sciences 2020) based on the comparison of CS2 generation at 25C and 70C*

Conversions

8,760	hr/yr	453.5929	g/lb	Wind adjustment factor Fw	1
2,000	lb/ton	3.28084	ft/m		
4,046.86	m2/acre	3,600	s/hr		

LIME PRODUCTION

Source Data

Source ID	Description	Throughput ton/day	Throughput ton/yr	PM Emissions lb/day	PM Emissions ton/yr
LS1	Limestone transfer to Primary Crusher Hopper			3.39	0.48
LS2	Primary Crushing and Associated Transfers In and Out			6.10	0.86
LS3	Primary Screening and Associated Transfers In and Out			28.25	3.97
LS4	Secondary Crushing and Associated Transfers In and Out			6.10	0.86
LS5	Secondary Screening and Associated Transfers In and Out			28.25	3.97
LS6	Limestone transfer to Ball Mill Feed Bin			3.39	0.48
LS7	Limestone transfer to Ball Mill Feed Conveyor			3.39	0.48
LS8	Ball Mill Feed transfer to Ball Mill			3.39	0.48
LSBM	Limestone Ball Mill			45.65	6.42
LS9	Limestone transfer to Kiln Feed Bin			0.80	0.12
LS10	Limestone transfer to Lime Kiln Feed Conveyor			0.80	0.12
LS11	Fines Screening and Associated Transfers In and Out			6.68	1.03
Subtotal LS1-11				136.18	19.28
LS12	Kiln Feed transfer to PFR Shaft Lime Kiln			0.80	0.12
LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	169	52,377	21.97	3.40
Subtotal LS12,LK				22.77	3.53
Total				158.95	22.80

HAP/TAP Emission Factors and Emissions

LS_pph LS_tpy LS12_pph LS12_tpy LK_pph LK_tpy lb/hr ton/yr

CAS No.	Pollutant	Concentration ppm[2]	LS1-11,LSBM lb/hr	LS1-11,LSBM ton/yr	LS12 lb/hr	LS12 ton/yr	Lime Kiln lb/hr	Lime Kiln ton/yr	Emissions[1] lb/hr	Emissions[1] ton/yr	TAP	A/C
7440-38-2	Arsenic	23	1.01E-04	4.43E-04	6.51E-07	2.85E-06	1.79E-05	7.83E-05	1.20E-04	5.24E-04	Y	C
7440-41-7	Beryllium	0.8	3.52E-06	1.54E-05	2.27E-08	9.92E-08	6.22E-07	2.72E-06	4.17E-06	1.82E-05	Y	C
7440-43-9	Cadmium	0.25	1.10E-06	4.82E-06	7.08E-09	3.10E-08	1.94E-07	8.51E-07	1.30E-06	5.70E-06	Y	C
7440-48-4	Cobalt	4	2.27E-05	7.71E-05	1.34E-07	4.96E-07	3.66E-06	1.36E-05	2.65E-05	9.12E-05	Y	A
7440-47-3	Chromium	15	8.51E-05	2.89E-04	5.01E-07	1.86E-06	1.37E-05	5.11E-05	9.93E-05	3.42E-04	Y	A
7439-97-6	Mercury [3]	0.02	1.13E-07	3.86E-07	6.68E-10	2.48E-09	2.82E-04	1.05E-03	2.82E-04	1.05E-03	N	
7439-96-5	Manganese	236.5	1.34E-03	4.56E-03	7.89E-06	2.93E-05	2.16E-04	8.05E-04	1.57E-03	5.39E-03	Y	A
7440-02-0	Nickel	5	2.20E-05	9.64E-05	1.42E-07	6.20E-07	3.89E-06	1.70E-05	2.60E-05	1.14E-04	Y	C
7439-92-1	Lead	3	1.70E-05	5.78E-05	1.00E-07	3.72E-07	2.75E-06	1.02E-05	1.99E-05	6.84E-05	N	
7440-36-0	Antimony	2.5	1.42E-05	4.82E-05	8.34E-08	3.10E-07	2.29E-06	8.51E-06	1.66E-05	5.70E-05	Y	A
7723-14-0	Phosphorus	130	7.38E-04	2.51E-03	4.34E-06	1.61E-05	1.19E-04	4.43E-04	8.61E-04	2.96E-03	Y	A
7440-22-4	Silver	0	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	Y	A
7429-90-5	Aluminum	22600	1.28E-01	4.36E-01	7.54E-04	2.80E-03	2.07E-02	7.69E-02	1.50E-01	5.15E-01	Y	A
7440-39-3	Barium	145	8.23E-04	2.79E-03	4.84E-06	1.80E-05	1.33E-04	4.94E-04	9.60E-04	3.31E-03	Y	A
1317-65-3	Calcium Carbonate	274500	1.56E+00	5.29E+00	9.16E-03	3.40E-02	2.51E-01	9.35E-01	1.82E+00	6.26E+00	Y	A
7440-50-8	Copper	5	2.84E-05	9.64E-05	1.67E-07	6.20E-07	4.58E-06	1.70E-05	3.31E-05	1.14E-04	Y	A
7439-89-6	Iron	10350	5.87E-02	1.99E-01	3.45E-04	1.28E-03	9.47E-03	3.52E-02	6.85E-02	2.36E-01	Y	A
7439-98-7	Molybdenum	0.5	2.84E-06	9.64E-06	1.67E-08	6.20E-08	4.58E-07	1.70E-06	3.31E-06	1.14E-05	Y	A
7440-28-0	Thallium	5	2.84E-05	9.64E-05	1.67E-07	6.20E-07	4.58E-06	1.70E-05	3.31E-05	1.14E-04	Y	A
7440-61-1	Uranium	5	2.84E-05	9.64E-05	1.67E-07	6.20E-07	4.58E-06	1.70E-05	3.31E-05	1.14E-04	Y	A
7440-62-2	Vanadium	15.5	8.79E-05	2.99E-04	5.17E-07	1.92E-06	1.42E-05	5.28E-05	1.03E-04	3.53E-04	Y	A
7440-33-7	Tungsten	5	2.84E-05	9.64E-05	1.67E-07	6.20E-07	4.58E-06	1.70E-05	3.31E-05	1.14E-04	Y	A
7440-66-6	Zinc	18	1.02E-04	3.47E-04	6.01E-07	2.23E-06	1.65E-05	6.13E-05	1.19E-04	4.10E-04	Y	A
Subtotal			1.75E+00	5.94E+00	1.03E-02	3.82E-02	2.82E-01	1.05E+00	2.04E+00	7.03E+00	9.0667	9.0667
7647-01-0	Hydrogen Chloride	0.14 lb/ton product[4]					0.99	3.67	0.99	3.67		chk

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

[2] *(M3 2018) Median concentrations of SGP limestone material. Metals with medians below the detection limit (DL) are set to 1/2DL.*

[3] *Hg emissions from the Lime Kiln are conservatively estimated assuming 100% volatilization of all Hg in the limestone*

[4] *(EPA 1999b)*

1E+6 parts/ppm

LIME PRODUCTION - CONTINUED

Source Data

Source ID	Description	PM Emissions lb/day	PM Emissions ton/yr
LS1L	Mill Lime Silo #1 Loading	0.248	0.002
LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	1.200	0.011
MillS2L	Mill Lime Silo #2 Loading	0.248	0.002
MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	1.200	0.011
ACS1L	AC Lime Silo #1 Loading	0.990	0.009
ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.304	0.042
ACS2L	AC Lime Silo #2 Loading	0.990	0.009
ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.304	0.042
ACS3L	AC Lime Silo #3 Loading	0.990	0.009
ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.304	0.042
ACS4L	AC Lime Silo #4 Loading	0.495	0.004
ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	2.304	0.021
Subtotal - Mill & AC Lime Silos		15.576	0.203
LCR	Lime Mill Crushing and associated transfers In and Out	6.828	1.058
LSL	Pebble Lime Silo Loading via Bucket Elevator	0.149	0.023
LSU	Pebble Lime Silo discharge to Lime Slaker	0.015	0.002
Subtotal - Lime Mfg		6.991	1.083
Total		22.567	1.286

HAP/TAP Emission Factors and Emissions

CAS No.	Pollutant	Concentration ppm[2]	Mill and AC lb/hr	Mill and AC ton/yr	Lime Mfg lb/hr	Lime Mfg ton/yr	Emissions[1] lb/hr	Emissions[1] ton/yr	TAP	A/C
7440-38-2	Arsenic	23	1.06E-06	4.66E-06	5.69E-06	2.49E-05	6.75E-06	2.96E-05	Y	C
7440-41-7	Beryllium	0.8	3.70E-08	1.62E-07	1.98E-07	8.67E-07	2.35E-07	1.03E-06	Y	C
7440-43-9	Cadmium	0.25	1.16E-08	5.07E-08	6.18E-08	2.71E-07	7.34E-08	3.22E-07	Y	C
7440-48-4	Cobalt	4	2.60E-06	8.11E-07	1.17E-06	4.33E-06	3.76E-06	5.14E-06	Y	A
7440-47-3	Chromium	15	9.74E-06	3.04E-06	4.37E-06	1.63E-05	1.41E-05	1.93E-05	Y	A
7439-97-6	Mercury	0.02	1.30E-08	4.05E-09	5.83E-09	2.17E-08	1.88E-08	2.57E-08	N	
7439-96-5	Manganese	236.5	1.53E-04	4.79E-05	6.89E-05	2.56E-04	2.22E-04	3.04E-04	Y	A
7440-02-0	Nickel	5	2.31E-07	1.01E-06	1.24E-06	5.42E-06	1.47E-06	6.43E-06	Y	C
7439-92-1	Lead	3	1.95E-06	6.08E-07	8.74E-07	3.25E-06	2.82E-06	3.86E-06	N	
7440-36-0	Antimony	2.5	1.62E-06	5.07E-07	7.28E-07	2.71E-06	2.35E-06	3.22E-06	Y	A
7723-14-0	Phosphorus	130	8.44E-05	2.63E-05	3.79E-05	1.41E-04	1.22E-04	1.67E-04	Y	A
7440-22-4	Silver	0	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	Y	A
7429-90-5	Aluminum	22,600	1.47E-02	4.58E-03	6.58E-03	2.45E-02	2.13E-02	2.91E-02	Y	A
7440-39-3	Barium	145	9.41E-05	2.94E-05	4.22E-05	1.57E-04	1.36E-04	1.86E-04	Y	A
1305-78-8	Calcium Oxide	740,000 [3]	4.80E-01	1.50E-01	2.16E-01	8.02E-01	6.96E-01	9.52E-01	Y	A
7440-50-8	Copper	5	3.25E-06	1.01E-06	1.46E-06	5.42E-06	4.70E-06	6.43E-06	Y	A
7439-89-6	Iron	10350	6.72E-03	2.10E-03	3.01E-03	1.12E-02	9.73E-03	1.33E-02	Y	A
7439-98-7	Molybdenum	0.5	3.25E-07	1.01E-07	1.46E-07	5.42E-07	4.70E-07	6.43E-07	Y	A
7440-28-0	Thallium	5	3.25E-06	1.01E-06	1.46E-06	5.42E-06	4.70E-06	6.43E-06	Y	A
7440-61-1	Uranium	5	3.25E-06	1.01E-06	1.46E-06	5.42E-06	4.70E-06	6.43E-06	Y	A
7440-62-2	Vanadium	15.5	1.01E-05	3.14E-06	4.52E-06	1.68E-05	1.46E-05	1.99E-05	Y	A
7440-33-7	Tungsten	5	3.25E-06	1.01E-06	1.46E-06	5.42E-06	4.70E-06	6.43E-06	Y	A
7440-66-6	Zinc	18	1.17E-05	3.65E-06	5.24E-06	1.95E-05	1.69E-05	2.31E-05	Y	A
Total			5.02E-01	1.57E-01	2.25E-01	8.38E-01	7.27E-01	9.95E-01		

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

[2] *See LIME PRODUCTION, page 10*

[3] *(NLA 2007) 40% to 74% CaO in lime*

1E+6 parts/ppm

AGGREGATE PRODUCTION

Source Data

Source ID	Description	PM Emissions lb/day	PM Emissions ton/yr
PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conve	15.00	2.74
PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conve	15.00	2.74
Total		30.00	5.48

HAP/TAP Emission Factors and Emissions

CAS No.	Pollutant	Concentration ppm[2]	Emissions[1] lb/hr	Emissions[1] ton/yr	TAP	A/C
7440-38-2	Arsenic	23	2.88E-05	1.26E-04	Y	C
7440-41-7	Beryllium	0.8	1.00E-06	4.38E-06	Y	C
7440-43-9	Cadmium	0.25	3.13E-07	1.37E-06	Y	C
7440-48-4	Cobalt	4	5.00E-06	2.19E-05	Y	A
7440-47-3	Chromium	15	1.88E-05	8.21E-05	Y	A
7439-97-6	Mercury	0.02	2.50E-08	1.10E-07	N	
7439-96-5	Manganese	236.5	2.96E-04	1.29E-03	Y	A
7440-02-0	Nickel	5	6.25E-06	2.74E-05	Y	C
7439-92-1	Lead	3	3.75E-06	1.64E-05	N	
7440-36-0	Antimony	2.5	3.13E-06	1.37E-05	Y	A
7723-14-0	Phosphorus	130	1.63E-04	7.12E-04	Y	A
7440-22-4	Silver	0	0.00E+00	0.00E+00	Y	A
7429-90-5	Aluminum	22600	2.83E-02	1.24E-01	Y	A
7440-39-3	Barium	145	1.81E-04	7.94E-04	Y	A
1317-65-3	Calcium Carbonate	274500	3.43E-01	1.50E+00	Y	A
7440-50-8	Copper	5	6.25E-06	2.74E-05	Y	A
7439-89-6	Iron	10350	1.29E-02	5.67E-02	Y	A
7439-98-7	Molybdenum	0.5	6.25E-07	2.74E-06	Y	A
7440-28-0	Thallium	5	6.25E-06	2.74E-05	Y	A
7440-61-1	Uranium	5	6.25E-06	2.74E-05	Y	A
7440-62-2	Vanadium	15.5	1.94E-05	8.49E-05	Y	A
7440-33-7	Tungsten	5	6.25E-06	2.74E-05	Y	A
7440-66-6	Zinc	18	2.25E-05	9.86E-05	Y	A
Total			3.85E-01	1.69E+00		

(1) *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

(2) *See LIME PRODUCTION, page 10*

1E+6 parts/ppm

Air Sciences Inc.	PROJECT TITLE: Stibnite Gold Project	BY: K. Lewis
	PROJECT NO: 335-20-3	PAGE: 13 OF: 19 SHEET: Calcs
AIR EMISSION CALCULATIONS	SUBJECT: HAP/TAP Emission Calculations	DATE: October 4, 2021

CONCRETE PRODUCTION

Source Data

	description	TP_unit/day	TP_unit/yr
		Throughput	
Source ID	Description	ton/day	ton/yr
CS1L	Cement/Shotcrete Silo #1 Loading	164	60,000
CS1U	Cement/Shotcrete Silo #1 Unloading	164	60,000
CS2L	Cement/Shotcrete Silo #2 Loading	164	60,000
CS2U	Cement/Shotcrete Silo #2 Unloading	164	60,000
CM	Central Mixer Loading	164	60,000
	Subtotal Cement Silo Filling	658	240,000
	Subtotal Central Mix Batching	164	60,000

HAP/TAP Emission Factors and Emissions

				CF_pph	CF_tpy	CM_pph	CM_tpy	lb/hr	ton/yr		
		Silo Fill	Central Mixer	Cement Silo L/U		Central Mix Batching		Total Emissions[3]			
CAS No.	HAP/TAP	lb/ton[2]	lb/ton[3]	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	TAP	A/C
7440-38-2	Arsenic	4.24E-09	2.96E-07	1.16E-7	5.09E-7	2.03E-6	8.88E-6	2.14E-6	9.39E-6	Y	C
7440-41-7	Beryllium	4.86E-10		1.33E-8	5.83E-8	--	--	1.33E-8	5.83E-8	Y	C
7440-43-9	Cadmium		7.10E-10	--	--	4.86E-9	2.13E-8	4.86E-9	2.13E-8	Y	C
7440-47-3	Chromium	2.90E-08	1.27E-07	7.95E-7	3.48E-6	8.70E-7	3.81E-6	1.66E-6	7.29E-6	Y	A
18540-29-9	Cr (VI)	5.80E-09	2.70E-08	1.59E-7	6.96E-7	1.85E-7	8.11E-7	3.44E-7	1.51E-6	Y	C
7439-92-1	Lead	1.09E-08	3.66E-08	2.99E-7	1.31E-6	2.51E-7	1.10E-6	5.49E-7	2.41E-6	N	
7439-96-5	Manganese	1.17E-07	3.78E-06	3.21E-6	1.40E-5	2.59E-5	1.13E-4	2.91E-5	1.27E-4	Y	A
7440-02-0	Nickel	4.18E-08	2.48E-07	1.15E-6	5.02E-6	1.70E-6	7.44E-6	2.84E-6	1.25E-5	Y	C
7723-14-0	Phosphorus		1.20E-06	--	--	8.22E-6	3.60E-5	8.22E-6	3.60E-5	Y	A
Total				5.73E-6	2.51E-5	3.91E-5	1.71E-4	4.49E-5	1.97E-4		

(1) *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

(2) *AP-42, Table 11.12-8, (06/06) Cement Silo Filing, Controlled.* 20% *Cr (VI), IDEQ email on 11/23/2020* 0.0002 0.0002

(3) *AP-42, Table 11.12-8, (06/06) Central Mix Batching, Controlled.* 21.29% *Cr (VI), IDEQ email on 11/23/2020* chk

Conversions

24 hr/day

CONCRETE PRODUCTION - CONTINUED

Source Data

PM_ppd PM_tpy

Source ID	description Description	PM Emissions lb/day	ton/yr
CAL	Aggregate Bin Loading	16.56	1.73
CAU	Aggregate Bin Unloading	16.56	1.73
Total		33.12	3.45

HAP/TAP Emission Factors and Emissions

lb/hr ton/yr

CAS No.	Pollutant	Concentration ppm[2]	Emissions[1] lb/hr	ton/yr	TAP	A/C
7440-38-2	Arsenic	23	1.81E-05	7.94E-05	Y	C
7440-41-7	Beryllium	0.8	6.30E-07	2.76E-06	Y	C
7440-43-9	Cadmium	0.25	1.97E-07	8.63E-07	Y	C
7440-48-4	Cobalt	4	5.52E-06	1.38E-05	Y	A
7440-47-3	Chromium	15	2.07E-05	5.18E-05	Y	A
7439-97-6	Mercury	0.02	2.76E-08	6.90E-08	N	
7439-96-5	Manganese	236.5	3.26E-04	8.16E-04	Y	A
7440-02-0	Nickel	5	3.94E-06	1.73E-05	Y	C
7439-92-1	Lead	3	4.14E-06	1.04E-05	N	
7440-36-0	Antimony	2.5	3.45E-06	8.63E-06	Y	A
7723-14-0	Phosphorus	130	1.79E-04	4.49E-04	Y	A
7440-22-4	Silver	0	0.00E+00	0.00E+00	Y	A
7429-90-5	Aluminum	22600	3.12E-02	7.80E-02	Y	A
7440-39-3	Barium	145	2.00E-04	5.00E-04	Y	A
7440-50-8	Copper	5	6.90E-06	1.73E-05	Y	A
7439-89-6	Iron	10350	1.43E-02	3.57E-02	Y	A
7439-98-7	Molybdenum	0.5	6.90E-07	1.73E-06	Y	A
7440-28-0	Thallium	5	6.90E-06	1.73E-05	Y	A
7440-61-1	Uranium	5	6.90E-06	1.73E-05	Y	A
7440-62-2	Vanadium	15.5	2.14E-05	5.35E-05	Y	A
7440-33-7	Tungsten	5	6.90E-06	1.73E-05	Y	A
7440-66-6	Zinc	18	2.48E-05	6.21E-05	Y	A
Total			4.63E-02	1.16E-01		

(1) *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

(2) *See LIME PRODUCTION, page 10*

1E+6 parts/ppm

FUEL STORAGE - GASOLINE

Source Data

Source ID	description Description	VOC_ppd VOC Emissions lb/day	VOC_tpy VOC Emissions ton/yr
TG1	Mine Site Gasoline Tank #1	5.25	0.96
TG2	Mine Site Gasoline Tank #2	5.25	0.96
Total		10.49	1.91

HAP/TAP Emission Factors and Emissions

CAS No.	Pollutant	Concentration wt. %[2]	lb/hr Emissions[1] lb/hr	ton/yr Emissions[1] ton/yr	TAP	A/C
71-43-2	Benzene	1.608%	7.03E-03	3.08E-02	Y	C
92-52-4	Biphenyl	0.010%	4.37E-05	1.91E-04	Y	A
110-82-7	Cyclohexane	0.240%	1.05E-03	4.60E-03	Y	A
110-54-3	Hexane	7.138%	3.12E-02	1.37E-01	Y	A
91-20-3	Naphthalene	0.444%	1.94E-03	8.50E-03	Y	A
108-95-2	Phenol	0.055%	2.40E-04	1.05E-03	Y	A
108-88-3	Toluene	7.212%	3.15E-02	1.38E-01	Y	A
25551-13-7	Trimethyl benzene	2.500%	1.09E-02	4.79E-02	Y	A
1330-20-7	Xylene	7.170%	3.13E-02	1.37E-01	Y	A
Total			1.15E-01	5.05E-01		

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.*

[2] *(EPA 1999a)*

MINING FUGITIVE EMISSIONS

Dust Emissions

Source Data **Model Scenario** **W3** **T-RACT Emissions**

Operating schedule 365 day/yr

Clean rock cap (CR) >50% (1)

(1) *(Perpetua 2021h) Percent of VMTs on haul roads capped with CR*

Roads outside of the pits and DRSFs are capped with CR

Source ID	Description	PM Emissions lb/day	PM Emissions ton/yr
YPP	Yellow Pine Pit	--	--
HFP	Hangar Flats Pit	--	--
WEP	West End Pit	338.16	61.71
BT	Bradley Tailings	--	--
YPPBL	Yellow Pine Pit Blasting	--	--
HFPBL	Hangar Flats Pit Blasting	--	--
WEPBL	West End Pit Blasting	643.03	117.35
BTBL	Bradley Tailings Blasting	--	--
STKP	PC Stockpile	--	--
FDRSF	Fiddle DRSF	--	--
HFDRSF	Hangar Flats DRSF	152.12	27.76
YPDRSF	Yellow Pine DRSF	--	--
WEDRSF	West End DRSF	--	--
HR000	Haul Roads	12,723.41	2,322.02
TSF	Tailing Storage Facility	--	--
ACCRD	Access Roads	38.10	6.95
UGEXP	Scout Portal	0.008	0.002
Total		13,894.82	2,535.81
TSF, ACCRD, UGEXP		38.11	6.95 chk 2535.81

HAP/TAP Emission Factors

CAS No.	Pollutant	ORE Concentration ppm(1)	DR Concentration ppm(1)	CR Concentration ppm(3)	HRD Concentration ppm(4)	Borrow Concentration ppm(5)	AR Concentration ppm
7440-38-2	Arsenic	667	667	90	378.5	2.5	2.5
7440-41-7	Beryllium	3.2	3.2		3.2		3.2
7440-43-9	Cadmium	0.5	0.5		0.5		0.5
7440-48-4	Cobalt	4	4		4		4
7440-47-3	Chromium	9	9		9		9
7439-97-6	Mercury (2)	0.96	0.6		0.6		0.6
7439-96-5	Manganese	299	299		299		299
7440-02-0	Nickel	2	2		2		2
7439-92-1	Lead	8	8		8		8
7440-36-0	Antimony	23	23		23		23
7723-14-0	Phosphorus	650	650		650		650
7782-49-2	Selenium	0.4	0.4		0.4		0.4
7440-22-4	Silver	0.5	0.5		0.5		0.5
7429-90-5	Aluminum	71000	71000		71000		71000
7440-39-3	Barium	800	800		800		800
1317-65-3	Calcium Carbonate	14000	14000		14000		14000
7440-50-8	Copper	5	5		5		5
7439-89-6	Iron	18200	18200		18200		18200
7439-98-7	Molybdenum	1	1		1		1
7440-28-0	Thallium	10	10		10		10
7440-61-1	Uranium	10	10		10		10
7440-62-2	Vanadium	28	28		28		28
7440-33-7	Tungsten	10	10		10		10
7440-66-6	Zinc	35	35		35		35

(1) *(Midas Gold 2017c)* *Median concentration of 55,000 SGP samples.* *1E+6 parts/ppm*

(2) *(Midas Gold 2018e)* *Median ore and development rock (DR) concentrations of 151,000 samples; resource block model.*

(3) *(Perpetua 2021g)* *Median concentration of 265 SGP samples.*

(4) *HRD: haul road - emissions calculated based on 50% of the total VMT occuring on CR*

(5) *(ALS 2018)* *Median concentration of 8 SGP samples.*

DR DR DR DR DR DR DR DR ORE DR DR DR DR HRD DR/AR

MINING FUGITIVE EMISSIONS - CONTINUED **Model Scenario W3** DR **T-RACT Emissions**

HAP/TAP Emissions

Hourly [1] YPP_pph HFP_pph WEP_pph BT_pph YPPBL_pph HFPBL_pph WEPBL_pph BTBL_pph STKP_pph FDRSF_pph HFDRSF_pph YPDRSF_pph WEDRSF_pph HR000_pph CCRD, UGE lb/hr

CAS No.	Pollutant	YPP lb/hr	HFP lb/hr	WEP lb/hr	BT lb/hr	YPPBL lb/hr	HFPBL lb/hr	WEPBL lb/hr	BTBL lb/hr	STKP lb/hr	FDRSF lb/hr	HFDRSF lb/hr	YPDRSF lb/hr	WEDRSF lb/hr	HR000 lb/hr	TSF, ACCRD, UGEXP lb/hr	Total lb/hr
7440-38-2	Arsenic	0	0	9.4E-3	0	0	0	0.018	0	0	0	4.2E-3	0	0	0.201	4.2E-6	0.232
7440-41-7	Beryllium	0	0	4.5E-5	0	0	0	8.6E-5	0	0	0	2.0E-5	0	0	1.7E-3	5.1E-6	1.9E-3
7440-43-9	Cadmium	0	0	7.0E-6	0	0	0	1.3E-5	0	0	0	3.2E-6	0	0	2.7E-4	7.9E-7	2.9E-4
7440-48-4	Cobalt	0	0	5.6E-5	0	0	0	1.1E-4	0	0	0	2.5E-5	0	0	2.1E-3	6.4E-6	2.3E-3
7440-47-3	Chromium	0	0	1.3E-4	0	0	0	2.4E-4	0	0	0	5.7E-5	0	0	4.8E-3	1.4E-5	5.2E-3
7439-97-6	Mercury	0	0	8.5E-6	0	0	0	1.6E-5	0	0	0	3.8E-6	0	0	3.2E-4	9.5E-7	3.5E-4
7439-96-5	Manganese	0	0	4.2E-3	0	0	0	8.0E-3	0	0	0	1.9E-3	0	0	0.159	4.7E-4	0.173
7440-02-0	Nickel	0	0	2.8E-5	0	0	0	5.4E-5	0	0	0	1.3E-5	0	0	1.1E-3	3.2E-6	1.2E-3
7439-92-1	Lead	0	0	1.1E-4	0	0	0	2.1E-4	0	0	0	5.1E-5	0	0	4.2E-3	1.3E-5	4.6E-3
7440-36-0	Antimony	0	0	3.2E-4	0	0	0	6.2E-4	0	0	0	1.5E-4	0	0	0.012	3.7E-5	0.013
7723-14-0	Phosphorus	0	0	9.2E-3	0	0	0	0.017	0	0	0	4.1E-3	0	0	0.345	1.0E-3	0.376
7782-49-2	Selenium	0	0	5.6E-6	0	0	0	1.1E-5	0	0	0	2.5E-6	0	0	2.1E-4	6.4E-7	2.3E-4
7440-22-4	Silver	0	0	7.0E-6	0	0	0	1.3E-5	0	0	0	3.2E-6	0	0	2.7E-4	7.9E-7	2.9E-4
7429-90-5	Aluminum	0	0	1.000	0	0	0	1.902	0	0	0	0.450	0	0	37.640	0.113	41.106
7440-39-3	Barium	0	0	0.011	0	0	0	0.021	0	0	0	5.1E-3	0	0	0.424	1.3E-3	0.463
1317-65-3	Calcium Ca	0	0	0.197	0	0	0	0.375	0	0	0	0.089	0	0	7.422	0.022	8.105
7440-50-8	Copper	0	0	7.0E-5	0	0	0	1.3E-4	0	0	0	3.2E-5	0	0	2.7E-3	7.9E-6	2.9E-3
7439-89-6	Iron	0	0	0.256	0	0	0	0.488	0	0	0	0.115	0	0	9.649	0.029	10.537
7439-98-7	Molybdenu	0	0	1.4E-5	0	0	0	2.7E-5	0	0	0	6.3E-6	0	0	5.3E-4	1.6E-6	5.8E-4
7440-28-0	Thallium	0	0	1.4E-4	0	0	0	2.7E-4	0	0	0	6.3E-5	0	0	5.3E-3	1.6E-5	5.8E-3
7440-61-1	Uranium	0	0	1.4E-4	0	0	0	2.7E-4	0	0	0	6.3E-5	0	0	5.3E-3	1.6E-5	5.8E-3
7440-62-2	Vanadium	0	0	3.9E-4	0	0	0	7.5E-4	0	0	0	1.8E-4	0	0	0.015	4.4E-5	0.016
7440-33-7	Tungsten	0	0	1.4E-4	0	0	0	2.7E-4	0	0	0	6.3E-5	0	0	5.3E-3	1.6E-5	5.8E-3
7440-66-6	Zinc	0	0	4.9E-4	0	0	0	9.4E-4	0	0	0	2.2E-4	0	0	0.019	5.6E-5	0.020
Total		0	0	1.490	0	0	0	2.834	0	0	0	0.670	0	0	55.918	0.167	61.079

[1] *Hourly emissions are based on annual throughput for the carcinogenic annual risk TAPs and daily throughput for the non-carcinogenic 24-hr TAPs.* chk 61.0794 61.0794

DR DR DR DR DR DR DR DR ORE DR DR DR DR HRD DR/AR

MINING FUGITIVE EMISSIONS - CONTINUED **Model Scenario W3** DR **T-RACT Emissions**

HAP/TAP Emissions

Annual

		YPP_tpy	HFP_tpy	WEP_tpy	BT_tpy	YPPBL_tpy	HFPBL_tpy	WEPBL_tpy	BTBL_tpy	STKP_tpy	FDRSF_tpy	HFDRSF_tpy	YPDRSF_tpy	WEDRSF_tpy	HR000_tpy	CCRD, UGE	ton/yr
		YPP	HFP	WEP	BT	YPPBL	HFPBL	WEPBL	BTBL	STKP	FDRSF	HFDRSF	YPDRSF	WEDRSF	HR000	TSF, ACCRD, UGEXP	Total
CAS No.	Pollutant	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr	ton/yr
7440-38-2	Arsenic	0	0	0.041	0	0	0	0.078	0	0	0	0.019	0	0	0.879	1.8E-5	1.017
7440-41-7	Beryllium	0	0	2.0E-4	0	0	0	3.8E-4	0	0	0	8.9E-5	0	0	7.4E-3	2.2E-5	8.1E-3
7440-43-9	Cadmium	0	0	3.1E-5	0	0	0	5.9E-5	0	0	0	1.4E-5	0	0	1.2E-3	3.5E-6	1.3E-3
7440-48-4	Cobalt	0	0	2.5E-4	0	0	0	4.7E-4	0	0	0	1.1E-4	0	0	9.3E-3	2.8E-5	0.010
7440-47-3	Chromium	0	0	5.6E-4	0	0	0	1.1E-3	0	0	0	2.5E-4	0	0	0.021	6.3E-5	0.023
7439-97-6	Mercury	0	0	3.7E-5	0	0	0	7.0E-5	0	0	0	1.7E-5	0	0	1.4E-3	4.2E-6	1.5E-3
7439-96-5	Manganese	0	0	0.018	0	0	0	0.035	0	0	0	8.3E-3	0	0	0.694	2.1E-3	0.758
7440-02-0	Nickel	0	0	1.2E-4	0	0	0	2.3E-4	0	0	0	5.6E-5	0	0	4.6E-3	1.4E-5	5.1E-3
7439-92-1	Lead	0	0	4.9E-4	0	0	0	9.4E-4	0	0	0	2.2E-4	0	0	0.019	5.6E-5	0.020
7440-36-0	Antimony	0	0	1.4E-3	0	0	0	2.7E-3	0	0	0	6.4E-4	0	0	0.053	1.6E-4	0.058
7723-14-0	Phosphorus	0	0	0.040	0	0	0	0.076	0	0	0	0.018	0	0	1.509	4.5E-3	1.648
7782-49-2	Selenium	0	0	2.5E-5	0	0	0	4.7E-5	0	0	0	1.1E-5	0	0	9.3E-4	2.8E-6	1.0E-3
7440-22-4	Silver	0	0	3.1E-5	0	0	0	5.9E-5	0	0	0	1.4E-5	0	0	1.2E-3	3.5E-6	1.3E-3
7429-90-5	Aluminum	0	0	4.382	0	0	0	8.332	0	0	0	1.971	0	0	165	0.494	180
7440-39-3	Barium	0	0	0.049	0	0	0	0.094	0	0	0	0.022	0	0	1.858	5.6E-3	2.029
1317-65-3	Calcium Ca	0	0	0.864	0	0	0	1.643	0	0	0	0.389	0	0	32.508	0.097	35.501
7440-50-8	Copper	0	0	3.1E-4	0	0	0	5.9E-4	0	0	0	1.4E-4	0	0	0.012	3.5E-5	0.013
7439-89-6	Iron	0	0	1.123	0	0	0	2.136	0	0	0	0.505	0	0	42.261	0.127	46.152
7439-98-7	Molybdenu	0	0	6.2E-5	0	0	0	1.2E-4	0	0	0	2.8E-5	0	0	2.3E-3	7.0E-6	2.5E-3
7440-28-0	Thallium	0	0	6.2E-4	0	0	0	1.2E-3	0	0	0	2.8E-4	0	0	0.023	7.0E-5	0.025
7440-61-1	Uranium	0	0	6.2E-4	0	0	0	1.2E-3	0	0	0	2.8E-4	0	0	0.023	7.0E-5	0.025
7440-62-2	Vanadium	0	0	1.7E-3	0	0	0	3.3E-3	0	0	0	7.8E-4	0	0	0.065	1.9E-4	0.071
7440-33-7	Tungsten	0	0	6.2E-4	0	0	0	1.2E-3	0	0	0	2.8E-4	0	0	0.023	7.0E-5	0.025
7440-66-6	Zinc	0	0	2.2E-3	0	0	0	4.1E-3	0	0	0	9.7E-4	0	0	0.081	2.4E-4	0.089
Total		0	0	6.527	0	0	0	12.412	0	0	0	2.936	0	0	245	0.731	268
															chk	267.5280	267.5280

MINING FUGITIVE EMISSIONS - CONTINUED

Mercury Evaporative Flux Emissions

Fugitive Mercury Flux and Emissions

			Area		Hg Flux	Emissions[1] lb/hr	ton/yr	lb/yr
CAS No.	Pollutant	Source	m^2	ha	$\mu g/m^2$-yr	lb/hr	ton/yr	lb/yr
		Stockpiles	52,623	5.3	556	7.37E-6	3.2E-5	6.5E-2
		Rock Dumps	2,063,990	206.4	76.2	3.96E-5	1.7E-4	0.35
		Tailings	1,338,158	133.8	2,144	7.22E-4	3.2E-3	6.32
		Pits	1,504,919	150.5	132.3	5.01E-5	2.2E-4	0.44
7439-97-6	Mercury					8.2E-4	3.6E-3	7.17

(1) *Hourly emissions based on:* 8,760 *hours per year of operation*

Fugitive Mercury Emission Factors

	Twin Creeks (TC)		Ore Hg Adjusted	Stibnite	
	Hg Flux (1)	Hg (2)	$\mu g/m^2/yr$	Hg Flux (3)	Hg (4)
Source	$\mu g/m^2$-yr	µg/g	TC	$\mu g/m^2$-yr	µg/g
Stockpiles	5,609	33	556	556	0.96
Rock Dumps	768	3.5	76.2	76.2	0.60
Tailings	21,621	33	2,144	2,144	0.96
Pits	1,334	9.5	132	132.3	0.60

(1) *(Eckley 2010)* *Table 1: Hg flux µg/m^2-yr*

(2) *(Eckley 2010)* *Table 1: Average Hg flux mg/g: " Stockpiles - high-grade stockpiles, Rock Dumps - waste rock dumps, Tailings - high-grade stockpiles as a surrogate; Pits - pit"*

(3) *(Eckley 2010)* *Figure 2: log(y) = m*log(x) + b*

y = Hg Flux (ng/m^2-d)
x = material Hg concentration (µg/g)]

Slope =	*Solar*	*TC*
	Low	*0.59*
	Medium	*0.6*
	High	*0.77*
	Average	*0.65*

(4) *(Midas Gold 2018e)*

Sample Calculation: m = log (y1/y2) / log(x1/x2)

m=	0.65	unitless
y1=	5,609	$\mu g/m^2$-yr
x1=	33	$\mu g/m^2$-yr
x2=	0.96	$\mu g/m^2$-yr
log(x1/x2)=	1.536243	unitless
log(y1/y2)=	1.003679	unitless
y1/y2=	10.08506	unitless
y2=	556.2	$\mu g/m^2$-yr

Conversions

2,000	lb/ton
10,000	m2/ha
453.593	g/lb

TABLE A-W3. HAP/TAP Emissions and Exemptions

T-RACT Emissions						MINING										LEACHING	
chk						*Mining*	*Model Scenario W3*									*CN Leach/PAX*	
						YPP,HFP,WEP,BT	YPPBL,HFPBL,WEPBL,BTBL		HR000		STKP, FDRSF, HFDRSF, YPDRSF, WEDRSF		TSF,ACCRD,UGEXP				
CAS	HAP/TAP	HAP	TAP			Pits		Blasting		Haul Roads		Stockpiles and DRFS		Tails, Access Road, Exploration		CN Leach and PAX	
	NSPS or NESHAP HAP/TAP -->		*Y*														
	Non-Carcinogenic Acute (A) or Carcinogenic (C) -->				A/C	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr
7440-38-2	Arsenic	Y	Y	Y	C	9.4E-3	0.041	0.018	0.078	0.201	0.879	4.2E-3	0.019	4.2E-6	1.8E-5		
7440-41-7	Beryllium	Y	Y	Y	C	4.5E-5	2.0E-4	8.6E-5	3.8E-4	1.7E-3	7.4E-3	2.0E-5	8.9E-5	5.1E-6	2.2E-5		
7440-43-9	Cadmium	Y	Y	Y	C	7.0E-6	3.1E-5	1.3E-5	5.9E-5	2.7E-4	1.2E-3	3.2E-6	1.4E-5	7.9E-7	3.5E-6		
50-00-0	Formaldehyde	Y	Y	Y	C												
7440-02-0	Nickel	Y	Y	Y	C	2.8E-5	1.2E-4	5.4E-5	2.3E-4	1.1E-3	4.6E-3	1.3E-5	5.6E-5	3.2E-6	1.4E-5		

TABLE A-W3. HAP/TAP Emissions and Exemptions

						0	0	0	0	1	1	1	1	0	0	1	1
T-RACT Emissions						**PROCESSING AND PRODUCTION**											
chk						***Ore Processing***				***Ore Concentration and Refining***				***Process Heating***			
						OC1-13		PS		AC		EW,MR,MF,CKD		ACB, CKB, PV, HS		LKC	
CAS	HAP/TAP	HAP	TAP			Crushers & Xfers		Prill Silos		Autoclave		EW, Preg Tank, Retort, Furnace, Carbon Kiln		POX Boiler, C. Kiln Comb., Prop. Vap., Sol'n Heater		Lime Kiln Combustion	
	NSPS or NESHAP HAP/TAP -->			***Y***		***LL***	***LL***			***7E***	***7E***	***7E***	***7E***			***5A***	***5A***
	Non-Carcinogenic Acute (A) or Carcinogenic (C) -->				**A/C**	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr
7440-38-2	Arsenic	Y	Y	Y	C	3.9E-3	0.017			2.3E-5	1.0E-4	3.8E-4	1.7E-3	1.5E-6	6.4E-6	3.7E-6	1.6E-5
7440-41-7	Beryllium	Y	Y	Y	C	1.9E-5	8.2E-5			2.3E-5	1.0E-4	3.8E-4	1.7E-3	8.7E-8	3.8E-7	2.2E-7	9.6E-7
7440-43-9	Cadmium	Y	Y	Y	C	2.9E-6	1.3E-5			2.3E-5	1.0E-4	3.8E-4	1.7E-3	8.0E-6	3.5E-5	2.0E-5	8.8E-5
50-00-0	Formaldehyde	Y	Y	Y	C									5.5E-4	2.4E-3	1.4E-3	6.0E-3
7440-02-0	Nickel	Y	Y	Y	C	1.2E-5	5.2E-5			2.3E-5	1.0E-4	3.8E-4	1.7E-3	1.5E-5	6.7E-5	3.9E-5	1.7E-4

TABLE A-W3. HAP/TAP Emissions and Exemptions

T-RACT Emissions						PROCESSING AND PRODUCTION - Continued													
chk						*Lime Production*						*Aggregate Prod.*		*Concrete Production*					
						LS1-11,LSBM		LK,LS12,LCR,LS-L/U		LS1-L/U,MillS2-L/U,ACS1-4		PCSP1,PCSP2		CM		CS1L,CS1U,CS2L, CS2U		CA-L/U	
CAS	HAP/TAP	HAP	TAP			Limestone Crushers, Screens, Mill, Xfers		Lime Kiln, Kiln Feed, Lime Mill, Pebble Lime Silo		Lime Silos and Lime Mill Crushing		Portable Crushers, Screens, Xfers		Central Mixer		Cement Silo #1 and #2 L/U		Aggregate Bin	
	NSPS or NESHAP HAP/TAP -->			*Y*		*OOO*	*OOO*	*5A*	*5A*			*OOO*	*OOO*					*OOO*	*OOO*
	Non-Carcinogenic Acute (A) or Carcinogenic (C) -->				*A/C*	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr
7440-38-2	Arsenic	Y	Y	Y	C	1.0E-4	4.4E-4	2.4E-5	1.1E-4	1.1E-6	4.7E-6	2.9E-5	1.3E-4	2.0E-6	8.9E-6	1.2E-7	5.1E-7	1.8E-5	7.9E-5
7440-41-7	Beryllium	Y	Y	Y	C	3.5E-6	1.5E-5	8.4E-7	3.7E-6	3.7E-8	1.6E-7	1.0E-6	4.4E-6			1.3E-8	5.8E-8	6.3E-7	2.8E-6
7440-43-9	Cadmium	Y	Y	Y	C	1.1E-6	4.8E-6	2.6E-7	1.2E-6	1.2E-8	5.1E-8	3.1E-7	1.4E-6	4.9E-9	2.1E-8			2.0E-7	8.6E-7
50-00-0	Formaldehyde	Y	Y	Y	C														
7440-02-0	Nickel	Y	Y	Y	C	2.2E-5	9.6E-5	5.3E-6	2.3E-5	2.3E-7	1.0E-6	6.3E-6	2.7E-5	1.7E-6	7.4E-6	1.1E-6	5.0E-6	3.9E-6	1.7E-5

TABLE A-W3. HAP/TAP Emissions and Exemptions

T-RACT Emissions						PROCESSING AND PRODUCTION - Continued						MINING and LEACHING - Totals									
chk						*HVAC*		*Emer. Power/Fire*		*Fuel Storage*		*HAP Total*		*Mercury Total*		*Mercury Total*		*TAP Total*		*TAP Total*	
						H1M,H2M,HM,HAC,HR,HA,HMO,HTS,HW		EDG1,EDG2,EDG3,EDFP		TG1,TG2				*Exempt*		*Non-Exempt*		*HAP-TAP addressed by NSPS/NESHAP*		*For EL Evaluation*	
CAS	HAP/TAP	HAP	TAP			Heaters		Emergency Generators and Fire Pump		Gasoline Fuel Tanks											
	NSPS or NESHAP HAP/TAP -->			*Y*				*4Z*	*4Z*	*6C*	*6C*										
	Non-Carcinogenic Acute (A) or Carcinogenic (C) -->				*A/C*	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr
7440-38-2	Arsenic	Y	Y	Y	C	3.6E-6	1.6E-5					0.232	1.017							0.232	1.017
7440-41-7	Beryllium	Y	Y	Y	C	2.1E-7	9.4E-7					1.9E-3	8.1E-3							1.9E-3	8.1E-3
7440-43-9	Cadmium	Y	Y	Y	C	2.0E-5	8.6E-5					2.9E-4	1.3E-3							2.9E-4	1.3E-3
50-00-0	Formaldehyde	Y	Y	Y	C	1.3E-3	5.9E-3	5.1E-5	2.2E-4												
7440-02-0	Nickel	Y	Y	Y	C	3.8E-5	1.6E-4					1.2E-3	5.1E-3					0	0	1.2E-3	5.1E-3

TABLE A-W3. HAP/TAP Emissions and Exemptions

T-RACT Emissions						PROCESSING AND PRODUCTION - Totals										ALL	ALL	ALL	TAP EL	
chk						*HAP Total*		*Mercury Total*		*Mercury Total*		*TAP Total*		*TAP Total*		*HAP*	*Hg*	*TAP*	*TAP*	
								Exempt		*Non-Exempt*		*HAP-TAP addressed by NSPS/NESHAP*		*For EL Evaluation*			*Non-Exempt*	*For EL Evaluation*	*Emission Screening Level (EL)*	
CAS	HAP/TAP	HAP	TAP																	
	NSPS or NESHAP HAP/TAP -->			*Y*															Non-car	Carcin
	Non-Carcinogenic Acute (A) or Carcinogenic (C) -->				*A/C*	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	lb/hr	ton/yr	ton/yr	ton/yr	lb/hr	lb/hr	lb/hr
7440-38-2	Arsenic	Y	Y	Y	C	4.5E-3	0.020					4.5E-3	0.020	8.2E-6	3.6E-5	1.037		0.232	--	1.5E-6
7440-41-7	Beryllium	Y	Y	Y	C	4.3E-4	1.9E-3					4.3E-4	1.9E-3	3.5E-7	1.5E-6	0.010		1.9E-3	--	2.8E-5
7440-43-9	Cadmium	Y	Y	Y	C	4.6E-4	2.0E-3					4.3E-4	1.9E-3	2.8E-5	1.2E-4	3.3E-3		3.2E-4	--	3.7E-6
50-00-0	Formaldehyde	Y	Y	Y	C	3.3E-3	0.015					1.4E-3	6.2E-3	1.9E-3	8.3E-3	0.015		1.9E-3	--	5.1E-4
7440-02-0	Nickel	Y	Y	Y	C	5.5E-4	2.4E-3					4.9E-4	2.2E-3	5.6E-5	2.4E-4	7.5E-3		1.2E-3	--	2.7E-5

Appendix B – Modeled Emissions per Modeling Scenario and Source

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Carcinogenic TAP Modeling

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TABLE B-Y1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-Y1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-Y1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: Y1	YPP	Yellow Pine Pit	0	0.024	0.051	5.585	0.063	1.101
	HFP	Hangar Flats Pit	0	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	4.5E-3	9.7E-3	1.063	0.012	0.210
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.065	0.141	15.394	0.173	3.035
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.102**	**0.220**	**24.705**	**0.278**	**6.987**

TABLE B-Y1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-Y1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-Y1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: Y1	YPP	Yellow Pine Pit	0	1.432	0	7.9E-4	2.2E-3
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0.272	0	1.5E-4	4.2E-4
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	3.946	0	2.2E-3	6.1E-3
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**6.380**	**2.030**	**3.9E-3**	**0.010**

TABLE B-Y2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-Y2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-Y2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: Y2	YPP	Yellow Pine Pit	0	0.024	0.051	5.585	0.063	1.101
	HFP	Hangar Flats Pit	0	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	3.6E-3	7.9E-3	0.858	9.7E-3	0.169
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.096	0.208	22.711	0.256	4.478
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.131**	**0.285**	**31.817**	**0.358**	**8.390**

TABLE B-Y2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-Y2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-Y2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: Y2	YPP	Yellow Pine Pit	0	1.432	0	7.9E-4	2.2E-3
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0.220	0	1.2E-4	3.4E-4
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	5.822	0	3.2E-3	9.0E-3
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**8.203**	**2.030**	**4.9E-3**	**0.013**

TABLE B-Y3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-Y3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-Y3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: Y3	YPP	Yellow Pine Pit	0	0.024	0.051	5.585	0.063	1.101
	HFP	Hangar Flats Pit	0	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	3.6E-3	7.9E-3	0.858	9.7E-3	0.169
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.155	0.337	36.835	0.415	7.263
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.191**	**0.415**	**45.941**	**0.517**	**11.175**

TABLE B-Y3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-Y3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-Y3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: Y3	YPP	Yellow Pine Pit	0	1.432	0	7.9E-4	2.2E-3
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0.220	0	1.2E-4	3.4E-4
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	9.442	0	5.2E-3	0.015
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**11.823**	**2.030**	**6.9E-3**	**0.019**

TABLE B-H1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-H1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-H1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: H1	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0.024	0.051	5.585	0.063	1.101
	WEP	West End Pit	0	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	WEPBL	West End Pit Blasting	0	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	4.5E-3	9.7E-3	1.063	0.012	0.210
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.105	0.228	24.940	0.281	4.918
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.142**	**0.308**	**34.252**	**0.385**	**8.870**

TABLE B-H1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-H1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-H1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: H1	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	1.432	0	7.9E-4	2.2E-3
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0.272	0	1.5E-4	4.2E-4
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	6.393	0	3.5E-3	9.8E-3
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**8.827**	**2.030**	**5.2E-3**	**0.014**

TABLE B-H2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-H2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-H2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: H2	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0.024	0.051	5.585	0.063	1.101
	WEP	West End Pit	0	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	WEPBL	West End Pit Blasting	0	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	3.6E-3	7.9E-3	0.858	9.7E-3	0.169
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.157	0.342	37.334	0.421	7.362
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.193**	**0.419**	**46.440**	**0.523**	**11.273**

TABLE B-H2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-H2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-H2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: H2	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	1.432	0	7.9E-4	2.2E-3
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0.220	0	1.2E-4	3.4E-4
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	9.570	0	5.3E-3	0.015
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**11.951**	**2.030**	**7.0E-3**	**0.019**

TABLE B-H3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-H3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-H3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: H3	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0.024	0.051	5.585	0.063	1.101
	WEP	West End Pit	0	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	WEPBL	West End Pit Blasting	0	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	3.6E-3	7.9E-3	0.858	9.7E-3	0.169
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.096	0.209	22.854	0.258	4.506
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.132**	**0.287**	**31.960**	**0.360**	**8.418**

TABLE B-H3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-H3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-H3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: H3	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	1.432	0	7.9E-4	2.2E-3
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0.220	0	1.2E-4	3.4E-4
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	5.858	0	3.2E-3	9.0E-3
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**8.239**	**2.030**	**4.9E-3**	**0.013**

TABLE B-H4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-H4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-H4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: H4	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0.024	0.051	5.585	0.063	1.101
	WEP	West End Pit	0	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	WEPBL	West End Pit Blasting	0	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	3.6E-3	7.9E-3	0.858	9.7E-3	0.169
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.123	0.268	29.277	0.330	5.773
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.159**	**0.346**	**38.383**	**0.432**	**9.685**

TABLE B-H4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-H4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-H4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: H4	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	1.432	0	7.9E-4	2.2E-3
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0.220	0	1.2E-4	3.4E-4
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	7.505	0	4.1E-3	0.012
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**9.886**	**2.030**	**5.8E-3**	**0.016**

TABLE B-W1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-W1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-W1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: W1	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0	0
	WEP	West End Pit	0	0.024	0.051	5.585	0.063	1.101
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	4.5E-3	9.7E-3	1.063	0.012	0.210
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.090	0.196	21.435	0.242	4.227
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.127**	**0.276**	**30.746**	**0.346**	**8.179**

TABLE B-W1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-W1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-W1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: W1	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	1.432	0	7.9E-4	2.2E-3
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0.272	0	1.5E-4	4.2E-4
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	5.495	0	3.0E-3	8.5E-3
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**7.928**	**2.030**	**4.8E-3**	**0.013**

TABLE B-W2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-W2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-W2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: W2	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0	0
	WEP	West End Pit	0	0.024	0.051	5.585	0.063	1.101
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	3.6E-3	7.9E-3	0.858	9.7E-3	0.169
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.145	0.316	34.484	0.389	6.800
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.181**	**0.393**	**43.590**	**0.491**	**10.711**

TABLE B-W2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-W2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-W2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: W2	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	1.432	0	7.9E-4	2.2E-3
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0.220	0	1.2E-4	3.4E-4
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	8.840	0	4.9E-3	0.014
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**11.221**	**2.030**	**6.6E-3**	**0.018**

TABLE B-W3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-W3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-W3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: W3	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0	0
	WEP	West End Pit	0	0.024	0.051	5.585	0.063	1.101
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	3.6E-3	7.9E-3	0.858	9.7E-3	0.169
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.208	0.452	49.397	0.557	9.740
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.244**	**0.530**	**58.504**	**0.659**	**13.652**

TABLE B-W3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-W3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-W3. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: W3	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	1.432	0	7.9E-4	2.2E-3
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0.220	0	1.2E-4	3.4E-4
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	12.662	0	7.0E-3	0.019
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**15.043**	**2.030**	**8.7E-3**	**0.024**

TABLE B-W4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-W4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-W4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: W4	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0	0
	WEP	West End Pit	0	0.024	0.051	5.585	0.063	1.101
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	3.6E-3	7.9E-3	0.858	9.7E-3	0.169
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.094	0.204	22.281	0.251	4.393
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.130**	**0.282**	**31.387**	**0.353**	**8.305**

TABLE B-W4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-W4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-W4. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: W4	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	1.432	0	7.9E-4	2.2E-3
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0.220	0	1.2E-4	3.4E-4
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	5.711	0	3.1E-3	8.8E-3
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**8.092**	**2.030**	**4.8E-3**	**0.013**

TABLE B-W5. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-W5. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-W5. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: W5	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0	0
	WEP	West End Pit	0	0.024	0.051	5.585	0.063	1.101
	BT	Bradley Tailings	0	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	BTBL	Bradley Tailings Blasting	0	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	3.6E-3	7.9E-3	0.858	9.7E-3	0.169
	HR000	Haul Roads	0	0.104	0.225	24.595	0.277	4.850
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.139**	**0.303**	**33.702**	**0.379**	**8.761**

TABLE B-W5. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-W5. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-W5. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: W5	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	1.432	0	7.9E-4	2.2E-3
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0.488	0	2.7E-4	7.5E-4
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0.220	0	1.2E-4	3.4E-4
	HR000	Haul Roads	0	6.305	0	3.5E-3	9.7E-3
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**8.686**	**2.030**	**5.2E-3**	**0.014**

TABLE B-B1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-B1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-B1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: B1	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0	0
	BT	Bradley Tailings	0	0.023	0.051	5.567	0.063	1.098
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	STKP	PC Stockpile	0	4.5E-3	9.7E-3	1.063	0.012	0.210
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.120	0.260	28.394	0.320	5.599
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.156**	**0.339**	**37.687**	**0.424**	**9.547**

TABLE B-B1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-B1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-B1. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: B1	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	1.427	0	7.8E-4	2.2E-3
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0.488	0	2.7E-4	7.5E-4
	STKP	PC Stockpile	0	0.272	0	1.5E-4	4.2E-4
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	7.278	0	4.0E-3	0.011
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**9.707**	**2.030**	**5.7E-3**	**0.015**

TABLE B-B2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to		LL	LL	0.010	1.2E-4	2.0E-3
	OC2	Grizzly to Apron Feeder		LL	LL	0.010	1.2E-4	2.0E-3
	OC3	Apron Feeder to Dribble Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC4	Apron Feeder to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC5	Dribble Conveyor to Vibrating Grizzly		LL	LL	0.010	1.2E-4	2.0E-3
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor		LL	LL	0.010	1.2E-4	2.0E-3
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor		LL	LL	0.089	1.0E-3	0.018
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile		LL	LL	0.010	1.2E-4	2.0E-3
	OC9	Stockpile Transfers to Reclaim Conveyors		LL	LL	0.049	5.5E-4	9.7E-3
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor		LL	LL	0.049	5.5E-4	9.7E-3
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	LL	LL	0.049	5.5E-4	9.7E-3
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	LL	LL	0.098	1.1E-3	0.019
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	LL	LL	0.011	1.3E-4	2.3E-3
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0.221	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	7E	7E	2.3E-5	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MR	Mercury Retort	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	7E	7E	9.6E-5	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	2.6E-7	0	0	3.1E-6	0
	CKB	Carbon Regeneration Kiln (Burners)	0	8.4E-7	0	0	9.7E-6	0
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	3.7E-8	0	0	4.3E-7	0
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	1.9E-6	0	0	2.2E-5	0
	LKC	PFR Shaft Lime Kiln Combustion	0	5A	5A	0	9.5E-5	0
	LS1	Limestone transfer to Primary Crusher Hopper	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS2	Primary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS3	Primary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323
	LS4	Secondary Crushing and Associated Transfers In and Out	0	OOO	OOO	5.7E-3	3.7E-5	0.070
	LS5	Secondary Screening and Associated Transfers In and Out	0	OOO	OOO	0.027	1.7E-4	0.323

TABLE B-B2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LS8	Ball Mill Feed transfer to Ball	0	OOO	OOO	3.2E-3	2.0E-5	0.039
	LSBM	Limestone Ball Mill	0	OOO	OOO	0.043	2.8E-4	0.522
	LS9	Limestone transfer to Kiln Feed Bin	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	OOO	OOO	7.5E-4	4.8E-6	9.2E-3
	LS11	Fines Screening and Associated Transfers In and Out	0	OOO	OOO	6.3E-3	4.0E-5	0.076
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	5A	5A	7.5E-4	4.8E-6	9.2E-3
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	5A	5A	0.021	1.3E-4	0.251
	LCR	Lime Mill Crushing and associated transfers In and Out	0	5A	5A	6.4E-3	4.1E-5	0
	LSL	Pebble Lime Silo Loading via Bucket Elevator	0	5A	5A	1.4E-4	9.0E-7	0
	LSU	Pebble Lime Silo discharge to Lime Slaker	0	5A	5A	1.4E-5	9.0E-8	0
	LS1L	Mill Lime Silo #1 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	MillS2L	Mill Lime Silo #2 Loading	0	2.4E-6	1.3E-6	2.3E-4	1.5E-6	0
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0	1.2E-5	6.5E-6	1.1E-3	7.3E-6	0
	ACS1L	AC Lime Silo #1 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS2L	AC Lime Silo #2 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS3L	AC Lime Silo #3 Loading	0	9.8E-6	5.4E-6	9.3E-4	6.0E-6	0
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
	ACS4L	AC Lime Silo #4 Loading	0	4.9E-6	2.7E-6	4.7E-4	3.0E-6	0
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0	2.3E-5	1.2E-5	2.2E-3	1.4E-5	0
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	OOO	OOO	0.014	9.1E-5	0.172
Concrete Production	CM	Central Mixer Loading	0	2.6E-5	8.2E-6	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	8.0E-7	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	8.0E-7	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	8.0E-7	0	0	0	0

TABLE B-B2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Cyanide 592-01-8	Manganese 7439-96-5	Phosphorus 7723-14-0	Aluminum 7429-90-5	Barium 7440-39-3	Calcium Carbonate 1317-65-3
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	8.0E-7	0	0	0	0
	CAL	Aggregate Bin Loading	0	OOO	OOO	0.016	1.0E-4	0
	CAU	Aggregate Bin Unloading	0	OOO	OOO	0.016	1.0E-4	0
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	1.5E-6	0	0	1.7E-5	0
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	9.3E-8	0	0	1.1E-6	0
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	1.9E-7	0	0	2.2E-6	0
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	7.5E-7	0	0	8.6E-6	0
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	1.1E-6	0	0	1.3E-5	0
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	4Z	4Z	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	4Z	4Z	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	6C	6C	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	6C	6C	0	0	0
Mining - Modeling Scenario: B2	YPP	Yellow Pine Pit	0	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0	0
	BT	Bradley Tailings	0	0.023	0.051	5.567	0.063	1.098
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	8.0E-3	0.017	1.902	0.021	0.375
	STKP	PC Stockpile	0	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	3.6E-3	7.9E-3	0.858	9.7E-3	0.169
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0	0
	HR000	Haul Roads	0	0.028	0.061	6.713	0.076	1.324
	TSF	Tailing Storage Facility	0.232	0	0	0	0	0
	ACCRD	Access Roads	0	4.7E-4	1.0E-3	0.113	1.3E-3	0.022
	UGEXP	Scout Portal	0	1.0E-7	2.3E-7	2.5E-5	2.8E-7	4.9E-6
		Total	**0.453**	**0.064**	**0.139**	**15.801**	**0.178**	**5.232**

TABLE B-B2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	0	2.7E-3	0	1.5E-6	4.1E-6
	OC2	Grizzly to Apron Feeder	0	2.7E-3	0	1.5E-6	4.1E-6
	OC3	Apron Feeder to Dribble Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC4	Apron Feeder to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC5	Dribble Conveyor to Vibrating Grizzly	0	2.7E-3	0	1.5E-6	4.1E-6
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	0	2.7E-3	0	1.5E-6	4.1E-6
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	0	0.023	0	1.3E-5	3.5E-5
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	0	2.7E-3	0	1.5E-6	4.1E-6
	OC9	Stockpile Transfers to Reclaim Conveyors	0	0.013	0	6.9E-6	1.9E-5
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	0	0.013	0	6.9E-6	1.9E-5
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	0	0.013	0	6.9E-6	1.9E-5
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	0	0.025	0	1.4E-5	3.9E-5
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	0	2.9E-3	0	1.6E-6	4.5E-6
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	0	2.3E-5	2.030	2.3E-5	2.3E-5
	EW	Electrowinning Cells and Pregnant Solution Tank	0	9.6E-5	0	9.6E-5	9.6E-5
	MR	Mercury Retort	0	9.6E-5	0	9.6E-5	9.6E-5
	MF	Induction Melting Furnace	0	9.6E-5	0	9.6E-5	9.6E-5
	CKD	Carbon Regeneration Kiln (Drum)	0	9.6E-5	0	9.6E-5	9.6E-5
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	0	0	0	0	1.6E-6
	CKB	Carbon Regeneration Kiln (Burners)	0	0	0	0	5.1E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	0	0	0	0	2.3E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	0	0	0	0	1.1E-5
	LKC	PFR Shaft Lime Kiln Combustion	0	0	0	0	5.0E-5
	LS1	Limestone transfer to Primary Crusher Hopper	0	1.5E-3	0	7.1E-7	2.2E-6
	LS2	Primary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS3	Primary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5
	LS4	Secondary Crushing and Associated Transfers In and Out	0	2.6E-3	0	1.3E-6	3.9E-6
	LS5	Secondary Screening and Associated Transfers In and Out	0	0.012	0	5.9E-6	1.8E-5

TABLE B-B2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	0	1.5E-3	0	7.1E-7	2.2E-6
	LS7	Limestone transfer to Ball Mill Feed Conveyor	0	1.5E-3	0	7.1E-7	2.2E-6
	LS8	Ball Mill Feed transfer to Ball	0	1.5E-3	0	7.1E-7	2.2E-6
	LSBM	Limestone Ball Mill	0	0.020	0	9.5E-6	2.9E-5
	LS9	Limestone transfer to Kiln Feed Bin	0	3.5E-4	0	1.7E-7	5.2E-7
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	0	3.5E-4	0	1.7E-7	5.2E-7
	LS11	Fines Screening and Associated Transfers In and Out	0	2.9E-3	0	1.4E-6	4.3E-6
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	0	3.5E-4	0	1.7E-7	5.2E-7
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	0	9.5E-3	0	4.6E-6	1.4E-5
	LCR	Lime Mill Crushing and associated transfers In and Out	0.211	2.9E-3	0	1.4E-6	4.4E-6
	LSL	Pebble Lime Silo Loading via Bucket Elevator	4.6E-3	6.4E-5	0	3.1E-8	9.6E-8
	LSU	Pebble Lime Silo discharge to Lime Slaker	4.6E-4	6.4E-6	0	3.1E-9	9.6E-9
	LS1L	Mill Lime Silo #1 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	MillS2L	Mill Lime Silo #2 Loading	7.6E-3	1.1E-4	0	5.2E-8	1.6E-7
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	0.037	5.2E-4	0	2.5E-7	7.8E-7
	ACS1L	AC Lime Silo #1 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS2L	AC Lime Silo #2 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS3L	AC Lime Silo #3 Loading	0.031	4.3E-4	0	2.1E-7	6.4E-7
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
	ACS4L	AC Lime Silo #4 Loading	0.015	2.1E-4	0	1.0E-7	3.2E-7
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	0.071	9.9E-4	0	4.8E-7	1.5E-6
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	0	6.5E-3	0	3.1E-6	9.7E-6
Concrete Production	CM	Central Mixer Loading	0	0	0	0	0
	CS1L	Cement/Shotcrete Silo #1 Loading	0	0	0	0	0
	CS1U	Cement/Shotcrete Silo #1 Unloading	0	0	0	0	0
	CS2L	Cement/Shotcrete Silo #2 Loading	0	0	0	0	0

TABLE B-B2. TAPs that Exceed the EL by Source chk **180,000 T/day Emissions**

	Source ID	Source Description	Calcium Oxide 1305-78-8	Iron 7439-89-6	Sulfuric Acid 7664-93-9	Thallium 7440-28-0	Vanadium 7440-62-2
			(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr	(24-hr) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	0	0	0	0	0
	CAL	Aggregate Bin Loading	0	7.1E-3	0	3.5E-6	1.1E-5
	CAU	Aggregate Bin Unloading	0	7.1E-3	0	3.5E-6	1.1E-5
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	0	0	0	0	9.0E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	0	0	0	0	9.0E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	0	0	0	0	5.6E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	0	0	0	0	1.1E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	0	0	0	0	4.5E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	0	0	0	0	6.8E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	0	0	0	0	0
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	0	0	0	0	0
Fuel Storage	TG1	Mine Site Gasoline Tank #1	0	0	0	0	0
	TG2	Mine Site Gasoline Tank #2	0	0	0	0	0
Mining - Modeling Scenario: B2	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	1.427	0	7.8E-4	2.2E-3
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0.488	0	2.7E-4	7.5E-4
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0.220	0	1.2E-4	3.4E-4
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0	1.721	0	9.5E-4	2.6E-3
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	0	0.029	0	1.6E-5	4.4E-5
	UGEXP	Scout Portal	0	6.4E-6	0	3.5E-9	9.8E-9
		Total	**0.696**	**4.097**	**2.030**	**2.7E-3**	**6.8E-3**

TABLE B-Y1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-Y1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-Y1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: Y1	YPP	Yellow Pine Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	5.7E-3	2.7E-5	4.3E-6	0	1.7E-5
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.065	5.5E-4	8.5E-5	0	3.4E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.098**	**7.1E-4**	**1.4E-4**	**1.9E-3**	**5.0E-4**

TABLE B-Y2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-Y2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-Y2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: Y2	YPP	Yellow Pine Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	4.2E-3	2.0E-5	3.2E-6	0	1.3E-5
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.094	7.9E-4	1.2E-4	0	5.0E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.125**	**9.5E-4**	**1.8E-4**	**1.9E-3**	**6.5E-4**

TABLE B-Y3. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-Y3. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-Y3. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: Y3	YPP	Yellow Pine Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	4.2E-3	2.0E-5	3.2E-6	0	1.3E-5
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.150	1.3E-3	2.0E-4	0	7.9E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.182**	**1.4E-3**	**2.5E-4**	**1.9E-3**	**9.5E-4**

TABLE B-H1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-H1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-H1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: H1	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	5.7E-3	2.7E-5	4.3E-6	0	1.7E-5
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.103	8.7E-4	1.4E-4	0	5.4E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.136**	**1.0E-3**	**1.9E-4**	**1.9E-3**	**7.0E-4**

TABLE B-H2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-H2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-H2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: H2	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	4.2E-3	2.0E-5	3.2E-6	0	1.3E-5
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.152	1.3E-3	2.0E-4	0	8.1E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.184**	**1.4E-3**	**2.5E-4**	**1.9E-3**	**9.6E-4**

TABLE B-H3. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-H3. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-H3. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: H3	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	4.2E-3	2.0E-5	3.2E-6	0	1.3E-5
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.095	8.0E-4	1.2E-4	0	5.0E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.126**	**9.6E-4**	**1.8E-4**	**1.9E-3**	**6.5E-4**

TABLE B-H4. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-H4. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-H4. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: H4	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	4.2E-3	2.0E-5	3.2E-6	0	1.3E-5
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.120	1.0E-3	1.6E-4	0	6.4E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.152**	**1.2E-3**	**2.1E-4**	**1.9E-3**	**7.9E-4**

TABLE B-W1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-W1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-W1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: W1	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	5.7E-3	2.7E-5	4.3E-6	0	1.7E-5
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.089	7.5E-4	1.2E-4	0	4.7E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.122**	**9.1E-4**	**1.7E-4**	**1.9E-3**	**6.3E-4**

TABLE B-W2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-W2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-W2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: W2	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	4.2E-3	2.0E-5	3.2E-6	0	1.3E-5
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.141	1.2E-3	1.9E-4	0	7.5E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.173**	**1.3E-3**	**2.4E-4**	**1.9E-3**	**9.0E-4**

TABLE B-W3. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-W3. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-W3. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: W3	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	4.2E-3	2.0E-5	3.2E-6	0	1.3E-5
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.201	1.7E-3	2.7E-4	0	1.1E-3
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.232**	**1.9E-3**	**3.2E-4**	**1.9E-3**	**1.2E-3**

TABLE B-W4. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-W4. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-W4. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: W4	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	4.2E-3	2.0E-5	3.2E-6	0	1.3E-5
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.092	7.8E-4	1.2E-4	0	4.9E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.124**	**9.4E-4**	**1.7E-4**	**1.9E-3**	**6.4E-4**

TABLE B-W5. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-W5. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-W5. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: W5	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	9.4E-3	4.5E-5	7.0E-6	0	2.8E-5
	BT	Bradley Tailings	0	0	0	0	0
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	BTBL	Bradley Tailings Blasting	0	0	0	0	0
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	4.2E-3	2.0E-5	3.2E-6	0	1.3E-5
	HR000	Haul Roads	0.101	8.6E-4	1.3E-4	0	5.4E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.133**	**1.0E-3**	**1.9E-4**	**1.9E-3**	**6.9E-4**

TABLE B-B1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-B1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-B1. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: B1	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	9.2E-3	4.4E-5	6.9E-6	0	2.8E-5
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	STKP	PC Stockpile	5.7E-3	2.7E-5	4.3E-6	0	1.7E-5
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	0	0	0	0	0
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.117	9.9E-4	1.5E-4	0	6.2E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.149**	**1.1E-3**	**2.1E-4**	**1.9E-3**	**7.7E-4**

TABLE B-B2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Ore Processing	OC1	Loader Transfer of Ore to	LL	LL	LL	LL	LL
	OC2	Grizzly to Apron Feeder	LL	LL	LL	LL	LL
	OC3	Apron Feeder to Dribble Conveyor	LL	LL	LL	LL	LL
	OC4	Apron Feeder to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC5	Dribble Conveyor to Vibrating Grizzly	LL	LL	LL	LL	LL
	OC6	Vibrating Grizzly to Primary Crusher or Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC7	Primary Crusher and Associated Transfers out to Coarse Ore Stockpile Feed Conveyor	LL	LL	LL	LL	LL
	OC8	Coarse Ore Stockpile Feed Conveyor Transfer to Stockpile	LL	LL	LL	LL	LL
	OC9	Stockpile Transfers to Reclaim Conveyors	LL	LL	LL	LL	LL
	OC10	Reclaim Conveyors to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	OC11	SAG Mill Feed Conveyor Transfer to SAG Mill	LL	LL	LL	LL	LL
	OC12	Pebble Crusher and Associated Transfers in (from SAG Mill) and out (to Pebble Discharge Conveyor)	LL	LL	LL	LL	LL
	OC13	Pebble Discharge Conveyor to SAG Mill Feed Conveyor	LL	LL	LL	LL	LL
	PSL	Prill Silos Loading (2 x 100 ton)	0	0	0	0	0
	PSU	Prill Silos Unloading (2 x 100	0	0	0	0	0
Mill Leaching	MILLTAN	Mill Leaching	0	0	0	0	0
Ore Concentration and Refining	AC	Autoclave	7E	7E	7E	7E	7E
	EW	Electrowinning Cells and Pregnant Solution Tank	7E	7E	7E	7E	7E
	MR	Mercury Retort	7E	7E	7E	7E	7E
	MF	Induction Melting Furnace	7E	7E	7E	7E	7E
	CKD	Carbon Regeneration Kiln (Drum)	7E	7E	7E	7E	7E
Process Heating	ACB	POX Boiler (17 MMBtu/hr Propane-Fired)	1.3E-7	7.7E-9	7.0E-7	4.8E-5	1.3E-6
	CKB	Carbon Regeneration Kiln (Burners)	4.1E-7	2.4E-8	2.2E-6	1.5E-4	4.3E-6
	PV	Propane Vaporizer (0.1 MMBtu/hr Propane-Fired)	1.8E-8	1.1E-9	9.9E-8	6.8E-6	1.9E-7
	HS	Strip Circuit Solution Heater (5 MMBtu, Propane-Fired)	9.0E-7	5.4E-8	5.0E-6	3.4E-4	9.5E-6
	LKC	PFR Shaft Lime Kiln Combustion	5A	5A	5A	5A	5A
	LS1	Limestone transfer to Primary Crusher Hopper	OOO	OOO	OOO	OOO	OOO
	LS2	Primary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS3	Primary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS4	Secondary Crushing and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS5	Secondary Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO

TABLE B-B2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
Lime Production	LS6	Limestone transfer to Ball Mill Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS7	Limestone transfer to Ball Mill Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS8	Ball Mill Feed transfer to Ball	OOO	OOO	OOO	OOO	OOO
	LSBM	Limestone Ball Mill	OOO	OOO	OOO	OOO	OOO
	LS9	Limestone transfer to Kiln Feed Bin	OOO	OOO	OOO	OOO	OOO
	LS10	Limestone transfer to Lime Kiln Feed Conveyor	OOO	OOO	OOO	OOO	OOO
	LS11	Fines Screening and Associated Transfers In and Out	OOO	OOO	OOO	OOO	OOO
	LS12	Kiln Feed transfer to PFR Shaft Lime Kiln	5A	5A	5A	5A	5A
	LK	Parallel Flow Regenerative (PFR) Shaft Lime Kiln	5A	5A	5A	5A	5A
	LCR	Lime Mill Crushing and associated transfers In and Out	5A	5A	5A	5A	5A
	LSL	Pebble Lime Silo Loading via Bucket Elevator	5A	5A	5A	5A	5A
	LSU	Pebble Lime Silo discharge to Lime Slaker	5A	5A	5A	5A	5A
	LS1L	Mill Lime Silo #1 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	LS1U	Mill Lime Silo #1 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	MillS2L	Mill Lime Silo #2 Loading	1.1E-8	4.0E-10	1.2E-10	0	2.5E-9
	MillS2U	Mill Lime Silo #2 Unloading to SAG Mill Conveyor	5.5E-8	1.9E-9	6.0E-10	0	1.2E-8
	ACS1L	AC Lime Silo #1 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS1U	AC Lime Silo #1 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS2L	AC Lime Silo #2 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS2U	AC Lime Silo #2 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS3L	AC Lime Silo #3 Loading	4.5E-8	1.6E-9	4.9E-10	0	9.9E-9
	ACS3U	AC Lime Silo #3 Unloading to Lime Slaker	2.2E-7	7.7E-9	2.4E-9	0	4.8E-8
	ACS4L	AC Lime Silo #4 Loading	2.3E-8	7.9E-10	2.5E-10	0	4.9E-9
	ACS42U	AC Lime Silo #4 Unloading to Lime Slaker	1.1E-7	3.8E-9	1.2E-9	0	2.4E-8
Aggregate Prod.	PCSP1	Portable Crushing and Screening Plant 1 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
	PCSP2	Portable Crushing and Screening Plant 2 (2 crushers (primary and secondary), 2 screens (primary and secondary), and 5 conveyor transfers)	OOO	OOO	OOO	OOO	OOO
Concrete Production	CM	Central Mixer Loading	2.0E-6	0	4.9E-9	0	1.7E-6
	CS1L	Cement/Shotcrete Silo #1 Loading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS1U	Cement/Shotcrete Silo #1 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CS2L	Cement/Shotcrete Silo #2 Loading	2.9E-8	3.3E-9	0	0	2.9E-7

TABLE B-B2. TAPs that Exceed the EL by Source chk **T-RACT Emissions**

	Source ID	Source Description	Arsenic 7440-38-2	Beryllium 7440-41-7	Cadmium 7440-43-9	Formaldehyde 50-00-0	Nickel 7440-02-0
			(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr	(annual) lb/hr
	CS2U	Cement/Shotcrete Silo #2 Unloading	2.9E-8	3.3E-9	0	0	2.9E-7
	CAL	Aggregate Bin Loading	OOO	OOO	OOO	OOO	OOO
	CAU	Aggregate Bin Unloading	OOO	OOO	OOO	OOO	OOO
HVAC	H1M	Mine Air Heater #1 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	H2M	Mine Air Heater #2 (4 MMBtu/hr Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HM	Mill HVAC Heaters (4 x 1.0 MMBtu Propane-Fired)	7.8E-7	4.7E-8	4.3E-6	2.9E-4	8.2E-6
	HAC	Autoclave HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HR	Refinery HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HA	Admin HVAC Heater (0.25 MMBtu Propane-Fired)	4.9E-8	2.9E-9	2.7E-7	1.8E-5	5.1E-7
	HMO	Mine Ops. HVAC Heaters (2 x 0.25 MMBtu Propane-Fired)	9.8E-8	5.9E-9	5.4E-7	3.7E-5	1.0E-6
	HTS	Truck Shop HVAC Heaters (2 x 1.0 MMBtu Propane-Fired)	3.9E-7	2.4E-8	2.2E-6	1.5E-4	4.1E-6
	HW	Warehouse HVAC Heaters (3 x 1.0 MMBtu Propane-Fired)	5.9E-7	3.5E-8	3.2E-6	2.2E-4	6.2E-6
Emer. Power/Fire	EDG1	Camp Emergency Generator (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG2	Plant Emergency Generator #1 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDG3	Plant Emergency Generator #2 (Mfr. Yr. >2007; diesel)	4Z	4Z	4Z	4Z	4Z
	EDFP	Mill Fire Pump (Mfr. Yr. >2009; diesel)	4Z	4Z	4Z	4Z	4Z
Fuel Storage	TG1	Mine Site Gasoline Tank #1	6C	6C	6C	6C	6C
	TG2	Mine Site Gasoline Tank #2	6C	6C	6C	6C	6C
Mining - Modeling Scenario: B2	YPP	Yellow Pine Pit	0	0	0	0	0
	HFP	Hangar Flats Pit	0	0	0	0	0
	WEP	West End Pit	0	0	0	0	0
	BT	Bradley Tailings	9.2E-3	4.4E-5	6.9E-6	0	2.8E-5
	YPPBL	Yellow Pine Pit Blasting	0	0	0	0	0
	HFPBL	Hangar Flats Pit Blasting	0	0	0	0	0
	WEPBL	West End Pit Blasting	0	0	0	0	0
	BTBL	Bradley Tailings Blasting	0.018	8.6E-5	1.3E-5	0	5.4E-5
	STKP	PC Stockpile	0	0	0	0	0
	FDRSF	Fiddle DRSF	0	0	0	0	0
	HFDRSF	Hangar Flats DRSF	4.2E-3	2.0E-5	3.2E-6	0	1.3E-5
	YPDRSF	Yellow Pine DRSF	0	0	0	0	0
	WEDRSF	West End DRSF	0	0	0	0	0
	HR000	Haul Roads	0.030	2.5E-4	4.0E-5	0	1.6E-4
	TSF	Tailing Storage Facility	0	0	0	0	0
	ACCRD	Access Roads	4.0E-6	5.1E-6	7.9E-7	0	3.2E-6
	UGEXP	Scout Portal	2.3E-7	1.1E-9	1.7E-10	0	7.0E-10
		Total	**0.061**	**4.1E-4**	**9.2E-5**	**1.9E-3**	**3.1E-4**

Appendix C – TAP Modeling Results

TABLE C. TAP Maximum Modeled Concentrations and AACs

	TAP Maximum Modeled Concentrations by Model Scenario														Max Scenario			
Pollutant	Y1 µg/m³	Y2 µg/m³	Y3 µg/m³	H1 µg/m³	H2 µg/m³	H3 µg/m³	H4 µg/m³	W1 [2] µg/m³	W2 [2] µg/m³	W3 [2] µg/m³	W4 [2] µg/m³	W5 [3] µg/m³	B1 µg/m³	B2 µg/m³	µg/m³	ID	AAC [4]	Compl-iance
Aluminum	1.13561	1.41646	1.13855	1.19028	1.28403	1.09010	1.17371	6.01079	5.27252	6.00999	4.97175	6.17075	1.17437	0.97352	6.17075	W5	500	Yes
Arsenic [1]	0.00030	0.00049	0.00029	0.00023	0.00053	0.00020	0.00021	0.00091	0.00095	0.00090	0.00087	N/A	0.00024	0.00012	0.00095	W2	0.0023	Yes
Barium	0.01279	0.01595	0.01282	0.01341	0.01446	0.01228	0.01322	0.06773	0.05941	0.06772	0.05602	0.06953	0.01323	0.01097	0.06953	W5	25	Yes
Beryllium [1]	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00001	0.00001	0.00001	0.00001	N/A	0.00000	0.00000	0.00001	W1	0.042	Yes
Cadmium [1]	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000	0.000002	0.000002	0.000002	0.000002	N/A	0.000000	0.000000	0.000002	W1	0.0056	Yes
Calcium Carbonate	0.34375	0.33431	0.37347	0.39124	0.38168	0.37132	0.38141	1.18652	1.04095	1.18637	0.98165	1.21807	0.39107	0.34851	1.21807	W5	500	Yes
Calcium Oxide	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	ALL	100	Yes
Cyanide	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	ALL	250	Yes
Formaldehyde [1]	0.00007	0.00007	0.00007	0.00007	0.00007	0.00007	0.00007	0.00007	0.00007	0.00007	0.00007	N/A	0.00007	0.00007	0.00007	ALL	0.77	Yes
Iron	0.29143	0.36343	0.29219	0.30525	0.32952	0.27957	0.30100	1.54079	1.35154	1.54058	1.27445	1.58179	0.30110	0.24962	1.58179	W5	50	Yes
Manganese	0.00477	0.00595	0.00478	0.00500	0.00538	0.00458	0.00493	0.02531	0.02220	0.02531	0.02094	0.02599	0.00494	0.00410	0.02599	W5	250	Yes
Nickel [1]	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00001	0.00001	0.00001	0.00001	N/A	0.00000	0.00000	0.00001	W1	0.42	Yes
Phosphorus	0.01036	0.01293	0.01039	0.01088	0.01169	0.00996	0.01073	0.05502	0.04827	0.05502	0.04551	0.05649	0.01074	0.00891	0.05649	W5	5	Yes
Sulfuric Acid	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	ALL	50	Yes
Thallium	0.00016	0.00020	0.00016	0.00017	0.00018	0.00016	0.00017	0.00085	0.00074	0.00085	0.00070	0.00087	0.00017	0.00014	0.00087	W5	5	Yes
Vanadium	0.00045	0.00056	0.00045	0.00047	0.00051	0.00043	0.00046	0.00237	0.00208	0.00237	0.00196	0.00243	0.00046	0.00039	0.00243	W5	2.5	Yes

[1] Carcinogenic TAP concentrations adjusted for 70-year exposure, as discussed in Section 3.4.4.

[2] Carcinogenic TAP concentrations adjusted for the West End pit LOM production limit, as discussed in Section 3.4.5.

[3] Modeling Scenario W5 is eliminated for carcinogenic TAP compliance, as discussed in Section 3.4.5.

[4] The AACs for carcinogenic pollutants are increased by a factor of ten per IDAPA 58.01.01.210.12(b); T-RACT adjustment.

Appendix D – Electronic Files

The electronic modeling files, emission inventory file, and Addendum references can be accessed via the following link:

https://drive.google.com/drive/folders/1o0-uNIu5DRds8hLShaD_0nPEBnlEJFCQ?usp=sharing

CERTIFICATE OF SERVICE

I hereby certify that on October 4, 2024, a true and correct copy of the foregoing EXPERT DECLARATION OF IAN H. VON LINDERN, P.E., Ph.D. was served on the following by electronic service:

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Ref.
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TABLE C. TAP Maximum Modeled Concentrations and Applicable AACs

TAP CAS	Name	Carcinogenic(1) TAP	TAP Maximum Modeled Concentrations by Model Scenario Y1 µg/m3	Y2 µg/m3	Y3 µg/m3	H1 µg/m3	H2 µg/m3	H3 µg/m3	H4 µg/m3	W1 µg/m3 (3)	W2 µg/m3 (3)	W3 µg/m3 (3)	W4 µg/m3 (3)	W5 µg/m3	B1 µg/m3	B2 µg/m3	Maximum Scenario µg/m3	Scenario ID	Applicable AAC(2) µg/m3	Compliance with TAP Rule	AAC/Impact
7429-90-5	Aluminum	No	1.13561	1.41646	1.13855	1.19028	1.28403	1.09010	1.17371	6.01079	5.27252	6.00999	4.97175	6.17075	1.17437	0.97352	6.17075	W5	500	Yes	2
7440-38-2	Arsenic	Yes	0.00030	0.00049	0.00029	0.00023	0.00053	0.00020	0.00021	0.00091	0.00095	0.00090	0.00087	N/A	0.00024	0.00012	0.00095	W2	2.3E-03	Yes	3675
7440-39-3	Barium	No	0.01279	0.01595	0.01282	0.01341	0.01446	0.01228	0.01322	0.06773	0.05941	0.06772	0.05602	0.06953	0.01323	0.01097	0.06953	W5	25	Yes	2450
7440-41-7	Beryllium	Yes	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00001	0.00001	0.00001	0.00001	N/A	0.00000	0.00000	0.00001	W1	4.2E-02	Yes	10867
7440-43-9	Cadmium	Yes	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000	0.000002	0.000002	0.000002	0.000002	N/A	0.000000	0.000000	0.000002	W1	5.6E-03	Yes	61250
1317-65-3	Calcium Carbonate	No	0.34375	0.33431	0.37347	0.39124	0.38168	0.37132	0.38141	1.18652	1.04095	1.18637	0.98165	1.21807	0.39107	0.34851	1.21807	W5	500	Yes	81
1305-78-8	Calcium Oxide	No	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	ALL	100	Yes	360
592-01-8	Cyanide	No	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	ALL	250	Yes	410
50-00-0	Formaldehyde	Yes	0.00007	0.00007	0.00007	0.00007	0.00007	0.00007	0.00007	0.00007	0.00007	0.00007	0.00007	N/A	0.00007	0.00007	0.00007	ALL	7.7E-01	Yes	674
7439-89-6	Iron	No	0.29143	0.36343	0.29219	0.30525	0.32952	0.27957	0.30100	1.54079	1.35154	1.54058	1.27445	1.58179	0.30110	0.24962	1.58179	W5	50	Yes	1272
7439-96-5	Manganese	No	0.00477	0.00595	0.00478	0.00500	0.00538	0.00458	0.00493	0.02531	0.02220	0.02531	0.02094	0.02599	0.00494	0.00410	0.02599	W5	250	Yes	9619
7440-02-0	Nickel	Yes	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00001	0.00001	0.00001	0.00001	N/A	0.00000	0.00000	0.00001	W1	4.2E-01	Yes	89
7723-14-0	Phosphorus	No	0.01036	0.01293	0.01039	0.01088	0.01169	0.00996	0.01073	0.05502	0.04827	0.05502	0.04551	0.05649	0.01074	0.00891	0.05649	W5	5	Yes	32
7664-93-9	Sulfuric Acid	No	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	ALL	50	Yes	122
7440-28-0	Thallium	No	0.00016	0.00020	0.00016	0.00017	0.00018	0.00016	0.00017	0.00085	0.00074	0.00085	0.00070	0.00087	0.00017	0.00014	0.00087	W5	5	Yes	5747
7440-62-2	Vanadium	No	0.00045	0.00056	0.00045	0.00047	0.00051	0.00043	0.00046	0.00237	0.00208	0.00237	0.00196	0.00243	0.00046	0.00039	0.00243	W5	2.5	Yes	1029

(1) Carcinogenic concentrations adjusted for 70-year exposure 16 70 years

(2) Carcinogenic AAC includes T-RACT 10 T-RACT

(3) WEP LOM production is limited to 50% of the total LOM production.

1000 mg/µg

			Y1	Y2	Y3	H1	H2	H3	H4	W1	W2	W3	W4	W5	B1	B2	MAX	_LocX_Acu	i_LocY_Acu	Ii_LocX_Chroni	LocY_Chro	Hi_LocX	Hi_LocY	
7429-90-5	Aluminum	No	1.13561	1.41646	1.13855	1.19028	1.28403	1.09010	1.17371	6.01079	5.27252	6.00999	4.97175	6.17075	1.17437	0.97352	6.17075	634399	4977484	634399	4977484	**634399**	**4977484**	
7440-38-2	Arsenic	Yes	0.00124	0.00206	0.00123	0.00102	0.00228	0.00082	0.00090	0.00672	0.00698	0.00662	0.00642	0.00824	0.00104	0.00050	0.00824					635125	4977834	<< Chroni
7440-39-3	Barium	No	0.01279	0.01595	0.01282	0.01341	0.01446	0.01228	0.01322	0.06773	0.05941	0.06772	0.05602	0.06953	0.01323	0.01097	0.06953	634399	4977484	634399	4977484	**634399**	**4977484**	
7440-41-7	Beryllium	Yes	0.00001	0.00002	0.00001	0.00001	0.00002	0.00001	0.00001	0.00005	0.00005	0.00005	0.00004	0.00007	0.00001	0.00001	0.00007	634700	4976934	634399	4977434	**634399**	**4977434**	
7440-43-9	Cadmium	Yes	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00001	0.00001	0.00001	0.00001	0.00001	0.00000	0.00000	0.00001	634399	4977384	634399	4977384	**634399**	**4977384**	
1317-65-3	Calcium Carbonate	No	0.34375	0.33431	0.37347	0.39124	0.38168	0.37132	0.38141	1.18652	1.04095	1.18637	0.98165	1.21807	0.39107	0.34851	1.21807	634399	4977484	634399	4977484	**634399**	**4977484**	
1305-78-8	Calcium Oxide	No	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	0.14837	634635	4974215	634635	4974215	**634635**	**4974215**	
592-01-8	Cyanide	No	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	0.19651	635100	4976434	635100	4976434	**635100**	**4976434**	
50-00-0	Formaldehyde	Yes	0.00031	0.00031	0.00031	0.00031	0.00031	0.00031	0.00031	0.00031	0.00031	0.00031	0.00031	0.00031	0.00031	0.00031	0.00031	634700	4975534	634700	4975534	**634700**	**4975534**	
7439-89-6	Iron	No	0.29143	0.36343	0.29219	0.30525	0.32952	0.27957	0.30100	1.54079	1.35154	1.54058	1.27445	1.58179	0.30110	0.24962	1.58179	634399	4977484	634399	4977484	**634399**	**4977484**	
7439-96-5	Manganese	No	0.00477	0.00595	0.00478	0.00500	0.00538	0.00458	0.00493	0.02531	0.02220	0.02531	0.02094	0.02599	0.00494	0.00410	0.02599	634399	4977484	634399	4977484	**634399**	**4977484**	
7440-02-0	Nickel	Yes	0.00001	0.00001	0.00001	0.00001	0.00001	0.00001	0.00001	0.00003	0.00003	0.00003	0.00003	0.00004	0.00001	0.00001	0.00004	634399	4976984	634399	4977434	**634399**	**4977434**	
7723-14-0	Phosphorus	No	0.01036	0.01293	0.01039	0.01088	0.01169	0.00996	0.01073	0.05502	0.04827	0.05502	0.04551	0.05649	0.01074	0.00891	0.05649	634399	4977484	634399	4977484	**634399**	**4977484**	
7664-93-9	Sulfuric Acid	No	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	0.41149	643352	4979986	643352	4979986	**643352**	**4979986**	
7440-28-0	Thallium	No	0.00016	0.00020	0.00016	0.00017	0.00018	0.00016	0.00017	0.00085	0.00074	0.00085	0.00070	0.00087	0.00017	0.00014	0.00087	634399	4977484	634399	4977484	**634399**	**4977484**	
7440-62-2	Vanadium	No	0.00045	0.00056	0.00045	0.00047	0.00051	0.00043	0.00046	0.00237	0.00208	0.00237	0.00196	0.00243	0.00046	0.00039	0.00243	634399	4977484	634399	4977484	**634399**	**4977484**	

<< Includes Hotspot, Chronic 16/

EX. NO. 304
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ASSOCIATED REPORTING & VIDEO

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BEFORE THE BOARD OF ENVIRONMENTAL QUALITY
STATE OF IDAHO

IN THE MATTER OF AIR QUALITY PERMIT TO CONSTRUCT P-2019.0047	)	Agency Case No. 0101-22-01
	)	OAH Case No. 23-245-01
NEZ PERCE TRIBE, IDAHO CONSERVATION LEAGUE, and SAVE THE SOUTH FORK SALMON	)	**EXPERT DECLARATION OF WILLIAM TIEDEMANN**
Petitioners,	)	
v.	)	
IDAHO DEPARTMENT OF ENVIRONMENTAL QUALITY,	)	
Respondent,	)	
and	)	
PERPETUA RESOURCES IDAHO, INC.	)	
Intervenor-Respondent.	)	

I, WILLIAM TIEDEMANN, declare and affirm as follows:

1. I am employed by the Idaho Conservation League as a Regulatory Conservation Associate. I have been in this position since April 2022.

QUALIFICATIONS AND EXPERIENCE

2. I received my Bachelors of Science (B.S.) in Mechanical Engineering from Gonzaga University, Spokane, WA, in 2013.

3. From 2013 to 2015, I worked at Haakon Industries as a Production Engineer.w I was responsible for managing compliance with federal and State of Washington environmental regulations including Clean Air Act (CAA) permitting and hazardous waste management at Haakon's Cheney, WA, manufacturing plant. There, I was the lead engineer in completing regular CAA permit and hazardous waste reporting requirements, and as well as leading several CAA permit modifications.

4. From 2017 to 2019, I was a CAA Permitting Engineer with the Idaho Department of Environmental Quality where I developed dozens of CAA air quality permits, including Permits to Construct (PTC), Title V Permits, and permit exemption documentation for various facilities. I worked with a variety of facilities, including gravel mining/processing, food manufacturing, landfills, among others. In developing these permits for these various operations, I was responsible for analyzing compliance with Idaho's toxic air pollutant (TAP) requirements. During this time, I became deeply familiar with Idaho Rules for the Control of Air Pollutions (Air Rules) found under IDAPA 58.01.01, as well as federal air permitting regulations 40 C.F.R. 60, 61, and 63.

5. From 2019 to 2022, I worked as a Senior Environmental Engineer at Brown and Caldwell Associates where I worked with a variety of clients on a multitude of projects on permitting and compliance projects, as well as site investigation and remediation. My work involved local, state, and federal environmental regulations within many frameworks including the CAA, Clean Water Act (CWA), Emergency Planning Community Right to Know Act (EPCRA), Spill Prevention Control and Countermeasure (SPCC), National Environmental Policy Act (NEPA), and cyanidation permitting. At the state level, my work included projects that spanned from Idaho, Oregon, Washington, Texas, Minnesota, New Jersey, and Massachusetts. Within the site investigation and remediation scope, my work included groundwater and surface water baseline monitoring, abandoned mine land site characterization, petroleum impacted site remedial action and monitoring, and dioxanes impacted site characterization. Within the CAA scope, my work included assisting clients with stationary source permitting compliance for a variety of industrial facilities, primarily in New Jersey and Idaho.

6. Since April of 2022, I have been employed at the Idaho Conservation League as a Regulatory Conservation Associate. Within this role, I review and provide comments on CWA and CAA permits, participate in federal and state rulemaking, and review CWA and CAA compliance/enforcement activities.

7. Through my career with private firms, the State of Idaho, and a non-profit organization, I have reviewed and/or developed hundreds of CAA permits, participated in dozens of negotiated rulemakings, and have reviewed thousands of pages of environmental rules and regulations across a variety of disciplines.

SCOPE OF REVIEW

8. I have been asked by the Petitioners Nez Perce Tribe, Idaho Conservation League, and Save the South Fork Salmon to review and evaluate the issues raised in the *Final Order in the Matter of Air Quality Permit to Construct P-2019.0047*[1] (Final Order) issued by the Board of Environmental Quality (Board) on May 9, 2024. Specifically, this declaration provides evidence and expert opinion on:

a. Whether DEQ's application of the 16/70 Project-specific adjustment factor to its analysis of ambient arsenic air concentration was appropriate to demonstrate compliance with the rule for carcinogenic TAPs found in IDAPA 58.01.01.586;

b. Whether using a 5-year rolling average for compliance with the rule for carcinogenic TAPs was appropriate and properly supported by the Permit conditions; and

c. Whether there is sufficient evidence to support the T-RACT analysis limiting the non-West End pit production limit.

DOCUMENTS REVIEWED

9. In preparation of this expert declaration, I reviewed the following documents:

- The historic TAPs rulemaking record from State of Idaho historical archives. The historic record includes hundreds of separate documents, including previous draft and final TAPs rules, public hearing transcripts, response to comment documents, emails, memorandums, letters between DEQ and industry stakeholders, hand written notes, and other various documents. Generally, these documents capture the 1991 to 1995 time period in which the original DEQ TAPs policy was formalized within the Idaho Negotiated Rulemaking Process and subsequently modified several times. I reviewed the historic TAPs rulemaking record in person, at the DEQ State office on two separate occasions on August 20, and September 10, 2024.

[1] REC 3695. *Final Order in the Matter of Air Quality Permit to Construct P-2019.0047*, Case Docket No. 0101-22-01, OAH Case No. 23-245-01 (May 9, 2024) (Final Order).

- Perpetua's application for a PTC, the draft PTC (Jan. 13, 2022), final PTC (June 17, 2022), the final Statement of Basis and Response to Comments (June 17, 2022) and associated attachments.
- Idaho's Air Rules, IDAPA 58.01.01.
- The Declarations of Kevin Schilling; Norka E. Paden, Ph.D.; Kevin Lewis; and Theresa Lopez, and each declarations' attached exhibits.
- The documents referenced in this declaration, which are attached as exhibits.

SUMMARY OF OPINIONS

10. Based on my review of case materials and extensive CAA permitting and compliance experience in private practice, with the State of Idaho, and with a non-profit organization, I conclude as follows:

a. DEQ's application of the 16/70 Project-specific adjustment factor to the ambient arsenic air concentration analysis, and the use of exposure duration adjustments like the 16/70 calculations is not supported by the historic TAPs rulemaking record. It was thus inappropriate for DEQ to use such an adjustment factor to demonstrate compliance with the Air Rules.

b. DEQ's interpretation of the TAPs AACCs as averaging periods rather than enforceable "standards" is misplaced and is not supported by the historic TAPs rulemaking record;

c. DEQ use of a 5-year rolling average for TAPs emission calculations is neither supported by the TAPs rule, the historic TAPs rulemaking record, nor by limitations under the Permit conditions; and

d. There was sufficient evidence to support the T-RACT analysis limiting the non-West End pit lifetime production limit, but West End Pit production is not properly constrained below the less than life-of-mine time frame.

OPINIONS

A. Application of the 16/70 Project-specific adjustment factor for assessing compliance with the TAPs rule is inconsistent with the rulemaking history, intent, and plain language of the TAPs rule.

11. When calculating arsenic emissions from the SGP for purposes of assessing compliance with the TAPs Rule, DEQ applied a Project-specific adjustment factor that took the SGP's estimated operational boundary arsenic concentration, multiplied it by 16 (representing the 16 year life of the SGP), divided that number by 70 years (representing an average human life-time), then compared that number the arsenic Ambient Concentration for Carcinogens (AACC) in order to demonstrate TAPs compliance.

12. The Declaration of Kevin Lewis (Lewis Declaration) claims that an "apples to apples" cancer risk comparison of the project's arsenic emissions and the AACC for arsenic cannot be made without the 16/70 Project-specific adjustment factor Lewis Decl. ¶ 58.

13.The Declarations of Norka E. Paden, Ph.D. (Paden Declaration), Kevin Schilling (Schilling Declaration), and Teresa Lopez (Lopez Declaration) all opine on this issue falling into the same problematic trap by relying on the same premise.

14. Based on my review of the historical records related to the development of the TAPs Rule, it is evident that the AACCs were developed as annual emission limits, with the intent that compliance is demonstrated on a year-over-year basis. The records demonstrate that

the use of an exposure duration adjustment,[2] like the 16/70 Project-specific adjustment factor used for the SGP, was directly considered by DEQ, and ultimately rejected. If implemented, using project-specific adjustment factors would create a permitting protocol that is antithetical to the intended protections of the TAPs Rule, the AACCs, and annual, year-over-year limits. My own personal experience working as a Permitting Engineer for DEQ, the Air Rules themselves, the historical TAPs Rule rulemaking record, and greater context of U.S. Environmental Protection Agency (EPA) guidance all support this conclusion.

15. As a Permitting Engineer for DEQ, I developed dozens of permits that required a TAPs compliance analysis. Many of those permits were for sources, such as portable rock crushers and concrete batch plants, that likely had limited term operations. In other words, more than five years, but less than 70 years. In all these instances I invariably applied DEQ's standard TAPs compliance protocol – to use the AACCs as annual compliance limits that a facility must meet year-over-year. In certain select instances where a facility specifically stated they did not intend to operate for more than 5 years, a ten-fold increase in the AACC was permitted, as allowed under Air Rule 58.01.01.007.08 and 210.15, but a permit condition limiting the facility's operation to no more than 5 years was included in the permit.

16. I never applied or was asked by supervising staff or an applicant to apply an adjustment factor for a TAPs emission calculation to account for exposure duration, like the 16/70 Project-specific adjustment factor at issue here. To my knowledge, DEQ introduced this type of Project-specific adjustment factor for the first time during the development of this PTC and such adjustment factors have never been used before for the permitting of other mines or other facilities.

[2] The concept of an "exposure duration adjustment" may also be appropriately referred to as "risk amortization" or "dose-averaging" as done within the Declaration of Ian H. von Lindern, P.E., Ph.D.

17. The Air Rules themselves and the historical TAPs rulemaking record reinforce my personal experience with TAPs compliance and demonstrate that, in its original TAPs rulemaking process, DEQ directly considered, but ultimately rejected, concepts like the 16/70 Project-specific adjustment factor and exposure duration adjustments generally, except for sources expected to operate for less than 5 years.

18. In an August 13, 1992 letter from DEQ's Mr. Frank Wilkoz to Ms. Joan Cloonan, Idaho Association of Commerce and Industry,[3] Mr. Wilkoz provided a first draft of the original TAPs rules for review while adding context within a "Explanation of Additions and Changes" section. Mr. Wilkoz served as DEQ's Technical Services Bureau Chief and was heavily involved in the development of the original TAPs rulemaking and subsequent modification while Ms. Cloonan served as an industry stakeholder and provided input to the process. Mr. Wilkoz's "Explanation of Additions and Changes" section provides insight to how DEQ intended to permit remediation and short term sources. Most significantly Mr. Wilkoz writes:

> However, a remediation source cannot be allowed to produce emissions that have the potential to expose human receptors to a full lifetime dose of a TAP over a short period of time, especially a carcinogen, even in the interest of environmental clean up. Further, a single very large dose of a carcinogen, while not a full lifetime dose, has the potential to cause toxics related cancers due to the nature of dose response interaction of carcinogens at the cellular level. To allow such doses would subvert the very purpose of a clean up.

19. In an email dated August 14, 1992, Idaho Deputy Attorney General Curt Fransen emailed DEQ's Mr. Tim Teater and Mr. Frank Wilkoz directly raising these questions regarding large-dose short-term exposures.[4] During the TAPs rulemaking period, Mr. Teater served as an

[3] See Exhibit A.
[4] See Exhibit B.

Air Quality Toxicologist and was also heavily involved in the development of the original TAPs rulemaking and subsequent modifications. In his email, Mr. Fransen questions:

> 16.01.01012,13.g.iii. and iv. The standard for remediation sources raises some questions of a general nature. I don't have any answers but wonder if it makes scientific sense to directly convert risk of additional cancer based on lifetime exposure to risk of additional cancer based on less than lifetime exposure by assuming a directly proportional relationship between years of exposure and risk. Sorry that I can't properly express that but you probably get the drift. Other questions that seem to arise from simply allowing higher exposure where the length of exposure is shorter include the unknown or potential combined and synergistic effect of many short term or remediation sources or other sources in the same area and the potential of serial (one after another) short term or remediation sources. Lastly, how will the operational life of a source be determined. What if an applicant says they only intend to operate for five years (for whatever reason) so want the higher emission number to apply. There is incentive for facilities to argue they will be short-term. The spectre of serial short-term sources arises. Perhaps the definition can be clarified so there is less wiggle room.[5]

20. In a later and related email sent from Mr. Teater to Mr. Wilkosz on August, 26, 1992,[6] Mr. Teater states:

> We will need to talk about the environmental remediation source limit of five years to get a break on emissions. I am opposed to making that greater than five years. It seems that after five years most remediation sources would have emission BRC (Below Regulatory Concern) anyway. If not then they need to be treated as any other source.

21. A further review of the historical TAPs rulemaking record provides support for treating the AACC as annual, year-over-years limit rather than supporting the use of unique operational scenarios and exposure duration adjustments. The Idaho Department of Health and

[5] In my review of the historical TAPs rulemaking record, no direct reply from either Mr. Teater or Mr. Wilkoz to Mr. Fransen was found.
[6] See Exhibit C.

Welfare (IDHW) response to draft rule comments from the same Idaho DEQ 1993 TAPs rulemaking document that is cited within the Lopez Declaration[7] states:

> **Comment #108**: Section 203.05.g. Unit Risk Factors are based on a 70-year exposure. This is not appropriate for an industrial park situation that will never be a residential application. The refined analysis should be liberalized to include a different model, actual meteorological data, more appropriate risk factors, actual hours of operation, more accurate emissions factors obtained through source testing, more accurate annual potential to emit scenarios and any other justifiable refinements. New wording for this section has been suggested to reflect this.
>
> **IDHW Response:** The rules have been changed in response to this comment. IDHW agrees that for industrial areas that will never be used for residential purposes, a 70 year risk base may be conservative. However, it is hard to predict future land use patterns. Examples of unforeseen new land uses with significant environmental and human health concerns have become quite common.
> IDHW has based its emission numbers on the best available data. IDHW has strived to take a balanced approach taking into account the needs of industry to operate and the need to protect human health and the environment. Since it is not possible to account for such real life factors as lifetime exposures, additive or multiplicative effects of exposures to the large variety of industrial chemicals in use in Idaho, it is necessary to make our emissions standards generally applicable and reasonably conservative.
>
> It is not possible for IDHW to carve out special exemptions or emissions factors for potential or hypothetical new or modified industrial sources or exposure scenarios. Our rules must take a balanced approach that is generally applicable and consistently applied. IDHW can not develop special emissions factors specifically for industry dominated areas. IDHW believes that the revised Section 210. 02 Quantification of Emissions Rates and Ambient Concentrations, which allows site specific data gives adequate flexibility in compliance with toxic standards.

22. I found no additional documentation regarding additional discussions of dose-response relationships in the historical TAPs rulemaking record. Regardless, and more

[7] *See* Lopez Decl., Memo. in Supp. of Decl. at 8, 10-12.

importantly, the only less-than-lifetime exposure duration adjustment DEQ ultimately included within the original TAPs rule (or any subsequent versions) was the less than 5-year, ten-fold adjustment factor currently contained under IDAPA 58.01.01.210.15.

24. The Lopez Declaration states that the EPA's 1984 Health Assessment Document for Inorganic Arsenic guidance (EPA 1984 Guidance) concludes that arsenic has a linear dose response relationship.[8] Said another way, there is a high concentration dose of arsenic received over a short duration that is equivalent in risk to some corresponding low concentration dose of arsenic received over a longer duration. This is the underlying assumption that DEQ relies on when it applied the 16/70 Project-specific adjustment factor to assessing TAPs compliance for the SGP Permit.

25. It is important to consider the broader context of the EPA 1984 guidance and the assumption of linear dose response relationships. The EPA 1984 Guidance does not include any exposure duration adjustment equations that are presented in the Paden[9] and Lopez Declarations,[10] such as EC = [CA x ET x ET x ED]/AT, and that is the basis for the 16/70 Project-specific adjustment factor used for assessing TAPs compliance in the Permit. This equation did not appear in EPA Superfund risk assessment guidance until 2009, as the Lopez Declaration itself cites,[11] well after the original TAPs Rule was developed and promulgated.

26. Furthermore, the historical TAPs rulemaking record shows DEQ specifically rejected previously existing EPA Superfund risk assessment guidance and its use of exposure duration adjustments in consideration of risk and TAP exposure. The following documents confirm this conclusion.

[8] Lopez Decl. ¶ 12; *id.*, Memo. in Supp. of Decl. at 3-4..
[9] *See* Paden Decl. ¶ 12.
[10] *See* Lopez Decl. ¶¶ 22, 24; *id*, Memo. in Supp. of Decl. at 10-12.
[11] Lopez Decl., Memo. in Supp. of Decl. at 9.

27. A undated TAPs rulemaking concept letter[12] (herein referred to as the TAPs Concept Letter) addressed to a "Robert" (presumably Robert Wilkoz) and presumably from another DEQ staffer outlines the rationale behind changes within a modified draft TAPs rule. Within the letter it is stated:

> We also do not accept the EPA superfund risk assessment guidelines. Superfund guidelines are based on the concept that the exposures are of limited duration and do not have a large potential for multiple exposures. We can not make those assumptions for sources in Idaho, many of which involve either long term exposures or exposures to substances with a potential for multiple exposures. In Idaho, we are attempting to protect the public from the deleterious effect of multiple sources of a given pollutant or the additive effects of multiple pollutants over the course of a 70 year lifetime. If we could assure only a single exposure occupance, then accepting higher temporary risk might be justifiable.
>
> In addition we must consider the effects of the pollutant on the elderly, the very young and the infirm. By using "worse case" assumptions we are then able, under very limited conditions and when the public health would not be compromised, to deviate from the one in a million standard and apply a one in one hundred thousand as noted in the NSR policy. The use of this conservative approach allows us to be sure that actual risk is no greater than the risk figure on which we base our policy.

27. A January 23, 1992 unsigned draft letter to Mr. Charles Woods, Marketing Manager for MDT Corporation[13] (a presumed TAPs rulemaking industry stakeholder) from a DEQ staffer (presumably Mr. Wilkoz)[14] states:

> Our policy is based on a 1:1,000,000 risk at the nearest public access to the source. Risk is computed by multiplying the predicted (by the model) ambient concentration by the unit risk factor (URF) as published by the US EPA. Idaho does not accept the Superfund

[12] See Exhibit D.
[13] See Exhibit E.
[14] The draft email has handwritten mark-up addressed to a "Tim". Given the frequent emails, letters, and notes discussing TAPs concepts within the TAPs historic rulemaking documents between Tim Teater and Robert Wilkoz and the similarity in style between those documents and the January 23, 1992 draft letter, this "Tim" is presumed to be Tim Teater and the author is presumed to be Robert Wilkoz.

> risk assessment method for computing risk except for single, relatively short term exposures. Our risk assessment for continuous industrial or other large sources is based on the possibility of multiple, long term exposures.

28. A TAPs rule that allows for exposure duration adjustments and a risk assessment approach creates a problematic precedent, as is made evident by the following hypothetical scenario. If the SGP (or any subsequent source) is allowed to operate using exposure duration adjustments, an adjacent receptor (i.e., a human being) would be exposed to more than the intended annual allowable concentration of arsenic (the AACC) for 16 years. If, before the SGP operations end, the receptor moves and lives or works next to another facility or a new facility starts operations next to the SGP that applies an exposure duration adjustment for TAPs compliance (a process which could repeat indefinitely), by the end of the receptor's lifetime, it has been exposed to a TAPs concentration over the AACC for its entire life and its lifetime risk exceeds the intended 1-in-100,000 cancer risk level. In this scenario, the "spectre of serial short-term sources," as feared by Mr. Fransen in his email,[15] is apparent. Allowing the SGP to use the 16/70 Project-specific adjustment factor opens the door to a world in which the current AACCs in the TAPs Rule are effectively replaced by higher concentrations due to shorter than 70-year sources.

9. Contrast a hypothetical scenario where exposure duration adjustments are not allowed and the TAP AACCs are annual limits that must be met year-over-year by every facility in Idaho. In this case, no facility may emit TAPs at a concentration greater than the AACCs and a 1-in-100,000 excess cancer risk is preserved no matter where a receptor lives, works, or travels in Idaho during their entire life, and no matter what other facilities start operations. This scenario creates a simple and easy to implement rule that is broadly protective of human health and the

[15] *Supra,* ¶ 19.

environment and, as the Schilling Declaration itself notes, was the intent of the originally TAP rulemaking process.[16] Furthermore, this scenario is supported by the historical TAPs rulemaking record and best fits the intent of DEQ.

30. Given the full review of the above evidence and based on my experience as a Permit Engineer at DEQ, I conclude as follows:

a. During the TAPs rulemaking process, DEQ specifically considered the use of exposure duration adjustments and use of calculations akin to the 16/70 Project-specific adjustment factor, but ultimately did not incorporate their use within the TAPs rules; and

b. DEQ intended the AACCs to be annual, year-over-year concentration limits and included only a single short-term adjustment factor within the original TAPs rule for sources operating for 5-years or less; and

c. DEQ's application of the 16/70 Project-specific adjustment factor to demonstrate compliance with TAPs is not supported by the intent or language of the TAPs rule, and results in a degradation of the protection of human health and the environment that is otherwise the purpose of the TAPs rule.

B. DEQ and Perpetua incorrectly assume the 1-in-100,000 cancer risk rate, rather than the AACC, is the applicable enforceable "standard."

31. The Lopez Declaration points out that DEQ states that TAPs AACs and AACCs "are expressed in terms of ambient air concentration, but they are not ambient air quality standards"[17] and interprets this quote, and other related DEQ statements, to reach the conclusion

[16] Schilling Decl. ¶ 13.
[17] Idaho DEQ, *Idaho Department of Health and Welfare, Responses to Comments and Questions Submitted During a Public Comment Period and Public Hearings on the Proposed Repeal and Reissuance of Rules for the Control of Air Pollution in Idaho* (1993) at 10 (Comment 31).

that, "The AACCs are not one-year limits. Compliance with IDAPA 586 is not based on comparing annual air concentrations from the model to an AACC"[18]. Instead of using the AACCs as the enforceable "standard" the Lopez, Schilling and Lewis Declarations argue that remaining below the 1-in-100,000 acceptable excess cancer risk is the ultimate standard in which a facility demonstrates compliance with the TAPs rule.

32. However, Lopez, Schilling, and Lewis's understanding of increments, standards, and enforceable limits is misplaced. Labeling AACCs as "increments" versus "standards" is simply a naming convention rooted in previously existing CAA policy; the enforceable standard is the AACC as a year-over-year limit.

33. There is a distinction between the National Ambient Air Quality Standards (NAAQS) as "standards" and the TAPs as "increments." Under stationary source permitting, the NAAQS set ambient air concentration standards for seven federal Criteria Pollutants (like Particulate Matter [PM] and Sulfur Dioxide); those standards consider both the existing ambient background concentration of a given criteria pollutant, as well as the addition of the same pollutant from the stationary source that is to be permitted. For example, the current PM_{10} 24-hour NAAQS is federally set at 150 ug/m^3. This means that the public is entitled to ambient air with a PM_{10} concentration no greater than 150 ug/m^3. Thus, a facility can be permitted to emit some amount of PM_{10}, but that amount, in addition to the existing background concentration of PM_{10}, can not create a PM_{10} concentration greater than 150 ug/m^3 at the facility's property/operation boundary.[19] Additions of PM_{10} may come from a variety of stationary or

[18] Lopez Decl., Memo. in Supp. of Decl. at 12.
[19] REC 0679-80. Statement of Basis, Appx. B (Ambient Air Quality Impact Analyses Review Memorandum), Table 24.

mobile, permitted or unpermitted sources, but maintaining an ambient concentration of PM_{10} below 150 ug/m^3 is the ultimate standard.

34. The AACCs as "increments" are different in that they do not consider background concentrations of TAPs. Unlike Criteria Pollutants, DEQ does not regularly monitor the ambient concentrations of TAPs. There simply are too many TAPs (there are over 80 carcinogenic TAPs alone listed in IDAPA 58.01.01.586), they are state-specific (unlike Criteria Pollutants), and the cost to do so is generally accepted as prohibitive. Thus, during the historic TAPs rulemaking process the AACCs were implemented as "increments" versus "standards." Said another way, while it is infeasible to monitor and enforce an ultimate TAPs concentration standard, it is feasible to estimate the incremental increase in TAPs concentrations that a facility would cause.

35. The concept and naming convention of "increments" is not novel to TAPs. In 1977, Clean Air Act amendments introduced the Prevention of Significant Deterioration (PSD) program.[20] The PSD program also created "increments." As defined by the EPA, "PSD increment is the amount of pollution an area is allowed to increase. PSD increments prevent the air quality in clean areas from deteriorating to the level set by the NAAQS. The NAAQS is a maximum allowable concentration 'ceiling.' A PSD increment, on the other hand, is the maximum allowable increase in concentration that is allowed to occur above a baseline concentration for a pollutant. The baseline concentration is defined for each pollutant and, in general, is the ambient concentration existing at the time that the first complete PSD permit application affecting the area is submitted."[21]

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[20] U.S. EPA, *Evolution of the Clean Air Act*, available at: https://www.epa.gov/clean-air-act-overview/evolution-clean-air-act (last visited Sept. 30, 2024).
[21] U.S. EPA, *Prevention of Significant Deterioration Basic Information* (Jan. 17, 2024), available at: https://www.epa.gov/nsr/prevention-significant-deterioration-basic-information (last visited Sept. 30, 2024).

36. Both the TAPs AACCs and PSD increments are maximum allowable increases from a specific source. In developing the TAPs Rules, DEQ would have certainly been aware of the concept and naming convention of "increments." The TAPs definition of increments is best viewed through the lens of a *compliance period*, rather than implying they represent an *averaging period*, as the Lewis Declaration does.[22]

37. Evidence from the historical TAPs rulemaking record reinforces this and the conclusion that the use of the term "increment" within TAPs was to differentiate them from including background concentrations as "standards" do. During the 1995 period, DEQ made revisions to the original and previously promulgated TAPs rule. As part of that process, DEQ developed a TAPs rule amendment summary document.[23] Within that document DEQ notes:

> The proposed rule will divide consideration of incremental increases of TAP emissions into individual source and facility wide categories. Net emissions is a concept that adds increases and decreases of emissions from new sources of TAP together to obtain a net amount. That net amount is then compared to acceptable ambient levels also called increments for a permitting decision. **The acceptable ambient level is referred to as an increment because TAP emissions increases are limited to an incremental increase as opposed to an absolute limited ambient concentration** (emphasis added).

38. On the other hand, if you assume DEQ intended the 1-in-100,000 cancer risk to be the enforceable standard and not the AACC as annual, year-over-year limits, it would have needed to incorporate additional variables into the TAPs Rule to guide applicants on how to assess that risk. Completing a risk assessment that analyzes a facility's excess cancer risk traditionally involves consideration of more variables and factors than just exposure duration.[24] Sensitive populations, comorbidities, and synergistic effects of combined toxic exposure all

[22] Lewis Decl. ¶ 29.
[23] See Exhibit F.
[24] *See* von Lindern Decl. ¶¶ 73-74

affect the ultimate cancer risk from a facility's airborne toxic emissions. . However, as mentioned above, the original TAPs rulemaking process rejected the risk assessment method and prioritized creating a simple and easy to implement rule that is still protective of human health and the environment. Ultimately, using the AACCs as the "enforceable standard" is a far more effective standard to use in fulfilling this goal.

39. Given the full review of the above evidence, I conclude as follows:

a. The labeling of the AACCs as "increments" versus "standards" is a naming convention rooted in previously existing CAA policy and is a distinction in the consideration of pollutant background concentrations rather than an averaging period concept.

b. DEQ intended the enforceable "standard" to be the AACC as an annual, year-over-year limit.

C. Use of a 5-year rolling average for demonstrating compliance with the TAPs ruleT-RACT is inappropriate and not supported by Permit conditions.

40. DEQ used a 5-year rolling average to calculate TAPs emissions from the SGP. However, such an approach does not comply with the intent of the original TAPs rulemaking process or with the language in the TAPs Rule stating that the AACCs are annual, year-over-year limits.

41. The Statement of Basis for the Permit partially acknowledges that the AACCs are annual limits while introducing the use of what it calls a more "refined" analysis. As stated under Section 4.2 of the TAPs Addendum Modeling Review Attachment to the Statement of Basis, "Annual average emissions of carcinogenic TAPs are typically used in the dispersion model to estimate maximum annual impacts. [Perpetua] refined the analyses by using source-specific

emission rates that are representative of a 5-year averaging period. This approach is appropriate because carcinogenic impacts are of concern from a long-term exposure basis."[25]

42. Using a 5-year rolling average on the calculated arsenic emissions from the SGP allows for some years of the SGP's TAPs emissions to be considerably higher–and above the AACC–as long as some years within the same period are comparably lower. So much so, that it would be possible for the SGP to have TAPs concentrations over the AACCs for the first four years of its operation as long as emissions from the fifth year were drastically reduced compared to the previous four.

43. This outcome creates a problematic precedent as is evident by another hypothetical scenario. Consider again the "spectre of serial short-term sources" and the scenario in which a receptor is exposed to consecutive sources that have applied an exposure duration adjustments discussed above in Paragraph 28. In a modified scenario, the receptor is adjacent to the SGP for four years of high TAPs emissions, but then relocates adjacent to a different TAPs source before a fifth year of low SGP TAP emissions occurs. The new TAPs source is also a less than 70-year source using exposure duration adjustments with TAPs concentrations above the AACCs. The receptor will be consistently exposed to TAPs concentration potentially well over the AACC, and is accruing an excess cancer risk level above 1-in-100,000. Again, the AACCs are effectively replaced by higher concentrations due to less than 70-year sources using exposure duration adjustment factors and/or emission period averaging.

44. In order to avoid such a scenario, the Air Rules and the historical TAPs rulemaking record speak for themselves. As stated within IDAPA 58.01.01.203.03, "Compliance with all applicable toxic air pollutant carcinogenic increments and toxic air pollutant

[25] REC 0698. Statement of Basis, TAPs Addendum Modeling Review Attachment.

non-carcinogenic increments demonstrates preconstruction compliance with Section 161 with regards to the pollutants listed in Sections 585 and 586." IDAPA 58.01.01.586 then simply states, "The AACC in this section are annual averages."

45. Given the full review of the above evidence, I conclude as follows:

a. Calculation of the SGP's arsenic emissions by using a 5-year rolling average is contrary to the intent of the original TAPs rulemaking process and the Air Rules stating that the AACC are an annual, year-over-year limit.

b. Using a 5-year rolling average inappropriately allows individual years of excess TAPs emissions to be masked within an averaged period.

D. There is insufficient evidence to support the T-RACT analysis limiting the non-West End pit production limit.

46. The Board in its *Final Order* questioned whether total life-of-mine ore production from non-West End pits was properly constrained by permit conditions.[26] I do not have specific concerns about whether production from non-West End pits was properly constrained over the life of the mine. However, the Board was right in questioning whether production from all pits was properly constrained.

47. The AACCs are limits for which compliance must be demonstrated on an annual, year-over-year basis. This requirement self-selects the highest maximum annual emission scenario as the emissions scenario that must be analyzed for AACC and TAPs compliance. As previously mentioned, the TAPs Addendum Modeling Review Attachment within the Statement

[26] REC 3725-27.

of Basis acknowledges this requirement: "Annual average emissions of carcinogenic TAPs are typically used in the dispersion model to estimate maximum annual impacts".[27]

48. It is unclear from the permitting record what exact emission sources and which period of time Perpetua and DEQ considered in developing the 5-year rolling averaging period for emissions. However, the von Lindern Declaration further investigates this issue, demonstrating that the likely maximum annual emissions scenario from the SGP would have considerably higher arsenic emissions than currently calculated within the Permit.[28]

49. In order to comply with the AACCs and demonstrate TAPs compliance, DEQ should have: (1) determined the worst arsenic generation scenario from any single year of the SGP (likely to include 100% production from the West End Pit); (2) compared the modeled operation boundary arsenic concentration from the worst generation scenario to the AACC to evaluate TAPs compliance; and (3) include a maximum annual ore generation permit limit from the pit(s) that correspond to the worst arsenic generation to ensure TAPs compliance.

50. Given the full review of the above evidence, I conclude as follows:

a. DEQ did not appropriately analyze the maximum annual emissions scenario from the SGP and instead diluted the SGP'd arsenic emissions through the 5-year rolling average calculation.

b. The permit does not sufficiently constrain ore production from the SGP's pit(s) on an annual basis.

[27] Analyzing the worst case scenario during permit development is a common permitting approach both at large and within DEQ specifically for fairly obvious reasons; if compliance with NAAQS, TAPs and any other applicable standards can be shown for a facility's worst case emissions/operation scenario then compliance for all other emissions/operation scenarios is inherently shown.
[28] *See* von Lindern Decl. ¶¶ 56-63

51. I declare under the penalty of perjury under the law of the State of Idaho that, to the best of my knowledge, information, and belief, the foregoing is true and correct.

DATED: October 3, 2024



William Tiedemann

Exhibit A

IDAHO DEPARTMENT
OF HEALTH AND WELFARE

DIVISION OF
ENVIRONMENTAL QUALITY

1410 North Hilton, Statehouse Mail, Boise, ID 83720-9000, (208) 334-0502 Cecil D. Andrus, Governor Richard P. Donovan, Director

August 13, 1992

Ms. Joan Cloonan,
Idaho Association of Commerce and Industry
P.O. Box 389
Boise, ID 83701

(HAND DELIVERED)

Dear Ms. Cloonan:

Enclosed per Orville Green's promise to you is:

> The First Draft of the Proposed Rules for the Control of Toxic Air Pollutants in Idaho.

> A brief explanation of the changes that have been made per our discussions at our last meeting.

This draft is to facilitate our discussions only. As I am sure you are aware, all actual regulatory proposals will have to undergo legal review and be reviewed by the U.S. EPA for compliance with the 1990 Clean Air Act Amendments.

If you have any questions on the above material please call me (334-0422). We are looking forward to continued productive discussions with you and IACI.

Sincerely,

Tim Teater
for

Robert Wilkosz
Bureau Chief
Technical Services Bureau
Division of Environmental Quality

:tt

Enclosures

cc: Dick Rush
Orville Green
Martin Bauer
Tim Teater
COF 1.1

Explanation of additions and changes.

The following is included as a brief discussion/explanation of the changes that the DEQ has made in our ideas for proposed toxic air pollutant rules. We have made every attempt to incorporate the suggestions made by IACI at the last IACI/DEQ meeting. These changes are for discussion only as they have not yet undergone legal review. The shaded portions are the changes made since our last meeting.

Environmental remediation source. This language was included for two reasons. First, we wish to encourage the rapid and effective remediation of environmental problems in other media. Remediation is a net benefit to the environment and as such, is to be encouraged when ever possible. However, we wish to reiterate that simply transferring a contaminant from one media to another is not acceptable remediation practice.

The second reason for this inclusion is that we do not think that it is reasonable to judge a source of five years or less duration by the same criteria as a permanent source. However, a remediation source cannot be allowed to produce emissions that have the potential to expose human receptors to a full lifetime dose of a TAP over a short period of time, especially a carcinogen, even in the interest of environmental clean up. Further, a single very large dose of a carcinogen, while not a full lifetime dose, has the potential to cause toxics related cancers due to the nature of dose response interaction of carcinogens at the cellular level. To allow such doses would subvert the very purpose of a clean up.

Short term source: This was included at the request of Mr. Dameworth of IACI to accommodate short term singular events. It was suggested, and we agree, that a source of five years or less should not necessarily be judged by the same criteria as permanent sources. However, as has been noted above, a short term source cannot be allowed to produce emissions that have the potential to expose human receptors to a full lifetime dose of a TAP especially a carcinogen. Again, as noted earlier, a single very large dose of a carcinogen, while not a full lifetime dose, has the potential to cause toxics related cancers due to the nature of dose response interaction of carcinogens at the cellular level. In view of the remediation adjustment factor, we consider an adjustment factor of 0.01 a reasonable compromise.

Environmental remediation or short term remediation adjustment factors. This language was included at the request of Mr. Dameworth of IACI. Mr Dameworth and others at IACI felt that language associating remediation sources with a one in ten thousand risk level (when figured in an equivalent manner as a permanent source) would inaccurately characterize the risk of these projects to the public. These draft adjustment factors are therefor added to make published risks for remediation sources seem equivalent to permanent sources. We are concerned, however, that these adjustment factors may serve to obscure the already minimal risks presented by remediation sources and compromise public confidence

in the permitting process.

The adjustment factors were arrived at in the following way. For remediation sources: five years divided by 70 years equals 0.070. This is roughly equivalent to a risk of one in ten thousand (actually a bit less). We have chosen not to make this a sliding scale calculation, ie 4/70, 3/70 etc. This was done for the reasons alluded to in the section above on environmental remediation sources.

For short term sources, it is our opinion that, since the purpose here is not necessarily to encourage operation of these sources, an adjustment factor equivalent to remediation sources is not appropriate. We do think, however, that allowing an increase in potential risk of one order of magnitude is acceptable. We believe that this factor would allow industry additional flexibility while still being adequately protective of the public health and the environment.

Approved fuels: This was deleted from the definitions at the request of IACI in order not to set precedent for other applications. This language was moved to the effected sections, 16.01.01012,02.d.vi and vii.

Section 16.01.01012,02.d.vii: This language was included to clarify the uses of laboratory equipment

Section 16.01.01012,02.d.x: This language was included to clarify the term recreational area.

Section 16.01.01012,13.g.ii,iii,&iv.: This language was included to clarify the procedures for permitting remediation and short term sources.

Section 16.01.01012,13.v: This section is included to clarify the modeling procedures. In general, we have attempted to describe the overall screening procedures from the most basic to the most sophisticated. Some of the specifics that are of interest are:

v.(a) This is a guide for the use of the TAP list in determining if further evaluation of TAP is necessary. As has been previously discussed, the TAP list with emissions screening levels is published in order that applicants have a ready reference to assist in the TAP permitting process. It has been our intent to make this list as comprehensive as possible in order that applicants have as much information at hand with out the need to do time consuming calculations and modeling when not necessary.

v.(b) Screening Modeling, first paragraph. The purpose here is not to re-approve EPA approved models, but to determine the appropriateness of the application. This is to save the applicant from doing work that ultimately will not be acceptable to the DEQ because an EPA model may have been used in an inappropriate application.

Because there are a large number of EPA approved models that can be used in the same general circumstances, DEQ review is to identify the most appropriate model for the situation. A modeling check list is available from DEQ to assist the applicant in this

process.

v.(c) This is the final step in quantification of emissions. As with screening level models, the language here is expressly to avoid the use of an inappropriate model in a given situation.

v. (d) This language is to give an explanation of how we will deal with TAP that have no OEL or URF. We looked for a more general procedure to use as opposed to a case by case method but we were unable to develop such a universal criteria. We have used the method described in the Draft Rules in the past in order not to impose a possibly unwarranted detection limit standard. By evaluating the physical and chemical properties of the substance in question, and comparing the results to chemicals for which exposure criteria are available, we were then able to propose an emissions limit that was acceptable to the applicant and DEQ.

Universal criteria that we have looked at have severe problems. Setting ELs at detection limits as has been done in the past may result in emissions limits that are unreasonably strict. A single value such as one pound an hour or one milligram per cubic meter etc. may be unreasonably strict in one instance but unreasonably liberal in another. Having no emissions or ambient criteria for TAP without an OEL or URF assumes that the lack of OEL or URF means that the compound in question is harmless. We would all agree that this assumption is unsupportable.

It is our position that the draft language represents a reasonable attempt to deal with this problem. In addition, the Division of Health is available to review the DEQ evaluation of the risk presented by a given emission level of a chemical.

Significant/significance. These terms are used throughout the Idaho Administrative Procedures Act (IDAPA). We believe that it would be difficult to remove this language entirely from the Toxics rules. We have attempted to address IACI concerns while at the same time preserving the integrity of the permitting process by adding the following language to the definitions Section 01.01003. 86, b. In reference to a net emissions increase or the potential of a source to emit a pollutant not listed in (a) above or in the New Source Review policy, any emission rate; or...

We would encourage IACI to bring specific proposals concerning the terms significant/significance to the next meeting for further discussion.

1ST DRAFT

PROPOSED RULES FOR THE CONTROL OF TOXIC AIR POLLUTION IN IDAHO

IDAPA 16.01.01003 -- DEFINITIONS.

~~*Approved Fuels. Natural gas, propane gas, liquified petroleum gas, distillate fuel oils, residual fuel oils, and diesel fuel; except that waste oil, gasoline, or refined gasoline are not approved fuels.*~~

Environmental Remediation Source. An emission source that functions to remediate or recover any release, spill, leak, discharge or disposal of any petroleum product or substance or any hazardous waste as defined by IDAPA 16.01.01003,44: from any soil or ground or surface waters. An Environmental Remediation Source shall have an operational life no greater than five (5) years from the inception of actual operations to the cessation of actual operations.

Short Term source. Any new source or major modification to an existing source, occurring one time only with an operational life no greater than five (5) years from the inception of actual operations to the cessation of actual operations. For the purposes of this act short term source includes pilot or experimental plants not covered in IDAPA 16.01.01012,02.d,x.

Pilot or Experimental Plant. An emission source that functions to test processing, mechanical, or pollution control equipment to determine full-scale feasibility.

Occupational Exposure Limit. Refers to airborne concentrations of substances and represents conditions under which it is believed that nearly all workers may be repeatedly exposed day after day without adverse effects. Occupational exposure Limits can be found in *Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices with Intended Changes for 1991-92 or the current edition*, adopted by the American Conference of Governmental Industrial Hygienists, or the National Institute for Occupational Safety and Health (NIOSH) current Relative Exposure Limit (REL), or the Occupational Health and Safety Administration (OSHA) Air Contaminate Standards, current Permissible Exposure Limit (PEL) or current Worker Protection Standards for Agricultural Pesticides promulgated by the Environmental Protection Agency under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA). The above references are listed in descending order of precedence.

Unit Risk Factor. *These factors describe the probability of developing excess cancers over a 70 year lifetime exposure to 1 ug/m^3 of a given carcinogen. Unit Risk Factors Can Be Found in the Federal Register Vol. 56 No. 35 / Thursday, February 21, 1991 / Rules and Regulations Appendix V. or listed on the Integrated Risk Information System (IRIS) of the U.S. Environmental Protection Agency or listed in the Health Effects Summary Tables promulgated by the U.S. Environmental Protection Agency Office of Health Effects Assessment and the Office of Air Quality Planning and Standards. In the absence of U.S. EPA accepted risk factors, risk factors under review by the EPA Carcinogen Risk Assessment Verification Endeavor (CRAVE) shall be used on an interim basis.*

Reasonably Available Control Technology (RACT): *Reasonably available control technology is that control technology that would achieve the lowest emissions of any toxic air pollutant applicable to a given source using reasonably available and economically feasible control equipment. This may require technology that has been applied to similar, but not necessarily identical sources.*

.01.01012, PROCEDURES AND REQUIREMENTS FOR PERMITS TO CONSTRUCT AND OPERATING PERMITS.

.01.01012,02 Permit To Construct:

No owner or operator may commence construction or modification of any stationary source, major facility, or major modification after the effective date of Section 01.01012 without first obtaining a permit to constructfrom the Department which satisfies the requirements of this Section. No exemptions shall apply to any modifications to a major facility which has not been issued a permit, except that no permit to construct is required for ~~the following classes of equipment which have actual and allowable emissions of less than one hundred (100) tons per year of any air contaminant or and would not significantly increase the emissions of a major facility~~ sources which:

a. Have actual and allowable emissions of less than one hundred (100) tons per year of any air contaminant; and

b. Would not significantly increase the emissions of a major facility; and

c. Will not have an ambient air concentration of any air contaminant that would, as demonstrated using Department-approved methods:

   i. Cause or significantly contribute to a violation of an ambient air quality standard; or

   ii. Cause an ambient concentration in excess of one percent of the Threshold Limit Value; or

   iii. Cause a cancer-risk probability in excess of one in one million.

d. Which belong to one of the following classes of equipment:

i. Air conditioning or ventilating equipment not designed to remove air contaminants generated by or released from equipment.

ii. Air contaminant detectors or recorders, combustion controllers, or combustion shutoffs.

iii. Fuel burning equipment for indirect heating and for heating and reheating furnaces using gas exclusively with a capacity of less than fifty (50) million BTU's per hour input.

iv. Other fuel burning equipment for indirect heating with a capacity of less than one million (1,000,000) BTU's per hour input.

v. Mobile internal combustion engines, marine installations and locomotives.

vi. Stationary internal combustion engines fueled by natural gas, propane gas, liquified petroleum gas, distillate fuel oils, residual fuel oils, and diesel fuel; except waste oil, gasoline, or refined gasoline shall not be used, and in accordance with the following:

100 horsepower or less -- unlimited hours of operation;
101 to 200 horsepower -- 450 hours per month;
201 to 400 horsepower -- 225 hours per month;
401 to 600 horsepower -- 150 hours per month.

vii. Stationary internal combustion engines used exclusively for emergency power generation fueled by natural gas, propane gas, liquified petroleum gas, distillate fuel oils, residual fuel oils, and diesel fuel except waste oil, gasoline, or refined gasoline shall not be used, and which operate less than 200 hours per year.

viii. Laboratory equipment used exclusively for chemical and physical analyses, research or education, including ventilating and exhaust systems for laboratory hoods.

ix. Environmental characterization activities including emplacement and operation of field instruments, drilling of sampling and monitoring wells, and any

other activities specifically exempted by the Director.

x. Pilot or experimental plants located at least 1/4 mile from any recreational area which, for the purpose of this Section, is defined as any area, available to the public used for any recreational activity such as, but not limited to, city, county, state or national parks or recreation areas, play grounds, swimming pools, stadiums or ball-game fields or residence or other structure not occupied or used solely by the owner of the facility or the owner of the property upon which the facility is located; which operate less than one year; and which also meet one of the following conditions:

(a) Use a slip stream from an existing process stream not to exceed ten percent of that existing process stream; or

(b) Have actual uncontrolled emissions which are not significant.

xi. Any emission source or sources provided that the actual uncontrolled facility-wide emissions are not significant, and the uncontrolled emissions would not significantly contribute to ambient air quality concentrations.

xii. Any other class or size of equipment specifically exempted by the Director. A list of those sources unconditionally exempted by the Director will be maintained by the Department, and made available upon request.

01.01012,13. Procedure for Issuing Permits

a. General procedures ...

b. Additional procedures ... attainment or unclassifiable area ...

c. Additional procedures ... federal Class I area ...

d. Procedures for operating permits ...

e. The Department ... fluid model ...

f. Modification of permits ...

g. *Additional procedures for demonstrating compliance with the toxic substances requirements in Section 01.01011,01.*

i. *For sources not recognized by the Department as environmental remediation or short term sources that cannot demonstrate, using Department approved methods, that emissions of carcinogens contribute an ambient air cancer risk probability of less than 1:100,000 and that emissions of non-carcinogens contribute to an ambient air concentration of less than one percent of the Threshold Limit Value, a permit cannot be issued unless the source ~~has achieved the greatest degree of emission reduction that has been adequately demonstrated~~ can demonstrate that reasonably available control technology (RACT) as defined in EPA guidelines or as approved by the Director, can be installed and properly operated. A permit may be issued without the installation and operation of RACT if the associated health risks to the public from the operation of the facility have been declared acceptable by the Department's Division of Health.*

ii. *For remediation sources that cannot demonstrate, using Department-approved methods which may include the application of a remediation adjustment factor of seventy thousandths (0.070), an emission rate or acceptable ambient level for a non-carcinogen (AAL) of one one hundredth (1/100) of the appropriate OEL, as listed on Appendix A1 of the TAP list or an acceptable ambient level for a carcinogen (AALC), as listed on Appendix A2 of the TAP list, ~~emissions of carcinogens contribute an ambient air cancer risk probability of less than 1:10,000 and or that emissions of non-carcinogens contribute to an ambient air concentration of less than ten percent of the Threshold Limit Value~~, a permit cannot be issued unless the source ~~has achieved the greatest degree of emission reduction that has been adequately demonstrated~~ can demonstrate that reasonably available control technology (RACT) as defined in EPA guidelines or as approved by the Director can be installed and properly operated. A permit may be issued without the installation and operation RACT if the associated health risks to the public from*

the operation of the facility have been reviewed and declared acceptable by the Department's Division of Health.

iii Short term sources shall be treated the same as remediation sources except that a short term adjustment factor of 0.01 instead of a remediation adjustment factor of 0.07 shall be applied.

iv. For sources that can demonstrate, using Department-approved methods, that emissions of carcinogens contribute an ambient air cancer risk probability of less than 1:1,000,000 and that emissions of non-carcinogens contribute to an ambient air concentration less than one percent of the Threshold Limit Value, no additional procedures are needed.

v. Department-approved methods will consist of the following:

(a) Emissions Screening:
Comparison of maximum potential emissions to the screening emission limits for carcinogens and non-carcinogens as documented in Appendix A1 or A2 of the Toxic Air Pollutant list ~~as promulgated by the Director~~. Maximum potential emissions can be determined by actual emissions testing using U.S. Environmental Protection Agency approved methods ~~subject to review and approval by the Division of Environmental Quality~~ or estimates of the maximum potential emissions using standard scientific and engineering principals and practices subject to review and approval by the Director. If maximum potential emissions as determined using department approved methods as described in this Section are less than or equal to the screening emissions levels as listed on Appendix A1 or A2 of the TAP list, no further procedures for demonstrating compliance with the toxic substances requirements in Section 01.01011,01 will be required.

(b) Screening Modeling:
Screening modeling, using only U.S.

Environmental Protection Agency (EPA) currently approved models, applied according to EPA's Guidelines on Air Quality Models, and as determined appropriate for the application by the Director, may be done to conservatively determine ambient concentrations of a toxic air pollutant.

To determine an acceptable ambient level for a TAP when using SCREEN, T-SCREEN or other EPA approved models which use arbitrary meteorological data and predict maximum one (1) hour concentrations, multiply the maximum hourly concentration output by the model for a distance not greater than the facility property boundary nearest the source or, with department approval, the closest point of public access by a persistence factor of 0.15 to convert the hourly average to an annual average.

For a carcinogen, no further procedures for demonstrating compliance with Section 01.01011,01 will be required if the resulting product is equal to or less than the AALC as listed on Appendix A2 of the TAP list or if the resulting product when multiplied by the unit risk factor results in an ambient air cancer risk probability less than or equal to one in a million.

For a non-carcinogen, no further procedures for demonstrating compliance with Section 01.01011,01 will be required if the resulting product is less than or equal to one one hundredth (1/100 of the appropriate occupational exposure limit as listed on Appendix A1 of the TAP list..

(c). Refined Modeling

Atmospheric dispersion modeling, using only U.S. EPA currently approved models determined appropriate for the application by the Director, applied according to EPA Guidelines on Air Quality Models may be done to determine an ambient concentrations of a TAP. The procedures will be the same as for screening modeling except that a persistence factor shall not

be used.

(d) For any TAP for which there is no OEL or screening emissions limit or AALC listed on Appendix A1 or A2, the screening emissions limit and AAL or AALC will be determined by evaluation of the physical, chemical and toxicological properties of the substance in question and by comparison to physically, chemically and toxicologically related substances if any, on a case by case basis by the Director or the Division's Department of Health.

(e) Any other method approved by the Director.

insert table 1 here

TABLE 1. SOURCE TYPE/PERMITABLE RISK LEVELS

	AJUST-MENT FACTOR	DEMINIMUS	PERMITTABLE	NOT PERMITTABLE
NEW SOURCE	N/A	≤ 1:1,000,000	≤ 1:100,000	≥ 1:100,000
REMEDIATION SOURCE	0.070	≤ 1:1,000,000	≤ 1:100,000	≥ 1:100,000
SHORT TERM SOURCE	0.010	≤ 1:1,000,000	≤ 1:100,000	≥ 1:100,000

Exhibit B

FROM: Fransen, Curt

TO: Teater, Tim
Wilkosz, Robert

DATE: 08-14-92
TIME: 11:51

CC:
SUBJECT: Toxic Air Rules
PRIORITY:
ATTACHMENTS:

My comments, briefly, are as follows:
-16.01.01.01012,02.d. By making this section an "or" section, in other words a section which categorically excludes certain classes of equipment from the permit requirement, some problems seem to arise with the less precisely defined classes from about viii onward. For instance, if a facility could jam themselves (such as INEL) into either the "laboratory equipment" or "pilot or experimental plant" class, the permit requirement would not appear to apply regardless of how large or hazardous the emission actually would be. I could see INEL argueing that everything they do is somehow for physical analyses or research (lab equipment class) or the testing of processing or mechanical stuff to determine full-scale feasibility (pilot or experimental plant class). The problem with these classes is that they are subjective and potentially broad as compared to the classes described by i through vii. Likewise, xi is vague and appears to duplicate at least some of the factors established by a, b and c.
-16.01.01012,13.g.iii. and iv. The standard for remediation sources raises some questions of a general nature. I dont have any answers but wonder if it makes scientific sense to directly convert risk of additional cancer based on lifetime exposure to risk of additional cancer based on less than lifetime exposure by assuming a directly proportional relationship between years of exposure and risk. Sorry that I cant properly express that but you probably get the drift. Other questions that seem to arise from simply allowing higher exposure where the length of exposure is shorter include the unknown or potential combined and synergistic effect of many short term or remediation sources or other sources in the same area and the potential of serial (one after another) short term or remediation sources. Lastly, how will the operational life of a source be determined. What if an applicant says they only intend to operate for five years (for whatever reason) so want the higher emission number to apply. There is incentive for facilities to argue they will be short-term. The spectre of serial short-term sources arises. Perhaps the definition can be clarified so there is less wiggle room.

Let me know if you want to discuss.

Exhibit C

FROM: Teater, Tim

TO: Wilkosz, Robert

DATE: 08-26-92
TIME: 15:28

CC:
SUBJECT: IACI toxics committee.
PRIORITY:
ATTACHMENTS:

---

1. Lori tells me that the AG's office has copies of all the state regs. Ill check on NY & NC.
2. We will need to talk about the environmental remediation source limit of five years to get a break on the emissions. I am opposed to making that greater than five years. It seems that after five years most remediation sources would have emissions BRC anyway. If not then they need to be treated as any other source.
3. The discussion on CRAVE was an increadable bunch of whining BS. Bitching for its own sake!
4. Section "d" about dealing with compounds that do not have emissions standards or URFs will be tough. As I mentioned to you, Pat and Dick Shultz supported my position on this. I can only think that we might come up with some rewording. I am totally opposed to the idea that if it has no emissions data then it should be uregulated.
5. Section "v" (a) we are asked to "prioritize emissions estimate data ie stack testing, AP-42, XWALK, etc. This is a stupid idea. I do not understand where Daimworth is coming from. Different emissions estimating techniques are appropriate for different situations. Stack testing is OK but even that depends on how much alike the processes and facilities are. Some of the stuff IACI has complained about is so self defeating.

REPLY FROM: Teater, Tim FROM: Wilkosz, Robert

TO: Teater, Tim

DATE: 08-26-92
TIME: 14:27

CC:
SUBJECT: IACI toxics committee.
PRIORITY:
ATTACHMENTS:

fyi

FORWARDED FROM: Wilkosz, Robert
FROM: Green, Orville

TO: Nagel, Joe

DATE: 08-26-92
TIME: 14:03

CC: Ledger, John
Wilkosz, Robert

SUBJECT: IACI toxics committee.
PRIORITY:
ATTACHMENTS:

We had a very good meeting. Even Mike Smith of FMC was helpful today. Joan Cloonan was on vacation. Dick Schultz and Pat McGavaran attended and helped considerably. Schultz was pleased with the meeting.

We have about a dozen items left, none unresolvable in my opinion, to work out. Wilkosz will chair the next meeting 9/14. We may schedule one more

meeting after that, but we are very close to referring the draft to the AG's office for review prior to public comment.

Afterwards, Dick Rush said that IACI was still discussing the issue, and he re-stated that they may still oppose the package once we conclude our discussions.

Exhibit D

Robert, this is a second draft - wadayathink? Please note that I'm shaky on the rational for using .15 for an annualization factor.'

This is to clarify the New Source Review Policy, as it regards its application to the construction of new sources of toxic air pollutants (TAP).

In applying the New Source Review policy to a potential source of TAP, the first aspect of the application that we look at is the screening emission limits. If the emissions out of the stack do not exceed our published emissions limits then the emissions are below regulatory concern for that process and pollutant.

If emissions are above the listed screening emissions limits then the SCREEN model is utilized to predict an ambient concentration. The DEQ, in order to have a conservative, "worse case" scenario, uses full meteorology, not just a particularly favorable stability class and or wind speed for the SCREEN model.

If predicted ambient concentrations are still above DEQ screening levels and if actual meteorological data is available, a more sophisticated model may be used to more accurately estimate dispersion data for TAP. Any model used must be EPA approved for the use and the results must be reviewed by our own meteorological staff.

When the TAP of concern are known or suspected carcinogens, the maximum hourly predicted concentrations are converted to an predicted annual concentration by multiplying the hourly concentrations by a conversion factor of .15. Derived from??

In the case of a substance of interest not being listed by DEQ or if there are no emission or ambient values listed, the substance must still be included in any emissions estimates and modeling. Potential risk associated with any unlisted substance or substance with out published values will be evaluated on a case by case basis by the DEQ.

Risk is calculated by multiplying the unit risk factor published by the EPA by the concentration obtained in the model. In general, the policy requires that risk at the facility fence line or the first point of public access from the source be equal to or less than one in a million.

We do not accept the first full time residence as the nearest point of public access except in very limited special circumstances. For instance, if a source was in an industrial area with very limited public access and the first regular public access was a nearby residence, then we may consider that residence as the first public access and analyze risk to the public accordingly.

We also do not except the EPA superfund risk assessment guidelines. Superfund guidelines are based on the concept that the exposures

are of limited duration and do not have a large potential for multiple exposures. We can not make those assumptions for sources in Idaho, many of which involve either long term exposures or exposures to substances with a potential for multiple exposures.

In Idaho, we are attempting to protect the public from the deleterious effect of multiple sources of a given pollutant or the additive effects of multiple pollutants over the course of a 70 year lifetime. If we could assure only a single exposure occupance, then accepting higher temporary risk might be justifiable.

In addition we must consider the effects of the pollutant on the elderly, the very young and the infirm. By using "worse case" assumptions we are then able, under very limited conditions and when the public health would not be compromised, to deviate from the one in a million standard and apply a one in one hundred thousand as noted in the NSR policy. The use of this conservative approach allows us to be sure that actual risk is no greater than the risk figure on which we base our policy.

For further information on the application of the New Source Review policy on TAP, please contact our office.

Exhibit E

DRAFT

January 23, 1992

Mr Charles Wood
Marketing Manager, Sterilization Equipment
MDT Corporation
P.O. Box 23077
Rochester, New York
14692-3077

Dear Mr. Wood,

Mr. Dan Heiser has asked me to respond to your recent enquiry about regulations concerning the emission of ethylene oxide (EO). The following explains the screening level review process for permits to construct new continuous industrial or other large sources.

Sources of EO emissions may be subjected to the Idaho New Source Review (NSR) policy for Toxic Air Pollutants (TAP) and may require a permit to construct (PTC). The screening level for emissions of EO into the ambient air is 6.7E-04 lb/hr. When that screening level is shown likely to be exceeded by mass balance or other acceptable engineering calculations, an Acceptable Ambient Level for a Carcinogen (AALC) is used as the next step in the screening process. The AALC was determined previously in the policy draft process. What we determine in the PTC or NSR process, is the ambient impact (concentration) of a given pollutant.

For EO the AALC is 1.0E-02 ug/m^3. In order to determine the AALC, the NSR policy requires that the source be modeled using SCREEN with full meteorology. If actual meteorological data is available, then that data should be used. If this modeling indicates that the screening AALC will be exceeded, then the applicant has the option of using a more sophisticated model to show that the AALC will meet NSR policy. Any model used must be US EPA approved for the use.

Our policy is based on a 1:1,000,000 risk at the nearest public access to the source. Risk is computed by multiplying the predicted (by the model) ambient concentration by the unit risk factor (URF) as published by the US EPA. Idaho does not accept the Superfund risk assessment method for computing risk, except for ~~single~~, relatively short term exposure. Our risk assessment for continuous industrial or other large sources is based on the possibility of multiple, long term exposures.

I have enclosed our NSR policy. That policy also outlines the decision guidelines for permitting sources of TAP based on risk or potential health impacts. If you have any further questions please feel free to contact me.

(334-....)

Sorry Tim I meant as this is tutorial sort of reminder to you

Tim my point is that we don't determine the AALC each PTC review, we determine the ambient level likely caused by the source & compare that to the AALC. right?

TR 5275

REC 6095

Exhibit F

Item No.:	Docket No.: 0101-9501	Program: Air Quality
Topic: Revision of the Toxic Air Pollutant Rules		
Status: Planned Rule	X Proposed Rule	Final Rule
Note:		
Date: Initial Publication 1/95	Board 6/95	Final Publication 8/95
Technical staff contact: Robert Wilkosz		Telephone: 334-5898

- This rule amends existing rules. The proposed rules address the permitting and exemptions from permitting, of new sources of toxic air pollution in Idaho.

- The proposed rule changes the regulatory basis on which Toxic Air Pollutants (TAP) are regulated. TAP were regulated based on the requirements to demonstrate compliance with the TAP Acceptable Ambient Concentration (AAC) increments. The proposed rule regulates TAP based upon the requirement to demonstrate compliance with section 161. This change was made to accommodate the other changes such as netting and interpollutant trading that provide for exceptions to the TAP increments.

- Below regulatory concern (BRC), Levels for TAP emissions have been established. These BRC levels have to do with record keeping, reporting, and self exemption from the requirements to obtain a permit to construct (PTC).

- The proposed rule will divide consideration of incremental increases of TAP emissions into individual source and facility wide categories. Net emissions is a concept that adds increases and decreases of emissions from new sources of TAP together to obtain a net amount. That net amount is then compared to acceptable ambient levels also called increments for a permitting decision. The acceptable ambient level is referred to as an increment because TAP emissions increases are limited to an incremental increase as opposed to an absolute limited ambient concentration.

  Source specific TAP emissions are those coming from one specific source within a whole facility under the following conditions: the emissions, without any air pollution controls must be less than the increment and with controls, the emissions must be less than or equal to the screening emissions level or the increment, which ever is greater.

- The proposed rule recalculates the way the increment for non-carcinogens is calculated. The current rules have increments based on an occupational exposure limit (OEL), divided by a total uncertainty factor of 100 with an annualized averaging time. The proposed rule will divide the OEL by 20 and decrease the averaging time to 24 hours.

- The proposed rule would eliminate remediation source factor and eliminate some TAP emissions from netting. The remediation source factor was a mathematical factor applied to the increment to allow a greater level of emissions for the short period of time (5 years) that a remediation source would operate. Remediation sources not specifically exempted from

netting requirements will be treated the same as other new sources. However, best available control technology (BACT) would be required if the TAP emissions from that source will exceed the AAC.

- The proposed rule will extend the concept of offsetting to TAP. Offsetting is allowing an increase in emissions of an air pollutant to be offset by a reduction in the same air pollutant from another source. In a circumstance that a source desires to construct a new source of TAP emissions but the new source can not meet the TAP emissions requirements, interpollutant trading provides an opportunity for that construction to go on while theoretically decreasing the over all risk from TAP emissions. The DEQ will use the EPA guidance contained in Section 112(g) of the clean air act or other EPA approved data bases or references to make all interpollutant trading determinations.

- This proposed rule is the result of numerous meeting with Idaho Association of Commerce and Industry, a number of other industrial representatives and some members of the public.

- Notification of the proposed rule will be published in the bulletin as well as various papers around the state. Public hearings are scheduled for Moscow, Pocatello and Boise. DEQ plans to submit the proposed rules the Board of Health and Welfare in June, 1995.

Item No.:	Docket No.: 01019501

CERTIFICATE OF SERVICE

I hereby certify that on October 4, 2024, a true and correct copy of the foregoing EXPERT DECLARATION OF WILL TIEDEMANN was served on the following by electronic service:

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s/ Julia Thrower
Julia S. Thrower

BEFORE THE BOARD OF ENVIRONMENTAL QUALITY
STATE OF IDAHO

IN THE MATTER OF AIR QUALITY PERMIT TO CONSTRUCT P-2019.0047	Agency Case No. 0101-22-01
NEZ PERCE TRIBE, IDAHO CONSERVATION LEAGUE, and SAVE THE SOUTH FORK SALMON, Petitioners, vs. IDAHO DEPARTMENT OF ENVIRONMENTAL QUALITY, Respondent, and PERPETUA RESOURCES IDAHO, INC., Intervenor-Respondent.	OAH Case No. 23-245-01

CONTESTED CASE HEARING

Date: April 2, 2025
Place: Idaho Department of Environmental Quality
1410 North Hilton Street, Boise, Idaho
Time: 9:06 a.m.
REPORTED BY:
ANDREA L. CHECK, CSR No. 748, RPR, CRR
Notary Public

A P P E A R A N C E S

Board Members:

DR. JOHN RANDY MacMILLAN, Chair

CLAYTON STEELE, Vice Chair

PAT PURDY

BETH ELROY

MARK BOWEN

LANCE BOYLAN

For the Board:

Office of the Attorney General

Deputy Attorney General

Energy and Natural Resources Division

BY: MS. ANN YRIBAR, ESQ.

P.O. Box 83720

Boise, Idaho 83720-0010

ann.yribar@ag.idaho.gov

For the Respondent Department of Environmental Quality:

Office of the Attorney General

Deputy Attorney General

Department of Environmental Quality

BY: MS. HANNAH M.C. YOUNG, ESQ.

1410 North Hilton, 2nd Floor

Boise, Idaho 83706

hannah.young@deq.idaho.gov

A P P E A R A N C E S (Continued)

For the Intervenor-Respondent Perpetua Resources Idaho, Inc.:

Stoel Rives, LLP
BY: MS. NICOLE C. HANCOCK, ESQ.
101 South Capitol Boulevard, Suite 1900
Boise, Idaho 83702
nicole.hancock@stoel.com

For the Petitioners Nez Perce Tribe and Idaho conservation League:

Advocates For the West
BY: MR. BRYAN HURLBUTT, ESQ.
P.O. Box 1612
Boise, Idaho 83701
bhurlbutt@advocateswest.org

For the Petitioner Save the South Fork Salmon:

Mountain Top Law, PLLC
BY: MS. JULIA THROWER, ESQ.
614 Thompson Avenue
McCall, Idaho 83638
jthrower@mtntoplaw.com

Also Present:

Diane Cutler, Elaine Ganino, Tiffany Floyd

P R O C E E D I N G S

CHAIRMAN MacMILLAN: Good morning, everyone. It is April 2nd, 2025, approximately 9:00 a.m. This is Dr. Randy MacMillan, chairman of the Idaho Board of Environmental Quality. I call to order this special meeting of the Idaho Board of Environmental Quality.

In addition to being a public meeting, we are also on the record In the Matter of Air Quality Permit to Construct Issued to Perpetua Resources Idaho, Incorporated, Agency Case No. 0101-22-01, OAH Case No. 23-245-01. This special meeting is being held in the state office of the Department of Environmental Quality.

For those present in the meeting room, please sign in on the sheet provided by the entrance. There won't be an opportunity for public comment today.

Elaine, could you please take the roll.

BOARD CLERK GANINO: Yes, Mr. Chairman.

Dr. Randy MacMillan?

CHAIRMAN MacMILLAN: Here.

BOARD CLERK GANINO: Clayton Steele?

VICE CHAIR STEELE: Here.

BOARD CLERK GANINO: Mark Bowen?

BOARD MEMBER BOWEN: Here.

BOARD CLERK GANINO: Beth Elroy?
BOARD MEMBER ELROY: Here.
BOARD CLERK GANINO: Pat Purdy?
BOARD MEMBER PURDY: Here.
BOARD CLERK GANINO: Lance Boylan?
BOARD MEMBER BOYLAN: Here.
BOARD CLERK GANINO: And Board Member Dennis Leikam is absent.
CHAIRMAN MacMILLAN: Thank you. Before we get started with the first agenda item, I'd like to take the opportunity to introduce the parties and talk about some of the logistics for today.
You will notice that unlike a normal DEQ Board meeting, we have a court reporter here today. The reporter will be on the record throughout our proceedings today, so please try to speak slowly and clearly, try not to talk over one another, and use "yes" or "no" instead of "uh-huh" or nodding your heads. That will make the reporter's job easier today.
I'd also like to take a moment to introduce the parties for the record so the reporter has those going forward.
Let's begin with introducing the parties.
The Petitioners in this matter are Nez Perce Tribe, Idaho Conservation League, and Save the Southfork

Salmon.

Would you all take a moment to please identify yourselves for the record.

MR. HURLBUTT: Bryan Hurlbutt representing Idaho Conservation League and the Nez Perce Tribe.

MS. THROWER: And Julia Thrower representing Save the Southfork Salmon.

CHAIRMAN MacMILLAN: Thank you.

The Respondents in this matter are the Department of Environmental Quality and Intervener-Respondent, Perpetua Resources Idaho, Incorporated.

Would you please identify yourselves for the record.

MS. YOUNG: Hannah Young representing the Department.

MS. HANCOCK: Nicole Hancock with Stoel Rives representing Perpetua.

CHAIRMAN MacMILLAN: Thank you.

Also in the room today we have Deputy Attorney General Ann Yribar. She is representing the Board.

Is there anyone else that I missed who wants their attendance put on the record?

(No response.)

CHAIRMAN MacMILLAN: So we'll move right on to

Agenda Item No. 1.

We will move on to the first agenda before the Board today, which is executive session pursuant to Idaho Code 74-206(1)(f). The Board may choose to go into executive session multiple times throughout the hearing.

Is there a desire at this point for any of the Board members to enter into an executive session to communicate with our legal counsel? If so, I'd entertain a motion to that effect.

BOARD MEMBER ELROY: Mr. Chairman, I move the Board enter into an executive session pursuant to 74-206(1)(f) to communicate with legal counsel for the public agency to discuss the legal ramifications of and legal options for pending litigation or controversies not yet being litigated but imminently likely to be litigated. I request that a roll call vote be taken and that vote be recorded in the minutes of this meeting.

CHAIRMAN MacMILLAN: Thank you. And for the record, that was Beth Elroy.

So there is a motion. Is there a second?

BOARD MEMBER BOWEN: Second.

CHAIRMAN MacMILLAN: Okay. Is there -- there is -- is there any discussion? Any discussion?

(No response.)

CHAIRMAN MacMILLAN: Hearing none, the motion has been made and seconded. We will now conduct a roll call vote. Board members, please respond by saying "aye" in favor of the motion or "nay" against the motion.

And, Elaine, if you could call that.

BOARD CLERK GANINO: Thank you, Mr. Chairman.

Dr. Randy MacMillan?

CHAIRMAN MacMILLAN: Aye.

BOARD CLERK GANINO: Clayton Steele?

VICE CHAIR STEELE: Aye.

BOARD CLERK GANINO: Pat Purdy?

BOARD MEMBER PURDY: Aye.

BOARD CLERK GANINO: Beth Elroy?

BOARD MEMBER ELROY: Aye.

BOARD CLERK GANINO: Mark Bowen?

BOARD MEMBER BOWEN: Aye.

BOARD CLERK GANINO: Lance Boylan?

BOARD MEMBER BOYLAN: Aye.

CHAIRMAN MacMILLAN: The motion is carried.

The Board is now off record and the room for executive session will be closed off. Attendees in the adjacent room are welcome to remain and wait until executive session concludes.

BOARD CLERK GANINO: Mr. Chairman, I actually

will have you move into Conference Room D.

CHAIRMAN MacMILLAN: Very good. Thank you.

(The Board convened into executive session off the record.)

CHAIRMAN MacMILLAN: So if I recall in the script correctly, we need a motion to come out of executive session.

BOARD MEMBER ELROY: Mr. Chairman, I move that the Board resolve out of executive session and that the meeting of the minutes reflect that no action was taken during the executive session.

CHAIRMAN MacMILLAN: That motion was read by Beth Elroy.

BOARD MEMBER PURDY: Second the motion.

CHAIRMAN MacMILLAN: We have Pat Purdy a second for the motion.

Is there any discussion?

(No response.)

CHAIRMAN MacMILLAN: The motion has been made and seconded. I guess we need to vote on it. The script doesn't --

MS. YRIBAR: Have Elaine do the roll call.

CHAIRMAN MacMILLAN: So, Elaine, if you could do a roll call vote to come out of executive session.

BOARD CLERK GANINO: Yes, Mr. Chairman.

Dr. Randy MacMillan?
CHAIRMAN MacMILLAN: Aye.
BOARD CLERK GANINO: Clayton Steele?
VICE CHAIR STEELE: Aye.
BOARD CLERK GANINO: Mark Bowen?
BOARD MEMBER BOWEN: Aye.
BOARD CLERK GANINO: Beth Elroy?
BOARD MEMBER ELROY: Aye.
BOARD CLERK GANINO: Pat Purdy?
BOARD MEMBER PURDY: Aye.
BOARD CLERK GANINO: Lance Boylan?
BOARD MEMBER BOYLAN: Aye.
CHAIRMAN MacMILLAN: Motion is carried.
Moving on to Agenda Item No. 2, which is oral arguments on Petitioners' petition for a review of January 7th, 2025, preliminary order, memorandum in support, and request for hearing.
I'd like to provide 30 minutes to each party to argue their case. In addition, there will be ten minutes allotted for each petitioner for rebuttal.
So let's begin with the petitioners. And according to my list, Idaho Conservation League is first.
BOARD MEMBER ELROY: Mr. Chairman?
CHAIRMAN MacMILLAN: Yes.

BOARD MEMBER ELROY: Do you want --

CHAIRMAN MacMILLAN: Oh, absolutely. And I should mention, particularly for the hearing reporter, that Beth Elroy will need to leave the meeting at about 11:00 o'clock or so and will come back, approximately, noon time.

We'll probably have lunch, if the lunch has arrived, about 11:30 today. And so that's the tentative plan. But, anyway, Beth Elroy will be leaving this meeting temporarily.

Thank you, Beth.

Brian, the floor is yours.

MR. HURLBUTT: Thank you, Board members.

And Julie Thrower, representing Save the Southfork, is also up here with me. We filed the petition together, and I'll be, you know, roughly covering, you know, the first half of the petition; she'll be covering the second half. But there's certainly overlap, and we can both be prepared to answer questions, if helpful, throughout these presentations.

So to set the stage, in May 2024, the Board remanded the permit to construct that DEQ issued for the Stibnite Gold Mine finding the DEQ had failed to properly account for arsenic pollution in three different ways: Number one, the Board found that DEQ

didn't act reasonably in using a five-year rolling average. Number two, there was insufficient evidence to support the T-RACT analysis limiting the West End Pit production limit. And Number three, DEQ didn't act reasonably in accordance with law when it applied the 16 over 70 calculation to the ambient air concentration analysis.

Since then, on remand, DEQ and Perpetua could have added permit conditions, such as requiring additional pollution control or by setting different operational limitations on the project, but instead of doing that, DEQ and Perpetua doubled down on what they had done when they issued the permit before. They haven't made any changes to the permit and have just tried to justify what they previously did.

We're asking that the Board should reject this, should stand by its final order from May 2024, and should again remand the permit.

As I'll explain in the first part of my argument, DEQ's and Perpetua's rationalizations on remand do nothing to fix the fundamental problem with the permit, which is that it does not comply with the Air Rules as they are written when it comes to arsenic.

Next, time permitting, I'll touch on, and then Ms. Thrower will get into this in more detail, but our

argument that the way arsenic was handled in this permit not only conflicts with the plain language of the rules, but it conflicts with the intent of the rules and the ways that they're designed to protect the health of Idahoans throughout the entirety of their life.

I'll be focusing, primarily, on the 16 over 70 issue as I go through these arguments, but I can talk about the five-year rolling average and West End Pit issues as well.

And, yeah, feel free to ask questions as I go. I know everyone has different levels of past involvement in this and different backgrounds and there are a lot of dense issues here.

So I'd like to start by just making sure we're on the same page about what relevant Air Rules provisions apply here. And so bear with me as I walk through some of those Air Rules positions.

But Section 161 of the Air Rules, which is about "Toxic Substances," says: "Any contaminant which is by its nature toxic to human or animal life or vegetation shall not be emitted in such quantities or concentrations as to alone, or in combination with other contaminants, injure or unreasonably affect human or animal life or vegetation."

That's kind of a broad general standard to

protect people and nature from toxics. And the rules go on to specify how it is that DEQ carries that out when issuing a permit. And that's in Section 203 of the Air Rules, the permit requirements for new and modified sources.

Under that section, subpart (03) for "Toxic Air Pollutants," it says that: "No permit to construct can be granted unless DEQ first determines "Using the methods provided in Section 210, the emissions of toxic air pollutants from the stationary source or modification would not injure or unreasonably affect human or animal life or vegetation as required under Section 161."

So it's saying DEQ needs to use the methods in Section 210 of the rules to make a determination about whether a source is going to unreasonably interfere with health due to toxics.

So turning to 210, what are those methods in Section 210 that DEQ must follow. There are a bunch of different subparts of Section 210, but subpart (01) requires identifying the different toxic pollutants at issue; subpart (02) requires estimating the emission rates of those various toxics; Section (03) then requires quantifying the ambient concentrations of those toxics. So estimating once this source is built and

operating, what's the ambient concentration of a toxic like arsenic going to be.

And then relevant here is subpart (08), "Controlled Ambient Concentrations." Once you know what those concentrations of arsenic or other toxic pollutants are, how do you see if they comply. And it says under part (08), subsection (a), "Compare the source's or modification's controlled ambient concentration at the point of compliance for the toxic air pollutant to the applicable acceptable ambient concentration listed in Sections 585 or 586."

So you compare the estimated toxic concentrations that will be coming from the source to those that are listed in Sections 585 and 586 of the rules. Relevant here is 586 which is for toxic carcinogens. 586 lists each toxic carcinogen, including arsenic highlighted here in yellow, and has a value, an AACC value and acceptable ambient concentration.

Those are provided as annual averages. This is stated in Section 586. And so DEQ has to compare the modeled concentrations of arsenic to the values listed here in Section 586.

Continuing on in Section 210, there are two relevant exceptions or adjustments to doing what was just described. One of those is for what's called

T-RACT. If the source demonstrates that it would be hard to achieve those standards using reasonably available controls, they can get a ten times adjustment.

Here in this case, Perpetua was granted a ten times T-RACT adjustment. So instead of comparing the concentrations of arsenic to the value listed in Section 586, they get to compare it to ten times that value.

There's another exception for short-term sources. This is Section -- subsection (15) within Section 10. Short-term sources are defined to be sources that operate for five years or less. The Stibnite Gold Project is a 16-year project, so not five years or less.

But there's also this -- in the rules, an applicant can also get a ten times adjustment to that ambient concentration in Section 586 if they are a short-term source. I'll note that the short-term source factor also says: "This method may be used for TAPs listed in Section 586 only and may be utilized in conjunction with standard methods for quantification of emission rates (Subsections 210.05 through 210.08)."

That's saying that the short-term source adjustment is not available for a T-RACT source. T-RACT's under 210.12, the short-term source is only

available for sources that are being approved through 210.05 through 08. So if the source gets a ten times adjustment because it qualifies for T-RACT, like the Stibnite Gold Project did, it cannot also get this short-term source factor.

That was kind of a lot but just, kind of, to summarize some of the high points of the rules, they explicitly require following the methods laid out in Section 210 to demonstrate compliance with toxic standards. These include estimating the toxic emissions and concentrations that will result from the new source and then comparing those to the values listed in Section 586.

There's the two relevant exceptions, T-RACT or short-term sources. For those you can compare to ten times that value listed in Section 586. The rules don't include any other relevant exceptions.

So turning to the Stibnite Gold Project, during the permitting process Perpetua and DEQ realized that the mine wouldn't meet the arsenic AACC even after getting a ten times adjustment for T-RACT. So the model of emissions for the project compared to ten times that value listed in the rules, the model value is still higher than that.

As described in DEQ's Kevin Schilling's

declaration -- this is in the record at 1241 through 44 -- DEQ modeled arsenic levels from the mine and determined "compliance could not be demonstrated using the typical approach." So DEQ then applied the T-RACT to the project getting that ten times increase in the level they need to meet. But even then, "The analysis still resulted in modeled arsenic impacts exceeding a value of ten times the AACC."

Next, even though the short-term source exception at 210.15 is only allowed for projects that are five years or less, and even though that short-term source exception is not available for projects that already got a T-RACT adjustment, DEQ then relied on that short-term source exception to create an analogous exception for this project, which is the 16 divided by 70 adjustment factor.

DEQ diluted the average modeling for the project, diluted the modeled annual average arsenic value by multiplying by 16; the life of the project, dividing by 70, the duration of an average human lifetime.

This resulted in DEQ comparing an arsenic value for the project that only represents 23 percent, about, of the actual arsenic concentrations that will occur during the mining.

So instead of comparing the actual modeled concentrations each year of the mine to ten times the AACC, the permit compared this artificially diluted number to ten times the AACC to find that it was a low enough value and that the permit could be approved.

And I want to be clear that DEQ had never done anything like this before. This is well supported in the record. For one example, Mr. Schilling wrote some memos during the permitting process when DEQ was considering whether to apply this 16 divided by 70 adjustment.

In one of those memos -- this is in the record at 1185 -- Mr. Schilling stated that following the methods laid out in Section 210 was certainly how DEQ had done permitting in the past.

In another memo Mr. Schilling described this new approach as "a complete change in the regulatory approach used to demonstrate compliance with toxics. It abandons the Section 210 approach used in the application for an arsenic Section 161/210 hybrid analysis." And that's in the record at 1194.

Not only DEQ had never done this before, but as I mentioned before, it's just simply not in the rules, and I'd like to point out that that's what the Board previously found.

In the Board's final order from May 9th of last year, I'll read what the Board said about this. This is on page 21 of your final order. "The Air Rules clearly provide an AACC standard in Section 586. They then clearly provide an adjustment to that AACC standard when T-RACT can be used to control emissions. The Air Rules also clearly allow for a ten times adjustment to the AACC when a project is going to operate for five years or less, but nowhere in the rules does it provide that a project that will operate for more than five years but less than 70 years may be adjusted in proportion to the amount of time it will operate."

The Board was right about this. This should be the end of the story on this issue. The Air Rules are legally binding, they have the force and effect of law, and they must be followed as written.

I'm going to mention a couple cases cited in our briefing, but just to get through them faster, the Idaho Supreme Court explained in a case called Mead v. Arnell that "Agency rules, like Air Rules, have the full force and effect of law."

The Idaho Supreme Court also stated in Herndon v. West that, "We must follow the law as written. If it's socially or economically unsound, the power to correct it is legislative not judicial."

So here the Air Rules are not mere suggestions or recommendations as to how DEQ might go about considering a new source and issuing a permit, they're binding rules. They must be followed as written.

If DEQ or Perpetua or the Board think that the rules are unsound, they're free to try to change the rules through the formal rulemaking process, but DEQ cannot deviate from the Air Rules when it's issuing a permit like the permit to construct to Perpetua.

Turning to the second point, which is a bit of a transition to Ms. Thrower's presentation, not only does the 16 over 70 adjustment conflict with the plain language of the Air Rules, but it conflicts with the intent of the rules and it fails to protect public health to the full degree of the rules.

By requiring all new sources to comply with the AACC values listed in 586, including that for arsenic, the Air Rules provide a clear and consistent way to ensure that every source in Idaho complies with Idaho's toxic limits.

This approach protects Idahoans throughout their entire life. Following the AACC's as they're written in the Air Rules as annual averages that sources must meet each year, no matter how long that source might be operating, ensures that Idahoans are never

exposed to more than the AACC on each and every year of their entire life.

These are good reasons for why the Air Rules are written the way they are. And by contrast, the new approach that's been utilized here to approve the Stibnite Gold Project is less protective of Idahoans. The 16 over 70 adjustment allows Idahoans to be exposed to higher than the AACC values that are set out in the rules during each year that the 16-year Stibnite Gold Mine operates.

Just to be clear about that, the AACC for arsenic that's in the rules in Section 586, as adjusted, being multiplied by ten for T-RACT, that value is .0023 micrograms per meter cubed.

Perpetua and DEQ's modeling, without using the 16 over 70 adjustment, expects that the mine will cause .0041 micrograms per meter cubed annually on average for the mine. That .0041 versus .0023 that's in the rules is nearly two times the acceptable level that's listed in the rules.

In trying to justify this, DEQ and Perpetua assumed that 16 years of heightened exposure to arsenic led to the same cancer risk as spreading that exposure out over 70 years. And Ms. Thrower will explain why that's not correct.

But even if it were correct for arsenic, it's certainly not correct for other carcinogenic air pollutants, including ones that have mutagenic effects. And this would create a dangerous precedent if DEQ were allowed to permit other sources following the same technique.

DEQ and Perpetua also assumed that a person who's exposed to 16 years of heightened arsenic levels won't encounter any other sources of arsenic during the rest of their 54 years, or potentially more, life. This ignores the problem of successive sources.

As just one example, the Stibnite Gold Project that this permit approves includes not just mining at the site but it includes additional exploration work to look for other opportunities to possibly mine in the future.

So it could be the case that after 16 years of exposure to excess arsenic, there could be a second phase of mining or a new mine or additional mining activities that could again cause elevated arsenic levels extending beyond the 16 years that were just considered here.

Following the rules as written in making the AACC's be met every single year would protect against this and would ensure that even if somebody is exposed

to successive sources, they're never up above those levels that are set within the rules.

This could also be the case if somebody was exposed to elevated arsenic from the Stibnite Gold Mine for the next 16 years and then moved somewhere else in Idaho where they encountered some other source of arsenic.

If the Board were to allow the 16 over 70 adjustment here, this will remove important protections from the Air Rules that afford Idahoans protection throughout their entire life. Protection from not just one source, like the Stibnite Gold Mine, but protection from any source that they might encounter.

Turning from the 16/70 issue to just a quick mention about the five-year rolling average and the West End Pit production. When it's for similar reasons that the 16/70 adjustment isn't allowed by the rules and runs counter to the rule's public health protections, the permit's also incorrect by using the five-year rolling average and by failing to properly limit the West End Pit production.

Both of these techniques that were used for the five-year rolling average in the West End Pit are averaging techniques that mask potential higher years of arsenic concentrations. But, again, the rules, the

AACCs listed in Section 586 state that those are annual averages. And by allowing averaging over multiple years it masks higher spikes in arsenic that could exceed those values by even more.

And with that, I will turn it over to Ms. Thrower unless there are questions for me now.

CHAIRMAN MacMILLAN: Any questions for Mr. Hurlbutt?

(No response.)

CHAIRMAN MacMILLAN: Not at this time anyway.

Please proceed.

MS. THROWER: All right. Thank you.

Mr. Chairman, Board members, good morning, and thank you for taking the time to have us speak to you today.

Before I get into the specific scientific issues that were presented to our hearing officer at the office administrative hearing through our expert, as well as the expert of DEQ and Perpetua, I want -- I think it would be useful to have a discussion of how this regulatory structure that we're dealing with here correlates with assessing cancer risk.

And part of what Perpetua and DEQ's experts talked about is that you don't really need to follow the AACC; really what we're talking about is following the

excess cancer risk that was established under the Idaho rules. And that is -- under T-RACT, that is the 1 in 100,000 excess cancer risk.

So there's been a lot of semantics thrown around in this case. For example, whether the AACC is an increment, not a standard, whether it's an annual average or an outer limit. I think all the parties agree that the AACC is an increment and not a standard.

And so what do we mean by that? And I'm going to talk about that in the context of assessing cancer risk. And that will dovetail into what our experts have testified to at the Office of Administrative Hearings.

So I'm going to start with a standard rather than an increment. And I'm going to use the regulatory structure that I believe we're all familiar with, the National Ambient Air Quality Standards or the NAAQS.

The NAAQS sets standards for air quality. Meaning, that it defines a maximum allowable concentration of a pollutant in the ambient air. So in the example -- for instance, as Mr. Hurlbutt was talking about successive sources.

For example, a source -- let's say source number one would get a permit to emit a certain amount of pollutant, an increment, as long as that concentration of that pollutant in the ambient air would

not exceed the set standard.

If a second source comes in, it also gets a permit to emit a certain increment of a pollutant. But, again, so long as that concentration of that pollutant in the ambient air does not exceed the set standard. And that's the same with the third source and so on.

So the point here is where you have a standard -- whether you have one, two, three, or more sources, the pollutant in the ambient air never exceeds that set standard. And, thus, if you apply this to a carcinogenic pollutant, the allowed cumulative risk over a lifetime is also never exceeded.

So that standard acts as a maximum allowable concentration, or you could call it a maximum allowable cancer risk or ceiling. And I want to contrast that with the AACC, which is an increment. And we don't have a standard associated with that under the Air Rules.

As an increment, the AACC defines the amount of a pollutant that an area is allowed to increase -- or that a source is allowed to increase in an area. It also, in the rules, does correlate to an acceptable excess cancer risk, which Idaho, decades ago, during their rulemaking process for the Toxic Air Pollutant rule or TAPs rule -- I might use that acronym, TAPs rule -- which determined that the acceptable cumulative

lifetime excess cancer risk was 1 in 1 million.

The rules also provide an exception under T-RACT, as Mr. Hurlbutt has discussed, to increase the acceptable cumulative lifetime excess cancer risk by tenfold to 1 in 100,000. In this example of three successive sources, the first source gets to emit an increment of pollutant such that the ambient air will not exceed the T-RACT amount of that pollutant.

And, you know, applying that in our case, as Mr. Hurlbutt said, that value is .0023 micrograms per cubic meter of arsenic. And that corresponds, again, to a lifetime excess cancer risk of 1 in 100,000.

So, Ms. Cutler, if you can please pull up Dr. von Lindern's Figure 1 from his expert declaration. And this is in the Agency record as Document 136, with a starting record number of 6100. And Figure 1 is on REC6111.

MS. CUTLER: This was Agency Document 136?

MS. THROWER: Yeah.

MS. CUTLER: All right.

MS. THROWER: I think you're way down into the exhibits there. That should be -- it's Record No. 6111. There you go. Right there. Thank you.

Okay. So if you look at this graph, the orange line at the top represents the maximum allowable

lifetime risk under the Air Rules with T-RACT applied. So, again, that's 1 in 100,000. The diagonal blue line represents the accumulation of the allowable lifetime cancer risk from an incremental source.

As you can see, as a person is exposed to the pollutant, there's a linear dose response. More exposure equals higher cancer risk. If the dose of that exposure is low enough, a person's accumulated lifetime cancer risk will not exceed that orange line.

When a second source comes in, it also gets to emit an increment of pollutant, again, here allowing the concentration of arsenic in the ambient air to increase by up to .0023 micrograms per cubic meter, which, again, corresponds to an excess cancer risk of 1 in 100,000. The same with the third, and so on.

So the point here is that because each source is allowed to emit its own increment of a pollutant, each source adds to the cumulative cancer risk over a person's lifetime.

And, Ms. Cutler, if you can move to Dr. von Lindern's figure 5A that's on REC6122. That will show what I'm -- that will show what happens with excessive or successive sources.

Figure 5A, yes, thank you.

So this figure, the same as in Figure 1, the

orange line represents the T-RACT allowable 1 in 100,000 excess cancer risk. The blue line represents a person's cumulative lifetime cancer risk. Now, the green line represents the cumulative lifetime cancer risk of a person when there are three successive projects.

So in this case, this graph shows three successive 6-year projects, but the same principle applies to 10-year projects, 16-year projects, 20-years projects, et cetera.

The point is that here you can see one project will emit enough arsenic to have a person accumulate a certain amount of cancer risk during the lifetime of that project. If another project comes in, it will add to that cumulative cancer risk, but it will not -- as long as the AACC or the rules are correctly applied, it will not exceed that lifetime cancer risk of 1 in 100,000.

The point is that if the TAPs rule is implemented without applying any project-specific adjustment factors, if it's implemented as it has been for decades since it was passed and has been implemented as our understanding is that DEQ has always implemented, never before using a project-specific adjustment factor for any permit, if it's implemented this way, the State can issue multiple successive projects -- permits for

projects without exceeding a person's cumulative lifetime cancer risk.

So what happens to this cumulative lifetime cancer risk when DEQ and Perpetua use a project-specific adjustment factor that focuses on the lifetime of the project rather than the lifetime of the person?

And, Ms. Cutler, if you can move back up to Figure 2 that's on REC6116.

Okay. So this graph shows what happens if we focus on the cumulative cancer risk of the project by applying adjustment factor that corresponds to the lifetime of the project.

A person will have accumulated the T-RACT allowable excess cancer risk within the short lifetime of the project, be it a 6-year project, a 16-year project, or 20-year project. While they will have to live out the rest of their life already having accumulated the maximum allowable cancer risk under the Air Rules.

Again, the orange line corresponds to the T-RACT allowable lifetime excess cancer risk. The blue line is the cumulative risk associated with the project. Again, this one shows a 6-year project. And what it shows is the person would accum ulate the full allowable lifetime excess cancer risk within six years. For the

Stibnite Gold Project it would be 16 years.

And, Ms. Cutler, if you can move to Figure 4 on page 6120.

Thank you.

So it's even worse if we consider successive projects, as is depicted in this graph. This figure shows the cumulative lifetime excess cancer risk of a person if there are three successive 6-year projects allowed that each emit an increment of pollutant if we apply a project-specific adjustment factor that is based on the project's lifetime rather than focusing on the human lifetime.

The result is that with each successive project after the first, a person will continue to accumulate cancer risk that exceeds the allowable T-RACT risk of 1 to 100,000.

Again, this graph shows three successive 6-year projects. It applies -- but the blue will just be shifted a little bit to apply to a 16-year project. But the point is this is applying to the length -- or the focus of the length of the accumulation of cancer risk is the project length and not the person's lifetime.

So, you know, this bears on DEQ and Perpetua's toxicologist's risk assessment, because what they do is

they focus on the project lifetime and not the human lifetime.

Their risk assessment, their approach may not be incorrect in all scenarios, but it is incorrect here under this regulatory structure when we are concerned about emissions, not just from Idaho DEQ. As an agency, the air permitting program as a program is concerned not about the public health implications of a single-source but also -- but also multiple sources, past emissions, as well as future sources that will come online in the future.

Perhaps in the Superfund context, which both Dr. Paden and Ms. Lopez's CVs demonstrate they have experience in, and that's where they've pulled this equation that they use, this adjustment factor that they use from EPA guidance from superfund sites, perhaps in this context maybe their analysis is appropriate, but that's not the context we're in here.

In this regulatory context, in this permit context we have to believe that decades ago when DEQ issued the TAPs rule and made the policy choice that the T-RACT allowable cumulative lifetime excess cancer risk of 1 in 100,000, that it was considering the human lifetime and not just the project lifetime, and it was considering the possibility that there would be more

than one source operating in Idaho's airshed in anyone's given lifetime.

I know there's a sense that this area is remote. You know, there's been some talk and discussions and through our hearing that, you know, cancer risk is based on exposure for 24 hours, 365 days a year, for 70 years. That's how cancer risk is assessed.

Scientifically, it's a complicated -- certainly, a complicated area of science. But I don't think we can discount protecting the public health because someone doesn't live there 24/365/70 years. We have people that recreate there, we have people that fish and hunt there, we will have mine workers that will be doing two-week shifts on and off that will be living in man camps there.

So there will be people there that will be exposed to this air, that will be exposed to this arsenic, and if we're not doing this right, we are really threatening the health of these people and the health of all Idahoans.

Allowing Perpetua to flip the focus of the T-RACT excess cancer risk to the project lifetime rather than human lifetime not only gives them the tenfold increase from T-RACT, which is allowable -- we don't

argue against that -- but this adjustment factor gives them almost a fivefold extra increase in cancer risk from using this project-specific adjustment factor.

Allowing Perpetua to flip the focus of the cancer risk to the project lifetime rather than a human lifetime creates a dangerous situation on the ground, or should I say, in the air for all Idahoans now during the operation of this project, as well as the future of all Idahoans.

Allowing Perpetua to flip the cancer risk again to a project lifetime focus rather than human lifetime creates a dangerous precedent, as Mr. Hurlbutt had discussed, when we approve the next source of arsenic emissions in Idaho's airshed, be it another mine, an antimony processing facility, or some other unassociated arsenic emitting source.

What this does is it significantly threatens the public health well beyond what the policymakers, when it passed the TAPs rule, had determined is acceptable to accommodate industry.

I'd like to make -- I'd like to shift gears a little bit and talk about the issue of agency deference when you're reviewing the material before you.

Agency deference to matters of technical expertise is something that you are allowed to consider,

but it is not absolute. And that means that there is still a rule and a responsibility for this board to review whether the agency had a rational basis for what it did or whether it was arbitrary and capricious, abused its discretion, or otherwise was not in accordance with the law.

So, you know, looking back at the hearing transcript, as I'm sure you either have done or will do, I think you should keep in mind of how much weight and deference you should give to Perpetua's and DEQ's toxicologists.

And, in particular, their assumption -- which is the basis for their whole risk assessment -- their assumption that a higher dose of arsenic over a shorter period of time is equivalent to a lower dose over a longer period of time in terms of excess cancer risk.

This assumption, again, is the basis for their flip from looking at the human lifetime perspective to the project lifetime perspective in excessive cancer risk. And the question is, was that assumption reasonable. And I think we need to think about this in the regulatory context as well.

As a purely scientific matter and specifically for this project, Perpetua's toxicologist quoted from a 2005 EPA Guidelines For Cancer Risk Assessment to

support their choice of a -- what is called a major default option; that higher doses for a shorter time is equivalent to lower doses at a longer time.

And I don't -- this EPA guideline that they quoted from was admitted as an exhibit in the hearing in front of the Office of Administrative Hearings. I don't see it in the Agency record in electronic form and that it was given a record number, so I have copies, paper copies of this guideline or excerpts of it that, Mr. Chairman, if I may, pass it out to the Board.

MS. YRIBAR: We can pass them out. I'm going to have to verify what was or was not admitted to the hearing officer before that's something that we can consider. But go ahead and pass them out.

MS. THROWER: Okay. And this was -- just for your ability to find this in the record, it was admitted as Exhibit 221. And during the hearing, it was handed out as a hard copy, but it was not attached to Dr. -- it was during Dr. -- or excuse me -- Ms. Lopez's testimony. It was not attached to her exhibit so that we had it electronically but a hard copy was handed out to us.

MS. YRIBAR: And do you have a transcript reference for where that was admitted into the record?

MS. THROWER: It's the first hearing day. And it will be around -- the number on the transcript is

TR0392.

MS. YRIBAR: Thank you.

MS. THROWER: Somewhere close to that. I think it may be a page before that. And that would be page 210 of the hearing transcript of day one.

MS. YRIBAR: And, Diane, for whatever reason, I can't access DEQ's website to bring the record up.

MS. CUTLER: Oh, it's not in here?

MS. YRIBAR: Well, no, the website won't even load. Pat couldn't get to it either. Is there maybe another -- maybe at a break we could find another Wi-Fi that would maybe allow us to get on the website and look at the record.

COURT REPORTER: Does this need to be on the record?

MS. YRIBAR: We can go off the record for just a minute while we figure out the Wi-Fi thing.

(Discussion held off the record.)

MS. THROWER: So Perpetua's toxicologist, Ms. Lopez, testified about this document. And she said that this "Lays out the foundation of how you evaluate carcinogens in risk assessment." She further testified that a single sentence from Appendix A of this 167-page document called "Major Default Options" was "Methodology that is required under the guidance documents in

conjunction with the use of an IRU or URF."

And as I said, this EPA document, as you pulled up, was entered as Exhibit 221. But if you look through the other pages of this document where it discusses the use of these major default options -- which there are several -- it talks about them as an exception, not a rule.

For example, major default options are not methodologies that are required, but quoting from page 1-6 -- and these, obviously, aren't highlighted, so you can go back through this transcript record and find the exact quotes later if you can't find it now -- but quoting from page 1-6, it says that: "These options are only to be used to address uncertainties or the absence of critical data."

On page 1.7 this document also talks about the major default options as: "Matters of policy concerning the appropriate way to bridge uncertainties that concern potential risks to human health."

And, again, on that same page under the section entitled -- I'm sorry, I lost my place here -- under the section entitled, "Key Features of the Cancer Guidelines," it states: "Rather than viewing default options as a starting point from which departures may be justified by new scientific information, these cancer

guidelines view a critical analysis of all available information that is relevant to assessing the carcinogenic risk as the starting point from which a default option may be invoked, if needed, to address uncertainty for the absence of critical information."

Neither Dr. Paden nor Ms. Lopez's expert declarations, using these default options as a method for cancer risk assessment, really discussed or had any critical analysis of available information and didn't use that as a starting point of their assessment, rather they started with this default option.

And to make matters worse, they just accepted the arsenic that -- the emissions factor -- the amount of emissions of arsenic that was going to be emitted from Perpetua and from DEQ without really analyzing that, without understanding whether that is really the maximum allowable -- or excuse me -- maximum annual average arsenic concentration, which is the term that they use in their equations to calculate cancer risk.

They just use these numbers without understanding that, really, the number that Perpetua and DEQ gave them was a five-year rolling average, not a maximum annual arsenic concentration; that it was an average of production from non-West End Pits and West End Pits, which is important because the West End Pit

production creates more emissions than the other pits. And the number that they were given was a combination, an average of an average of all these scenarios of production that are not limited by any of the permit conditions.

But, really, what they do -- what it did was to mask the -- what the maximum annual average arsenic concentration really was. And so in the end what that means is their cancer risk assessment is underestimated.

So as I said, both experts just blindly accepted this number without understanding what that number represented. They just took a statement from an appendix of an 165-page document and assumed that they would just start there with a major default option because that was easier and that was -- that's it. You know, that made the arsenic concentration low enough to be able to make it appear like they're complying with the Air Rules.

So when you look at this, when you're comparing the declarations from these different experts, think about these things, and when you're weighing how much deference to give to the Agency on this matter. Because the basis for how they determined to use this major default option is not reasonable, is not supported by the evidence, and is arbitrary and capricious.

I'm not going to touch much on the five-year rolling average issue and the West End production pit issue. I think our post-hearing brief lays out those calculations. And it's never fun for anybody to hear someone talk about equations, so I think that unless there are questions about that, maybe it's just left for you to review the materials with a calculator.

But the point is, is that both of these two factors end up diluting the maximum annual average arsenic concentration that is capable of being emitted under the permit conditions. So what that ends up doing is it lowers the number that is supposed to be compared -- that is compared to the annual average listed of T-RACT, annual average listed in Section 586 artificially dilutes that number.

So as I said, I'm going to just rely on you all to review our briefs on those issues. And I'll take any specific questions on those two issues or what I just talked about beforehand.

CHAIRMAN MacMILLAN: Thank you, Ms. Thrower and Mr. Hurlbutt.

Any questions from board members to either of these two presenters?

BOARDMEMBER BOWEN: Mr. Chairman?

Just a follow-up question. You somewhat

alluded to this. If somehow the Board were to find in favor of allowing this approach to the rule, from your perspective, what kind of precedent would that set in the future?

MS. THROWER: Go ahead, Mr. Hurlbutt.

MR. HURLBUTT: Yeah. Talking specifically about the 16/70 adjustment, it would seem to open the door to any project that is less than 70 years in duration trying to seek a similar adjustment factor. So that could be a 50-year project, a 30-year project, a 16-year project similar to this one, and possibly even much shorter-term projects.

Maybe a 3-year project would decide that instead of getting the 10 times adjustment in the rules, they'd rather get a 3 divided by 70 adjustment factor that would allow them even higher levels of toxic pollutants.

And this also opens the door to allowing sources that get -- already are getting a T-RACT adjustment to now also get an adjustment based on their duration; whereas, I discussed that short-term source exception that's in the rule is not available for projects that already get a T-RACT adjustment. So that opens the door to that.

How many sources out there can plausibly

claim, you know, a duration under 70 years, I don't know, but potentially any, I'm not really sure. But it could lead to a situation where a lot of new sources are able to take advantage of this.

And the result could be emitting more than what's allowable on an annual basis under the AACCs from multiple different sources throughout the state and during successive stages of people's lives. So I think that that would be a big problem.

MS. THROWER: I think -- if I could follow up -- I think the precedent there, you know, is the rules already have a project-focused regulation or rule, you know, the five year, the short-term thing that takes into account the project lifetime.

And Idaho, at that time, made the policy choice that that level -- allowing those sources to have a higher risk of cancer emitting amount of arsenic or toxic air pollutant that allows a higher risk of cancer, they made that policy choice at the five-year mark or less.

Anything beyond that is -- falls under the other rule, the T-RACT or just the regular, you know, AACC, but in this case the T-RACT. So, I mean, you know, allowing a project-specific adjustment factor in this case, which would allow project-specific adjustment

factor for future permits, I mean, this is a policy change.

This is not something that should be done in the context of a single permit. This should be done through rulemaking through the public comment process and a change in the rule that people can -- permitees and the public can understand and follow what that means for the public health of Idaho.

BOARDMEMBER BOWEN: Thank you, Mr. Chairman.

BOARD MEMBER PURDY: And I have a follow-up question to that, if it pleases.

So you're saying that there's no precedent for the Agency having the latitude to make project-specific exceptions in any prior permits, that this is the first time that that's ever happened where they've had to interpret a rule, where they may be exercising latitude in a rule to accommodate specific project, I guess, situations that may be unusual or different than what they normally come across or what the rules were written for?

MR. HURLBUTT: That's correct. The evidence that -- and some of this is pointed out in our brief, and I referenced Mr. Schilling's memo, said this would be a change in practice. This hasn't been done before --

BOARD MEMBER PURDY: First time the 16/70 has been used, but --

MR. HURLBUTT: Yeah.

BOARD MEMBER PURDY: -- in general --

MS. THROWER: Any other claim.

BOARD MEMBER PURDY: -- any other project-specific exception that you're aware of?

They just don't make those?

MR. HURLBUTT: I don't know.

MS. THROWER: That is our understanding. When we were in the process of discovery during this case, we asked the Agency, as a discovery request, if there were any other permits that had used any kind of project-specific adjustment factors, not just 16/70, but the project-specific adjustment factor, and the response was no.

So it is our understanding that there have not been any other projects that have utilized a project-specific adjustment factor that focuses on the lifetime of the project.

BOARD MEMBER PURDY: So follow-up. You believe, then, that the DEQ scientists should not be given that kind of latitude to, in their best judgement, make those kind of exceptions for projects that, maybe, are outside the scope of the normal -- the rules that

are currently in place, then?

MR. HURLBUTT: Correct.

MS. THROWER: Well, yeah. Yeah, no, because we have the rules. I mean, the rules need to be followed. There's no room for, well, if you know an applicant can't meet this Section 586 rule, then we can go to this process. There's no room for alternative risk assessments, alternative scientific methods for risk assessment in the rules.

Sorry, I cut you off.

MR. HURLBUTT: Yeah. No, I mean, just to kind of echo that, you know, DEQ needs to follow the methods in Section 210. Those don't include some method whereby if they don't satisfy the AACCs based on T-RACT and the other factors we talked about, there's not an additional method listed there saying, well, as a backup you can do a risk assessment to consider this project.

MS. THROWER: And Dr. von Lindern's declaration discusses states that do have risk assessments as the means to show compliance with the state's permitting program. And it is a very complicated process.

And the state puts out guidelines for what should be considered and, you know, methods that should be used in consideration of cancer risk assessment. So

it's, you know, at least cabined, at least the public and the applicant know what the correct methods are.

There's no -- not as much, I'll say. I shouldn't say no -- but, you know, there's not going to be arguments about -- as much argument about methodology, this one uses that one, or whatever. And those -- you know, those were all, you know, passed through their regular agency rulemaking, you know, and guidance process, and not through a single permit application.

BOARD MEMBER PURDY: Thank you.

CHAIRMAN MacMILLAN: Other questions?

So I have one: Are you suggesting that -- well, I think this is correct, and so help me out here: But doesn't establishing the T-RACT conditions, that gives the Agency quite a bit of deference of defining what those things could be, doesn't it?

MR. HURLBUTT: What do you mean by "the T-RACT conditions"?

CHAIRMAN MacMILLAN: Well, my recollection is that the Department decides -- makes recommendations to the permitee on what they can do to meet the AACC, for example.

Is that incorrect?

MS. THROWER: Are you talking about the

methods for calculating the emissions?

CHAIRMAN MacMILLAN: No. No. I'm speaking about methods a mining operation, for example, could use to comply with the emission requirements. So that's --

MR. HURLBUTT: Yeah, so --

CHAIRMAN MacMILLAN: It's not so -- that part of the rule isn't so specific that you have to do "X," "X," "X," "N," "N," "N." You can do "X" plus "N" plus "B" plus "C" to get at the emission requirement.

MS. THROWER: So, perhaps, as has been discussed as part of our case before, their fugitive dust emission control?

Is that what you mean, like that.

CHAIRMAN MacMILLAN: That could be like that, perhaps.

MS. THROWER: Right. Right.

CHAIRMAN MacMILLAN: Methods that are alternatives to what a permitee is proposing. And maybe they would work better or -- you know, the engineers have quite a bit of knowledge about that stuff.

MR. HURLBUTT: And so in the T-RACT section of the rules, this is in Section 210 of the rules, Part 12 on T-RACT, Part D, kind of after going through the T-RACT and seeing whether the concentrations now meet the AACCs or not, part D under this T-RACT section says,

"The Department shall include emission limits and other permit terms for the toxic air pollutant in the permit to construct that assure the facility will be operated in the manner described in the demonstration."

So I think that shows that the Department can help develop permit limits and conditions, as needed, to bring emission levels down such that they would meet the T-RACT adjusted AACC.

CHAIRMAN MacMILLAN: Thank you.

MS. THROWER: But the 16/70 factor is not a condition --

CHAIRMAN MacMILLAN: Understood.

MS. THROWER: -- it's a math trick.

CHAIRMAN MacMILLAN: Any other questions?

(No response.)

CHAIRMAN MacMILLAN: Okay. Thank you very much. And -- well, 11:16, are we ready to just break for lunch?

MS. YRIBAR: I don't know if it's here.

CHAIRMAN MacMILLAN: We could have a long bathroom break.

MS. GANINO: Mr. Chairman, the lunch is scheduled to be delivered at 11:30, so I don't know if you want to do a break before then.

(Simultaneous speaking.)

CHAIRMAN MacMILLAN: Well, our lead attorney is suggesting that we push through. So bathroom break for board members not needed.

Okay. So we can have the -- let's hear from the Respondents, the Department of Environmental Quality and Perpetua.

MS. YOUNG: If I may make a suggestion. Two things: One, we would -- I guess the Department would prefer and hope that Perpetua actually go before us, because we understand they have a demonstrative there, and they're going to provide some background of the project to maybe refresh your memory or for new board members.

So the first request, I suppose, is that the interveners go and then the Department could follow. I guess we'd also appreciate the opportunity to take a break for lunch and then be heard, but, obviously, defer to the Board.

CHAIRMAN MacMILLAN: Why don't we just break now for lunch and plan to come back at noon. Does that work?

MS. YRIBAR: I'd make a motion to adjourn for lunch -- somebody can make a motion to adjourn for lunch.

CHAIRMAN MacMILLAN: Somebody make a motion.

VICE CHAIR STEELE: So moved.
CHAIRMAN MacMILLAN: There's a motion to break for lunch.
BOARD MEMBER BOWEN: Second.
CHAIRMAN MacMILLAN: Seconded.
All those in favor say "aye."
(Chorus of Ayes.)
THE COURT: Motion carried. We'll be back at about noon.
(Lunch break taken.)
CHAIRMAN MacMILLAN: I call this board meeting back to order. And we'll begin with the presentation from Perpetua.
MS. HANCOCK: Thank you. If it's okay, I'd like to pass out a copy of the electronic presentation that we'll be looking at.
Am I okay to proceed?
CHAIRMAN MacMILLAN: Oh, please, I'm sorry.
MS. HANCOCK: That's okay.
CHAIRMAN MacMILLAN: Could you introduce yourself, please.
MS. HANCOCK: Sure. My name is Nicole Hancock, and I'm an attorney with Stoel Rives. I'm here to represent Perpetua Resources Idaho.
I'm going to walk through the PowerPoint

presentation, but I'm open to questions at any time, and I'll address some of the questions that have already been raised as well.

I'm going to move to the next slide, please.

I'd like to start by first providing a little bit of context about the project itself. Perpetua submitted its application for an air permit related to the Stibnite gold and antimony project.

Antimony is a critical element that's needed through the national defense and clean energy needs. It is the only domesticated reserve of military-grade antimony. It's used by the United States Department of Defense for many nonreplaceable munitions and components.

To date, through federal grants, the project has received over $70 million in support for the project. This project will bring many well-paying jobs and employment and business opportunities to very rural areas of Idaho.

When this project was originally mined over 100 years ago, we didn't have the regulations that we have today, so it was left in a tough state. The current project will help to remediate the current existing state, it will improve the water quality, restore the waterway passages for endangered fish at

this 100-year-old abandoned mine site.

It will also restore natural resources habitat, including streams and wetlands. And then it cleans up a legacy contamination source that otherwise is going to be left in its current existing state.

If you'd move to the next slide.

By way of additional backdrop, Governor Little issued an executive order in January of this year establishing the SPEED Council. "SPEED" stands for Strategic Permitting Efficiency and Economic Development.

And he tasked the agencies with expediting permit review, increasing collaboration with the project proponents and boosting public transparency. Governor Little is quoted as saying, "Idaho leads the nation in streamlining regulations and promoting good government, but there is always more we can do to improve. ... There is a renewed focus on efficiency in government [and] we are going to take even more steps to make sure state government does not get in the way of projects that support our economy."

If you'd go to the next slide.

At the federal level, it has declared through an executive order in January, there's a national energy emergency. And again in March of 2025, through another

executive order, was issued immediate measures to increase American mineral production. And it was declared to be an imperative to immediately facilitate maximum domestic mineral production in the United States because of our security -- national and economic security threats to the country.

If we can move forward.

This permit has -- or this project has already been the subject of 50 state and federal permits, and as recently as March of this year IDEQ issued the cyanidation permit approving the first phase of the project. The Idaho Department of Lands approved the mine's reclamation plan and the cyanidation facility's permanent closure plan.

Through the finalization of these permits, in anticipation of them being completed in 2025, all of that is necessary in order to timely deliver antimony to the federal government that wouldn't occur until 2028 if all permits are granted in calendar year 2025. So the sum here is that timing is critical for this project.

If we move to the next slide.

This permit has actually been in the works for six years. Perpetua initially submitted the permit application in August of 2019, went through three full years of different public -- three sets of public

comments over those three years, through a review, an analysis with DEQ working to negotiate the current conditions that are in the permit.

And so over the last six years that's brought us to today, the permit has repeatedly been approved and then subjected to multiple challenges by petitioners up until the point that we're at, the one that we're here for today, which was filed in January of 2025, following the January 7th hearing officer's findings of fact, conclusions of law in the preliminary order.

If we can move forward.

As this Board knows, you were all remanded three questions back to the hearing officer following the May 2024 board meeting. Those three questions are presented here.

The first one, whether DEQ acted reasonably in using a five-year rolling average in its T-RACT analysis. Number two, whether there was sufficient evidence to support DEQ's T-RACT analysis regarding the non-West End Pit production. And, three, whether DEQ acted reasonably and in accordance with the law when it applied the 16/70 adjustments to the arsenic exposure concentration.

Importantly, this Board clarified that what it was seeking was the development of a full, factual

record on the arsenic issue, specifically, including the development and use of expert opinions.

Everybody was on notice, the petitioners, DEQ, and Perpetua were on notice that when this issue was remanded back to the hearing officer, that it was for the purposes of developing a full, factual record on the arsenic issue to determine if all of the rules were met in analyzing the cancer risk presented by this project.

If we move forward.

The petitioners are the parties who carry the burden here. And we will submit that the petitioners have not been able to meet that burden. This Board is tasked with the question of whether DEQ has acted reasonably in accordance with the law, but the petitioners have to show you how DEQ has not acted reasonably or in accordance with the law.

And that's a preponderance of the evidence standard, which means they don't get the deference if it's -- all things being equal their position prevails. They have to convince you that it was more probably true than not that DEQ has somehow acted unreasonably and violated the law in its application of assessing cancer risks presented by this permit.

I'm going to cover a few of the pertinent regulations that were at issue at the hearing before the

officer and that have been applied by DEQ. These permit -- the pertinent regulations that we're looking at here, they're of paramount importance to your analysis and your evaluation of whether DEQ complied with the rules.

And what we heard was that these were the appropriate rules from the petitioners, but we didn't actually see the application by them of these rules. What we heard instead was items that they wanted to be included in these rules or additions to these rules that are nowhere present in the language of the rules.

If we start with the actual definition of toxic air pollutants, we can see that it specifically provides that these are ambient air quality increments. Now, that "increments" is of real importance here because it is looking at the individual increments over a 70-year lifetime of exposure. That means exposure continuously for 70 years based on increments of exposure along those 70 years.

If we look at Section 586, which is the Toxic Air Pollutant Carcinogenic Increments -- again, it uses the word "increments" -- it provides the tables that were used through the AACC. And it specifically provides that those AACC levels that are used in the section are annual averages. They are not lifetime

limits, they are not an emissions standard, they are annual averages measured in increments.

So then we get to Section 210. This is the section that allows for the T-RACT controls, again, saying that this is now an emissions standard. And it specifically provides that the emission standards may be based on the application of a design, equipment, work practice, or operational requirement, or any combination thereof. And what this allows for is for DEQ to use its own authority and its own discretion to apply conditions and requirements to limit the emissions that come from any kind of permitted project.

If we'd go to the next page.

The next page is a continuation of the pertinent regulations under 210. Under 210.02 it allows DEQ to use standard scientific and engineering principles to estimate the emission rate, which means -- this is the use of the experts.

The experts are allowed to use their own scientific methodologies and engineering principles in order to determine what the actual emission rate is for any specific project. Now, mind you, this is a project-specific evaluation that's performed.

Under 210.02 (d), it requires that the calculation that the DEQ provides is based on the

maximum capacity of the source. Based on its interpretation of how those operational limitations will be applied specific to that permit.

So what that means is, that DEQ is tasked with using that scientific evaluation, the modeling that could be done, at maximum capacity based on the production limits that would be imposed in that permit.

So this would be a rule-based mathematical calculation based on the project limitations that are specific to this permit. Under 210.12 (c), if that calculation, that scientific calculation, applying those production limits, based on the maximum capacity of exposure falls under a 1 in 100,000 cancer risk probability, then no further procedures for demonstrating preconstruction compliance is required.

So in other words, as long as the cancer risk with those production limits is under that 1 in 100,000, the permit complies with the law.

If we move to the next page.

Now, with those rules in place, all of the parties went back to the hearing and presented their own experts.

The two experts that you see here are the petition ers' experts, Ian von Lindern and Will Tiedemann. Now, von Lindern is not a -- neither one of

these are toxicologists. von Lindern testified that the calculations that he performed, he didn't know if the permit conditions were included or factored in.

Testimony confirms that, in fact, the calculations he performed did not include the permit conditions and the production limitations that were included within those permit conditions. He wasn't able to re-create his own calculations. He relied on Kevin Schilling's calculations that did not include those production limits.

He said that he had a toxicologist on staff but that he didn't believe that bringing a toxicologist was necessary. He admitted that exposure duration -- the actual exposure duration does matter, but he did not factor it into his calculation.

Instead, he provided what he believed was -- what he wished would be included in the rules, which is the margin of safety. Now, that margin of safety will look familiar because we just looked at it when the petitioners were showing their graphs.

He wished that the margin of safety was included in the rules, even though he admits that it's not. And he also believes that EPA should have factored in what he believes is a mutagenic mode of action for arsenic emissions, even though EPA, as he's admitted,

does not believe that arsenic -- it has a mutagenic mode of action.

He states that his cumulative exposure modeling shows additional exposure beyond the production limits and admits that his calculations are based on 70 years' worth of continued exposure, not based on what is the maximum emission amounts that would be calculated in this project using the production limits.

Now, Mr. Tiedemann also is not a toxicologist. In fact, he has some conflicts of interest. He worked at Brown and Caldwell and even admits that he reviewed Perpetua's permit as part of the work that he did at Brown and Caldwell and never saw anything impermissible in the submission.

He's admitted he has a moral dilemma working on mining projects and a value-based system that's more in line with the Idaho Conservation League with whom he works today. He admitted that the annual concentration does not exist in the rules, but it's something that he has proffered should be included in the rules.

In fact, the evidence that he put into the record, he selected pieces of historical documents from rulemaking that never made it into the final rules. And even the evidence that he did select was incomplete and taken out of context and proffered into the record

without the full contextual information. He never provided any calculations of emissions or cancer risks, and from that that was the totality of the evidence that the petitioners put forth in the record.

If we can move forward one slide.

The hearing officer commented on this in his own findings of fact and conclusions of law. And he said that their witnesses, Mr. Tiedemann and Dr. Von Lindern, testified regarding what they wished the Air Rules said rather than what they actually said.

And then he goes on to say that many of the exhibits that they offered consisted of isolated references from prior rulemaking that lacked explanation of their context or relevance to the interpretation of the plain language of the existing Air Rules.

What the hearing officer found is their evidence fell far short of the burden that they hold in order to prove that the existing air permit was unreasonable or out of the context of the existing laws.

If we move forward.

You contrast that with the expert s that DEQ proffered. Norka Paden is a toxicologist specializing in risk assessment. She has 25 years of experience and performed over 50 risk assessments. She said that the EPA's URFs account for sensitive populations already.

That's built-in to the risk factors that the EPA adopted.

She modeled using scientific methodologies the maximum concentrations -- that's the amount that was required under 210 -- for the carcinogenic TAPs accounting for a life of mine production limit exposure.

So what that means is she modeled the actual exposure based on the production limits that are contained in the permit. Based on those actual exposure limits, on the highest annual concentrations, she said that was the appropriate methodology for measuring the exposure. She calculated those emissions.

And that exposure duration, mind you, is based on 24 hours a day, 7 days a week, 365 days in the year, with 70 years of full-time exposure. So she took that as the backdrop -- that's under the AACC -- she took that as the backdrop, and she applied this specific permit, including its permit conditions, and she modeled it out using her own scientific methodology that went unchallenged by any petitioner.

And she said, using those permit conditions at 24 hours a day, 7 days a week, 365 days a year, the maximum number of years of emissions you would reach would be 16 years. That is the exact same if you worked 12 hours a day, 7 days a week, 365 days a year for

32 years. Because if you work 12 hours a day instead of 24 hours a day, it would take you twice as long in order to reach those production limits.

But it didn't matter because under either scenario, no matter how fast or how quickly you work to mine all of the finite amount of production limits that are allowed under the permit, you come to the exact same allowance -- or the exact same exposure amounts, which all fall under the 1 in 100,000 risk.

Now, Kevin Schilling was the other DEQ expert. He's been with IDEQ doing stationary source air modeling for 20 years. He's provided permit process and TAPs analysis throughout his career. He recognizes that the AACCs are an expression of risk of 1 in a million over 70 years of continuous, nonstop exposure.

He provided the calculations that he performed using the T-RACT analysis to ensure project emission cancer risk, specific to this project, using this project limitation, and ensured that it complied with under the 1 in 100,000 cancer risk under the T-RACT.

He acknowledged that the TAPs provide an incremental risk over a general risk of developing cancer, which means you just look at this specific project, not all of the other projects that would be outside of this project, you do a project-specific

review.

He acknowledged that the EPA's URF is a project-based risk analysis. All of this is provided under the rules. And he, likewise, ensured using his own calculations and methodology, including the five-year rolling average, that the compliance would be less than the 1 in 100,000 T-RACT analysis.

That testimony is all before the hearing officer and in the hearing record before the Board.

If we move to the next one.

In addition, Perpetua provided its own two experts, Theresa Lopez, who is here to my left. She's a toxicologist who's been at this for 32 years performing, specifically, cancer risk assessments. This is her job. This is what she does.

And she acknowledged that the AACCs are not annual limits, they are an annual average based on, again, that 24 hours a day, 7 days a week, 365 days a year, 70 years' worth of continued exposure.

And she acknowledged that you can compare that air concentration and then adjust it for the actual exposure of the project-specific permit that 's being considered in this case.

The EPA's URF is a cancer risk probability from the exposure to the arsenic. I want to take a

little bit of a deviation here for just a moment. The petitioners showed you two pages of a 166-page exhibit, which was identified in the hearing record as Exhibit 221.

And they talked about how Ms. Lopez had used this in her testimony. Except for what they didn't tell you is that what Ms. Lopez was explaining and responding to was the fact that this document that was titled, "Guidelines for Carcinogen Risk Assessment" is guidance for determining the URF, not for assessing risk from the exposure.

She brought this document into the record, and you can find her testimony about this beginning on page 211, line 20, and continuing through page 214, line 5. What she specifically described was when the petitioners were challenging what was included and what did the URFs actually take into account, including whether sensitive populations or children were factored into those unit risk factors, she brought this document into the record to ensure that, in fact, the URF does, in fact, take into account those sensitive pop ulations.

To the extent that you have any questions about her use of that document, I encourage you to refer to that section of her testimony.

So if I'm back to Ms. Lopez's testimony as a

toxicologist before the hearing officer, she also talked about DEQ's use of a five-year rolling average and how that did not increase any cancer risk beyond what had already been calculated and factored into the T-RACT analysis.

And if you have any questions about the five-year rolling average, we can walk through that as well. But her calculations considered whether having a five-year rolling average presented, even in an individual day or in an individual year, if it provided any excess cancer risks, and she testified that it did not, and provided those calculations in the record.

She also talked about her utilization and verification that DEQ's exposure duration, the use of the exposure duration, specifically the 16 over 70, it was a proper scientific method for calculating the cancer risk provided in this project.

And that's because when you look at the AACCs, that's based on a 70-year lifetime of exposure. But when you look at a 24-hour operation, 7 days a week, every single day for 70 years, that's not what this project will ever provide for.

So you have to do a mathematical adjustment based on what the actual exposure would be in this case. And she calculated that risk of being less than 1 in

100,000. In fact, specifically, she calculated it to be 1 in 240,000, so nearly two and a half times under that T-RACT allowance of the risk.

Kevin Lewis also testified. Kevin Lewis is a chemical engineer for 33 years. He's been providing modeling for air emissions and air permitting as an expert. He's performed hundreds of air quality analyses for mining projects.

He modeled and mapped the arsenic emissions and dispersions that are in Figure 1 of his report. He ran 14 different modeling scenarios using the worst-case scenarios that he could come up with. And then of those 14 modeling scenarios, he took the worst of the worst of the worst, the highest scenario, and then he used that scenario for making and submitting Perpetua's air permit.

So he looked at it in the worst possible condition using the most conservative estimates out of all of those scenarios and then took the worst one and applied it. And even using all of those analyses and the worst modeling scenarios, at best, he comes up with 41 percent of the T-RACT allowance of that 1 in 100,000. So he only gets to 41 percent of that allowance, not even halfway.

And that's applying the permit conditions that

limit the life of the mine, which, in turn, limit the emissions in this case. And he also performed that calculation again for the five-year rolling average. And even if you look at one isolated year, you're at worse case in one isolated year of a five-year rolling average, 55 percent of the T-RACT allowance. You would never exceed anything beyond the 55 percent of the 1 in 100,000.

If we can move to the next slide.

So based on this testimony that the hearing officer heard firsthand, he also had the opportunity to ask his own questions and delve into what he believed was any kind of unanswered areas, he concluded that the production limits calculating the shortest possible amount of operating period, which would be 16 years, which is the maximum production allowed under the PTC, that's what Section 210 requires the calculation to be conducted under, it results in the 1 in 240,000 excess cancer risk over a lifetime of arsenic emissions.

If the operation extends beyond 16 years -- because this is a finite amount of production that can come out of this mine -- a lifetime risk, even if you took 70 years to get the same production limit, you would never exceed the 1 in 240,000 excess cancer risk.

It all falls under the T-RACT allowance, and

he believed that the permit was, therefore, allowable. And he specifically cited his analyses and evaluations of the two most relevant permit conditions, but mind you, there's many in there, but, specifically, Permit Condition No. 3.6, which limits the lifetime total mine production to 788.4 million tons, and then of that, 50 percent could come from the West End permit.

And then under Permit Condition 3.5, the five-year rolling average, he specifically made findings that ensured that even with the five-year rolling average, and you look at any one given day, one given year, it would never exceed any kind of T-RACT allowance.

To put it bluntly, we talked specifically with the witnesses and asked them: "Do you slice and dice this in any creative way that would allow you to play fancy with this permit that will exceed what is allowed under Rule 210?" And all of the witnesses for DEQ and for Perpetua said, "No."

The toxicologists said, "No, there is no way to slice and dice this in a fancy way that will allow you to calculate this permit to end run around what the rules will allow. We've calculated it multiple ways, and every way that we calculate it, we ensure that you are always under the T-RACT allowance."

CHAIRMAN MacMILLAN: Question.

MS. HANCOCK: Sure.

CHAIRMAN MacMILLAN: So are you saying that if the mine ran for 70 years -- sorry, I just had some hearing aid notice. Sorry.

MS. HANCOCK: That's okay. We can't hear it from here.

CHAIRMAN MacMILLAN: So, anyway, if the mine operated for 70 years at the worst-case scenario of emissions, it would still meet the T-RACT?

MS. HANCOCK: Yes.

CHAIRMAN MacMILLAN: Well, then why is there an issue?

Why did DEQ say, well, it doesn't meet their modeling expectations, so we need to go adopt a 16/70 adjustment?

MS. HANCOCK: So the 16/70 is just a mathematical calculation.

CHAIRMAN MacMILLAN: Sure.

MS. HANCOCK: It's not its own permit limitation. What DEQ is modeling when they look at 16/70 is if under Rule 10 it requires that you look at and evaluate -- it requires that DEQ look at and evaluate the permit based on the maximum amount of emissions that come out of the plant; right?

And so if you operate the plant at 24 hours a day, 7 days a week, 365 days a year up until that production limit, then that would take 16 years; right?

It's not reasonable. You're going to have weather events, you're going to have holidays, you're going to have other things that are going to shut that down. So you're not really going to only operate the mine for 16 years, but that's the maximum amount of exposure at the highest concentration levels that will ever come out of the plant.

And so if you operate the plant over a longer period of time but up until that same production limit, you will never exceed that cancer risk that was calculated by the toxicologist. So if you took 70 years, you're still limited by the 788.4 million tons of finite product that's in the mine, and that's all you can mine out of this mine. You can't mine anything more, and so you'll never have a greater emission level.

BOARD MEMBER PURDY: Can I follow up?

CHAIRMAN MacMILLAN: Please.

BOARD MEMBER PURDY: So that maybe -- I've maybe misled myself. So the 16 years was a calculated number; that's not a permit condition number?

MS. HANCOCK: That's correct.

BOARD MEMBER PURDY: So I was misunderstanding

that the 16 years, you know, was the expected life of the mine. The 16 years is if they were as aggressive as possible, meeting absolute maximum daily limits on production, it would take 16 years. Not realistic, obviously, like you mentioned. They're not going to be that efficient, so odds are that this facility will operate for, who knows, 20 or 25 years, potentially, to extract the permit condition limits?

MS. HANCOCK: That's right.

BOARD MEMBER PURDY: And those exposures will then still be well within, because they're, obviously, spread out over 20 years or 25 years or 30 years, whatever it takes to get that limit out.

MS. HANCOCK: Yep, that's right. And if you look at page 10 of the slides -- when you go back, it's under the pertinent regulations under Rule 210.02 (d) -- DEQ was required to do that calculation based on maximum capacity of the source. And so they had to calculate it at that level, but this is not -- 16 years is not a permit condition, and, in fact, wouldn't make sense for this permit.

BOARD MEMBER PURDY: It's a maximum theoretical capability if they had all the trucks running, all the shovels running, everything working just perfectly, they could get it done in 16 years, but

that's not going to happen?

MS. HANCOCK: That's correct.

BOARD MEMBER ELROY: So, Mr. Chairman?

Randy, I want to follow up on your question so that I clearly understand the answer. The comment about no way you could slice or dice it to increase the exposure even up to 70 years, is it fair to say the production of the mine is capped at "X," and using the fastest you could do that, being 16 years, the max exposure you could get is at that 16 years? And then over time if you go to 20 years, 25 years, the exposure actually reduces year over year the longer you operate past the 16 years?

Does that make sense?

So the comment about the highest exposure level would be using a 16-year model, if I'm understanding correctly. It makes clear sense to me, because the longer you operate the mine, the lower those exposure levels go down.

MS. HANCOCK: I think that's right. And I'm going to show you a graph in just a second that will, hopefully, give you a visualization of what you just described. Because you're right, yeah.

CHAIRMAN MacMILLAN: So just, again, if the mine was operated for 16 years with the T-RACTs in

place, the emissions in that 16 -- each period of time, the annual or five-year average, the emissions would not be sufficient to increase the cancer risk to something greater than 1 in 100,000.

MS. HANCOCK: You would never exceed the 1 in 240,000 no matter how long you took to mine the amount of production that is allowed under this permit. It is the production limit that, in turn, limits the emissions of arsenic from that production.

And if you take a longer time to mine that -- if you take a longer time to mine the product, you reduce fewer emissions along the way. So you would never exceed that amount. If you bear with me for two slides, I'll show you a graph that might help, and then we could answer more, if that works.

This slide we looked at with the petitioners. And they showed this -- this is Figure 1 from Dr. von Lindern's calculations saying that this supports 16/70. Mind you, his testimony at the hearing was in his calculations he did not take into account the production limits.

But what he admitted was -- this is his testimony from the hearing day two. And you can see the line and page numbers there, 477 line 10 through 478 line 5. And I asked him this question related to his

own graph.

And you can see on the bottom there there's the years. And he does it in ages. Like, if you had somebody who was one years old -- or zero, starting out at zero being exposed at the mine.

So standing under, you know, whatever emission is out there, if they were standing there and went for 16 years on his graph, and I asked him the question: "If there's no more emittance from the project, and therefore no more exposure [after the 16th year], there's nothing to add to it for the following year, is there."

And he said, "No." And I said, "So then you would just stop at year 16 and that's how much you've been exposed to based on those years of exposure; is that right?" He says, "That's right."

If we go to the next slide.

So this is what it looks like. So this is his same graph. At the top you can see the orange line at the very top. That would be the T-RACT allowance. If you look at the orange line that goes up for the first 16 years, that's the maximum amount of exposure. If you mined at that 24 hours a day, 7 days a week, as fast as you could to the maximum production limit, you would be -- at 16 years -- you would be done with all of your

emissions from the project, and it would have no more emissions from this project. It would present no further additional cancer risks.

That green line is just modeling it if you took 32 years, so double the amount of time. So if you worked 12-hour shifts but every day, you know, 7 days a week, 365 days a year, it would take you 32 years to mine up to that production limit. You still get to the exact same exposure level, but it takes you longer to get there. But you would still never exceed that exposure level.

Does that help answer the question that you were asking?

CHAIRMAN MacMILLAN: I think so.

MS. HANCOCK: And this is what all of the toxicologists agreed on, that this is the proper methodology for evaluating the arsenic emissions and the exposure to -- or the cancer risk that is presented by the emissions from this project.

CHAIRMAN MacMILLAN: So just to reiterate. So 16 years of mine operation with the permit conditions, that's not going to -- if you just look at 16 years, not 70 years -- you know, formally you could use 70 years -- but if you just use 16, you do a cancer risk analysis, it stays -- it's 1 to 240,000?

MS. HANCOCK: That's correct. If you mined round the clock.

CHAIRMAN MacMILLAN: Which is unlikely.

MS. HANCOCK: Which is unlikely.

And it's the production limit that provides the protection. That's what DEQ implemented in the permit to ensure that this project, no matter how long you take to mine, is not going to ever exceed the cancer risk. It's the production limit that provides that protection. And that's what differentiates this project from other lifetime projects; right?

If you're looking -- when they say, "Well, isn't this creating some kind of new precedent?" This isn't creating new precedent. It's the petitioners' proposal that will create new precedent because the petitioners are proposing that you look at this in a stacking way.

We looked at their -- they showed their -- the demonstrative. And they said, well, if you add permit one plus permit two plus permit three plus some hypothetical in the future, that you might somehow give some extra exposure for cancer risk. That's not what the rules provide at all.

The rules require that you look at the permit that is being applied for and you do the rule-based math

based on what that permit is going to emit and you evaluate the cancer risk that is proposed by that permit.

There is no stacking of additional permits. There's no stacking of historical permits or hypothetical future permits, because we don't know what's going to happen, and there's no way to account for that. And, basically, there would be no end to the dialogue, then, because you're always hypothesizing about something that hasn't yet even happened. That would be setting new precedent.

What Perpetua's proposing is a project that has -- now it has project limitations that ensures that it complies, that it won't ever exceed the cancer risk. And that's different; right?

Most of the time when you're talking about a plant that's operating, that's building something, they're going into perpetuity. It's a business; right? They want to keep operating forever, and so there aren't these kind of production limits.

The difference here is that you actually have a finite amount of product in the ground that they have to get out. And if they found more, they're going to have to get a different permit. It's never going to be allowed under this permit.

And so you don't ever look at what's happening outside of it. You evaluate it based on the four corners of this permit. And when we look at that and you apply the actual mathematical calculation, it will never exceed the cancer risk that is allowed under the rules.

Does that make sense?

CHAIRMAN MacMILLAN: I think so.

MS. HANCOCK: Okay. I'll go on to the --

CHAIRMAN MacMILLAN: I'll have to sleep on it.

MS. HANCOCK: Okay. I'll go to the next slide, please.

So the petitioners have presented their arguments to you today, and it's the same as what they argued in their petition for a review that they filed in January. And it's the same arguments that they've been making for years now.

And they're saying that the 16/70 adjustment is unlawful and it sets a dangerous new precedent, it is not supported by the evidence. And then they also talk about how the five-year rolling average is not reasonable to assess compliance with the arsenic limits and they're not sufficient to limit the production.

And what they argued to you today is that somehow this is going to set a new precedent that's

going to create risk and it's going to dilute what would otherwise be allowed under the rules. And that's not the case.

They had an opportunity to bring their own toxicologist to do their own math to conduct their own analysis in front of the hearing officer, and they didn't present any toxicologist, they didn't present any of their own calculations.

The only calculation that they put forth was through Dr. Von Lindern, and he didn't take into account the production limits, which is the very type of tailoring that the DEQ is allowed to do in order to ensure compliance with the rules.

And that's what the DEQ did, and that's what all of the toxicologists who testified concluded using their own mathematically calculated risk using scientifically-sound methodology as corroborated by the hearing officer making credibility findings of the witnesses who testified in person and as completely unrefuted by the petitioners' experts. All of those conclusions were that this permit falls under that allowance.

If we move to the next slide.

So the hearing officer answered the questions that this Board presented to him, and he -- "Did DEQ act

reasonably in using a 5-year rolling average for the T-RACT analysis?"

He concluded, "Yes. At 180 tons a day, this is the maximum amount in the 5-year rolling average" -- this is Condition 3.5 -- "at 180,000 tons a day for a maximum number of days within any 5-year period" -- so that a total of five years -- "the average would never exceed 135, the arsenic emissions did not exceed the cancer risk allowed."

Kevin West testified about this where he performed that calculation at 180,000 tons a day. That was the 55 percent of the T-RACT analysis. Under Question 2: "Was there sufficient evidence to support DEQ's T-RACT analysis regarding the non-West End Pit production?"

He said, "Yes. Based on those 14 different modeling scenarios, using conservative estimates and the maximum arsenic emission numbers" -- which is what's required under the rules -- "applying those permit conditions" -- also required under the rules -- "all of the toxicologists agreed that the cancer risk would not exceed the T-RACT limitations. 41 percent using the five-year rolling average, or even at its peak of 55 percent, if you look at any one -- the maximum amount under one small time period, always falling under the

T-RACT allowance."

And then No. 3: "Did DEQ act reasonably and in accordance with the law when it applied the 16/70 adjustment to the acceptable ambient air concentrations for arsenic?"

He answered "Yes. AACC is lifetime on a lifetime of exposure." That's that 24/7, 365. And you have to account for the actual exposure duration in assessing the cancer risk. So even using that maximum production, even if it could have gone beyond 16 years, the production limit will always, based on that life of mine, fall under the T-RACT allowance.

And then if we go to the next slide.

This timeline has been going on for six years. The permit was applied for in August of 2019. June of 2022 it was issued but then challenged by petitioners. In October of '23, the hearing officer ruled in favor on 13 different challenge claims of error, and, again, the petitioners appealed. It went back again. January 7th the hearing officer issued his findings of fact and conclusions of law and preliminary order, and they challenged yet again.

I propose to you that we're here before you April 2nd of 2025, six years into this permit application, this permit has been evaluated, and time

and time again has been concluded to be a proper and safe protection to ensure that there is no undue risk to the public.

DEQ has done their analysis. Perpetua has done their analysis. It has been confirmed time and time again. We submit that it is time for this permit to be approved once and for all, because we believe that the evidentiary record behind it supports that this is not going to present any undue risk to the public.

And I'd stand for any other questions you have. Otherwise, just thank you for your time.

CHAIRMAN MacMILLAN: Thank you.

So any questions from board members?

(No response.)

CHAIRMAN MacMILLAN: Seeing none.

Thank you.

MS. YOUNG: I'm assuming it's my turn.

CHAIRMAN MacMILLAN: If you could introduce yourselves for the reporter, please.

MS. YOUNG: Yes. Thank you. Good morning.

CHAIRMAN MacMILLAN: Afternoon.

MS. YOUNG: Oh, afternoon. Where does time go?

MS. FLOYD: Time flies.

MS. YOUNG: Good afternoon. My name is Hannah

Young. I represent the Department. And sitting here to my left I have Tiffany Floyd, who is now DEQ's deputy director.

So good afternoon, Chairman and members of the Board.

As you've heard, we are here today on the petitioners' second petition to the Board. And when the Board first issued it's decision last May, it remanded the case back to the hearing officer for the development of further evidence on one issue, the Department's analysis of the project's arsenic emissions. And we're now back to the Board on this one issue.

In hearing this matter for the second time, the standard of review remains the same. The standard of review is as follows: The Board must determine whether DEQ acted reasonably and in accordance with the law when it issued the permit and, specifically, in its analysis of the arsenic emissions.

So while the subject matter is very complex -- we are all aware how technically detailed this is -- the task at hand is actually very straightforward. The Board must review DEQ's analysis and determine those two things, was DEQ reasonable, was DEQ lawful.

And, in fact, considering the voluminous record before you and the evidence that was put forward

at the evidentiary hearing, it would be very difficult to now look at the record, look at the evidence, and not find that DEQ was both.

Now, when this matter was first before the Board, as I mentioned, there were four complex issues before you, and in presenting the arsenic issue to the Board, I did not anticipate the necessary level of detail and explanation that would be and should be needed. And so I failed to provide it, quite frankly.

For example, nowhere in my brief or nowhere in the oral argument did I explain to you what a unit risk factor or URF is. Nowhere did I explain to you how those unit risk factors are part of the AACC. I didn't explain to you the difference between an annual standard and a project increment. And I also failed to explain that project risk is the cornerstone of the TAPs rules.

So all of this information was in the record, of course. And it was in the record because these facts have been the basis of DEQ's analysis since permit inception. But simply put, I did not explain it to you. I did not get far enough into the weeds to explain a technically complicated analysis.

And I think this is really the first time that the fundamental underpinning of the TAPs rules have been questioned and analyzed to this degree. But I, simply

put, took for granted how complicated this analysis is.

So where does that leave us today? The answer is simple, because the Board gave DEQ the opportunity to provide the evidence, to provide the explanation, DEQ did. And during the two-day evidentiary hearing the hearing officer heard directly from all of the expert witnesses and concluded that DEQ was both reasonable and lawful.

The experts that the Board asked to hear from, specifically the two and only toxicologists, decisively concluded that DEQ was reasonable and unlawful. In the words of DEQ's toxicologist Norka Paden, the cancer risk estimates were accurately calculated, the methodology for the calculations adheres to toxicological guidance and analytical practices to modify exposure duration and did not underestimate risk.

In the words of Perpetua's toxicologist, Theresa Lopez, the 16/70 calculation was consistent with good scientific methodology for assessing cancer risk and is consistent with applicable rules. The evidence, the explanation is before you now.

There is a mountain of evidence through which DEQ has continued to explain, in great detail, how it performed its analysis and how it implemented the Air Rules. The mountain of evidence before you is the

result of an exhaustive, thorough process.

As you just heard, for almost three years now DEQ has been asked to show its work. DEQ has defended its permit and its analysis in front of the hearing officer on several occasions and now twice before the Board, and at every turn DEQ has demonstrated how it was reasonable and lawful at every turn.

DEQ is answering the questions being asked. But at some point, DEQ should be made to answer the questions asked, and then when they demonstrate they complied with the rules, the process should conclude. Under Idaho Code 39107, which is the statute that governs the board, an aggrieved party is afforded the opportunity for a fair hearing.

The statute states this hearing may be conducted by the Board or the Board may designate hearing officers who shall have the power and authority to conduct hearings in the name of the Board. And the Board has now done both.

The Board has designated a hearing officer to conduct hearings in the name of the Board, and the Board is now hearing the matter directly. So in simple terms, you've done your job. The obligation is complete. This review process cannot simply continue. At some point, DEQ should be made to show its work and then not keep

answering the questions asked time and time again. We've briefed this specific arsenic issue six times now, and we've heard oral argument on it four times.

Now, as long as DEQ's answers are reasonable and lawful, the hearing officer's decision should stand. But I do not want you to mistake me, I think that being subject to review is, obviously, very important.

DEQ should be required to show its work. But the evidence is piling up, and the Board directed the hearing officer to establish the additional necessary evidence, and he did. So we cannot now look at this mountain of evidence and find that DEQ was unreasonable or lawful [sic].

The task at hand is not to decide what the rules should do, what any one of us would like the rules to do, what makes sense to someone individually, the job is to look at the rules as they exist today and determine if DEQ was reasonable and lawful.

DEQ's task is to issue legally defensible environmentally protective permits. And DEQ also did its job. The evidence demonstrates that the permit is reasonable and lawful.

So with that, I will turn to the merits of the arsenic issue. And just as a bit of a roadmap, I will discuss the basis of the TAP rules first. Next I'll

walk through the rules in more detail. And then I will discuss how DEQ's analysis was protective of public health. Finally, I'll touch on the rulemaking history.

And, please, any questions, interrupt me at any time.

So, first, the key to understanding DEQ's arsenic emissions analysis is to understand that the cornerstone of the TAP or Toxic Air Pollutant rules is that total increased cancer risk from a project over the project's life cannot exceed the lifetime cancer risk limit imposed by the rules.

In other words, the TAPs rules do not create annual standards like you see for annual compliance with NAAQS, for example. The rules create an increment that is a 1 in a million increased risk over a lifetime of exposure, or 1 in 100,000 if you're using T-RACT. Once you accept and understand this premise, the rest of the analysis follows.

So what does that mean here with the project when I say that the TAPs rules are increment based and that the increment is a 1 in a million increased risk over a lifetime of exposure?

I mean, simply, that under the TAP rules, DEQ is analyzing the increased cancer risk from arsenic at the Stibnite Gold Project that is created over the life

of that project and ensuring that that increased risk from the project is no more than 1 in a million or 1 in 100,000 depending on use of T-RACT.

Now, petitioners, obviously, take issue with this approach. And they have claimed, and you just heard, that it sets a dangerous new precedent. But there's no departure from precedent here because the reality is there's no precedent. This is a unique situation.

During a two-day evidentiary hearing, DEQ's expert, Kevin Schilling, testified that he's never been confronted with this situation before. He's never imposed a total production limit in the TAPs rules, because typically applicants don't assume a finite operational period.

They assume to operate permanently, or if they do know how long they're going to -- or if not permanent, they don't know. They're just permitting a project that they hope exists as long as it can.

But here that's simply not the case. We knew that the project was not going to operate for -- on a permanent basis, it had a finite operation. So we know it's not a permanent source. And where the TAPs rules are focused on a lifetime of exposure, an adjustment based on the known lifetime, which 16 years at maximum

capacity, as you just heard, then the adjustment was reasonable.

And as the hearing officer found, projects such as the Stibnite Gold Project in which exposure is known to be less than 70 years, failure to account for true exposure results in overstating emissions from the project.

And I just wanted to note, based on some questions that I heard earlier, that in other standards, which are annual standards, like NAAQS, DEQ does limit -- does use project-specific adjustments and creates limits for projects. For example, like a portable source that's only going to operate for a year.

And in those cases, DEQ uses the same methodologies and clearly uses its authority to create project-specific adjustments. So if they're only going to operate for one year, but there's a three-year average for the standard, they do whatever was happening the first year, and they put zeros in for the next two years.

So this is not unheard of. In fact -- so the point here is that it's not a departure from precedent. And in the TAPs rules it's just a unique situation, like I said, because most projects -- all projects, except for now this one, have come in saying I'm going to

operate on a permanent basis when they've been analyzed under the TAPs rules.

Next I want to discuss how this adjustment was lawful by discussing what the rules provide and then what the rules don't provide. So there are two critical rules that are necessary in understanding DEQ's analysis in understanding how DEQ was lawful.

The first is Section 586, obviously, which contains the AACCs. And it lists each carcinogenic toxic air pollutant. It provides the applicable, acceptable ambient concentration, as well as the unit risk factor or the URF.

The URF is developed by EPA, and it's the risk probability from exposure to 1 microgram per cubic meter of a substance continuously for 24 hours a day, 365 days a year over the lifetime exposure assumed to be 70 years.

The AACC then is calculated by taking the acceptable lifetime risk, which is 1 in a million or 1 in 100,000 and dividing it by the URF. So the URFs are listed in the rules, and the AACC is based on the URF.

And DEQ's experts, Norca Paden and Kevin Schilling, both testified at the hearing that the inclusion of the URF in Section 586 demonstrates conclusively that it is a project cancer risk that is

the focus, not an annual strict standard.

That's because the URF developed by EPA is based on a lifetime project risk. And the second important piece is the definition of a toxic air pollutant carcinogenic increment. And I apologize, I'll read it to you. It's a little bit lengthy.

It's defined as follows: Those ambient air quality increments based on the probability of developing excess cancers over a 70-year lifetime exposure to 1 microgram per cubic meter of a given carcinogen and expressed in terms of a screening emission level or an AACC for carcinogenic toxic air pollutant. They are listed in Section 586.

And you may have noticed that in that definition it references the emission levels. So if you look at the table in Section 586, you'll see there's another column -- we haven't talked about it much -- but it's those emission levels.

And those emission levels were simply created by DEQ and said -- based on some hypothetical modeling -- and they say, if you meet these levels, then you're done, you don't have to go into any more analysis.

So, basically, the definition is referencing, you know, either the AACC or those emission levels. But

the definition, what's important here is that it references the 1 in a million cancer risk as being the criteria, and that the AACCs are an expression of that for a continuation exposure over a lifetime. So, again, if this sounds repetitive, it's because it is. It's all based on the same principles.

The use of the word "expressed" in Mr. Schilling's opinion, as he testified at the hearing, makes it clear that the focus is a total project imposed cancer risk not specific year by year. So based on these two sections, DEQ's adjustment was clearly lawful.

And the hearing officer agreed finding based on the plain language of Air Rule 161, 210, 586, and the evaluation of toxic air pollutant emissions under those rules, it's inherently project specific and focused on the increased project cancer risk posed by the specific project proposed by the air permit application.

So those are the two rules that I think are worth highlighting, but I want to take a moment to -- I know this has been done already a few times, so bear with me, but there are a lot of rule sections that are applicable to the analysis, and so I have a flow chart here that I'm going to pass around. It's just a demonstrative. It doesn't need to be admitted into evidence, but I'll pass them around.

And then, Diane, if you don't mind pulling it up. It might not fit on the screen super easily. But I did at least print it on oversized paper so that it wasn't as, maybe, overwhelming and tiny.

But this document is, basically, a flow chart of the rules and how DEQ complied with the rules.

Thank you. I've got my own here. And I know it's a lot of information, but it's a lot of information because it's a complicated analysis, so we did our best to really parse it down, but this was -- we didn't want to skimp on the necessary information here.

So I want to bring your attention to the green boxes. You can see in the upper, left-hand corner it says, "Start here for Air Rules." And then if you follow those arrows, you follow the green boxes. Those green boxes contain the primarily applicable Air Rules.

Oh, I'm sorry. I meant to provide you guys with one of those too back there?

Do you have extras?

MS. CUTLER: Yeah.

MS. YOUNG: Thank you.

So, again, if you look at the green boxes, you will see that that tracks the applicable Air Rules. And if you look to the right, you will see that's DEQ's analysis and how DEQ complied with the Air Rules.

The additional red boxes simply provide some additional detail that's, I think, helpful in the analysis.

So as you've heard, and I'll try to be brief, because I don't want to do this too many times here, but if you start in that top, left corner, you can see that the starting place is Section 161, which provides the overarching policy that applies to the emission of toxic air pollutants like arsenic. It provides that toxic emissions cannot be emitted to injure or unreasonably effect human life or vegetation.

Moving to Rule 203, that's the rule that provides that in order to obtain a permit, an applicant must demonstrate that it will comply with 161. So if you want a permit, you need to do a TAPs review, you need to look at what toxic air pollutants might be emitted by the project.

Now, 203 states that you demonstrate compliance with 161 using the processes in 210. So, naturally, that leads us to 210. And much of the remaining boxes there are Section 210, the various process.

So 210.01 and 02, the applicant identifies and quantifies any TAP emissions, which DEQ did. If you look to the right there, emissions were calculated for

64 different toxic air pollutants.

If you move down to 210.07, DEQ compares the controlled TAP emissions to the screening levels that I had mentioned earlier in 586. DEQ did that and found that 50 were below and 14 were above.

So you move down to 210.08, then you compared the controlled TAP emissions through some modeling to the 586 AACCs. Doing that, DEQ found that 13 were below and arsenic was the only one above.

So, really, I think a lot of what we just talked about is probably just additional background context, because that's what leads us to being, ultimately, at the arsenic issue, which is where we're at today.

So when DEQ found that the arsenic emissions were above the AACC, then the permit applicant determined to use T-RACT. And T-RACT can be used pursuant to Section 210.12.a to demonstrate compliance with the 586 carcinogens.

And if you look to the right there, you see that T-RACT was applied. And then if you follow that arrow again, just for some additional information, you can see the operational and T-RACT limits, some of which we've been discussing, that were applied. So when we talk about what those T-RACT limits were, that's what

you have.

Now, what we know based on this discussion is that the AACCs are inherently expressed as the annual average concentration over the course of a 70-year lifetime, and so using those fundamental principles from 586, as well as the definition I just read to you in 006.125.

So per 586, EPA's formula, the highest modeled annual average concentration was adjusted to account for what you'll see there as T-RACT limit 3, which is the 788.4-million-ton lifetime limit. So because this had a finite operation, because the permit contained an overarching limit to the amount of production, the adjustment of 16 years, which, again, 16 just demonstrates max capacity, operating max capacity, that adjustment was performed.

COURT REPORTER: Can you slow down a little bit. Thank you.

MS. YOUNG: Oh, I'm sorry. Am I going -- I'm trying to zoom, and I'm talking fast. Thank you.

Let's see here. I was on a roll. That's why I was talking so fast.

Let's see, if you go down to 210.12.b and c -- so we're on the green boxes, second from the bottom -- now you compare the T-RACT concentration to the T-RACT

AACC, and you see there that DEQ did so.

The approved ambient T-RACT concentration .00095 micrograms per cubic meter was then compared -- if you look to the left, just for your information, the T-RACT arsenic AACC was provided -- .0023, you can see that the permit was found to be in compliance.

And the last green box there is just ensuring that the permit contains those T-RACT limits to make sure that the project isn't going to -- you know, that the permit actually makes sure that they're going to comply with the limits. So this is a lot of information, like I said.

Yes, Chairman.

CHAIRMAN MacMILLAN: So, Hannah, again -- so if we look at the box that you were just on -- so why did you go to -- why did you have to apply 16/70 adjustment factor?

MS. YOUNG: Right. It's a great question. And I wish that the DEQ experts were up here instead of me answering this question. But, essentially, the adjustment was -- let's see here, I had a note I wanted to make sure. Well, it was somewhere in here.

The modeling was based on, you know, the maximum for each year. And that modeling assumes that you're going to operate for, you know, 70 years, for

example.

And when you didn't apply that analysis -- oh, sorry -- then you had -- it didn't meet the T-RACT AACC, right, if you didn't apply the 16/70 adjustment. But without that adjustment, you were also overstating emissions, because you were assuming that you're going to operate at that max capacity for at least 70 years.

BOARD MEMBER PURDY: Can I just clarify that?

MS. YOUNG: Yeah.

BOARD MEMBER PURDY: Because of this Condition No. 3, this Permit Condition No. 3, this T-RACT Limit No. 3, 788.4 million tons of lifetime facility weight, if you don't apply that, like you said, it assumes 135 tons per day going out for 70 years --

MS. YOUNG: Right.

BOARD MEMBER PURDY: -- which is not going to happen.

MS. YOUNG: Absolutely.

BOARD MEMBER PURDY: It's going to stop at -- it will take 16 years, but it might take 20, it might take 25, it make take 30, it might take 32.

MS. YOUNG: Right. But no matter -- exactly. And I'm sorry for interrupting, Mr. Purdy. But the operational limit of the amount of ore will stay the same. So either it takes you 60 years and you go at a

higher concentration for 60 years -- or 16 years, and then it drops off, or you do a lower amount because of the overall ore operational.

BOARD MEMBER PURDY: 16 years was just the worst-case scenario that you were required --

MS. YOUNG: Right.

BOARD MEMBER PURDY: -- to apply?

MS. YOUNG: But without the adjustment, you're assuming that you're operating at that worst-case scenario for 70 years, and you're not. That's an impossibility.

BOARD MEMBER PURDY: So you significantly overestimate the emissions, because you could be done in 16 years, but you're still counting emissions for the next, whatever, 34 years or 44 years or whatever --

MS. YOUNG: Right.

BOARD MEMBER PURDY: -- that aren't happening?

MS. YOUNG: Right. Absolutely. And so the emissions being calculated for that scenario aren't representative of the reality.

BOARD MEMBER BOYLAN: Mr. Chair?

CHAIRMAN MacMILLAN: Yes.

BOARD MEMBER BOYLAN: So kind of tying in to what you were saying there, that maximum production limit, just doing a unit analysis, effectively, in

engineering terms, you have three different variables here. You have the denominator, which is the base assumption of a 70-year project, but then you have 16 above it, that's what we're talking about. But when we're describing the maximum production over a 16-year timeframe applied at that tonnage, that's where you come up with the .00414?

MS. YOUNG: I'm sorry, can you ask that last question again?

BOARD MEMBER BOYLAN: So the maximum production is where you get the .00414 --

MS. YOUNG: Right. Right.

BOARD MEMBER BOYLAN: -- applied over the 16 years. So if you were then just taking a step back and said, all right, we're going to change that to 20 years, that .00414 drops --

MS. YOUNG: Right.

BOARD MEMBER BOYLAN: -- in the calculation? And that's just looking at it as a unit analysis type of review.

MS. YOUNG: Right. This number is based on operating at max capacity.

BOARD MEMBER BOYLAN: Yeah. That's where your worst-case scenario comes in is in that portion of the equation.

MS. YOUNG: Right. And the petitioners' claim that the max was diluted using averaging, which is patently false. There was no averaging that occurred.

And Dr. von Lindern, during the hearing, tried to discuss the averaging, and when he was asked questions about it on cross-examination, he could not explain the numbers. He could not come up with an answer. Because it's complicated. So I don't fault him for that.

But that's just an inaccurate representation. What did occur was the maximum at West End Pit and the maximum non-West End Pit and 50 percent production of each, which is also worstcase scenario, because the permit limits West End Pit, which is the -- based on all the modeling that potentially create the highest emissions, 50 percent was the max on the West End Pit. And then 50 percent of the other.

But that's, again, worst case, because it's very possible that only 25 percent of the West End Pit is mined and 75 percent comes from non-West End Pit deposits. And if that's the case, then, obviously, that max overestimates it, which is fine because that's part of the modeling is you take the maximum impacts. But there was no averaging, so I take specific note of that, because that's something that I heard again today.

CHAIRMAN MacMILLAN: So another question: So DEQ is saying that the 16/70 is a T-RACT requirement?

MS. YOUNG: So the T-RACT AACC was never adjusted. The AACC, in and of itself, was never adjusted. What was adjusted was the exposure concentration. And then that exposure concentration was compared to the T-RACT AACC.

So it was part of the refinement in developing or -- I probably am not going to come up with the best word, because I'm just a lawyer and not a technical person, but in coming up with the exposure concentration from the mine to compare to the T-RACT AACC. That's where the project-specific adjustment came into play. So they're not adjusting the T-RACT itself.

CHAIRMAN MacMILLAN: So, again, once again, could you tell me why you did 16/70?

MS. YOUNG: Yes, I can. Without the 16 over 70, the assumption was that the emissions from the mine would be at a capacity that's based -- I guess, without the 16/70, you don't take into account the finite limits in the permit for overall operation. The 788.4-million-tons lifetime facility-wide total mining limit, which is the condition 3.6 in the permit. So without that 16/70, you're assuming this maximum over an entire lifetime, which, again, is never going to occur.

BOARD MEMBER PURDY: So could I -- because I want to clarify that, if I could. Because the T-RACT AACCs are the average annual concentration over a 70-year period, this mine will not operate for 70 years?

MS. YOUNG: Correct.

BOARD MEMBER PURDY: This mine will operate for some period less than that; correct?

MS. YOUNG: Correct.

BOARD MEMBER PURDY: So Perpetua -- I mean, Perpetua could have, as an alternate approach, could have said, well, we're not going to mine that much per day, then we're going to reduce our overall total mining activity and take this out over 25 years --

MS. YOUNG: Yeah, Perpetua wanted --

BOARD MEMBER PURDY: -- instead of 16?

MS. YOUNG: Yes. I'm sorry to interrupt.

BOARD MEMBER PURDY: They could have extended the maximum production capacity of the mine to 20 or 25 years and met the requirement --

MS. YOUNG: Yes, absolutely.

BOARD MEMBER PURDY: -- just, boom, right there?

MS. YOUNG: Yes, absolutely, they could have. But they wanted the ability to mine as fast as possible. That's part of it. Essentially, they needed the

adjustment -- or they needed to look at it at max 16 years because they wanted to consider whether or not they could meet the AACC if they were, although unlikely, operating at max capacity.

Now, they're not going to, but they would have done a different calculation if they would have, for example, accepted that it would have taken them longer. And I am more than happy to talk to DEQ's experts, because I want you to have the best information here and provide a written answer to follow up with the Board.

Because, obviously, you've homed in on something very important. This is something that went into great detail during the evidentiary hearing. And so, you know, we went through that process, and we told the hearing officer -- the actual experts explained to the hearing officer, and the hearing officer agreed and understood that it was lawful.

And so, you know, I would, again, hope that we would give credence to that process and uphold the hearing officer's decision, but I'm also more than happy to continue to have the actual experts at DEQ explain this complicated analysis.

CHAIRMAN MacMILLAN: Well, and, Ms. Young, the 16/70 has been a major stumbling block --

MS. YOUNG: Absolutely.

CHAIRMAN MacMILLAN: -- for us in trying to understand in some of the earlier hearing -- well, when Kevin Schilling had said, I came up with this 16/70, and it just kind of was a flag, for at least some of us -- or at least one of us.

And ever since then it's been a real concern to us. But you're saying, DEQ is saying, and Perpetua said the same thing, I think, I'm pretty sure, that without the 16/70 adjustment, the mining operation would still meet --

MS. YOUNG: The AACC.

CHAIRMAN MacMILLAN: -- the AACC?

MS. YOUNG: Yes. Yes. So I hear what you're saying. I understand the concern that you're expressing. You've raised a couple of things. I want to make sure I address all of them.

And one of them is, I think petitioners raised Kevin Schilling's memorandum where he said, you know, this is new, I want to talk about this, and expressed some concerns, and that's fair. But it was something they'd never considered before because nobody had ever -- no applicant had ever come in under the TAPs rules and said, "I have a finite operation, I'm not going to be a permanent source," and so it was new.

At that time, and this is in the record in

Kevin's declarations, he consulted with the lead DAG at the time. There was a lot of conversations about it. And, ultimately, that analysis was vetted and determined to, based on Kevin's understanding of the cornerstone of the rules being project risk over a lifetime, it was determined to be lawful and appropriate and reasonable.

I don't think that that memo or that conversation from Kevin is a red flag. I think it just shows DEQ doing its due diligence and not accepting what a permitee offers up, but saying, hey, this is something I've never seen before, this is new, let's vet it and make sure it complies.

And they wouldn't have issued a permit based on principles that they -- you know, if Kevin wouldn't have testified at the hearing saying he was confident in the analysis if the result of that process didn't provide him confidence, ultimately.

But the adjustment, the 16/70 was necessary to account for the overall 788.4-million-ton limit, because that limit, that finite limit limits the duration of the mine. Now, at max capacity, it limits duration to 16 years.

If the mine operates at that max capacity, that .000414, it cannot operate for more than 16 years. So if it's operating at 16 years, that's the max

capacity, and you're not putting in that 16/70 adjustment, you are way overestimating the emissions from the source.

CHAIRMAN MacMILLAN: And I know we need to move along, and we all need to think about all this.

So if the mine operates one day, and it emits arsenic in the dust or emits dust and arsenic in the dust, so the concentration -- the emission concentration will not be greater than .004 -- whatever the number is?

MS. YOUNG: 414.

CHAIRMAN MacMILLAN: -- 414; is that what you're saying?

MS. YOUNG: I'm sorry, I was still looking for my note. Will you repeat that one more time? I apologize.

CHAIRMAN MacMILLAN: So if the mine operates one day, and it does whatever -- there's a limit on, I don't know, how many tons they can pull out in one day, they process that, they run their trucks and do all the things mines do, the emission concentration of arsenic would not exceed .0041 -- 3? 6? 4?

MS. YOUNG: 4, right. That is the mine operating at max capacity, based on not only the overall limit, but the daily and five-year rolling average limit. Because there's also limits on how much they can

pull out in a single day, which is part of those operational limits that were, you know, part of the calculation in determining worst-case impact.

CHAIRMAN MacMILLAN: So in the record, then, could you direct us to where it says something like that?

MS. YOUNG: Yes, I would be happy to do so. I mean, it occurred at the evidentiary hearing. If I can, I could supplement or provide citations to the exact point in the record to the Board in a -- you know, something submitted after the fact, some sort of supplemental document. And I would be more than happy to point you to the parts of the record. Because, as you point out, this is of critical importance.

CHAIRMAN MacMILLAN: Thank you.

MS. YOUNG: Okay. So what I wanted to demonstrate -- and this was, obviously, important discussion about what the rules require -- but the chart, I think, does a couple of things as well. And what I want you to see through this is that DEQ used a very thoughtful and very logical approach that was reasonable and based on all of the applicable rules.

During the evidentiary hearing and throughout the briefing, we've heard from petitioners as to what they would have liked the rules to provide. And you saw

the quotes from the hearing officer about, you know, the petitioners testifying regarding what they wished the Air Rules did versus what they actually say.

Even in their petition to the Board here, petitioners waste precious pages of their brief discussing what the state of Washington does, including concepts like health impact assessments, which are, of course, found nowhere in DEQ's rules.

They continue to discuss concepts like mutagenic modes of action, noncarcinogenic risk. Today you heard them discuss things like understanding, like, this increment stacking. Again, these are things that are not in the rules, and the increment is based only on the specific project.

For better or worse, despite what you might think about the TAP rules, what they do is they only look at the one project before it. DEQ isn't keeping --

VICE CHAIR STEELE: Mr. Chair?

So on that note, I mean, if you had three projects in downtown Boise, you would look at it on a project-by-project basis; correct?

MS. YOUNG: Correct.

VICE CHAIR STEELE: You wouldn't stack those?

MS. YOUNG: Correct. That's not what the TAPs rules do. Now, other rules, like the NAAQS, for

example, would consider, potentially, you know, what the ambient air quality was, but not under the TAP rules.

VICE CHAIR STEELE: Okay. Thanks.

MS. YOUNG: That is correct. And, again, that's -- you know, for better or worse, that's just how the rules are written.

So, ultimately, the hearing officer agreed with DEQ's interpretation and application and disagreed with the petitioners' version of the rules.

BOARD MEMBER BOYLAN: Mr. Chairman?

CHAIRMAN MacMILLAN: You had a question?

BOARD MEMBER BOYLAN: Can you clarify, don't the rules, the TAPs rules require that maximum assessment; is that right? Did I hear that correctly?

MS. YOUNG: The maximum assessment?

BOARD MEMBER BOYLAN: Yeah, as a worst-case scenario to establish the baseline of the evaluation?

MS. YOUNG: Yes.

BOARD MEMBER BOYLAN: I just wanted to make sure.

MS. YOUNG: Yeah.

So as I stated earlier, once you understand that the cornerstone of the TAP rules creates an increment that is a 1 in a million increased risk over a lifetime of exposure, then the rest of DEQ's analysis

follows as reasonable.

And this is particularly important for understanding DEQ's use of the five-year rolling average for determining compliance. Since petitioners continue to wrongly assert that the AACCs provide annual compliance limits, then they also continue to assert that the five-year rolling average is insufficient.

DEQ's expert, Kevin Schilling, testified that as long as the project-imposed risk is the criteria -- and here we're assuming, at maximum, that that's 16 years -- at the fastest, right, the shortest duration -- what really matters for demonstrating whether it complies or not is where we're at at 16 years. That's the compliance period.

However, DEQ used a five-year averaging period for limiting process rates, which easily accomplishes the requirement for a project with a 16-year duration, and it provides reasonable periodic assurance of compliance with the long-term limit. And those limits are the daily -- the amount of production.

So the hearing officer agreed, finding that this was not only a reasonable approach, but that it, for projects like the Stibnite Gold Project with highly variable emissions, a five-year rolling average of emissions is actually more representative from the

project than evaluating emissions on an annual basis.

So you might have a year where there is much more limited production, which might not be an accurate representation of how the mine is actually functioning. Five years would be a better picture.

So as to the West End Pit issue, in the interest of time, I think it's been a good discussion, but we've probably used much of my time, so I'll just rely on the briefing and the hearing officer's decision on that, unless there are any specific questions, which I'm happy to take.

Okay. I still have time. I have a few more.

CHAIRMAN MacMILLAN: Yes, go please.

MS. YOUNG: Thank you.

So I think it's very critical to understand that this approach is not only lawful and reasonable, but it is protective of public health. During the remand, DEQ and Perpetua's toxicologists -- again, the only two toxicologists presented -- testified that DEQ's arsenic analysis was equally or more protective.

Both experts explained that using EPA's methodology for calculating cancer risk, the use of the project-specific adjustment factor did not unreasonably increase the risk and was, in fact, in compliance with the T-RACT AACC. As you've heard, the result was 1 in

240,000, which meets the risk -- the AACC T-RACT of 1 in 100,000.

And I do want to take issue with a comment that I heard earlier from petitioners that the toxicologists were simply fed numbers during their analysis. And during the evidentiary hearing, both toxicologists were asked if they specifically looked at the underpinning to how those numbers were come up with, did they look at the formula, did they look at the calculation, and both were borderline offended and said, yes, absolutely, they did consider the underlying analysis, they weren't simply fed that information.

Both Dr. Paden and Ms. Lopez calculated the risk from the project using EPA's formula for human health risk assessments where cancer risk calculations are done always using a variable exposure duration and assumed 70-year lifetime.

So both testified that adjusting for the exposure duration is a critical factor in calculating risk. That's because the calculation of cancer risk is an evaluation of chronic exposure, how long you're going to be exposed to something.

And the calculation is linear. Meaning, it's a function of two variables, exposure concentration and exposure duration. Again, how long is the exposure

going to occur. And the duration is clearly critical in understanding the risk.

The result of those calculations by both toxicologists demonstrated that emissions from the project resulted in a .0095 micrograms per cubic meter arsenic concentration averaged over a lifetime again, which is 1 in 240,000.

Petitioners claim that DEQ employed averaging tactics to dilute the impact. I've already discussed that. Again, this is false. There was no averaging. DEQ took the maximum after looking at each scenario and then used the maximum emissions from each scenario modeled.

And, obviously, as you've heard, the scenarios use a lot of conservative assumptions, for example, with the potential that they would be operating 24 hours a day, which we know is not -- simply not going to occur.

CHAIRMAN MacMILLAN: I'm sorry.

MS. YOUNG: You're fine.

CHAIRMAN MacMILLAN: So did you just say that using the 16/70 for a 70-year duration for analysis, that the AACC would be .009?

MS. YOUNG: Yeah, as I was reading that, I think we got a little off base in our conversation with the flow chart earlier, because that .00414 number is

the number before the 16 over 70 adjustment.

CHAIRMAN MacMILLAN: But the key for me was it's one 1 of 240,000?

MS. YOUNG: Right.

CHAIRMAN MacMILLAN: Does that happen with the .00414 --

MS. YOUNG: No.

CHAIRMAN MacMILLAN: -- or does that happen with the .009?

MS. YOUNG: Right. Yes.

CHAIRMAN MacMILLAN: The .009?

MS. YOUNG: Yes. That is the 1 in 240,000. Because the .00414 is unadjusted with the project-specific adjustment.

CHAIRMAN MacMILLAN: So what does the .00414 give you?

MS. YOUNG: The .00414 represents the highest modeled annual average concentration, but it does not account for the T-RACT limit 3 or the operational limit 3, which is the total tons of lifetime mining limit.

So the .00414 is the highest modeled annual average concentration, but it doesn't account for, again, the limit on the mine, which, you know, for ease of this conversation, we could say is 16 years at max capacity, then it doesn't account for that.

But that is a limit in the permit, it's a limit to production, and so it has to be accounted for, which is why DEQ took that .00414 and times it by the 16 over 70 project-specific adjustment.

BOARD MEMBER BOYLAN: So can I --

CHAIRMAN MacMILLAN: Please.

BOARD MEMBER BOYLAN: So, yeah, just because I brought up the .414, I guess what I was trying to tease out was when you're doing this analysis and you're beginning from the foundation of worst-case scenario, highest production limit, you would land at the .414, just that's the worst, absolute worst-case scenario?

THE WITNESS: Right.

BOARD MEMBER BOYLAN: But the uniqueness of this, as I'm hearing it, is that rate, emissions rate will deplete within 16 years?

MS. YOUNG: Right.

BOARD MEMBER BOYLAN: Which is why apply the factors?

MS. YOUNG: Right.

BOARD MEMBER BOYLAN: You can't assume -- if I'm understanding this rationale correctly, you can't assume the .00414 across the 70-year timeframe because --

MS. YOUNG: Right.

BOARD MEMBER BOYLAN: -- you're a finite source of material that played out with the 16 at that rate.

MS. YOUNG: Exactly. If you recall the figure that Perpetua put up, the line goes up, you know, for the 16 years, but then it evens out. You stop having additional emissions because you would run out of ore to mine at that point. So you're exactly right.

BOARD MEMBER BOYLAN: So then my next train of thought was confirming that that's what the rule requires, that you have to assume worst-case scenario?

MS. YOUNG: Right.

BOARD MEMBER BOYLAN: But hearing -- which I didn't, prior to today, understand was that the reality is that rate of production would not be achieved, certainly not on a continuous basis --

MS. YOUNG: Correct.

BOARD MEMBER BOYLAN: -- because it's unreasonable to assume you'd never have a down day?

MS. YOUNG: Right.

BOARD MEMBER BOYLAN: So that number, even without the adjustment factor, if you were to take the actual years of production, whether it's 20, 25, or 30, that emissions rate will automatically drop --

MS. YOUNG: Correct.

BOARD MEMBER BOYLAN: -- because you're extending the resource out?

MS. YOUNG: Correct. Chairman, if you have further questions, I would direct you to --

BOARD MEMBER BOYLAN: I was just trying to clarify.

MS. YOUNG: -- Mr. Boylan.

CHAIRMAN MacMILLAN: So, again, the .00414, that's the worst-case scenario concentration --

MS. YOUNG: Correct.

CHAIRMAN MacMILLAN: -- prior to applying the 16/70 adjustment factor?

MS. YOUNG: Right.

CHAIRMAN MacMILLAN: But if you didn't apply the 16/70 adjustment factor, you would be exceeding --

MS. YOUNG: Correct.

CHAIRMAN MacMILLAN: -- the AACC?

MS. YOUNG: You would. That's why the 16/70 adjustment factor was necessary, because you were going to exceed it. The problem, however, with not applying the adjustment factor is that you are incorrectly assuming that that emission rate is going to occur indefinitely, or at least 70 years, which is not the case. And that's a necessary part of the analysis if you're using -- you know, if you're understanding how

the AACCs and how the URFs are applied.

So as the hearing officer found, without using that project-specific adjustment, you are grossly overestimating emissions.

BOARD MEMBER PURDY: Can I make a simple analogy? You have the -- the AACC's are based on a 70-year time period?

CHAIRMAN MacMILLAN: Correct.

BOARD MEMBER BOWEN: The exposure over 70 years.

BOARD MEMBER PURDY: Exposure over 70 years.

We'll call that a half --

BOARD MEMBER BOWEN: That's 24/7, 7 days a week.

BOARD MEMBER PURDY: The .00414 is calculated over maximum capacity, pedal to the metal, 24 hours a day, 7 days a week, .00414 over 16 years. You cannot compare that to a 70-year exposure number. Those are two different numbers. The denominators, they're not the same, they're not over the same time period.

So to be able to compare those two numbers, you have to divide -- you have to multiply it by 16 over 70 to take that number, spread it out over 70 years, because the AACCs are an average concentration over 70 years, not over 16 years.

MS. YOUNG: Right. So if you look at the --

BOARD MEMBER PURDY: Over 70 years, not over 16 years. So you have to correct the .00414 number to put it out over 70 years.

MS. YOUNG: So if you look at the declaration of Dr. Paden, she -- exactly what you're talking about, this would be at 3876 and 3877 in the record. She does this calculation where you have the highest annual concentration, and you times it by the amount of time that the, you know, mine would operate at that highest concentration, and then you divide it over 70 years, which is exactly what your point is.

So if you look at her declaration, she explains how those calculations were performed and why you needed to include in order to have the same -- you know, compare apples to apples of what would really occur over 70 years. Because the rules are looking at what's occurring over 70 years. At .00414, that cannot occur for 70 years.

CHAIRMAN MacMILLAN: Could it occur for one day?

MS. YOUNG: I don't feel like I'm a technical expert to say that. I don't know if it could occur in one day. Again, we're really into the weeds, which is fine, and I want the Board to understand this

information.

The Board remanded for this explanation to the hearing officer, and we had a two-day hearing. And the hearing officer was able to view all of this information, hear directly from the experts, which is what I wish you could do today is hear directly from the experts.

BOARD MEMBER PURDY: Mr. Chairman, I would suggest that we need to go back and look at the evidence that was submitted during the hearing. And I don't think that we can ask her to answer technical questions.

So like she suggested, I think we need to -- if we have these questions, we need to go back and look at the evidence that was submitted during the hearings from the various toxicologists, because I think they answer this question.

CHAIRMAN MacMILLAN: Well, I have looked, Pat, and it's still very confusing, because you can't tell, at least with the records that I've looked at, which is quite a bit, that they have not applied the 16/70 adjustment factor -- or they have applied the 16/70 adjustment factor to their analyses and reporting .009, for example.

And the question really is: Are sensitive people, sensitive populations, are they being exposed,

during the course of the mine's operation -- whether it's for daily, weekly, 16 years, or 32 years, or 70 years -- are they being exposed to a higher risk of cancer?

MS. YOUNG: The toxicologists testified at the evidentiary hearing that sensitive populations are already accounted for in the development of the URF. And so as long as DEQ is applying the AACC in the URF, then sensitive populations are already being accounted for, and the toxicology is already embedded into the analysis.

So I would offer, and the Board can consider this or not, that you hear directly -- if you have these questions still, you could hear from the experts. I mean, Kevin is here today and Theresa Lopez is here today. To the extent you have questions, the Board has the ability to take in additional evidence under 39-107 and under the contested case rules.

And if you have questions, I mean, again, I would continue to assert that the hearing officer asked the questions he needed pursuant to the remand, he made a decision, and that's what we're here today is to make sure that the hearing officer had a reasoned decision.

That being said, DEQ clearly stands by its analysis, and I don't want the Department to lose out on

an opportunity to explain something that could be explained. I don't want to throw a monkey wrench in there. I don't want to speak out of turn or say the wrong thing. I think we're on the same page as far as what that does.

And I could follow up, you know, with staff on this specific issue of if the mine operated for one day, what would the emission limit be. I don't know if they know that. I don't know if they modeled that.

CHAIRMAN MacMILLAN: Well, so from a -- I'm a biologist and pathologist, and so the -- for me, one of the critical issues is just if a population is exposed for 5 years, 10 years, 15, 16 years at an increased concentration of a carcinogen, they could be significantly impacted by that -- those events. And their cancer, if they were to develop it, wouldn't show up, maybe, for 20 or 30 years.

MS. YOUNG: Right. And the toxicologists testified at the hearing that exposure is chronic. So it's not what happens on day one. Day one -- and their expertise is in, you know, human health assessments and cancer risk to humans.

And they were definitively saying that it's chronic, and it's based on duration. And so, again, to the extent you have questions beyond what they've

testified and you want to ask those questions, again, Ms. Lopez is here, but I don't want to get us off track.

CHAIRMAN MacMILLAN: So any objection to --

MS. YRIBAR: I think we would need to discuss that in executive session.

CHAIRMAN MacMILLAN: Okay. Well, why don't you go ahead and finish, and then we'll move on.

MS. YOUNG: Let's see here. I guess the final point that I will make is on the rulemaking history, as this did come up during the evidentiary hearing. And to the extent that we're looking or questioning what the rules do, the DEQ's application of the TAPs rules is supported by the rulemaking history.

DEQ's expert, Kevin Schilling, testified at the evidentiary hearing that based on his experience as personally participating in the development of these rules in the early '90s, that the TAP AACCs were established to ensure that impacts of any carcinogenic TAPs from a project or facility would not cause a lifetime cancer risk over 1 in a million or 1 in a 100,000 when using T-RACT.

He explained what I have already said to you, that the cornerstone was focused on project risk and that for any particular project, whether it's a new facility or a modification, not causing a risk to exceed

1 in a million or 1 in 100,000.

And I think this is important for two reasons: It helps explain DEQ's rationale in approaching this permitting action. If DEQ's staff understood that lifetime risk was the cornerstone, then its use of the project-specific adjustment for a nonpermanent source would be reasonable.

And, second, I think it's important in addressing petitioners' claim that DEQ is acting, as they've said in some of their briefing, in some sort of ad hoc manner. It's inconceivable that DEQ now would only come up with this approach when it's been the underpinning of the TAP rule since their creation in the '90s.

So with that, Chairman and members of the Board, I would submit that DEQ has conducted an analysis and issued a permit that was reasonable, lawful, and protective of public health. DEQ did not depart from any precedent, has not provided any ad hoc justification, and petitioners have failed to prove that DEQ committed any errors in its thorough and diligent permit analysis. And this is supported by the record and by the experts that the hearing officer heard from during the evidentiary hearing.

Thank you.

CHAIRMAN MacMILLAN: Thank you, Ms. Hannah.

So are there any other questions for Ms. Young?

(No response.)

CHAIRMAN MacMILLAN: Hearing none, we do have -- we have plenty of time today, Pat, so there is time for rebuttal from petitioners if they have any rebuttal.

COURT REPORTER: I need a break, though. I need to take a break before we keep going.

CHAIRMAN MacMILLAN: So we can just take a break for ten minutes.

MS. YRIBAR: Off the record.

CHAIRMAN MacMILLAN: Off the record.

(Break taken.)

CHAIRMAN MacMILLAN: So we're back on the record. And there's opportunity for rebuttal from the petitioners, so whichever one of you wants to lead.

MR. HURLBUTT: Yeah, I think we'll go in the same order as before.

Thank you, Board members. I'd like to focus first -- I have just a few points of things to clarify -- but first on this 0.00414 number that came up a lot, and make sure everyone understands exactly what that is and what that means.

So that is the number using the five-year rolling average and non-West End Pit production limits that Perpetua's modelers came up with for what the concentration of arsenic will be while the project's underway if it operates at a somewhat maximum level over 16 years.

Ms. Young admitted correctly that that number is higher than the T-RACT adjusted AACC. Multiplying the AACC number that's clearly stated here in the rules by ten, that's 0.0023. This number that Perpetua's calculated of 0.00414 is, roughly, you know, twice as high.

So the AACC adjusted for T-RACT is, you know, this much arsenic, and Perpetua's projecting that for 16 years they will be at nearly twice as much up here. And that's the key issue here for the Board to decide is, is that allowed under the rules and/or is that adequately protective of public health.

There's no dispute that if they do that in 16 years then stop, they will no longer be generating arsenic. And I'm not really sure why that keeps coming up, that somehow the levels that are projected to occur for 16 years are somehow wrong because they're going to stop eventually.

For 16 years, as modeled, there will be this

.00414 level that's nearly twice as high as what's allowed right here in the Air Rules, if you accept that these are annual averages that needed to be met year over year for any particular project.

BOARD MEMBER PURDY: Are those annual averages over an assumed 70-year life, or are those absolute annual averages, or was that based on the 70-year life of the project?

MR. HURLBUTT: These annual averages were developed based on risk factors and a 70-year life. Perpetua's and DEQ's experts have been trying to kind of undo all of this and get back to just doing some kind of risk assessment specific to this project, but the rules are clear, the rules need to be followed as written.

And if you, again, you know, recall that DEQ has to follow the methods in Section 210. The methods for a T-RACT source say that you -- I'll read what it says. This is in 210 subsection (12) for T-RACT sources. And under part (b), it says: "Compare the source's or modification's approved T-RACT ambient concentration at the point of compliance for the toxic air pollutant to the amount of the toxic air pollutant that would contribute an ambient air cancer risk probability of less than one to one hundred thousand (which amount is equivalent to ten times the applicable

acceptable ambient concentration listed in 586)."

So, yes, this is all based on a 1 in 100,000 risk level, but the rules have already taken all the guess work and risk assessment stuff out of it by saying those are the values listed here in Section 586. For a T-RACT source, you just multiply it by ten, and you compare it to that. That's it. That's all you do. It's a plain and simple process. It doesn't require going back through and calculating some -- doing a whole new risk assessment to consider whether a project makes sense. And, again, that's protective. That also helps ensure somebody is protected throughout their entire life, so if they exposed to something that exceeds the AACCs -- so that they couldn't be exposed to something that exceeds the AACCs for 16 years, recognizing they might be exposed to arsenic at later periods.

And, again, these values, they say in Section 586, the AACCs in this section are annual averages and DEQ has always in the past interpreted the rule s as requiring a project to comply with these each year of the project.

Another point I'd like to make is that there were some arguments suggesting that this idea that a source might not operate for 70 years is some shockingly new thing that's never been heard of before. That's not

true. The rules already have an exception for short-term sources. This is Section 210.15.

A short-term source defined as five years or less can get a ten times adjustment in the levels that they need to meet for the AACCs. It's already in the rules. It's something that was already thought about. Why five years or less? I don't know.

You may agree or disagree that five years is the appropriate cutoff for what kinds of short-term sources should be -- should get some kind of additional allowance here, but the rules are what they say. Five years or less, those are the only short-term sources that get some kind of exception.

And by the way, that exception is not allowed for a source that already gets T-RACT. And here Stibnite project is getting a ten times adjustment already for it's T-RACT demonstration and seeking, by analogy, some kind of short-ish term adjustment, the 16/70 adjustment, which is just not found anywhere in the rules.

The final thing I'd like to touch on is Board Member Boylan touched on something interesting, which is that the .00414 level that's expected to happen for 16 years at the project, if the project still stuck to the same production limits but spread those out over

some longer period of time, then, yes, that would be a lower number each year.

And the important thing to note about that is that that shows how there are ways that the project could meet the annual levels of .0023, such as by having further operational limits that got it down to that level, which might have the mine operate for longer, but would potentially achieve compliance with these annual levels that we are arguing have to be met under the rules.

With that, I'll turn it over to Julie or take any questions.

CHAIRMAN MacMILLAN: Any questions?

BOARD MEMBER ELROY: So, Mr. Chairman, I do have kind of a general question, and whether the two of you have the answer, or possibly someone from DEQ, but this concept of 70 years, there are other mines, I assume, in Idaho that have been -- have obtained air permits, and so this is, from what I understand, the first time we're doing something around the 16 divided by 70.

But the other mines that we've permitted in the past, just from a benchmarking perspective, it sounds like this was not required for that. And maybe that's a DEQ question, but are you aware of how other

mines have been permitted in Idaho and how this wasn't necessary.

MR. HURLBUTT: So, I mean, as Ms. Thrower mentioned before, during discovery we asked DEQ for any other examples of permits that used some kind of adjustment factor like this that accounted for the life of the project, and they did not turn over any other documents.

And, again, the record's pretty clear that DEQ says this is a new approach, it's not how they've ever done this before. For other mines that have been permitted, you know, yeah, apparently, they were able to meet these limits on an annual basis and never had to propose creative approaches like this that take the .00414 number and multiply it by something to reduce it to about a quarter or a fifth about what it actually will be when the mine's operating.

CHAIRMAN MacMILLAN: Any other questions for Mr. Hurlbutt?

MS. THROWER: Thank you.

Mr. Chairman, members of the Board, I'm going to touch on -- I think Mr. Hurlbutt's argument here today has made it clear that the rules have one method of complying with the AACC limits, and that is just your emissions are under that number on an annual average.

However, we have this expert testimony, we've gotten ourselves into this expert testimony about cancer risk as an alternative method to complying with the TAPs rule. I'd just like to point out again that I think you should really consider how much weight you give to DEQ's and Perpetua's experts.

Both of them relied on superfund guidance to pull out an equation that they used in this context, in a very different context -- regulatory context for permitting air permits that are, you know, considerably possibly more complex, but definitely different in their considerations of how emissions are calculated, how emissions might be emitted on a yearly basis, whether they're constant, whether they're not, for how long.

Both experts did not actually develop the maximum annual average in emissions that they used in their calculations. And -- which I'll go into a little bit later here, but it turns out it is not the maximum emissions that the mine can emit under the proposed capacity under the permit conditions that are imposed on it.

Both relied on the single default option that I talked about from the EPA cancer risk assessment guidance as their starting point of this analysis without any justification of why they have to go through

that default option, why there was uncertainty or missing information that led them to use that default option.

Neither of them accounted for how spreading out the emissions -- so, basically, they took -- they just totaled the 16 years of emission and divided it by 70. That's what they're doing to come up with their .0095 micrograms per cubic meter annual emissions. Neither of them explained how that accounts for sensitive populations.

And, Mr. Chairman, you hit on that exactly, how exposure to children and other vulnerable populations, women of reproductive age, elderly populations, how a higher dose, even for a shorter amount of time, may impact them more. You know, spreading out the dose over 70 years artificially doesn't account for that. 70 years is a construct of cancer risk assessment; it is not a criteria for the project's life. So I think focusing on the 70-year thing is -- we're going the wrong direction here.

The URF, you know, DEQ said that takes in account sensitive populations, but the URF is averaged over a lifetime. The dose and risk is not the same when it's imposed on sensitive populations, and pediatric exposures can manifest later in life. So the URF is

not -- it's not a perfect measure for making sure that our most sensitive populations are protected from this type of cancer risk.

I want to go back to this number. Because the DEQ's and Perpetua's toxicologists have this equation, as I've said, from the superfund guidance, from EPA's superfund guidance that uses the highest annual concentration times 16 years divided by 70 years.

So that highest annual concentration, that is a yearly concentration, not spread out over anything. That is the highest annual concentration. They used the .00414 as a basis as the start of their calculations. That is with the 16/70 backed out; right? So that's the number that Mr. Hurlbutt was talking about that does not meet the AACC limit. But that is not the maximum annual concentration.

Mr. Lewis testified that that amount is based on -- it's 135,000 tons per day annual average. If you go back to petitioners' post-hearing brief, about page 15, we start talking about this, all the citations are there to the testimony, to the record documents, you know. And Mr. Lewis testified that, yeah, that's about a 33 percent difference between the permit limit of 180,000 tons per day.

So under a five-year rolling average, Perpetua

can, for three years, still do 180,000 tons per day as an annual average, and then there will be two years of less production.

But if we take that number, .00414, do a back-of-the-envelope calculation, like what Mr. Lewis did in his testimony and pretend that we're actually looking at 180,000 tons per day production per year, then we add on 33 percent, and that gets us to .0055. Now, there's one more dilution factor, and that is the West End Pit production.

Now, Dr. Von Lindern testified -- he knew at this point when he was testifying what that number was made up of. He did not understand that during the comment period during the permit development period how DEQ came up with their maximum annual average number, and so he asked Mr. Schilling. And Mr. Schilling told him that their number is based on an average of seven non-West End Pit production scenarios, plus the West End Pit production scenario. 100 percent West End Pit scenario. And then that's all averaged out.

Now, under the permit conditions, there is a condition that limits Perpetua from 50 percent of total production from the West End Pit, but that limit does not limit Perpetua's ability to produce ore from the West End Pit at 100 percent in any given year.

In fact, they could produce product from the West End Pit for -- it's in our brief. I don't remember exact numbers -- I believe for five years total, 100 percent production for five years just from the West End Pit. And Mr. Schilling testified -- and, again, the citation is in our brief -- that that's sort of a normal scenario is that, you know, mining companies will start production in one pit and move to another one and move to another one.

So, really, what we're looking at is a maximum annual concentration that has to be calculated is 100 -- is the potential to mine 180,000 tons per year -- or excuse me -- per day for a year along with all that production coming from West End Pit production.

If you look at some tables that were Exhibit 304 in the hearing that we had before the Office of Administrative Hearings -- and, again, this is all in our brief -- that number for West End Pit production at -- that number -- and if you take away the five-year rolling average and do it at 180,000 tons per day, that number, that maximum annual concentration turned out to be 0.0092.

That is the number that if Perpetua and DEQ's toxicologists really wanted to calculate the cancer risk using this equation from the superfund guidance, the

number they should have been using is .0092.

BOARD MEMBER PURDY: Mr. Chairman, can I ask a question about --

THE WITNESS: Or it's a back envelope calculation, but, you know.

BOARD MEMBER PURDY: Can I ask you a question?

MS. THROWER: Yes, absolutely.

BOARD MEMBER PURDY: You're repeating that number. Do you have that number on the record in evidence from testimony of an expert, or is that your number? Is that an expert? Is that a number we can see the calculations on it?

MS. THROWER: Yeah, that is in our post-hearing brief. And Dr. von Lindern testified that when he talked -- he talked to Kevin Schilling about how they came up with that number. And you can see it in the --

BOARD MEMBER PURDY: So that's not a number that one of your toxicologists -- that somebody that's qualified to calculate that number and then came up with, that's a number that --

MS. THROWER: That's a number that if you -- I mean, if you look at the numbers and the charts and everything that was in the record, then you can look at that number and you can go ahead and say, okay, West End

Pit production is this number, the emissions are this number. How they derived the number that they actually use, the .00414, is a compilation of these other numbers, and --

BOARD MEMBER PURDY: So, again, my question: Will we find that in evidence somewhere?

MS. THROWER: Yes.

BOARD MEMBER PURDY: Can we find that statement in evidence somewhere?

MS. THROWER: I believe so. And, again, if you go to our post-hearing brief, we've cited to the testimony on that, we've cited to the record documents that demonstrate that.

BOARD MEMBER PURDY: Okay. I'll look for that. I just want to make sure that that's a -- that that's not -- that's a real number.

MS. THROWER: Yeah. And that's in the second half.

And I'm saying it's not a number -- it's a real number in the sense that you can back calculate this. Is this a number that DEQ actually calculated? No.

DEQ admitted in testimony that they have never calculated the maximum annual average. They used the five-year rolling average to do all their calculations.

That's one thing. They used an average of West End Pit and non-West End Pit to do their calculations.

BOARD MEMBER PURDY: Because we heard earlier today that -- just a few minutes ago that their calculations were based on multiple worst-case scenarios, and that they used -- picked the worst case of the worst-case scenarios for their application.

MS. THROWER: And that is false.

BOARD MEMBER PURDY: So you're say that that's not true.

MS. THROWER: That is not true.

And I'm probably getting to the end of my time here, so I would just like to point out one more thing. Again, Mr. Chairman, I think your question about, you know, can they do things like the -- control fugitive dust, everything like that. You know, that's where our scientific expertise is; right?

And that's where DEQ's scientific expertise is, is to figure out permit conditions, how this mine can operate with Perpetua's experts to figure out conditions to get the emissions down to the level of the AACC to meet the rules, to meet the compliance under the rules. That is their role that they can still do that.

They can still do that. And they don't need to use the 16/70 adjustment factor and change the rules

on us. They can put up conditions that adjust the maximum output and do it over 20 years. You know, there are other conditions about the silt content in the road that limits the dust, about, you know, the fugitive dust control efficiency.

There are other things they can do to try and make this mine comply with the rules that we have, rather than trying to make up some other rules and come up with exceptions. Because this is not, necessarily, a unique or exceptional mine, it's just that nobody else has ever asked DEQ to do this for them.

And I think that is -- I think I will just stop there.

CHAIRMAN MacMILLAN: Okay. Thank you Ms. Thrower.

Any questions for Ms. Thrower?

VICE CHAIR STEELE: Has anyone suggested to not use EPA's URFs?

MS. THROWER: Well, the URF is already built in to the AACC. So that was a policy choice when they developed those numbers. And so I would not really think that would be a good idea to come up with our own number. I mean, that's --

VICE CHAIR STEELE: I was just wondering.

MS. THROWER: Yeah. Yeah.

VICE CHAIR STEELE: All right. Thank you.

CHAIRMAN MacMILLAN: Other questions?

(No response.)

CHAIRMAN MacMILLAN: Thank you very much.

MS. THROWER: Thank you.

MR. HURLBUTT: Thank you.

CHAIRMAN MacMILLAN: So the next step: Is there a desire at this point by any of the Board members to enter into an executive session to discuss the arguments with legal counsel?

If so, I'd entertain the motion to that effect.

BOARD MEMBER PURDY: Mr. Chairman, I'd like to make a motion.

CHAIRMAN MacMILLAN: You have it.

BOARD MEMBER PURDY: I move the Board enter into an executive session pursuant to Idaho Code 74-206(1)(f) to communicate with legal counsel for the public agency to discuss the legal ramifications of and legal options for pending litigation, or controversies not yet being litigated but imminently likely to be litigated. I request that a roll call vote be taken and that vote be recorded in the minutes of this meeting.

CHAIRMAN MacMILLAN: And that was read by Pat Purdy.

Is there a second on the motion?

VICE CHAIR STEELE: Second.

CHAIRMAN MacMILLAN: There's a second on the motion. Is there any discussion?

(No response.)

CHAIRMAN MacMILLAN: A motion has been made and seconded. We'll now conduct a roll call vote. Board members, please respond by saying "aye" in favor of the motion or "nay" against the motion.

Elaine, could you call roll.

BOARD CLERK GANINO: Yes, Mr. Chairman.

Dr. Randy MacMillan?

CHAIRMAN MacMILLAN: Aye.

BOARD CLERK GANINO: Clayton Steele?

VICE CHAIR STEELE: Aye.

BOARD CLERK GANINO: Pat Purdy?

BOARD MEMBER PURDY: Aye.

BOARD CLERK GANINO: Beth Elroy?

BOARD MEMBER ELROY: Aye.

BOARD CLERK GANINO: Mark Bowen?

BOARD MEMBER BOWEN: Aye.

BOARD CLERK GANINO: Lance Boylan?

BOARD MEMBER BOYLAN: Aye.

CHAIRMAN MacMILLAN: Motion is carried. So the Board will go in the other room.

(Break taken.)

CHAIRMAN MacMILLAN: We'll start back up again.

Is there a motion to reconvene?

BOARD MEMBER PURDY: Yes, I'd like to make a motion. I move that the Board resolve out of executive session and that the meeting of the minutes reflect that no action was taken during the executive session.

BOARD MEMBER ELROY: Second.

CHAIRMAN MacMILLAN: Is there any discussion?

(No response.)

CHAIRMAN MacMILLAN: Hearing none, I guess we can do roll call or not?

MS. YRIBAR: Yes.

CHAIRMAN MacMILLAN: Elaine, could you real the roll.

BOARD CLERK GANINO: Yes, Mr. Chairman.

Dr. Randy MacMillan?

CHAIRMAN MacMILLAN: Aye.

BOARD CLERK GANINO: Clayton Steele?

VICE CHAIR STEELE: Aye.

BOARD CLERK GANINO: Pat Purdy?

BOARD MEMBER PURDY: Aye.

BOARD CLERK GANINO: Beth Elroy?

BOARD MEMBER ELROY: Aye.

BOARD CLERK GANINO: Mark Bowen?
BOARD MEMBER BOWEN: Aye.
BOARD CLERK GANINO: Lance Boylan?
BOARD MEMBER BOYLAN: Aye.
CHAIRMAN MacMILLAN: Motion is carried. We are back on the record after our executive session.
So is there a need to continue this oral argument until tomorrow?
(No response.)
CHAIRMAN MacMILLAN: No.
So the Board will take this matter under advisement. We will hold an additional public meeting to make our decision. And we will issue an order within 56 days of today.
And just to clarify, the Board will have an executive session that is closed just to the Board, obviously, on April 28th. And you're welcome to come, but we'll just adjourn immediately upon meeting into executive session, and then no decisions will be made at that time.
And then on May 15th, I believe -- I think that's correct -- we'll have another Board meeting in which we will vote on how -- on our decision. And you're certainly welcome to attend that.
Did I get that right?

MS. YRIBAR: Uh-huh. Yep.

CHAIRMAN MacMILLAN: So at this point, I would entertain a motion to adjourn.

BOARD MEMBER BOWEN: Mr. Chairman, I move we adjourn.

CHAIRMAN MacMILLAN: Is there a second?

VICE CHAIR STEELE: Second.

CHAIRMAN MacMILLAN: We stand adjourned.

(Meeting adjourned at 3:07 p.m.)

REPORTER'S CERTIFICATE

I, ANDREA L. CHECK, CSR No. 748, Certified Shorthand Reporter, certify;

That the foregoing proceedings were taken before me at the time and place therein set forth, at which time the witness was put under oath by me;

That the testimony and all objections made were recorded stenographically by me and transcribed by me or under my direction;

That the foregoing is a true and correct record of all testimony given, to the best of my ability;

I further certify that I am not a relative or employee of any attorney or party, nor am I financially interested in the action.

IN WITNESS WHEREOF, I set my hand and seal this 7th day of April, 2025.



ANDREA L. CHECK, CSR No. 748, RPR, CRR
Notary Public
1109 West Main Street, Suite 220
Boise, Idaho 83702
My Commission expires July 20, 2028.

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Idaho Rules of Civil Procedure

Rule 30

(e) Review by the Witness; Changes.

(1) Unless waived by the deponent and the parties, the deponent must be allowed 30 days after being notified by the officer that the transcript or recording is available in which (A) to review the transcript or recording; and (B) if there are changes in form or substance, to sign a statement listing the changes and the reasons for making them. (2) Changes indicated in the Officer's Certificate. The officer must note in the certificate prescribed by Rule 30 (f)(1) whether a review was requested and, if so, must attach any changes the deponent makes during the 30-day period. (3) Witness Failure to Sign. (A) In General, If the deposition is not signed by the witness within the 30-day period, the officer must sign it and state on the record the fact of the waiver of signature, or of the illness or absence

of the witness or the fact of the refusal to sign the deposition together with any reason given for not signing. (B) Use of Unsigned Deposition. The deposition may be used as if it were signed, unless pursuant to Rule 32 (d)(4) the court determines that the reasons given for the refusal to sign require rejection of the deposition in whole or in part.

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BOARD OF ENVIRONMENTAL QUALITY

IN THE MATTER OF:	) AGENCY CASE NO.
AIR QUALITY PERMIT TO CONSTRUCT	) 0101-22-01
ISSUED TO PERPETUA RESOURCES IDAHO, INC.	) OAH CASE NO.
_____	) 23-245-01

BOARD OF ENVIRONMENTAL QUALITY

SPECIAL MEETING

BEFORE

CHAIRMAN: DR. JOHN RANDY MACMILLAN

Date: May 15, 2025 - 9:00 a.m.

Location: Idaho Department of Environmental Quality
1410 N. Hilton Street
Boise, Idaho

REPORTED BY:

COLLEEN P. DOHERTY, CSR 345

Notary Public

APPEARANCES:

The Board of Environmental Quality:

Dr. John R. MacMillan, Chair (Present Remotely)

Mr. Clayton Steele (Present Remotely)

Mr. Lance Boylan (Present Remotely)

Mr. Pat Purdy

Mr. Mark Bowen

Mr. Dennis Leikam

For the Board of Environmental Quality:

IDAHO STATE DEPUTY ATTORNEY GENERAL

Energy and Natural Resources Division

BY MS. ANN YRIBAR

P.O. Box 83720

Boise, Idaho 83720-0010

ann.yribar@ag.idaho.gov

Also Present: Elaine Ganino

Diane Cutler

Ginny Simms

CHAIRMAN MacMILLAN: All ready to proceed? Okay.

Today is Thursday, May 15th, 2025, at 9:00 a.m. This is Randy MacMillan, Chairman of the Idaho Board of Environmental Quality.

I call to order this special meeting of the Idaho Board of Environmental Quality. In addition to being a public meeting, we are also on the record in the Matter of Air Quality Permit to Construct Issued to Perpetua Resources Idaho, Inc., Agency Case No. 0101-22-01; OAH Case No. 23-245-01.

This special meeting is being held in the State office of the Department of Environmental Quality. For those present today in the room, please sign in on the sheet provided by the entrance. There will not be an opportunity for public comment today.

Elaine, could you please take the roll call, do a recall?

MS. GANINO: Yes, Mr. Chairman.

Randy MacMillan?

CHAIRMAN MacMILLAN: Here.

MS. GANINO: Clayton Steele.

MR. STEELE: Here.

MS. GANINO: Pat Purdy.

MR. PURDY: Here.

MS. GANINO: Mark Bowen.

MR. BOWEN: Here.

MS. GANINO: Dennis Leikam.

MR. LEIKAM: Here.

MS. GANINO: Lance Boylan.

MR. BOYLAN: Here.

MS. GANINO: Beth Elroy is absent.

CHAIRMAN MacMILLAN: Thank you. And we do have a quorum.

The Board intends to take action at this meeting. No additional statements or oral argument will be taken at this meeting.

We will now move on to the agenda items. Agenda item No. 1, executive session pursuant to Idaho Code Section 74-206(1)(f).

I will entertain a motion.

MR. BOWEN: Mr. Chairman, I move the Board enter into executive session pursuant to Idaho Code Section 74-206(1)(f) to communicate with legal counsel for the public agency to discuss the legal ramifications of and legal options for pending litigation or controversies not yet being litigated, but imminently likely to be litigated.

I request that a roll call vote be taken, and that vote be recorded in the minutes of this meeting.

CHAIRMAN MacMILLAN: That motion was read by Mark Bowen. Is there a second on the motion?

MR. PURDY: I'll second that.

CHAIRMAN MacMILLAN: That motion was seconded by Pat Purdy.

Is there any discussion?

Elaine, if you'll conduct a roll call vote.

And Board members, please respond by saying "aye" in favor of the motion, or "nay" against the motion.

MS. GANINO: Randy MacMillan.

CHAIRMAN MacMILLAN: Aye.

MS. GANINO: Clayton Steele.

MR. STEELE: Aye.

MS. GANINO: Pat Purdy.

MR. PURDY: Aye.

MS. GANINO: Mark Bowen.

MR. BOWEN: Aye.

MS. GANINO: Dennis Leikam.

MR. LEIKAM: Aye.

MS. GANINO: Lance Boylan.

MR. BOYLAN: Aye.

CHAIRMAN MacMILLAN: The motion is carried. The Board is now off the record and the room for executive session will be closed off. Attendees in the

adjacent room are welcome to remain and wait until executive session concludes.

(The Board is in executive session.)

CHAIRMAN MacMILLAN: Okay. We are set to go then. So we need a motion to exit executive session.

MR. STEELE: I move that the Board exit out of executive session. And that the meeting of the minutes reflect that no action was taken during the executive session.

CHAIRMAN MacMILLAN: Is there a second on the motion?

MR. PURDY: I'll second that.

CHAIRMAN MacMILLAN: The motion has been made and seconded. We are back on the record after the executive session.

MS. YRIBAR: Randy, let's do a roll call vote on that.

CHAIRMAN MacMILLAN: Okay. Let's do a roll call vote on that. Elaine, could you take a roll call vote for us.

MS. GANINO: Randy MacMillan.

CHAIRMAN MacMILLAN: Aye.

MS. GANINO: Clayton Steele.

MR. STEELE: Aye.

MS. GANINO: Pat Purdy.

MR. PURDY: Aye.

MS. GANINO: Mark Bowen.

MR. BOWEN: Aye.

MS. GANINO: Dennis Leikam.

MR. LEIKAM: Aye.

MS. GANINO: Lance Boylan.

MR. BOYLAN: Aye.

CHAIRMAN MacMILLAN: The motion is carried.

So Agenda Item No. 2 is an action item, petition for review, petitioners' petition for review of the January 7th, 2025 preliminary order, memorandum in support, and request for hearing. We are here today to make our final decision on a petition for review.

Board members, is there any discussion on that topic?

MR. BOWEN: Mr. Chairman, I move the petitioners' petition for review of the January 7, 2025 preliminary order is denied. The Board finds there was sufficient evidence to demonstrate that DEQ acted reasonably and in accordance with the law, in not including additional permit conditions limiting the non-west end pit production limit. And there was sufficient evidence to demonstrate that DEQ acted reasonably, and in accordance with the law, when it applied the 16 over 70 adjustment. This order is final

as to all issues presented, as well as to all issues previously decided in the final order issued on this matter, May 9th, 2024.

CHAIRMAN MacMILLAN: That motion was read by Mark Bowen.

Is there a second to the motion?

MR. PURDY: I'll second that.

CHAIRMAN MacMILLAN: That motion, a second was made by Pat Purdy.

Is there any discussion, Board members?

MR. PURDY: Well, Mr. Chairman, I guess I have some comments that I would like to make.

I think that, you know, this has been, I guess, to speak to the petitioners, and to speak to the Board, I think we've been through a very detailed and meticulous process here. And I think the DEQ has, you know, after our review by the Board, we realize that the DEQ has gone through a very thorough and meticulous review of this permit to construct.

It's been reviewed again in detail, at least two different times by a Hearing Officer, with extensive testimony, and technical review. And then it's been, again, thoroughly and independently reviewed by this Board.

And again, all the findings have been

consistent that this is a -- that the DEQ has done their job, and has complied with statute, and regulations. And that it appears to be, time to move this forward. I think that this has been thoroughly vetted and thoroughly investigated. And so I think we're at the end of the road here, I believe.

CHAIRMAN MacMILLAN: Thank you, Pat.

Any other comments from the Board members?

MR. BOWEN: Mr. Chairman, this is Mark Bowen. I would like to just comment how appreciative the Board is of everybody's effort on this lengthy conversation, particularly relative to protection of Idaho citizens and the environment. And just understand and acknowledging the intent of everybody here is to be protective of both those.

And I think for me, individually, the detailed exploration and investigation that has ensued here, has given me a high level of confidence in the competency of our staff, and the intent of everybody involved. And I'm really, I'm confident with the outcome here. I feel like moving forward. We truly are doing what's in the best interest of the State of Idaho and its citizens.

CHAIRMAN MacMILLAN: Thank you, Mark.

Any other comments from Board members?

I would like to make a few comments. I

support the Hearing Officer's conclusions. In my view, the permit to construct meets the requirements of our air quality rules. DEQ's decisions in this case are reasonable and legal. They are based on sound, widely used, scientific and engineering models.

In my view, the air quality rule appears to give DEQ considerable discretion relative to the models and guidance the parties use to estimate emissions and their impact. This would logically include cancer risk analysis. There are no identified prohibitions in our rules with regard to models, but the methods must be scientifically sound.

The EPA and cancer risk guidance appears to be scientifically sound. The EPA guidance recognizes the scientifically established toxicologic and pharmacologic principle, the dose, as well as duration of dose, are key to eliciting an effect. The EPA guidance would be acceptable to estimate cancer risks for projects less than 70 years.

My review of the extensive efforts of DEQ to ensure operation of Stibnite Gold Mine was in conformance with Idaho's air quality rules gives me considerable comfort. Admittedly, I'm not an expert in air quality regulation; and certainly, barely knowledgeable about mines.

But I do know a little bit of cancer biology. In that regard, I was impressed with the expert declaration of Dr. Patent, and the other toxicologists. They made what appeared to me, to be very sound, scientifically, in cancer biology credible, technical presentations. Dr. Patent's inclusion of scientific papers, from reputable scientific journals greatly enlightened me, and I'm most appreciative of their particular report.

I was also impressed with Dr. Van Linden's (phonetic) analyses. I think he's quite right to be concerned about margins of safety, and applaud his presentation. His comments caused me to wonder, could there be a better formula for estimating cancer risks? And given a more robust and long-term dataset, it seems reasonable in the future, in future cancer risk predictions, that they could provide greater confidence. The scientific papers referenced by Dr. Patent, I like the knowledge challenged that.

For me, it is terribly difficult to estimate cancer risks, from one exposure, or a lifetime exposure of potential carcinogens. As Dr. Patent pointed out, there are multiple factors that influence susceptibility to a carcinogen; the variety of carcinogen activities, dose and duration attributes, the role of toxicity,

itself, and chronic inflammation in inducing cancer makes estimating risks a significant challenge.

So I would like to applaud DEQ and the staff for their continued efforts, to protect the health of the people, animals, and the plants of Idaho. It is a daunting task.

Are there any other comments from Board members?

We will now conduct the roll call vote. Board members please respond by saying "aye" in favor of the motion, or "nay" against the motion.

Elaine.

MS. GANINO: Yes, Mr. Chairman.

Randy MacMillan.

CHAIRMAN MacMILLAN: Aye.

MS. GANINO: Clayton Steele.

MR. STEELE: Aye.

MS. GANINO: Pat Purdy.

MR. PURDY: Aye.

MS. GANINO: Mark Bowen.

MR. BOWEN: Aye.

MS. GANINO: Dennis Leikam.

MR. LEIKAM: Aye.

MS. GANINO: Lance Boylan.

MR. BOYLAN: Aye.

CHAIRMAN MacMILLAN: The motion is carried.

We have reached the end of our agenda for today. The next step in the process will be for the Board to serve its final written order on the parties. We will do that within 58 or 56 days from the date of the oral argument. And that will be by May 28th, 2025.

And before we close, I would like to thank Ms. Yribar; Ms. Cutler; and before her, Ms. Wilson; and the administrative staff of DEQ, Ms. Ganino, and Ms. Simms, for making this contested case less challenging for the Board.

At this time, I will entertain a motion to adjourn.

MR. PURDY: Mr. Chairman, I would like to make a motion to adjourn.

CHAIRMAN MacMILLAN: We stand adjourned on May 15th, 2025 of the Idaho Board of Environmental Quality.

MS. YRIBAR: Hey, Randy, let's have a second and a voice vote.

MR. BOWEN: Second.

CHAIRMAN MacMILLAN: Do I have a second to adjourn?

MR. BOWEN: Second.

CHAIRMAN MacMILLAN: So do we need a roll call vote?

MS. YRIBAR: Just a voice vote.

CHAIRMAN MacMILLAN: Okay. All those in favor say "aye."

THE BOARD MEMBERS: Aye.

CHAIRMAN MacMILLAN: The motion is carried. We stand adjourned.

The May 15, 2025 special meeting of the Idaho Board of Environmental Quality is adjourned.

Thank you very much, everyone.

(Proceedings concluded at 10:51 a.m.)

REPORTER'S CERTIFICATE

I, COLLEEN P. DOHERTY, CSR No. 345, Certified Shorthand Reporter, certify:

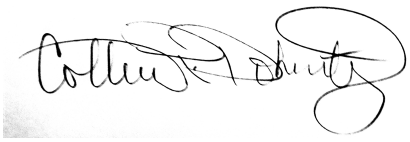
That the foregoing proceedings were taken before me at the time and place therein set forth, at which time the witness was put under oath by me;

That the testimony and all objections made were recorded stenographically by me and transcribed by me or under my direction;

That the foregoing is a true and correct record of all testimony given, to the best of my ability;

I further certify that I am not a relative or employee of any attorney or party, nor am I financially interested in the action.

IN WITNESS WHEREOF, I set my hand and seal this 1st day of June, 2025.



COLLEEN P. DOHERTY, CSR 345
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1109 West Main Street, Suite 220
Boise, Idaho 83702

My commission expires September 7, 2029.

[0101-22-01 - bowen]

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